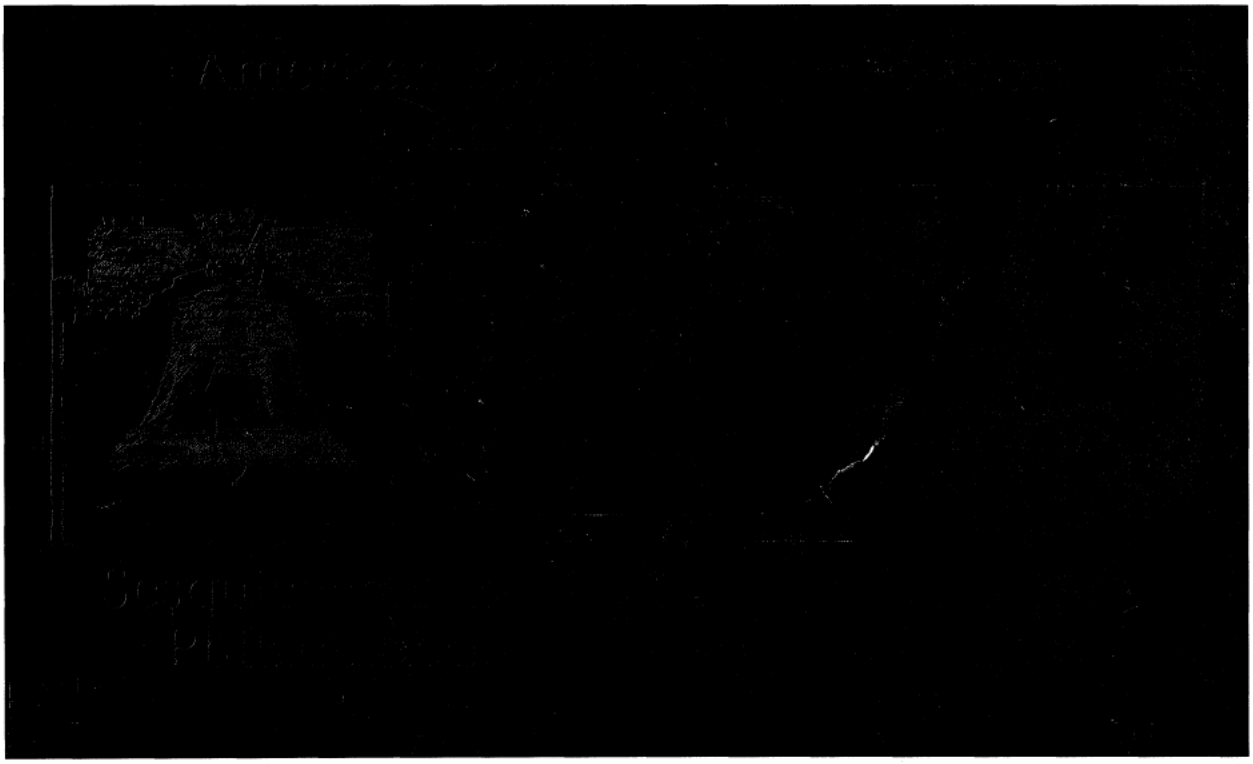
1994 ANNUAL MEETING

New Research Program and Abstracts



PROGRAM
AND
ABSTRACTS ON NEW RESEARCH

IN SUMMARY FORM

THE SESQUICENTENNIAL ANNUAL MEETING OF THE AMERICAN PSYCHIATRIC ASSOCIATION

PHILADELPHIA, PA
May 21-26, 1994

SUBCOMMITTEE ON NEW RESEARCH OF THE SCIENTIFIC PROGRAM COMMITTEE

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Scientific Program Committee
New York, NY

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New York, NY

APA Annual Meeting Philadelphia, Pennsylvania, May 21-26, 1994

Sesquicentennial Celebration 1844-1994

1400 K Street, N.W.
Washington, DC 20005
Telephone: (202) 682-6000
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May 21, 1994

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 1994 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.

The program begins Monday, May 23, 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 genetics, mood disorders, AIDS and schizophrenia. The Young Investigators' Oral/Slide Sessions 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 24, through Thursday, May 26, from 9:00 a.m.-10:30 a.m. Sessions will focus on schizophrenia; aggression; C/L; AIDS and HIV; and research issues (Tuesday); schizophrenia and other psychotic disorders; mood disorders; suicide; and psychopharmacology (Wednesday); and infant and childhood; alcohol and substance abuse; anxiety; mood disorders; and psychopharmacology (Thursday). Poster Sessions will be held Tuesday and Wednesday from 12 noon-2:00 p.m. and 3:00 p.m.-5:00 p.m., and on Thursday from 12 noon-2:00 p.m. These sessions will be devoted to mood disorders; treatment techniques and issues; premenstrual dysphoric disorder; suicide; anxiety disorders; schizophrenia and other psychotic disorders; neuropsychiatry; and genetics (Tuesday); cross-cultural and minority psychiatry; other psychiatric, personality, alcohol and substance abuse disorders; biological psychiatry; religious issues; AIDS and HIV-related disorders; C/L and emergency psychiatry; geriatrics; psychoimmunology; organic mental, sleep, somatoform disorders; violence and terrorism; and stress (Wednesday); and economic issues; infant and childhood disorders; child and adolescent psychiatry; psychopharmacology and other somatic therapies; eating disorders; diagnostic issues; epidemiology; psychiatric education; stigma; social psychiatry; resident and medical student, gender issues; presidential theme: Our Heritage, Our Future; couple and family, behavior and cognitive therapies; forensic, and community psychiatry (Thursday).

The 48 oral/slide papers (including 12 Young Investigators) and 613 poster presentations (including 146 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.
Chairperson
New Research Subcommittee of the
Scientific Program Committee

Outside Reviewers for the New Research Program

Hagop S. Akiskal, M.D.
Nancy C. Andreasen, M.D.
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Jack D. Barchas, M.D.
Wade H. Berrettini, M.D.
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Joseph T. Coyle, M.D.
Raymond R. Crowe, M.D.
Glen C. Davis, M.D.
Marshal F. Folstein, M.D.
Arnold J. Friedhoff, M.D.
Abby J. Fyer, M.D.
Elliott S. Gershon, M.D.
Judith H. Gold, M.D.
Jack M. Gorman, M.D.
Igor Grant, M.D.
Katherine A. Halmi, M.D.
Dilip V. Jeste, M.D.
Herbert D. Kleber, M.D.
Donald F. Klein, M.D.
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Donald S. Kornfeld, M.D.
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Robert W. McCarley, M.D.
John M. Morihisa, M.D.
Charles B. Nemeroff, M.D.
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William Z. Potter, M.D.
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Murray A. Raskind, M.D.
Stephen G. Rayport, M.D.
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Elliott Richelson, M.D.
Peter P. Roy-Byrne, M.D.
Michael H. Sacks, M.D.
Charles A. Shamoian, M.D.
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Robert L. Spitzer, M.D.
Barbara Stanley, Ph.D.
James J. Strain, M.D.
Trey Sunderland, M.D.
Kenneth J. Tardiff, M.D.
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Gary J. Tucker, M.D.
Fred R. Volkmar, M.D.
B. Timothy Walsh, M.D.
Daniel R. Weinberger, M.D.
George E. Woody, M.D.
Stuart C. Yudofsky, M.D.

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The American Psychiatric Association requires disclosure of the existence of any significant financial interest or other relationship a presenter has with the manufacture(s) of any commercial product(s) discussed in an educational presentation. The existence of such relationships does not necessarily constitute a conflict of interest, but the prospective audience must be informed of the presenter's affiliation with a commercial sponsor by way of an acknowledgement in this printed *New Research Program and Abstracts Book.* This policy is intended to openly identify any potential conflict so that the audience in an educational activity is able to form their own judgements about the presentation.

The following presenters on this year's new research program have indicated a significant financial relationship with the manufacturer(s) of a commercial product(s). The presenter's name and final program number(s), and the manufacturer's name, as they appear in this *New Research Program Book* are listed below:

Presenter	Manufacturer(s)	Final Program #
Alderman, Jeffrey A.	Pfizer Pharmaceuticals	NR610
Andreasen, Nancy C.	Medi-Physics, Inc., an Amersham Company	NR272
Barr, Linda C.	Solvay Pharmaceuticals	NR602, NR603
Bell, Iris R.	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company;	NR235, NR531
Boyer, William F.	SmithKline Beecham Pharmaceuticals	NR234
Bresnahan, David B.	The Upjohn Company	NR442
Ciraulo, Domenic A.	The Upjohn Company	NR393
Clark, Duncan B.	Eli Lilly and Company	NR243
Coccaro, Emil F.	Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Miles Pharmaceuticals; Solvay Pharmaceuticals; The Upjohn Company; Roerig, Division of US Pharmaceuticals Group of Pfizer Inc.; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR159
Cottraux, Jean A.	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR656
Daniel, David G.	Janssen Pharmaceutica Inc.	NR356
Dewan, Mantosh J.	Medi-Physics, Inc., an Amersham Company	NR253, NR438
Fava, Maurizio	Eli Lilly and Company; Pfizer Pharmaceuticals; SmithKline Beecham Pharmaceuticals; Burroughs Wellcome Co.	NR651
Feinberg, Michael	Syntex	NR224
Fossey, Mark D.	Burroughs Wellcome Co.	NR613
Galinowski, Andre J.	Lipha (Anphar-Rollaovo)	NR66
Gergel, Ivan P.	SmithKline Beecham Pharmaceuticals	NR559
Grebb, Jack A.	Abbott Laboratories	NR502
Green, Alan I.	Janssen Pharmaceutica Inc.	NR614
Gyulai, Laszlo	Abbott Laboratories; SmithKline Beecham Pharmaceuticals	NR222
Hellerstein, David J.	Pfizer Pharmaceuticals; Dista Products Company, a division of Eli Lilly and Company	NR215
Hirsch, Alan R.	Marsh Enterprises	NR655
Hudson, James I.	The Upjohn Company	NR620
Jones, Lynne	Sandoz Pharmaceuticals Corporation	NR276
Kline, Neal A.	Pfizer Pharmaceuticals	NR246
Kronig, Michael H.	Janssen Pharmaceutica Inc.	NR355
Lauriello, John	Sandoz Pharmaceuticals Corporation	NR316
Lindenmayer, Jean-Pierre	Janssen Pharmaceutica Inc.	NR324, NR617
McCafferty, James P.	SmithKline Beecham Pharmaceuticals	NR195
McGrath, Patrick	Eli Lilly and Company	NR561
Mintzer, Jacobo E.	Glaxo; Janssen Pharmaceutica Inc.; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Pfizer Pharmaceuticals; Eli Lilly and Company	NR343
Nierenberg, Andrew A.	Eli Lilly and Company	NR183
Pava, Joel A.	Eli Lilly and Company; Pfizer Pharmaceuticals; SmithKline Beecham Pharmaceuticals	NR193
Prichep, Leslie S.	Cadwell Laboratories	NR432
Richelson, Elliott	Roerig, Division of US Pharmaceuticals Group of Pfizer Inc.; Eli Lilly and Company; Wyeth-Ayerst Laboratories	NR560
Ring, Howard A.	Medi-Physics, Inc., an Amersham Company	NR77
Risch, Samuel Craig	Sandoz Pharmaceuticals Corporation	NR595
Satterlee, Winston G.	Eli Lilly and Company	NR601

Selph, Jeff	Burroughs Wellcome Co.	NR166
Shriqui, Christian L.	Janssen Pharmaceutica Inc.	NR618
Steiner, Martin	SmithKline Beecham Pharmaceuticals	NR555
Thase, Michael E.	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Pfizer Pharmaceuticals; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Burroughs Wellcome Co.	NR194
Tollefson, Gary D.	Eli Lilly and Company	NR362
Tran, Pierre V.	Eli Lilly and Company	NR357
Trestman, Robert L.	Dista Products Company, a division of Eli Lilly and Company; Mead Johnson; Pharmaceuticals, a Bristol-Myers Squibb Company; SmithKline Beecham Pharmaceuticals	NR381
Weisler, Richard H.	Burroughs Wellcome Co.	NR611
Wilson, William H.	Eli Lilly and Company; Sandoz Pharmaceuticals Corporation; Abbott Laboratories	NR593, NR594
Wirshing, William C.	Janssen Pharmaceutica Inc.	NR418

NEW RESEARCH

Monday, May 23, 1994, 9:00 a.m.-10:30 a.m.

New Research 1 – Poster Session – Exhibit Hall D, Street Level, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Harold Alan Pincus, M.D. and Charles B. Nemeroff, M.D.

NR1 Personality Disorders in HIV Positive Persons: Association with Other Measures of Psychiatric Morbidity
Jeffrey J. Richards, M.D., Susan E. McManis, M.D., Robert A. Zachary, Ph.D., George R. Brown, M.D.

NR2 Gender Differences in AIDS-Related Bereavement
Jacquelyn Summers, Andres Sciolla, M.D., Sidney Zisook, M.D., J. Hampton Atkinson, M.D., Janet Chandler, M.D., Igor Grant, M.D.

NR3 Suicidality and HIV Status
Stephan F. Baum, M.D., Diana O. Perkins, M.D., Carol E. Murphy, M.P.H., Robert N. Golden, M.D., Dwight L. Evans, M.D.

NR4 Apathy and Psychomotor Functioning in A-Symptomatic HIV-Seropositive Gay Men
Stephan F. Baum, M.D., Susan G. Silva, Ph.D., Robert A. Stern, Ph.D., Nicole Chaisson, B.A., Robert N. Golden, M.D., Dwight L. Evans, M.D.

NR4-A Attitudes and Preferences Regarding Treatment Among AIDS Patients: Minority Issues
Kenneth B. Ashley, M.D., Joel J. Wallack, M.D., Murray Alpert, Ph.D.

NR5 Diazepam Loading: A Novel Technique for Alcohol Detoxification
Todd R. Cheever, M.D., Mark C. Hyatt, M.D., William Fisher, M.D.

NR6 Substance Use and Psychiatric Disorders in Adolescents
Deborah Deas-Nesmith, M.D., Kathleen T. Brady, M.D., Mark Wagner, M.D., Sallie Campbell, M.S.W

NR7 A New Method to Screen for Anabolic Steroid Abuse
Elena M. Kouri, Ph.D., Harrison G. Pope, Jr., M.D., David L. Katz, M.D.

NR8 Comparison of Sleep Architecture for Stimulant and Alcohol Abusers in Acute Withdrawal
Peter M. Thompson, M.D., Shahrokh Golshan, Ph.D., Michael R. Irwin, M.D., Christian J. Gillin, M.D.

NR9 Alcoholics in General Hospital Evaluation and Treatment
Cecelia P. Kane, M.D., Francis J. Kane, M.D.

NR10 Substance Abuse/Dependence in Pregnancy: New Jersey Obstetrical Deliveries, 1984-1988
Mary Elizabeth Witt, M.D., Mary B. Breckenridge, Ph.D.

NR11 Disulfiram Improves Quality of Life in Alcoholics
Maria Gerber, Peter Widler, M.D., Richard Joyce, Ph.D., Hans-Ulrich Fisch, M.D.

NR12 Early Penetrating Sexual Abuse and Early Intravenous Drug Users
William C. Holmes, M.D., Barbara C. Bix, M.D.

NR13 Outpatient Benzodiazepine Detoxification Using Clonazepam in Methadone Patients
Todd I. Muneses, M.D., Robert P. Schwartz, M.D., Jeannette L., Johnson, Ph.D., Leroy C. Bell, M.D., Nicole E. Posner, B.A.

NR14 One-Year Outcome of Early and Late Onset Alcoholics
Sanaa Helmi, M.D., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Elizabeth J. Nickel, M.A., Mikel H. Thomas, M.D., Barry J. Liskow, M.D.

NR15 Neuroanatomical Studies of Addiction
Herbert W. Harris, M.D., Eric J. Nestler, M.D.

NR16 Role of Parkinsonism and Antiparkinsonian Therapy in the Subsequent Development of Tardive Dyskinesia
Kelly Elliott, B.S., Rif S. El-Mallakh, M.D., Susan Lewis, Ph.D., Stephen W. Looney, Ph.D., Robert Caudill, M.D., Teresita Bacani-Oropilla, M.D.

NR17 Treatment and Predictive Factors of Catatonia
Harold W. Goforth, M.A., Brendan T. Carroll, M.D.

NR18 Symptomatic Change After One Week of Treatment and Response to Clozapine in Schizophrenia
Robert G. Stern, M.D., Rene S. Kahn, M.D., Michael Davidson, M.D., Rena M. Nora, M.D., Kenneth L. Davis, M.D.

NR19 Entorhinal Cortex Volume in Schizophrenia: A Controlled MRI Study
Sarita K. Sharma, B.S., Henry A. Nasrallah, M.D., Marla N. Kemmerer, B.S., Robert Martin, Stephen C. Olson, M.D., Mary B. Lynn, M.A.

NR20 Increased Hippocampal Volume in Bipolar Disorder
Marla N. Kemmerer, B.S., Henry A. Nasrallah, M.D., Sarita K. Sharma, B.S., Robert Martin, Stephen C. Olson, M.D., Mary B. Lynn, M.A.

NR21 Short- and Long-Term Outcome in First-Episode and Chronic Schizophrenia
Fiona Gallacher, M.S., Derri L. Shtasel, M.D., Roland J. Erwin, Ph.D., Bruce Turetsky, M.D., Kimberly A. Hambrose, R.N., Raquel E. Gur, M.D.

NR22 Effects of Naltrexone on Stereotypic Behaviors
Julia A. Becker, M.D., Morris B. Goldman, M.D., Daniel J. Luchins, M.D., Mohammed Y. Alam, M.D.

NR23 Executive and Motor Impairments in Schizophrenia: Relation to Increased Spread of Activation in Semantic Networks
John H. Poole, Ph.D., Sophia Vinogradov, M.D., Emily Marton, B.A., Beth A. Ober, Ph.D., Gregory K. Shenaut, Ph.D.

NR24 The Impact of Self-Medication on the Knowledge of Discharge Medications in the Psychotic Patient
Douglas N. Shaffer, M.D., Avni Cirpili, M.S.N., John H. Gilmore, M.D., Diana O. Perkins, M.D.

NR25 Neuroleptic Response at the Onset of Psychosis
Russell E. Scheffer, M.D., Elizabeth Correnti, M.D., Sukdeb Mukherjee, M.D.

NR26 Serotonin Function in Drug Naive Schizophrenics
Russell E. Scheffer, M.D., Bruce I. Diamond, Ph.D., Elizabeth Correnti, M.D., Jian Wang, B.S., Richard L. Borison, M.D., Sukdeb Mukherjee, M.D.

NR27 Reduced Left Hemisphere Dominance for Language in Schizophrenia: Relation to Positive Symptoms
Esther Rabinowicz, Ph.D., Gerard Bruder, Ph.D., Xavier Amador, Ph.D., Dolores Malaspina, M.D., Charles A. Kaufmann, M.D., Jack M. Gorman, M.D.

NR28 Blood-Brain Barrier Permeability in Schizophrenia
Mary E. Donovan, M.D., Robert C. Alexander, M.D., Chan H. Park, M.D., Kenneth M. Certa, M.D.

NR29 Early Weight Gain During Clozapine Treatment as Predictor of Response
Daniel S. Umbricht, M.D., John M. Kane, M.D., Simcha Pollack, Ph.D., Jeffrey A. Lieberman, M.D.

NR30 Suicidality in Recent Onset Schizophrenia
Alexander S. Young, M.D., Keith H. Nuechterlein, Ph.D., Joseph Ventura, M.A., Michael J. Gitlin, M.D.

NR31 The Effects of Caffeine and Nicotine on Smooth Pursuit Eye Movements in Schizophrenic Patients
John S. Simpson, M.D., Donald E.N. Addington, M.D., William A. Fletcher, M.D.

NR32 Prolactin Level and Clinical Response to Clozapine
Jayendra K. Patel, M.D., Alan I. Green, M.D., Howard H. Chang, M.D., Anthony G. Kalinowski, Ph.D., Nancy J. Jaretz, R.N., Joseph J. Schildkraut, M.D.

NR33 Detrusor Hyperreflexia in Schizophrenic Patients with Incontinence
David R. Hunter, M.D., William W. Bonney, M.D., Sanjay Gupta, M.D., Stephan Arndt, Ph.D., Nancy C. Andreasen, M.D.

NR34 Atypical Antipsychotics, Serotonin and Weight Gain
Donna Ames, M.D., Lisa Harmon, Andrew Berisford, M.A., William C. Wirshing, M.D., Stephen R. Marder, M.D.

NR35 Neurologic Deficits, Tardive Dyskinesia and Medication Status
Donna Ames, M.D., William C. Wirshing, M.D., Byron Waters, Robert Moghimi, B.S., Andrew Berisford, M.A.

NR36 Withdrawal-Emergent Dyskinesia in Patients with Schizophrenia During Antipsychotic Discontinuation
Susan K. Schultz, M.D., Steve Ziebell, B.S., Delwyn Miller, M.D., Nancy C. Andreasen, M.D.

NR37 Evidence for a Neuroprotective Effect of Benzodiazepines in an Animal Model of Psychosis
Rona J. Hu, M.D., S. Paul Berger, M.D.

NR38 Working Memory Dysfunction in Schizophrenia
Kirsten Fleming, Ph.D., Terry E. Goldberg, Ph.D., Daniel R. Weinberger, M.D.

NR39 Psychosocial Correlates of Chronic Fatigue
Cecilia M. Sunnenberg, M.D., James C. Coyne, Ph.D., N. Cary Engleberg, M.D., Jon K. Zubieta, M.D., Mark A. Demitrack, M.D.

NR40 Low Platelet MAO Activity in Spanish Bullfighters
Jose L. Carrasco, M.D., Jeronimo Saiz-Ruiz, M.D., Juan J. Lopez-Ibor, M.D., Jesus Cesar, M.D.

NR41 Prolactin Response to Buspirone Challenge in the Presence of Dopaminergic Blockade
Douglas D. Maskall, M.D., Athanasios Zis, M.D., Raymond W. Lam, M.D., Annie Kwan, B.Sc.

NR42 The Effects of Desipramine on Serotonin Function in Depressed Patients and Healthy Subjects
Martha E. Leatherman, M.D., Joseph M. Bebchuk, M.D., R. David Ekstrom, M.P.H., Amy L. Durr, M.S., Stanley W. Carson, Pharm.D., Robert N. Golden, M.D.

NR43 The Role of Serotonin$_3$ Receptors in the Psychobiological Response to the Clomipramine Challenge Test
Martha E. Leatherman, M.D., Joseph M. Bebchuk, M.D., R. David Ekstrom, M.P.H., Stanley W. Carson, Pharm.D., George A. Mason, Ph.D., Robert N. Golden, M.D.

NR44 Orthostatic Response in Panic and Depressed Patients
Juan M. De Lecuona, M.D., Gregory M. Asnis, M.D., William C. Sanderson, Ph.D.

NR45 Clozapine Response in Chronic Schizophrenia and Brain Morphology on MRI: A Preliminary Report
Jeffrey S. Aronowitz, M.D., Houwei Wu, M.D., Simcha Pollack, Ph.D., Robert Bilder, Ph.D., John M. Kane, M.D., Allan Safferman, M.D.

NR46 PET Changes in OCD Versus Depression with Paroxetine Treatment: Preliminary Data
Sanjaya Saxena, M.D., Arthur J. Brody, M.D., Mark Colgan, M.E., Lewis R. Baxter, M.D.

NR47 PET Study of Cerebral Activation in Normal and Schizophrenic Subjects Performing Cognitive Challenge Tests
Ralph B. Lewis, M.D., Shitij Kapur, M.D., Robert Zipursky, M.D., Gregory Brown, M.D., Sylvain Houle, M.D.

NR48 Normal Aging and Frontal Lobe CBF: A PET Study
Brenda S. Kirkby, M.Sc., Giuseppe Esposito, M.D., Jill L. Ostrem, B.A., John D. Van Horn, Ph.D., Daniel R. Weinberger, M.D., Karen F. Berman, M.D.

NR49 Monte Carlo Simulation of PET Region of Interest Data Sets
John D. Van Horn, Ph.D., Alex Terrazas, B.S., Daniel R. Weinberger, M.D., Karen F. Berman, M.D.

NR50 Effects of Cohort Size on PET Cognitive Activation Studies
Jill L. Ostrem, B.A., Brenda S. Kirkby, M.Sc., John D. Van Horn, Ph.D., Giuseppe Esposito, M.D., James Gold, Ph.D., Daniel R. Weinberger, M.D., Karen F. Berman, M.D.

NR51 The Phenomenon of Dysautonomia in OCD
Srinivasan S. Pillay, M.B., S. Nassir Ghaemi, M.D., Anthony B. Joseph, M.D., Jonathan O. Cole, M.D.

NR52 Complex Partial Seizures and Panic Disorders: A Truly Complex Relationship
Nelson Handal, M.D., Prakash Masand, M.D., Jeff Weilburg, M.D.

NR53 Psychiatric Disorders in Epileptic Patients
Thania V. Quesada, M.D., Rene A. Poveda, M.D., M. Beatriz Currier, M.D.

NR54 Psychiatric Disorders and Functional Disability in Ambulatory Traumatic Brain Injured Patients
Jesse R. Fann, M.D., Wayne J. Katon, M.D.,

NR55 Excited Catatonia: Prevalence and Phenomenology
George Bush, M.D., Georgios Petrides, M.D., Andrew Francis, M.D.

NR56 The Immune Effects of a Medical Stressor
JoAnn Difede, Ph.D., Lawrence B. Jacobsberg, M.D., Dana Bovbjerg, Ph.D, Daniel Goodman, M.D., Samuel W. Perry III, M.D.

NR57 Interleukin-6 in Depression and Schizophrenia
Ulrich H. Frommberger, M.D., P. Haselbauer, A. Fraulin, J. Bauer, M.D., M. Berger, M.D.

NR58 Does Clozapine Cause OCD?
S. Nassir Ghaemi, M.D., Carlos A. Zarate, Jr., M.D., Anand P. Popli, M.D., Srinivasan S. Pillay, M.B., Jonathan O. Cole, M.D.

NR59 Lack of Potentiation of Neuroleptic Action by Clonidine in Psychosis
Scott T. Hedges, M.D., Rif S. El-Mallakh, M.D.

NR60 Sertraline Pharmacotherapy in Patients with Social Phobia
Eduina A. Martins, M.D., Teresa A. Pigott, M.D., Suzanne Bernstein, B.S., Brian B. Doyle, M.D., Virginia M. Smolka, Billinda Dubbert, M.S.N.

NR61 Clinical Implications of Adjunctive Valproic Acid Use in Clozapine Treated Psychiatric Patients
Lance P. Longo, M.D., Carl Salzman, M.D., Alan I. Green, M.D.

NR62 Clozapine Use in the Dually Diagnosed Mentally Retarded: Three Case Studies
Lance P. Longo, M.D., Mark J. Hauser, M.D., Michael L. Commons, Ph.D.

NR63 Idazoxan Effects on Attention in Normal Volunteers
Annick Vincent, M.D., Robert Risinger, M.D., Mark Schmidt, M.D., Philippe Baruch, M.D., Sophie Lemelin, BPS, William Z. Potter, M.D.

NR64 Trimethapham for Blood Pressure Control During ECT
Georgios Petrides, M.D., Farrokh Maneksha, M.D., Iannis Zervas, M.D., Andrew Francis, M.D.

NR65 The Estrogen Antagonist Tamoxifen Causes Treatment Resistance to Antidepressants
Jacqueline Quak, M.D., Susanna Goldstein, M.D., Uriel Halbreich, M.D.

NR66 Double-Blind Randomized Trial Comparing the Efficacy and Tolerability of Medifoxamine and Imipramine in Major Depressive Disorder
Andre J. Galinowski, M.D., Jean P. Olie, M.D., P. Lehert, Ph.D., F. Lemonnier, M.D., H. Loo, M.D.

NR67 Evaluation of Neuroleptic-Induced Hyperprolactinemia
David M. Klahr, M.D., Lewis A. Opler, M.D., Nereida Correa, M.D., Andrew G. Frantz, M.D., Paul Michael Ramirez, Ph.D., Michael Y. Hwang, M.D.

NR68 Are Spine Films Medically Necessary Prior to ECT?
Miguel A. Perez, M.D., Jose E. Ribas, M.D., David Loewenstein, Ph.D.

NR69 Seizures During an Inpatient Psychiatric Hospitalization
Anand P. Popli, M.D., Judith C. Kando, Pharm.D., Srinivasan S. Pillay, M.B., Mauricio Tohen, M.D., Jonathan O. Cole, M.D.

NR70 The McLean Hospital First-Episode Psychoses Family Study
Carlos A. Zarate, Jr., M.D., Bruce Cohen, M.D., Mauricio Tohen, M.D., James Heggarty, M.D., Franca Centorrino, M.D., Michelle Weiss, M.S.

NR71 Liver Function Tests and Anticonvulsants
Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D., German Baraibar, M.D., Jong-Won Kim, M.D., Jose Castillo-Ruiz, M.D., Judith Kando, Pharm.D.

NR72 Demographic Characteristics of Patients Referred to the University of Miami/Jackson Memorial Hospital Adult Outpatient Psychiatric Clinic
Eusebio G. Hernandez, M.D., Seana Shaw, M.D.

NEW RESEARCH

Monday, May 23, 1994, 1:00 p.m.-2:30 p.m.

New Research 2 – Oral/Slide Session – Exhibit Hall D-1, Street Level, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

Chp.: David Pickar, M.D.

NR73	Personality Dimensions and Anxiety Disorders Vladan Starcevic, M.D., Eberhard H. Uhlenhuth, M.D., Brian A. Roberts, M.D., Stephanie Fallon, M.D.	1:00 p.m.
NR74	Craniofacial Anomalies in Schizophrenia: Clues to the Timing of Developmental Disturbance Abbie Lane, M.B., Anthony Kinsella, FIS, Patrice Murphy, M.B., John L. Waddington, D.Sc., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.	1:15 p.m.
NR75	A Computer Simulation of the HPA Axis Joseph M. Gonzalez-Heydrich, M.D., Ronald J. Steingard, M.D., Isaac Kohane, M.D.	1:30 p.m.
NR76	Regulation of Early Gene Expression in the CNS by Antipsychotics Patrick J. Rogue, M.D., Guy Vincendon, M.D.	1:45 p.m.
NR77	Striatal Dopamine Receptor Binding in Epileptic Psychoses Howard A. Ring, M.B., Michael R. Trimble, M.B., Durval O. Costa, Ph.D., John Moriarty, M.B., Paul Verhoeff, M.D., Peter Ell, M.D.	2:00 p.m.
NR78	Apolipoprotein E-4 Allele Frequency in Two Different Populations of Patients with Alzheimer's Disease Debby W. Tsuang, M.D., Walter A. Kukull, Ph.D., Elaine Peskind, M.D., Gerald D. Schellenberg, Ph.D., Murray A. Raskind, M.D., Steve Edland, M.S.	2:15 p.m.

NEW RESEARCH

Monday, May 23, 1994, 1:00 p.m.-2:30 p.m.

New Research 3 – Oral/Slide Session – Exhibit Hall D-2, Street Level, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

Chp.: Charles L. Bowden, M.D.

NR79	Prescribing Patterns of Newer Antidepressants in a Resident Outpatient Psychiatry Clinic Amar N. Bhandary, M.D., Joe Medicis, M.D., Prakash Masand, M.D.	1:00 p.m.
NR80	Is Childhood Sexual or Physical Abuse a Risk Factor for Psychotic Depression? Adele C. Viguera, M.D., Anthony J. Rothschild, M.D.	1:15 p.m.
NR81	Gender Differences Among Psychiatric Inpatients with Comorbid Cocaine and Alcohol Use Disorders Ihsan M. Salloum, M.D., Dennis Daley, M.S.W.	1:30 p.m.
NR82	Retinal Effects of Chronic Lithium Use Suzanne M. Allain, M.D., Raymond W. Lam, M.D.	1:45 p.m.
NR83	Untoward Effects of Lithium Treatment in Very Young Hospitalized Children Owen R. Hagino, M.D., Elizabeth B. Weller, M.D., Mary Fristad, Ph.D., Douglas Washing, B.A., Ronald A. Weller, M.D.	2:00 p.m.
NR84	Acute Psychiatric Response to the Explosion at the World Trade Center JoAnn Difede, Ph.D., William J. Apfeldorf, M.D., Lisa Spielman, Ph.D., Marylene Cloitre, Ph.D., Samuel W. Perry III, M.D.	2:15 a.m.

NEW RESEARCH

Monday, May 23, 1994, 3:00 p.m.-5:00 p.m.

New Research 4 – Poster Session – Exhibit Hall D, Street Level, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Susan J. Fiester, M.D.

NR85 Sexual Abuse in Female Psychiatric Outpatients
Sylvie Lombardo, B.A., Robert Pohl, M.D.

NR86 Cognitive Distortions in Various Anxiety Disorders
Vladan Starcevic, M.D., Eberhard H. Uhlenhuth, M.D., William Matuzas, M.D., Dorothy Pathak, Ph.D.

NR87 OCD in College Students: Presentation, Impairment and Treatment
Lacramioara Spetie, M.D., Brendan T. Carroll, M.D.

NR88 Carbon Dioxide Sensitivity Following Tryptophan Depletion in Patients with Panic Disorder
Justine M. Kent, M.D., Jose Martinez, M.A., Laszlo A. Papp, M.D., Jack M. Gorman, M.D.

NR89 PTSD and Severe Motor Vehicle Accidents
Josie C. Ramos, M.D., Daniella David, M.D., Thomas A. Mellman, M.D., Diane Gonzalez, R.N., Jeffrey Augenstein, M.D.

NR90 Psychiatric Morbidity Following Hurricane Andrew
Daniella David, M.D., Thomas A. Mellman, M.D., Lourdes M. Mendoza, M.D., Renee Kulick-Bell, B.A., Gail Ironson, M.D., Neil Schneiderman, Ph.D.

NR91 Social Phobia Subtyping: Correlates to Severity
Lisa B. Shea, M.D., Michele T. Pato, M.D.

NR92 The Rollback Phenomenon in Major Depression
John J. Worthington III, M.D., Maurizio Fava, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Katharine G. Davidson, B.A., Jerrold F. Rosenbaum, M.D.

NR93 Panic Disorder in Emergency Ward Patients with Chest Pain
John J. Worthington III, M.D., Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Thomas Lee, M.D., Susan A. Sabatino, B.A., Jerrold F. Rosenbaum, M.D.

NR94 Reaction Times and Event-Related Brain Potentials to Traumatic Words in PTSD
Linda J. Metzger, Ph.D., Scott P. Orr, Ph.D., Lawrence A. Farwell, Ph.D., Roger K. Pitman, M.D.

NR95 Sertraline in Social Phobia
Violetta D. Czepowicz, M.D., Michael R. Johnson, M.D., Naresh P. Emmanuel, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

NR96 Attributional Style in Social Phobia: Comparison with Major Depression
Gerardo Villarreal, M.D., Michael R. Johnson, M.D., Naresh P. Emmanuel, M.D., Violetta D. Czepowicz, M.D., Mark Walsh, M.D., Olga Brawman Mintzer, M.D.

NR97 Differences Between Subtypes in Panic Disorders
Ulrich H. Frommberger, M.D., Raimund Buller, M.D., Christoph Kappler, Ph.D., Otto Benkert, M.D.

NR98 Self-Mutilation, Dissociative Experiences and Alexithymia
Caron Zlotnick, Ph.D., Teri Pearlstein, M.D., Elizabeth Simpson, M.D., Ann Begin, Ph.D., Ellen Costello, Ph.D.

NR99 Dissociative Experiences, Psychopathology and Maladaptive Schemas
Caron Zlotnick, Ph.D., Ann Begin, Ph.D., M. Tracie Shea, Ph.D., Teri Pearlstein, M.D., Elizabeth Simpson, M.D, Ellen Costello, Ph.D.

NR100 Dissociative Experiences and Self-Mutilation in BPD
Beth Brodsky, M.A., Rebecca A. Dulit, M.D., Marylene Cloitre, Ph.D.

NR101 Characteristics of Abuse in Psychiatric Outpatients
Deborah S. Lipschitz, M.D., Margaret L. Kaplan, Ph.D., Gregory M. Asnis, M.D.

NR102 Dissociative Symptomatology and Characteristics of Childhood Abuse
Deborah S. Lipschitz, M.D., Margaret L. Kaplan, Ph.D., Gregory M. Asnis, M.D., Gianni L. Faedda, M.D., Jodie Sorkenn, C.S.W., Alessandra Scalmati, M.D.

NR103 Trauma and Dissociation in Two Populations
Howard C. Wetsman, M.D., Elizabeth David, M.D., Edward Morse, Ph.D.

NR104 A Comparison of DSM-III-R Versus DSM-IV Criteria for Melancholic Depression
Beny Lafer, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D., Madeleine Carey, B.A., Jerrold F. Rosenbaum, M.D.

NR105 Effects of Thiopental Dose on ECT-Induced Cardiovascular Physiological Changes
Rama Prayaga, M.D., Cheng-Jen Chen, M.D.

NR106 Comorbid Panic Disorder in a Bipolar Family Study
Dean F. Mac Kinnon, M.D., Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., J. Raymond De Paulo, Jr., M.D.

NR107 Treatment of Chronic Major Depression with Desipramine
Nina L. Miller, M.A., James H. Kocsis, M.D.

NR108 Does Succinylcholine Affect ECT-Induced Seizure Duration?
Luis M. Del Rio, M.D., Cheng-Jen Chen, M.D.

NR109 Compliance with Pharmacological Treatment in Patients with Mania
Sean P. Stanton, B.S., Jerry A. Bennett, Pharm.D., Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D., Karen C. Tugrul, B.S.N., Stephen M. Strakowski, M.D.

NR110 Geropsychiatric Effects of Mild Subclinical Hypothyroidism
Sharon M. Esposito, M.D., John J. Haggerty, Jr., M.D., Robert A. Stern, Ph.D., Mark E. Williams, M.D., George A. Mason, Ph.D., Arthur J. Prange, Jr., M.D., Michael A. Senger, M.A.

NR111 Attention Deficit in Mixed and Pure Mania
Kenji W. Sax, M.S., Stephen M. Strakowski, M.D., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Scott A. West, M.D., Sean P. Stanton, B.S.

NR112 Comorbidity of ADHD in Adolescent Mania
Scott A. West, M.D., Susan L. McElroy, M.D., Stephen M. Strakowski, M.D., Paul E. Keck, Jr., M.D., Brian J. Mc Conville, M.D.

NR113 Transitional Objects and Borderline Personality
William Cardasis, M.D., Jamie Hochman, B.A., Kenneth R. Silk, M.D.

NR114 The Utility of SCID-II for Diagnosing Personality Disorders
Joshua McDavid, M.D., Suzan Clark, M.Ed., Paul A. Pilkonis, Ph.D., Brian Neighbors, M.A., Kathy Reilly, M.A., Joe Proletti, M.S.

NR115 Concomitant Personality Disorders in Patients with Social Phobia
Billinda Dubbert, M.S.N., Teresa A. Pigott, M.D., Suzanne Bernstein, B.S., Eduina A. Martins, M.D., Brian B. Doyle, M.D., Laurel Northup, M.D., Vinita Leslie, B.S., Virginia M. Smolka

NR116 Gender Differences in Personality Disorders
Mayana Golomb, M.D., Maurizio Fava, M.D., Melissa Abraham, B.A., Jerrold F. Rosenbaum, M.D.

NR117 Temperament and Character Inventory Predicted Probability of Personality Disorder Changes with Treatment of Depression
Kevin John Black, M.D., Yvette I. Sheline, M.D.

NR118 Alexithymia: Relationship to Personality Disorders
Michael Bach, M.D., Martina De Zwaan, M.D., Diann Ackard, M.D., Detlev O. Nutzinger, M.D., James E. Mitchell III, M.D.

NR119 Day Treatment: Patients at Risk for Relapse
Nuchanart Venbrux, M.D., Richard Fonte, M.D., Edward O. Bixler, Ph.D., Pat Taksen, M.S.W., Thomas C. Lillis, M.Ed.

NR120 The Role of Discussion on Television Effects on Children
Nuchanart Venbrux, M.D., Paul A. Kettl, M.D., Edward O. Bixler, Ph.D., Errin W. Crowell, B.S., James Douglas, B.S.

NR121 Sleep/Wake Patterns in Abused Children
Carol A. Glod, M.S.N., Martin H. Teicher, M.D., Carol Hartman, D.N.S., Thomas Harakal

NR122 Untoward Effects and Their Clinical Management in Young Autistic Children Treated with Clomipramine
Laura E. Sanchez, M.D., Jeanette E. Cueva, M.D., Jorge L. Armenteros, M.D., Magda Campbell, M.D.

NR123 Patient Knowledge of Medication at Discharge
Michael R. Lavin, M.D., Steven Budoff, D.O., Barbara Galkowski, C.S.W., Simcha Pollack, Ph.D., Michael H. Kronig, M.D.

NR124 Homelessness and Substance Use in Severe Mentally Ill Patients
Deborah White, B.A., Lisa Dixon, M.D., Anthony F. Lehman, M.D., John Belcher, Ph.D.

NR125 Transfers of Hospitalized Psychiatric Patients to a General Hospital Emergency Service for Adverse Drug Reactions
Anand P. Popli, M.D., James Hegarty, M.D., Arthur J. Segal, M.D., Judith C. Kando, Pharm.D., Mauricio Tohen, M.D., Ross J. Baldessarini, M.D.

NR126 Psychiatric Interview and Psychometric Predictors of Survival in Cardiac Transplant
Jennifer G. Gotto, M.D., Ranjit Chacko, M.D., Robert G. Harper, Ph.D., James Young, M.D.

NR127 Assessment of Personality Disorders in Patients with Reflex Sympathetic Dystrophy
Daniel A. Monti, M.D., Christina Herring, M.D., Robert Schwartzman, M.D.

NR128 The Provider-Patient Relationship in Young Adults with Type I Diabetes Mellitus
Ramona Dvorak, M.D., Allen Jacobson, M.D., Stuart T. Hauser, M.D., Robert S. Lagos, B.S., Charlotte Cole, Ed.D.

NR129 MMPI-2 and Ethnicity in the Basic Trainees of the United States Air Force
Curtis H. Holder, M.D., Edna Fiedler, Ph.D.

NR130 Suicide in the Elderly Cuban-American Population of Dade County Florida: 1990-1993
Yolanda B. Zarate, M.D., Maria D. Llorente, M.D., David Loewenstein, Ph.D.

NR131 Alcohol Use Among Undergraduate Asian-Americans
Edward Ma, B.S., Henry Chung, M.D., Jean Mueller, Ph.D., John C. Mahler, M.D., James Hull, Ph.D.

NR132 Mental Disorders in Black Nursing Home Residents
Luis G. Allen, M.D., Blaine S. Greenwald, M.D., Ronald Brenner, M.D., Richard Hodder, M.D., Arthur Risbrook, M.D.

NR133 Delusions of Theft in Probable Alzheimer's Disease
Jesus Rivero, M.D., Steven Sevush, M.D.

NR134 Tridimensional Personality Characteristics of Mentally Ill Offenders and Non-Offenders
Barry J. Mills, M.D., E. Ross Taylor, M.D., John A. Chiles, M.D., Jeff S. Seward, M.D.

NR135 Pseudopsychopathy and Conditional Release Failure in Mentally Ill Offenders
Barry J. Mills, M.D., E. Ross Taylor, M.D., John A. Chiles, M.D.

NR136 Understanding Firearms and the Mentally Ill
Nicole F. Wolfe, M.D.

NR137 Committing the Patient Who Doesn't Meet Criteria
Mitchell H. Dunn, M.D.

NR138 Psychiatric Consultations in Persons 80 Years of Age and Older: Is There a Difference?
Tarak Vasavada, M.D., Prakash Masand, M.D., Pushpi Chaudhary, M.D.

NR139 Incidence of Post-ECT Delirium in Geriatric Patients
Amaryllis Sanchez, B.A., Paul A. Kettl, M.D.

NR140 Instrumental Assessment of Psychomotor Slowing
Mary E. Wylie, M.D., Robert Sweet, M.D., Robert Nebes, Ph.D., Bruce Pollock, M.D., Edythe Halligan, M.A.

NR141 A Prospective Study of Factors Associated with Discharge From Hospitalization Among Older Psychiatric Inpatients
Raymond L. Ownby, M.D.

NR142 Fluoxetine Treatment for Elderly Patients with Dysthymic Disorder: A Pilot Study
Mitchell S. Nobler, M.D., D.P. Devanand, M.D., Tara M. Singer, B.A., Steven P. Roose, M.D., Harold A. Sackeim, Ph.D.

NR143 Age of Onset and the Rate of Cerebral Degeneration in Alzheimer's Disease: Magnetic Resonance-Based Volumetric Study
Ju Han Kim, M.D., Dong Soo Shin, M.D., Jin Hyeong Jhoo, M.D., Dong Young Lee, M.D., Jung Hie Lee, M.D., Jong Inn Woo, M.D.

NR144 WITHDRAWN

NR145 The Treatment of Depression in Dementia Patients
Linda D. Lewis, MN, Sharon R. Burnside, M.D., Jacobo E. Mintzer, M.D., William Wellborn, Ph.D., L.R. Waid, Ph.D., Kerry Herman, B.A.

NR146 Plasma Homovanillic Acid and Cognition in Geriatric Depression
Olurotimi L. Bajulaiye, M.D., George S. Alexopoulos, M.D., Robert C. Young, M.D.

NR147 Religion and the HIV-Positive Patient
Mark A. McClurg, M.D., Shimon S. Waldfogel, M.D., Stephan Hauptman, D.O., Roberta A. Benjamin, B.S.N.

NR148 A Study on PTSD in China: Clinical Features and Crisis Intervention of 64 Cases
Yalin Zhang, M.D., Suizhen Chen,, Xiaoyin Huang,

NR149 PTSD Symptomatology in Children: The Columbus Day School Bus Accident
Stephanie D. Young-Azan, M.D., Jon A. Shaw, M.D.

NR150 Why Do Clinicians Miss Past Suicidal Behavior?
Katalin Szanto, M.D., Kevin M. Malone, M.D., Elizabeth Corbitt, Ph.D., J. John Mann, M.D.

NR151 Suicidal Behavior, Axis II Disorder and Major Depression
Elizabeth Corbitt, Ph.D., Kevin M. Malone, M.D., Gretchen L. Haas, Ph.D., J. John Mann, M.D.

NR152 Suicide Risk Factors Among Asian Patients
Raymond D. Tam, M.D., Joana Law, C.S.W., John M. Herrera, Ph.D.

NR153 Communal Ties Mediating Violence and Its Effects
Karyn J. Horowitz, B.A., Stevan M. Weine, M.D., James F. Jekel, M.D.

NR154 PTSD Symptoms Profiles in Female Urban Adolescents
Karyn J. Horowitz, B.A., Stevan M. Weine, M.D., James F. Jekel, M.D.

NR155 Gender and Medical Comorbidities of Recurrent Depression in Older Inpatients
Daniel P. Chapman, Ph.D., Joan K. Miller,, Donald K. Blackman, Ph.D.

NR156 Patients Who Request a Female Therapist
Melinda Fudge, M.D., Timothy Smith, M.D., Salman Akhtar, M.D., Steven E. Samuel, Ph.D.

NR157 Body Dysmorphic Disorder in Atypical Depression
Katharine A. Phillips, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

NR158 Skin Picking: A Symptom of Body Dysmorphic Disorder
Katharine A. Phillips, M.D., Sarah L. Taub, B.A., Katherine D. Atala, M.D.

NR158-A Quality of Life in Women with Metastatic Cancer
Tim Gendron, Teresa A. Rummans, M.D., Michelle Taylor, Ph.D., Roger Evans, Ph.D., Paul Novotny, Ruth Johnson, M.D., Lynn Hartmann, M.D., Ann Marie Dose, R.N., Marilyn Stiles, Ph.D.

NEW RESEARCH

Tuesday, May 24, 1994, 9:00 a.m.-10:30 a.m.

New Research 5 – Oral/Slide Session – Exhibit Hall D-1, Street Level, Convention Center

SCHIZOPHRENIA/AGRESSION

Chp.: Andrew E. Skodol, M.D.

NR159	Heritability of Irritable Aggression: A Twin Study Emil F. Coccaro, M.D., C.S. Bergeman, Ph.D., Richard J. Kavoussi, M.D.	1:00 p.m.
NR160	Decreased Hippocampal Volume Over Time in Schizophrenia: Evidence of Neurodegeneration Henry A. Nasrallah, M.D., Marla Ketterer, B.S., Sarita K. Sharma, B.S., Stephen C. Olson, M.D., Robert Martin, Mary B. Lynn, M.A.	1:15 p.m.
NR161	Cognitive Impairment in Geriatric Schizophrenic Patients: Clinico-pathological Studies Michael Davidson, M.D., Vahram Haroutunian, Ph.D., Steven Gabriel, Philip D. Harvey, Ph.D., Peter Powchik, M.D., Julia A. Golier, M.D., Kenneth L. Davis, M.D.	1:30 p.m.
NR162	Gender Differences in Regional Cortical Glucose Metabolism in Schizophrenia Benjamin V. Siegel, M.D., Monte S. Buchsbaum, M.D.	1:45 p.m.
NR163	Linkage on the 11q21-22 Region in a Severe Form of Schizophrenia Michel Maziade, M.D., Maria Martinez, Ph.D., Denis Cliche, M.D., Jean-Pierre Fournier, M.D., Yvon Garneau, M.D., Chantal Merette, Ph.D.	2:00 p.m.
NR164	The Diagnosis of Schizophrenia in DSM-IV: How Different? Michael A. Flaum, M.D.	2:15 p.m.

NEW RESEARCH

Tuesday, May 24, 1994, 9:00 a.m.-10:30 a.m.

New Research 6 – Oral/Slide Session – Exhibit Hall D-2, Street Level, Convention Center

CONSULTATION/LIAISON; AIDS AND HIV-RELATED DISORDERS; AND RESEARCH ISSUES

Chp.: William Z. Potter, M.D.

NR165	Neural Networks for Studying Psychiatric Decisions Eugene Somoza, M.D., Jon Marvel, M.S.	1:00 p.m.
NR166	Analgesic Profiles of Bupropion Jeff Selph, B.S., Felicia R. Cochran, Ph.D., Mark A. Collins, B.S., Kwen-Jen Chang, Ph.D., Gary L. Grebe, B.S., Frank E. Soroko, B.S.	1:15 p.m.
NR167	Functional Status in Coronary Artery Disease: Biomedical and Psychosocial Correlates Mark D. Sullivan, M.D., Andrea Lacroix, Ph.D., Carl Baum, M.D., Wayne J. Katon, M.D., Arthur J. Resnick, M.D., Edward Wagner, M.D	1:30 p.m.
NR168	Stress, Cortisol and Killer Lymphocytes John M. Petitto, M.D., Jane Leserman, Ph.D., Diana O. Perkins, M.D., Robert N. Golden, M.D., Carol E. Murphy, M.P.H., Dwight L. Evans, M.D.	1:45 p.m.
NR169	Stress and Immunity in Men Infected with HIV Jane Leserman, Ph.D., John M. Petitto, M.D., Diana O. Perkins, M.D., Robert N. Golden, M.D., Carol E. Murphy, M.P.H., Dwight L. Evans, M.D.	2:00 p.m.
NR170	Cognitive Impairment Predicts Death in HIV-Positive Men Igor Grant, M.D., Robert K. Heaton, Ph.D., J. Hampton Atkinson, M.D., Reena Deutsch, M.S., Julie Nelson, B.S., J. Allen McCutchan, M.D.	2:15 p.m.

NEW RESEARCH

Tuesday, May 24, 1994, 12:00 noon-2:00 p.m.

New Research 7 – Poster Session – Exhibit Hall D, Street Level, Convention Center

MOOD DISORDERS; TREATMENT TECHNIQUES AND ISSUES; PREMENSTRUAL DYSPHORIC DISORDER; SUICIDE; AND ANXIETY DISORDERS

Moderator: Tana A. Grady, M.D.

NR171 Prevalence of Seasonal and Non-Seasonal Depression
Anthony J. Levitt, M.D., Michael H. Boyle, Ph.D.

NR172 Stress-Induced Alterations in Depression
Rand J. Gruen, Ph.D., Raul Silva, M.D., Joshua Ehrlich, M.A., Stacey Greenwald, Jack Schweitzer, Ph.D., Arnold J. Friedhoff, M.D.

NR173 Antidepressant Effects of Total Versus Partial Sleep Deprivation
Martin Szuba, M.D., Lewis R. Baxter, M.D., Lori L. Altshuler, M.D., Barry H. Guze, M.D., Jeffrey M. Schwartz, M.D.

NR174 Fenfluramine Challenge Test in Mania
Lakshmi N. Yatham, M.D., Margaret Brock, R.N.

NR175 Outcome of One Versus Two Weeks Phototherapy in SAD
Lawrence A. Labbate, M.D., Beny Lafer, M.D., Jerrold F. Rosenbaum, M.D., Amy Thibault, B.A., Gary S. Sachs, M.D.

NR176 The Relationship of Alprazolam and Clonazepam Dose to Steady-State Plasma Concentration
Lawrence A. Labbate, M.D., Mark H. Pollack, M.D., Michael W. Otto, Ph.D., George Tesar, M.D., Jerrold F. Rosenbaum, M.D.

NR177 Hyposomnia as Predictor of Anticonvulsant Response in Bipolar Affective Disorder
Dale A. D'Mello, M.D., John A. McNeil, D.O., Bhekumusa Msibi, D.O.

NR178 Predictive Profiles of Antidepressant Response
Fabrice Duval, M.D., M-Claude Mokrani, Ph.D., Martine Jautz, Psych, Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Thahn Son Diep, M.D., Eduardo De Andrade, M.D., Jean-Paul Macher, M.D.

NR179 Depression Screening in Primary Care: A Validity Study
Marijo B. Tamburrino, M.D., Denis J. Lynch, Ph.D., Rollin Nagel, M.A., Nancy J. Stadler

NR180 The Effects of Gender and Age of Onset of Depression on Mortality
Robert A. Philibert, M.D., George Winokur, M.D., Larry L.. Richards, D.O.

NR181 Order of Onset of Major Depression and Drug Abuse
Henry D. Abraham, M.D., Maurizio Fava, M.D.

NR182 Social Vocational Adjustment in Mood Disorders: Episodic Major Depression, Dysthymic Disorder and Double Depression
Susan Evans, M.A., Marylene Cloitre, Ph.D., James H. Kocsis, M.D., Daniel N. Klein, Ph.D., Charles Holzer, Ph.D., Michael B. First, M.D., Leah Gniwesch, M.A.

NR183 Are Neurovegetative Symptoms Stable in Recurrent Atypical Depressive Episodes?
Andrew A. Nierenberg, M.D., Joel A. Pava, M.D., Kathy Clancy, B.A., Maurizio Fava, M.D.

NR184 Prodromal and Residual Symptoms in Bipolar Disorder
Gabor I. Keitner, M.D., Christine E. Ryan, Ph.D., David A. Solomon, M.D., Ivan W. Miller, Ph.D., Ellen Frank, Ph.D.

NR185 ADHD Among Adults with Major Depression
Jonathan E. Alpert, M.D., Anne B. Maddocks, B.A., Andrew A. Nierenberg, M.D., Richard L. O'Sullivan, M.D., Joel A. Pava, Ph.D., John J. Worthington, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR186 Antiglucocorticoid Treatment of Depression
Owen M. Wolkowitz, M.D., Victor I. Reus, M.D., Theresa Chan, B.A., Francesca Manfredi, B.A., Jonathan Canick, Ph.D., Susan Ormiston, R.N., Louann Brizendine, M.D., Jonathan Ingbar, M.D.

NR187 Thyroid Indices and Cerebral Metabolism in Mood Disorders
Lauren B. Marangell, M.D., Terence A. Ketter, M.D., Mark S. George, M.D., Peggy J. Pazzaglia, M.D., Ann M. Callahan, M.D., Paul J. Andreason, M.D., Priti J. Parekh, B.A., Barry Horowitz, M.D., Peter Herscovitch, M.D., Robert M. Post, M.D.

NR188 Cholesterol and Cerebral Metabolism in Mood Disorders
Ann M. Callahan, M.D., Terence A. Ketter, M.D., Mark S. George, M.D., Lauren B. Marangell, M.D., Peggy J. Pazzaglia, M.D., Paul J. Andreason, M.D., Priti J. Parekh, B.S., Barry Horwitz, Ph.D., Peter Herscovitch, M.D., Robert M. Post, M.D.

NR189 Depression in Adolescents: Clinical Outcome in Early Adulthood
Uma Rao, M.D., Neal D. Ryan, M.D., Boris Birmaher, M.D., Ronald E. Dahl, M.D., Douglas E. Williamson, B.A.

NR190 Recurrence of Unipolar Depression in Adolescents: Psychobiological Predictors
Uma Rao, M.D., Neal D. Ryan, M.D., Ronald E. Dahl, M.D., Boris Birmaher, M.D., Douglas E. Williamson, B.A., Radhika Rao, M.S.

NR191 Diurnal Plasma 3-methoxy-4-hydroxyphenylglycol, Cortisol and Autonomic Rhythms in Acute and Remitted Depression
Bonnie J. Steinberg, M.D., Robert L. Trestman, M.D., Irene Lopez, B.A., Damon Mitchell, B.A., Larry J. Siever, M.D.

NR192 Changes in Folate with Antidepressant Therapy
Virginia Wesson, M.D., Anthony J. Levitt, M.D., Russell T. Joffe, M.D.

NR193 Residual Symptoms in Major Depression: A Comparison with Normal Controls
Joel A. Pava, Ph.D., Andrew A. Nierenberg, M.D., Madeleine Carey, B.A., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR194 Undertreatment of Chronic Depression
Michael E. Thase, M.D., George Trapp, M.D., Charles Holzer, Ph.D., John M. Zajecka, M.D., A. John Rush, M.D., Robert Howland, M.D.

NR195 Paroxetine in a Clinical Practice Setting
James P. McCafferty, B.S., David E. Wheadon, M.D., Ivan P. Gergel, M.D.

NR196 Shortened REM Latency and ECT
Leon J. Grunhaus, M.D., James E. Shipley, M.D., Alan Eiser, Ph.D., Anna L. Remen, M.A., Atul C. Pande, M.D., Rajiv Tandon, M.D., John F. Greden, M.D.

NR197 Modelling the Seizure in ECT: Critical Indicators of Therapeutic Response
James S. Lawson, Ph.D., Felix Juan J. Letemendia, M.D., Nicholas J. Delva, M.D., James Inglis, D.Sc., Martin Rodenburg, M.D., John J. Waldron, M.B., Dennis W. Lywood, MIEEE

NR198 Higher Levels of Cholesterol in Depressive Patients
Claudi Udina, M.D., Josep Tresserra, M.D., Vicens Valles, M.D., Rosa Catalan, M.D.

NR199 Leukocyte Adhesiveness/Aggregation in Major Depression
Zvi Zemishlany, M.D., Cynthia Klein, M.D., Dov Aizenberg, M.D., Ilan Modai, M.D., Moshe Aronson, Ph.D., Abraham Weizman, M.D.

NR200 DST and Clinical Outcome in Elderly Depressed Patients
N.P. Vasavan Nair, M.D., Mohammed Amin, M.D., Nmk NG Ying Kin, Ph.D., P. Holm, M.Sc., P. Kragh-Sorensen, M.D., C. Katona, M.D.

NR201 Psychosocial Correlates of Postpartum Mood
Francois Borgeat, M.D., Marc Berthiaume, M.P.S., Helene David, Ph.D., Jean-Francois Saucier, M.D., Odette Bernazzani, M.D.

NR202 Plasma Lithium Elevation at the End of Mania
Simavi Vahip, M.D., Bekir Ozkan, M.D., Alp Ayan, M.D., Serdar Korukoglu, Ph.D., Isik Tuglular, M.D.

NR203 Outcome in Single and Dual Diagnosis Patients
Sally Caldecott-Hazard, Ph.D., Richard C.W. Hall, M.D.

NR204 Six-Month Clinical Outcome of Outpatients with Early-Onset Chronic Depression
Vito Agosti, M.S.W.

NR205 Norplant Associated Major Depression and Panic Disorder
Karen D. Wagner, M.D., Abbey Berenson, M.D.

NR206 Television and Growth of Major Depression in Youth
Paul A. Kettl, M.D., Michelle Sredy, M.D.

NR207 Affective Disorders and Seasonality in Brazil
Florence Kerr-Correa, M.D., Lucijane B. Sousa

NR208 Discrimination of Anxiety and Depression with Cognition Data
John B. Jolly, Psy.D., David C. Wiesner, Ph.D., David S. McCray, M.D., Nickolaus Paal, Ph.D., J. Chris Rule, B.A., Janet M. Jolly, M.D.

NR209 Pharmacoeconomic Evaluation of Oral Therapies in the Management of Major Depressive Disorder
Thomas R. Einarson, Ph.D., Steven R. Arikian, M.D., Robert E. Lee

NR210 A Poisson-Erlang Model Analysis of Cognitive Retardation in Depression
Sophie Lemelin, BPS, Philippe Baruch, M.D., Francois Brisebois, M.Sc., Annick Vincent, M.D., James Everett, Ph.D., Louis-Paul Rivest, Ph.D.

NR211 Predictors of Response to Cognitive Therapy
Jacqueline A. Samson, Ph.D., Martha T. Dewitt, Ph.D., Joseph J. Schildkraut, M.D., Alan F. Schatzberg, M.D., Jonathan O. Cole, M.D.

NR212 Sertraline Administered for Eight Weeks to Depressed Patients Did Not Alter Sleep Architecture: A Preliminary Report
Andrew Winokur, M.D., Nedra Lexon, Kathleen Allen, Dan Reed, William Breitmeyer

NR213 Discriminating Apathy and Depression Using Items From the Hamilton Rating Scale for Depression
Robert S. Marin, M.D.

NR214 Co-Occurence of Bipolar Disorder and Personality Disorder
Reed D. Goldstein, Ph.D., Alan M. Gruenberg, M.D., Gary S. Bruss, Ph.D., Jacques P. Barber, Ph.D.

NR215 Dysthymia: Assessing Symptoms and Treatment Response with the Cornell Dysthymia Rating Scale
David J. Hellerstein, M.D., Lisa W. Samstag, M.A., Suzanne Little, M.A., Philip Yanowitch, M.D.

NR216 Comparison of Quality of Life in Outpatients Suffering From Affective Disorders
Patrick M. Martin, Ph.D.

NR217 Effects of Buspirone and 1-PP in Animal Models of Panic Attacks
Patrick M. Martin, Ph.D., Jean-Michel Chignon, M.D.

NR218 Suppressibility and Recovery of the Thyroid Axis in Major Depression
Patricia R. Mourilhe, M.D., Peter E. Stokes, M.D., Christophe Huston, B.A., Jessica E. Story, B.A., Marie H. Jhin, B.A., Betty J. Lasley, Ph.D.

NR219 Fixed and Titrated Dose RUL ECT in the Elderly
W. Vaughn McCall, M.D., Andy Farah, M.D., David Reboussin, M.D., Christopher C. Colenda, M.D.

NR220 Physiological Correlates of ECT
Veronika Solt, M.D., Cheng-Jen Chen, M.D.

NR221 Possible Iatrogenic Cardiovascular Risks for Older Patients Receiving ECT
Cheng-Jen Chen, M.D., Peter E. Stokes, M.D.

NR222 Cerebral Blood Volume and Oxygenation During ECT
Laszlo Gyulai, M.D., Larry Lipton, Ph.D., William Ball, M.D., Chilton Alter, B.S., Britton Chance, Ph.D.

NR223 Identification of Markers of Mild Delirium in the Elderly
Ira R. Katz, M.D., Jana Mossey, Ph.D., Luisa Skoble, M.D.

NR224 Effective Treatment for Premenstrual Syndrome with a Gonadotropin-releasing Hormone Agonist and an Oral Contraceptive
Michael Feinberg, M.D., Mona M. Shangold, M.D.

NR225 Serious Suicide Attempts in Children and Adolescents
Atilla Turgay, M.D., Lillian Mok, M.D., Anne Marie D'Aloisio, M.S.W., JoAnne Sheehan, R.N.

NR226 Driven to Suicide? Adolescent Needs and Drives
Catherine A. Martin, M.D., Arch G. Mainous, Ph.D., Michael J. Oler, M.D., Eric T. Richardson, M.D., Amy S. Haney, M.D.

NR227 Anger Impulsivity and Coping Styles in Suicidal Patients
Elie Lepkifker, M.D., Netta Horesh, Ph.D., Zipi Rolnick, M.A.

NR228 Childhood Abuse and Suicidal Behavior in Psychiatric Outpatients
Margaret L. Kaplan, Ph.D., Deborah S. Lipschitz, M.D., Gregory M. Asnis, M.D.

NR229 Comorbidity in Alcoholics Who Attempted Suicide
Jean-Michel Chignon, M.D., Patrick M. Martin, Ph.D., Catherine Dissoubray, M.D., Eric Souetie, M.D., Jean Ades, M.D.

NR230 Buspirone Induced Panic: Possible Role of 1(2-Pyrimidinyl) Piperazine
Jean-Michel Chignon, M.D., Patrick M. Martin, Ph.D., Jean-Pierre Lepine, M.D.

NR231 Catecholamine Neurons of Suicides: Ultrastructure
Marietta R. Issidorides, Ph.D., Virginia Kriho, B.A., George D. Pappas, Ph.D.

NR232 Efficacy of Alprazolam in Selective Serotonin Reuptake Inhibitor-Induced Jitteriness
Jay D. Amsterdam, M.D., Mady Hornig-Rohan, M.D., Greg Maislin, B.S.

NR233 A High-Risk Pilot Study of Social Phobia
Michael A. van Ameringen, M.D., Catherine Mancini, M.D., Peter Szatmari, M.D., Christina Fugere, B.Sc., Michael H. Boyle, Ph.D.

NR234 Serotonin Reuptake Inhibitors Are Superior to Alprazolam and Imipramine in Panic: A Meta-analysis
William F. Boyer, M.D.

NR235 Childhood Shyness and Psychophysiological Disorders: Personal and Family Psychiatric and Medical Histories
Iris R. Bell, M.D., Gary E. Schwartz, Ph.D., Julie M. Peterson, B.S.

NR236 Phenomenology of OCD and Tourette's Syndrome
Euripedes C. Miguel, M.D., Barbara J. Coffey, M.D., Lee Baer, Ph.D., Cary R. Savage, Ph.D., Scott L. Rauch, M.D., Michael A. Jenike, M.D.

NR237 Comorbidity of OCD and Personality Disorders
Albina R. Torres, M.D., Jose A. Del Porto, M.D.

NR238 Relationship of Panic to Suicide in an Emergency Psychiatry Population: Demographic Data
Joseph J. Zealberg, M.D., Susan J. Hardesty, M.D.

NR239 Platelet Benzodiazepine Receptors in PTSD
Ronit Weizman, M.D., Nathaniel Laor, M.D., Miri Bidder, M.D., Uri Muller, M.D., Ahuva Reiss, M.D., Moshe Gavish, Ph.D.

NR240 Platelet Imipramine Binding in PTSD
Ronit Weizman, M.D., Nathaniel Laor, M.D., Ayala Schvjovitzry, M.D., Leo Wolmer, M.D., Pnina Abramovitz-Schnaider, M.D., Moshe Rehavi, Ph.D.

NR241 Conditionability and Post-Traumatic Stress
Tuvia Peri, M.A., Gershon Bensachar, Ph.D., Arieh Y. Shalev, M.D.

NR242 Trauma and PTSD in Female Psychiatric Inpatients
Jean-Michel Darves-Bornoz, Patricia Ayache, M.D., Andree Degiovanni, M.D., Jean-Pierre Lepine, M.D.

NR243 A Double-Blind Placebo-Controlled Pilot Study of Fluoxetine for Panic Disorder
Duncan B. Clark, M.D., Rolf G. Jacob, M.D.

NR244 Soft Signs in OCD
Margo L. Thienemann, M.D., Lorrin M. Koran, M.D.

NR245 Sleep and Noradrenergic Measures in Chronic PTSD
Thomas A. Mellman, M.D., Adarsh Kumar, M.D., Renee Kulick-Bell, B.A., Mahendra Kumar, Ph.D., Bruce Nolan, M.D.

NR246 Sertraline or Fluoxetine in the Treatment of PTSD: Early Responses Positive and Negative
Neal A. Kline, M.D.

NR247 Panic Disorder and/or Epilepsy: Can Anticonvulsives Play a Role in the Treatment of Panic Disorder?
Karl Dantendorfer, M.D., Michaela Amering, M.D., Wolfgang Baischer, M.D., Peter Berger, M.D., Johann Windhaber, M.D., Heinz Katschnig, M.D.

NR248 Psychosis with PTSD
Nita Kumar, M.D., Gary S. Kutcher, Ph.D., Thomas A. Mellman, M.D.

NR249 Hypercholesterolemia in Female Inpatients with PTSD
M. Michele Murburg, M.D., Judith Stewart, Ph.D., Susan A. Ballagh, M.D.

NR250 Clinician Administered PTSD Scale Weekly: Reliability, Validity, and Sensitivity to Change
Linda M. Nagy, M.D., Dudley Blake, Ph.D., Steven M. Southwick, M.D., Frank Weathers, Ph.D., Terry Keane, Ph.D., Fred Gusman, M.S.W., Dennis S. Charney, M.D.

NR251 Uncoupling of the Noradrenergic: HPA Axis in Panic Disorder Patients
Jeremy D. Coplan, M.D., Daniel Pine, M.D., Laszlo A. Papp, M.D., Jack M. Gorman, M.D., Donald F. Klein, M.D.

NR252 Carbon Dioxide-Induced Panic and Lack of Cortisol Response
Jeremy D. Coplan, M.D., Daniel Pine, M.D., Laszlo A. Papp, M.D., Jose Martinez, M.A., Donald F. Klein, M.D., Jack M. Gorman, M.D.

NR253 SPECT Changes After Behavior Therapy or Clomipramine Treatment in OCD
Mantosh J. Dewan, M.D., John Tanquary, M.D., Prakash Masand, M.D., R. Sprafkin, Ph.D., F.D. Thomas, M.D., N. Szeverenyi, Ph.D.

NR254 Panic Disorder During Pregnancy and the Puerperium: A Prospective Study
Lee S. Cohen, M.D., Laura M. Robertson, B.A., Deborah A. Sichel, M.D., Stephen V. Farrone, Ph.D., Jacqueline A. Dimmock, B.A., Jerrold F. Rosenbaum, M.D.

NR255 Avoidance of the Present in the Dreams of Vietnam Veterans with PTSD and Depression
Bruce M. Dow, M.D., J. Christian Gillin, M.D.

NR256 Lack of Anxiogenic Effects of Flumazenil in PTSD
Penny Randall, M.D., J. Douglas Bremner, M.D., Steven M. Southwick, M.D., John H. Krystal, M.D., Dennis S. Charney, M.D.

NR257 Intravenous Administration of the Benzodiazepine Partial Inverse Agonist Iomazenil to Healthy Volunteers
Penny Randall, M.D., Adam Darnell, M.D., J. Douglas Bremner, M.D., Keith A. Hawkins, Psy.D., Michael Serynok, M.D., Scott W. Woods, M.D., J. Seibyl, M.D., John H. Krystal, M.D., Robert B. Innis, M.D., Dennis S. Charney, M.D.

NR258 Heart Rate Variability in Panic: Autonomic Balance
Phebe Tucker, M.D., Phil Adamson, M.D., Beverly Corbin, R.N., Dottie Williams, LPN, Jodie Groff

NR259 Trauma History in Social Phobia and Panic Disorder
Diane Majcher, M.D., Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Susan A. Sabatino, B.A., Jerrold F. Rosenbaum, M.D.

NR260 Anxiety Disorders in General Practice in France
Corinne Martin, M.D., Sylvie Maurice-Tison, M.D., Jean Tignol, M.D.

NR261 Increased Platelet MAO Activity in Patients with Panic Disorder
Sergio Gloger, M.D., Mario Seguel, M.D., Patricio G. Fischman, M.D., Francisco O'Ryan, M.D., Rafael Torres, M.D., Vilma Vidal, B.S.

NR262 Panic Associated Suicide and Violence
Martin L. Korn, M.D., Robert Plutchik, Ph.D., Herman van Praag, M.D.

NEW RESEARCH

Tuesday, May 24, 1994, 3:00 p.m.-5:00 p.m.

New Research 8 – Poster Session – Exhibit Hall D, Street Level, Convention Center

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS; NEUROPSYCHIATRY; AND GENETICS

Moderator: Ronald O. Rieder, M.D.

NR263 Gender Differences in Schizophrenia: Phenomenology and Neuroleptic Response
Debra A. Pinsky, M.D., Anil K. Malhotra, M.D., Alan F. Breier, M.D., David Pickar, M.D.

NR264 Neurodevelopmental Brain Anomalies in Schizophrenia
Peggy C. Nopoulos, M.D., Victor Swayze, M.D., Michael A. Flaum, M.D., Nancy C. Andreasen, M.D.

NR265 Racial Comparisons in Schizophrenic Veterans
William B. Lawson, M.D., Brian J. Cuffel, Ph.D.

NR266 Dystonia in Schizophrenic Drug Abusers
William B. Lawson, M.D.

NR267 Randomly Assigned Haldol Plasma Levels for Acute Psychosis
Philip G. Janicak, M.D., Javaid I. Javaid, Ph.D., Rajiv P. Sharma, M.D., Anne Leach, M.D., Sheila Dowd, B.S., John M. Davis, M.D.

NR268 Clinical Neuropsychiatric and Treatment Findings in Obsessive Compulsive Schizophrenics: Preliminary Report
Michael Y. Hwang, M.D., Lewis A. Opler, M.D., Marc Vital-Herne, M.D., David M. Klahr, M.D., Daphne Simeon, M.D.

NR269 Cognitive Status of Axis I Disorders
Keith A. Hawkins, Psy.D., William H. Sledge, M.D., Ralph E. Hoffman, M.D., Donald M. Quinlan, Ph.D., Jaak Rakefeldt, Ph.D., Nancy M. Docherty, Ph.D.

NR270 Plasma 5-hydroxyindoleacetic Acid Reflects Central Serotonin Activity in Medicated and Unmedicated Schizophrenic Patients
William A. Wolf, Ph.D., Lynda L. Hulst, M.A., Larry D. Alphs, M.D.

NR271 Neuronal Morphometric Studies of the Hippocampal Formation in Schizophrenia
Steven E. Arnold, M.D., Bryan Franz, B.A., Ruben C. Gur, Ph.D., Raquel E. Gur, M.D., John Q. Trojanowski, M.D.

NR272 Is the Neuropsychological Deficit in Schizophrenia Progressive?
Nancy C. Andreasen, M.D., Sanjay Gupta, M.D., Laura A. Flashman, Ph.D., Michael A. Flaum, M.D., Peggy C. Nopoulos, M.D., Daniel S. O'Leary, Ph.D.

NR273 Schizophrenia: Neuropsychological and MRI Findings
Paul G. Nestor, Ph.D., Martha E. Shenton, Ph.D., Cynthia G. Wible, Ph.D., Matthew O. Kimble, B.A., Lloyd Smith, M.S., Robert W. McCarley, M.D.

NR274 Qualitative and Quantitative Behavioral Response to Methylphenidate in First-Episode Schizophrenia
Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Darlene Jody, M.D., Jose Ma. J. Alvir, Dr.P.H., Miranda Chakos, M.D., David Meyerhoff, M.D.

NR275 The Behavioral Effects of m-Chlorophenylpiperazine and Methylphenidate in First-Episode Schizophrenia and Normal Controls
Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Sally R. Szymanski, D.O., Miranda Chakos, M.D., Jose Ma. J. Alvir, Dr.P.H., Rafael Munne, M.D.

NR276 The Effect of Clozapine on the Rate of Hospitalizations and Status of Schizophrenics
Lynne Jones, R.N., Michael Reinstein, M.D., Chris Mullally, B.S.

NR277 Neuropsychological Functions and Clinical Outcome
Marshall L. Silverstein, Ph.D., Michael Silver, M.D., Martin Harrow, M.D.

NR278 Insight and Cognitive Impairment in Schizophrenia
Paul Lysaker, Ph.D., Morris D. Bell, Ph.D.

NR279 Negative Symptoms and Work Capacity in Schizophrenia
Paul Lysaker, Ph.D., Morris D. Bell, Ph.D.

NR280 Polydipsia-Hyponatremia: Prevalence and Outcome
David B. Schnur, M.D., Scott Smith, M.A., Susan Frick, R.N.

NR281 Adolescent Schizophrenia: Reduced Memory and Brain
Lee Friedman, Ph.D., John T. Kenny, Ph.D., Diane Cola, M.A., Jason Buck, Robert L. Findling, M.D., S. Charles Schulz, M.D.

NR282 Social Unrelatedness and Schizophrenic Phenomenology
Lewis A. Opler, M.D., Paul Michael Ramirez, Ph.D., Jean-Pierre Lindenmayer, M.D., David M. Klahr, M.D.

NR283 Clozapine Levels and Treatment Response
Michael H. Kronig, M.D., Rafael Munne, M.D., Simcha Pollack, Ph.D., Thomas Cooper, M.A., John M. Kane, M.D., Jeffrey A. Lieberman, M.D.

NR284 Prevalence of Tardive Dystonia in a Chronically Mentally Ill Population
William F. Hoffman, M.D., Mary A. Bagdanoff, George A. Keepers, M.D., Thomas E. Hansen, M.D.

NR285 An Investigation of Drug Abuse in Schizophrenic Patients
Jack F. Samuels, Ph.D., Gerald Nestadt, M.D., Paula S. Wolyniec, M.A., Ann E. Pulver, Sc.D.

NR286 Disorientation: A Primary Feature in Schizophrenia
Janel Lombardi, M.A., Philip D. Harvey, Ph.D., Leonard White, Ph.D., Michael J. Parrella, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

NR287 Secondary and Drug-Induced Catatonic Syndromes: Application of Criteria and a Review of the Literature
John C. Kennedy, M.D., Brendan T. Carroll, M.D., Theodore J. Anfinson, M.D.

NR288 Dopamine Metabolism in Relatives of Schizophrenic Probands
Farooq Amin, M.D., Jeremy Silverman, Cecilia Wentzel, Christoper J. Smith, Peter J. Knott, Larry J. Siever, M.D.

NR289 Selective Attention and Intention in Schizophrenia
Ede Frecska, M.D., Lawrence Greenberg, M.D., Jeffrey Sparks, R.N., Kathy Piscani, R.N.

NR290 Fluctuating Dermatoglyphic Asymmetry, HLA Homozygosity and Schizophrenia
Diana O. Perkins, M.D., John H. Gilmore, M.D., Christine Sears, B.A.

NR291 Impaired Memory and Attention Associated with Abnormal Brain Morphology in Schizophrenia Multiplex Families
Karen J. Shedlack, M.D., Gregory R. Lee, M.A., Michael Sakuma, M.A., John R. Pepple, Ph.D., Anne L. Hoff, Ph.D., Lynn E. DeLisi, M.D.

NR292 HLA Homozygosity: Genetic Risk for Schizophrenia
John H. Gilmore, M.D., Diana O. Perkins, M.D., James D. Folds, Ph.D., Emily G. Reisner, Ph.D.

NR293 Soft Neurological Signs: Reliability and Validity
Nigel M. Bark, M.D., Sandra Grochowski, B.A.

NR294 Soft Neurological Signs and Dimensions of Schizophrenia
Nigel M. Bark, M.D., Sandra Grochowski, B.A., Denize Da Silva, M.D., Jorge Barros-Beck, M.D., Jean-Pierre Lindenmayer, M.D.

NR295 Temporal Lobe Asymmetries in Functional Psychoses
James M. Russell, M.D., Javier Villanueva-Mey, M.D., Terrence S. Early, M.D., Justin L. Martin, B.A.

NR296 A Controlled Study of Early Intervention in Schizophrenia
Marvin I. Herz, M.D., J. Steven Lamberti, M.D., Suzanne W. Brown, M.P.A., Ruth A. Scott, M.S.N., Susan P. O'Dell, M.S.N., Syed I. Mustafa, M.D.

NR297 Written Sentence Production in Schizophrenia
Brian F. O'Donnell, Ph.D., Maria C. Van Der Pahlen, B.A., Margaret A. Niznikiewicz, Ph.D., Matthew O. Kimble, B.A., S.N. Sridhar, Ph.D., Robert W. McCarley, M.D.

NR298 Event Related Potential and MRI Evidence of Deterioration in Schizophrenia
Brian F. O'Donnell, Ph.D., Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Martha E. Shenton, Ph.D., Matthew O. Kimble, B.A., Paul G. Nestor, Ph.D.

NR299 Event Related Potential Indices of Language Problems in Schizophrenia
Margaret A. Niznikiewicz, Ph.D., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

NR300 The Relationship of Brain Dopamine Functioning to Intellectual Performance in First-Episode Schizophrenia
Brian Sheitman, M.D., Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Gail Reiter, M.A., Jose Ma. J. Alvir, Dr. P.H., Miranda Chakos, M.D.

NR301 Increased Inter-Putamen Distance-Brain Width Ratio in First-Episode and Chronic Schizophrenic Patients
Houwei Wu, M.D., Rafael Munne, M.D., Robert Bilder, Ph.D., Bernhard Bogerts, M.D., Jeffrey A. Lieberman, M.D.

NR302 Sexual Dysfunctions in Male Schizophrenic Patients
Dov Aizenberg, M.D., Zvi Zemishlany, M.D., Pnina Dorfman-Etrog, M.D., Abraham Weizman, M.D.

NR303 Multi-Assessment of Risperidone Effects: A Retrospective Study
Roch Hugo Bouchard, M.D., Emmanuelle Pourcher, M.D., F. Chasse, Ph.D., Marie-Josee Filteau, M.D., Philippe Baruch, M.D., W. Pilon, Ph.D.

NR304 Quantitative Autoradiography of 5-HT1a Receptors in Schizophrenia and Nonpsychotic Suicide Patients
Donald C. Ohuoha, M.D., Thomas M. Hyde, M.D., Mary M. Herman, M.D., Joel E. Kleinman, M.D.

NR305 Geriatric Schizophrenic Inpatients Versus Outpatients
Katherine M. Putnam, M.A., John M. Herrera, Ph.D., Philip D. Harvey, Ph.D., Donald M. Quinlan, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

NR306 1H-Magnetic Resonance Spectroscopy in Schizophrenia: Putative Neurodevelopmental and Cognitive Correlates
Peter Buckley, M.D., Constance Moore, Ph.D., Helen Long, B.A., Conall Larkin, M.B., Fiona Mulvany, B.A., John L. Waddington, D.Sc.

NR307 Affective Reactivity of Language in Schizophrenic Patients and Their Parents
Nancy M. Docherty, Ph.D.

NR308 Working Memory, Attention and Language in Schizophrenia
Nancy M. Docherty, Ph.D., Keith A. Hawkins, Psy.D., William H. Sledge, M.D., Ralph E. Hoffman, M.D., Donald M. Quinlan, Ph.D., Jaak Rakfeldt, Ph.D.

NR309 Work and Symptom Change in Schizophrenia
Morris D. Bell, Ph.D., Paul Lysaker, Ph.D.

NR310 Symptoms and Work Performance in Schizophrenia
Morris D. Bell, Ph.D., Paul Lysaker, Ph.D.

NR311 Is Schizophrenia Primarily a Right Sided, Rhinencephalic Defect?
Murray A. Cowen, M.D., David N. Bertollo, B.A., Maurice R. Green, M.D.

NR312 Effects of Medication History on Resting EEG Measures in Schizophrenia
Roland J. Erwin, Ph.D., Ruben C. Gur, Ph.D., Raquel E. Gur, M.D.

NR313 Diagnoses in Child Schizophrenic Relatives
Marge C. Lenane, M.S.W., Kathleen McKenna, M.D., Jean Frazier, M.D., Judith L. Rapoport, M.D.

NR314 The Effects of Clozapine on Cognition in Schizophrenia
Theo C. Manschreck, M.D., Crystal R. Blyler, M.A., Brendan A. Maher, Ph.D., Deborah A. Redmond, M.A., Scott M. Beaudette, B.A.

NR315 Schizophrenia, Lung Cancer and Vitamin C
J. Daniel Kanofsky, M.D., Edward P. Norkus, Ph.D., Barry Geller, B.A., Robert Lowinger, M.D., Paul B. Kanofsky, Ph.D., Gary J. Kennedy, M.D.

NR316 MRI Predictors of Clozapine Response: A Preliminary Study
John Lauriello, M.D., Daniel H. Mathalon, Ph.D., David L. Ringo, M.D., Edith V. Sullivan, Ph.D., Kelvin O. Lim, M.D., Adolf Pfefferbaum, M.D.

NR317 Does Diminished Affective Expression in Schizophrenia Reflect Affective Deficit or Neuromotor Dysfunction?
Scott C. Clark, M.D., Robert H. Dworkin, Ph.D., Xavier F. Amador, Ph.D., Lewis A. Opler, M.D., Stephanie R. White, B.A., Jack M. Gorman, M.D.

NR318 Lateralized P300 Voltage Asymmetries in Left-Handed and Right-Handed Schizophrenic Subjects: An Update
Dorothy P. Holinger, Ph.D., Curtiss J. Durand, M.D., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

NR319 Syndrome Typology Effects Upon Engagement and Outcome in Schizophrenic Substance Abusers
Richard N. Rosenthal, M.D., David J. Hellerstein, M.D., Christian Miner, Ph.D.

NR320 The P50 and Mismatch Detection in Normal Volunteers: Implications for the Study of Sensory Gating in Schizophrenia
Nashaat N. Boutros, M.D., Brandy Barker, Michael Torello, Ph.D.

NR321 How Do Schizophrenics Discriminate the Origin of Information?
Sophia Vinogradov, M.D., Emily Marton, B.A., John H. Poole, Ph.D., Beth A. Ober, Ph.D., Gregory K. Shenaut, Ph.D., Leora Benioff, Ph.D.

NR322 A Poisson-Erlang Model Analysis of Choice Reaction Time in Negative Schizophrenia
Philippe Baruch, M.D., Marie-Josee Filteau, M.D., Sophie Lemelin, BPS, Roch Hugo Bouchard, M.D., Emmanuelle Pourcher, M.D., James Everett, Ph.D.

NR323 Premorbid Function in Schizophrenia and Mania
Scott Smith, M.A., David B. Schnur, M.D., Shaoshan Li, M.S.W., Elizabeth Horwitz, M.D., Adam Smith, Ph.D.

NR324 Cognitive Deficits and Psychopathology in Elderly Schizophrenics: Does Old Age Affect the Phenomenology of Schizophrenia?
Jean-Pierre Lindenmayer, M.D., Shilpa A. Shah, M.D., Arnaldo Negron, M.D., Ruth B. Hyman, Ph.D., Gary J. Kennedy, M.D.

NR325 Memory Activation in Late Onset Schizophrenia
John M. Herrera, Ph.D., Hung Lee, M.D., Donald M. Quinlan, Ph.D., Victoria Ongsiako, M.D., Dinshaw Bamji, M.D., Richard Mohs, Ph.D.

NR326 Schizophrenic Premorbid Adjustment: Event-Related Potential and Memory
James J. Levitt, M.D., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D., Paul G. Nestor, Ph.D., Martha E. Shenton, Ph.D., Jennifer E. Haimson, B.A.

NR327 Amygdala-Anterior Hippocampus Shrinkage in Male Schizophrenia: A Magnetic Resonance Controlled Study
Alessandro Rossi, M.D., Paolo Stratta, M.D., Fabrizio Mancini, M.D., Paolo Mattei, M.D., Massimo Casacchia, M.D.

NR328 Neuroleptic Discontinuation in Schizophrenics
Andre Tapp, M.D., Rajiv Tandon, M.D., Alan B. Douglass, M.D., Evelyn Dudley, R.N., Robert Scholton, R.N., Michael J. Underwood, M.A.

NR329 Depression in Severe Chronic Schizophrenia
Andre Tapp, M.D., Rajiv Tandon, M.D., Alan B. Douglass, M.D., Evelyn Dudley, R.N., Robert Scholton, R.N., Michael J. Underwood, M.D.

NR330 Brain Impairment and Adaptation in Schizophrenia
Rosemary Farmer, Ph.D., Anand K. Pandurangi, M.D.

NR331 Medication Adherence and Outcomes in Schizophrenia
Richard R. Owen, M.D., Ellen P. Fischer, Ph.D., Brian J. Cuffel, Ph.D., G. Richard Smith, M.D.

NR332 Facial Affect Recognition and Visual Attention in Schizophrenia
Jean M. Addington, Ph.D., Donald E.N. Addington, M.D.

NR333 The Positive and Negative Syndrome Scale in a French Population of Schizophrenics
Christophe Lancon, Jean Luc Martinez, Pascal Auquier, P. Michel Llorca, Thierry Bougerol

NR334 New Onset Echolalia in a Chronic Institutionalized Schizophrenic: Focal Neurological Deficit or Chronic Regression?
Emmanuel Hriso, M.D., Teresa A. Bielawski, M.D., Paul A. Hriso, M.D.

NR335 Electroencephalograms in Patients with Catatonic Disorders
Brendan T. Carroll, M.D., Nashaat N. Boutros, M.D.

NR336 Treatment of Clozapine-Induced Agranulocytosis
J. Steven Lamberti, M.D., Terrence J. Bellnier, M.P.A., Eugene Schneider, M.D., John P. Veneron, R.Ph., Steven B. Schwarzkopf, M.D.

NR337 Clinical Characteristics of Psychotic Adolescents
John D. O'Brien, M.D., Manuel D. Reich, D.O., Barbara Cornblatt, Ph.D., Michael Obuchowski, M.A.

NR338 P300's Latency and Response to Neuroleptics
Thierry Bougerol, Abdel Benraiss, P. Michel Llorca, Christophe Lancon

NR339 Unifying Aspects of OCD and Schizophrenia
Jose A. Yaryura-Tobias, M.D., Theresa Campisi, M.A., Dean McKay, Ph.D.

NR340 Correlates of Suicidality in Schizophrenia
Naveed Iqbal, M.D., Lloyd Goldsamt, Ph.D., Bruce J. Schwartz, M.D., Gregory M. Asnis, M.D., Robert Plutchick, M.D., Alec Cecil, Ph.D.

NR341 Pallidothalamic Circuits in Post-Stroke Mania
Edward C. Lauterbach, M.D., Ami N. Wilson, B.A., Spencer T. Price, B.S., Joseph G. Jackson, M.D.

NR342 Post-Stroke Depression: Pallidothalamic Circuits
Edward C. Lauterbach, M.D., Spencer T. Price, B.S., Ami N. Wilson, B.A., Joseph G. Jackson, M.D.

NR343 Clozapine in Psychotic Demented Patients
Jacobo E. Mintzer, M.D., Janet Pitner, Ph.D., Sharon R. Burnside, M.D.

NR344 Psychotic Symptoms and Neuropsychological Deficits
Blaine S. Cloud, M.D., Wendy E. Shumway, M.D., Steven D. Targum, M.D., David J. Libon, Ph.D., Robyn Resh, M.A., H.L. Gitlin, M.A.

NR345 Cerebral Blood Flow During Memory and Executive Task Performance: A PET 150 Study of Normal Control Subjects
J. Daniel Ragland, Ph.D., Ruben C. Gur, Ph.D., David Censits, B.A., Robin Smith, Ph.D., Abass Alavi, M.D., Raquel E. Gur, M.D.

NR346 Brief Neuropsychiatric Cognitive Examination and MRI, CT Scan Data
Joseph M. Tonkonogy, M.D., James R. Armstrong, Ph.D.

NR347 Superior Effect of Clozapine in Comparison with Typical Neuroleptics on Cognitive Function in Schizophrenia
Myung A. Lee, M.D., Corinne Hagger, Ph.D., Paul Thomas, Ph.D., Herbert Y. Meltzer, M.D.

NR348 SPECT Imaging Studies in Cortical Lobar Atrophies
Sophie Auriacombe, Marc Auriacombe, M.D., Martine Guyot, M.D., Jean Tignol, M.D.

NR349 The Accuracy of Standardized Substance Abuse Instruments in Patients with Traumatic Brain Injury
Eric Fishman, Ph.D., Mark Fuller, M.D., Nicholas Carosella, M.D., Ravi Kant, M.D.

NR350 Functional Differences in Dopamine Receptor Phenotypes
Fabrice Duval, M.D., Marc-Antoine Crocq, M.D., Antonia Mayerova, M.D., Pierre Sokoloff, M.D., Ernst Natt, M.D., Lars Lannfelt, M.D., M-Claude Mokrani, Ph.D., Paul Bailey, M.D., Jean-Charles Schwartz, M.D., Jean-Paul Macher, M.D.

NR351 An Association Between Bipolar Disorder and a Highly Polymorphic DNA Marker From Tyrosine Hydroxylase
Jeronimo Saiz-Ruiz, M.D., Jose F. Piqueras, Ph.D., Consuelo Llinares, M.D., Javier Santos, Ph.D., Ignacio P. de Castro, Ph.D., Guillermo Visedo, Ph.D.

NR352 Tourette's Syndrome and ADHD: Evidence Against a Genetic Relationship
Valsamma Eapen, M.B., Mary Robertson, M.D.

NEW RESEARCH

Wednesday, May 25, 1994, 9:00 a.m.-10:30 a.m.

New Research 9 – Oral/Slide Session – Exhibit Hall D, Street Level, Convention Center

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS

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

NR353 Thyroid Function in Lithium-Free Bipolar Patients
Jose L. Ayuso-Gutierrez, M.D., Jesus Valle, M.D., Jose L. Ayuso-Mateos, M.D.

NR354 Predictors of Tardive Dyskinesia
Miranda Chakos, M.D., Jose Ma. J. Alvir, Dr. P.H., Robert Bilder, Ph.D., Margaret Woerner, Ph.D., John M. Kane, M.D., Jeffrey A. Lieberman, M.D.

NR355 Risperidone for Treatment Refractory Schizophrenia
Michael H. Kronig, M.D., Antony D. Loebel, M.D., Alan Mendelowitz, M.D., Curt Pinchuck, M.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.

NR356 Risperidone Versus Clozapine in Psychosis
David G. Daniel, M.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D., David Pickar, M.D., Tracy Williams, R.N., Lisa Lubick, MPP

NR357 Clinical Efficacy and Safety of Olanzapine: A New Atypical Antipsychotic Agent
Pierre V. Tran, M.D., Charles M. Beasley, M.D., Gary D. Tollefson, M.D., Todd Sanger, Ph.D., Winston G. Satterlee, M.D.

NR358 New Evidence for the Clinical Utility of Haloperidol Plasma Levels
William H. Coryell, M.D., Delwyn D. Miller, M.D., Paul J. Perry, Ph.D.

NEW RESEARCH

Wednesday, May 25, 1994, 9:00 a.m.-10:30 a.m.

New Research 10 – Oral/Slide Session – Exhibit Hall D, Street Level, Convention Center

MOOD DISORDERS; SUICIDE; AND PSYCHOPHARMACOLOGY

Chp.: Stuart C. Yudofsky, M.D.

NR359 Anticipation in Bipolar Disorder: May Be Influenced by the Sex of the Affected Parent
Francis J. McMahon, M.D., Melvin G. McInnis, M.D., Mary C. Blehar, Ph.D., Elliot S. Gershon, M.D., John I. Nurnberger, Jr., M.D., Theodore Reich, M.D., J. Raymond DePaulo, Jr., M.D.

NR360 Low Serum Cholesterol and Attempted Suicide
Julia A. Golier, M.D., Peter M. Marzuk, M.D., Andrew C. Leon, Ph.D., Cindy Weiner, M.A., Kenneth J. Tardiff, M.D.

NR361 Suicidal Behavior Among Twins
Alec Roy, M.D., Nancy Segal, Ph.D., Marco Sarchiapone, M.D., Veronika Solt, M.D., John Williams, M.D.

NR362 Do [3H]-IMI Platelet Studies Reflect Treatment Outcome of Major Depression-Agitated Subtype?
Gary D. Tollefson, M.D.

NR363 Increased Lactate Levels and Post ECT Agitation
Marc Auriacombe, M.D., Jean P. Reneric, M.D., Daniel Usandizga, M.D., Francis Gomez, M.D., Isabelle Combourieu, M.D., Jean Tignol, M.D.

NR364 An Asymmetric Bilateral ECT Electrode Placement
Conrad M. Swartz, M.D.

NEW RESEARCH

Wednesday, May 25, 1994, 12:00 noon-2:00 p.m.

New Research 11 – Poster Session – Exhibit Hall D, Street Level, Convention Center

CROSS-CULTURAL AND MINORITY PSYCHIATRY; PERSONALITY, ALCOHOL AND SUBSTANCE ABUSE; BIOLOGICAL PSYCHIATRY; AND BRAIN IMAGING

Moderator: Charles P. O'Brien, M.D.

NR365 Role Strains, Role Fit and Psychological Distress in Immigrant Muslim Women: An Exploratory Study
Pascale Des Rosiers, M.D., Ellen Corin, Ph.D., Cecile Rousseau, M.D., Normand Peladeau, M.Sc.

NR366 The Identification of Culture-Specific Syndromes, as Proposed for the DSM-IV, in Children and Adolescents from Xhosa, South Africa
Brian A. Robertson, M.D., Karin Ensink, M.A., Gerard Drennan, M.A.

NR367 Race and Benzodiazepine Use Among Opioid Abusers
D. Daniel Rajna, M.D., Juliana Pakes, Scott W. Woods, M.D., Boris Meandzija, M.D., Thomas R. Kosten, M.D., Richard S. Schottenfeld, M.D.

NR368 Psychological Impact of Civil War on Liberian Children
Dana L. Sanderson, M.D., Grace L. Kennedy, M.D., Edward O. Bixler, Ph.D., John W. Getz, M.A., H. Allen Handford, M.D.

NR369 Total Quality Management Reduces Costs of Managing High-Risk Patients
Diane M. Pinchoff, M.A., George Molnar, M.D., Jeffrey Grace, M.D.

NR370 Critical Clinical Variables Mediating a Short Length of Stay
Geetha Jayaram, M.D., Patricia Sullivan, R.N.

NR371 What Happens When Psychiatric Beds Are Cut By Sixty Percent?
Alex Richman, M.D.

NR372 Referral and Non-Attendance at a Psychiatric Clinic
Rosemary M. Morrison, Ph.D.

NR373 Adults and Children Admitted with Adjustment Disorder Diagnoses: Clinical Correlations and Two-Year Rehospitalization
David N. Rosenfeld, M.D., Eddy A. Ortega, M.D., William M. Greenberg, M.D.

NR374 Presurgical Psychiatric Assessment of Medically Refractory Epileptic Patients
Rahul Manchanda, M.D., Betsy Schaefer, B.A., Richard McLachlan, M.D., Warren T. Blume, M.D.

NR375 Family Environment and BPD
Jody Shachnow, Ph.D., John F. Clarkin, Ph.D., Norman Shachnow, M.D., Cynthia Smith, M.S.W., Fran Thuraton, M.S.W., James Hull, Ph.D., Edward N. Shearin, Ph.D.

NR376 Agreement of Direct Interview and Family History of Diagnosed Personality Disorders
Tova Ferro, M.A., Daniel N. Klein, Ph.D.

NR377 Asymmetrical Alpha Power in Schizotypes
Dean F. Salisbury, M.D., Martina M. Voglmaier, Ph.D., Robert W. McCarley, M.D., Larry J. Seidman, Ph.D., Evana Goodreau, B.A.

NR378 Cholinergic Challenge and Affective Instability in Personality Disorder Patients
Bonnie J. Steinberg, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Emil F. Coccaro, M.D., Larry J. Siever, M.D.

NR379 Serum Cholesterol and Impulsivity in Mood and Personality Disorders
Antonia S. New, M.D., Robert L. Trestman, M.D., Maki Kano, B.A., Scott Gettinger, B.S., Larry J. Siever, M.D.

NR380 The Factor Structure of Schizotypy
Andrea J. Bergman, M.D., Vivian Mitropoulou, M.A., Robert L. Trestman, M.D., Larry J. Siever, M.D.

NR381 SPECT Imaging of Cognition in Schizotypals
Robert L. Trestman, M.D., Monte S. Buchsbaum, M.D., Benjamin V. Siegel, M.D., Miklos F. Losonczy, M.D., Claire Schaefer, Ph.D., Larry J. Siever, M.D.

NR382 Depressive Experiences in Borderline Inpatients
Kenneth N. Levy, B.A., John Kolligian, Ph.D., Donald M. Quinlan, Ph.D., Daniel F. Becker, M.D., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR383 Dependent and Self-Critical Personality Disorders
Kenneth N. Levy, B.A., John Kolligian, Ph.D., Donald M. Quinlan, Ph.D., Daniel F. Becker, M.D., William S. Edell, M.D., Thomas H. McGlashan, M.D.

NR384 Does Antidepressant Treatment Change Personality?
Ron G. Goldman, M.D., Patrick J. McGrath, M.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D.

NR385 The Clinical Utility of Self-Defeating Personality Disorder
Lora K. Heisler, M.S., Michael J. Lyons, Ph.D., John G. Goethe, M.D.

NR386 The Development of Psychopaths: A Cognitive Model
Robert J. Blair, Ph.D.

NR387 Physicians' Beliefs About Benzodiazepines
Edward K. Silberman, M.D.

NR388 Gender Differences in Cocaine Dependence
Kimberly A. White, M.D., Kathleen T. Brady, M.D., Susan Sonne, Ph.D.

NR389 Carbamazepine for Cocaine Dependence
Henry R. Kranzler, M.D., Lance Bauer, Ph.D., David F. Hersh, M.D.

NR390 Validity of the SCID in Substance Abuse Patients
Henry R. Kranzler, M.D., Bruce J. Rounsaville, M.D., Howard Tennan, Ph.D.

NR391 Comorbidity in Adolescent Inpatient Drug Abusers
Carlos M. Grilo, Ph.D., Kenneth N. Levy, B.A., Daniel F. Becker, M.D., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR392 Nicotine Stimulates Gene c-fos Expression in Human Leukocytes In Vivo
Andrew B. Norman, Ph.D., Herbert R. Thompson, B.S., Sean P. Stanton, B.S., Brian J. Mc Conville, M.D., Eugene Somoza, M.D.

NR393 The Effects of Benzodiazepines, Buspirone and Placebo Treatment on Mood and EEG Activity in Alcoholics and Normal Subjects
Domenic A. Ciraulo, M.D., Ofra Sarid-Segal, M.D., Jamie Barnhill, Ph.D., Ann Marie Ciraulo, R.N., Clifford M. Knapp, Ph.D., David Greenblatt, M.D.

NR394 Traumatic Exposure and PTSD Symptomatology Among Substance Abusers
Patricia Ryan Recupero, M.D., Pamela J. Brown, Ph.D., Robert Stout, Ph.D., Jessica Wolfe, Ph.D., Sharon Morello, R.N.

NR395 Clinical Course of Mentally Ill Substance Abusers
Jonathan D. Berman, M.D., Roland M. Atkinson, M.D.

NR396 Effect of Alpha-methyl-para-tyrosine on Response to Cocaine Challenge
Susan M. Stine, M.D., Ismene Petrakis, M.D., Peter I. Jatlow, M.D., John H. Krystal, M.D., Sally L. Satel, M.D., Dennis S. Charney, M.D.

NR397 Reporting and Representation of Sociodemographic Groups in Cocaine Pharmacotherapy Studies
David A. Gorelick, M.D., Ivan D. Montoya, M.D.

NR398 Combination of Bupropion and Bromocriptine for Treatment of Cocaine Dependence
David A. Gorelick, M.D., Ivan D. Montoya, M.D.

NR399 Obsessive Compulsive Personality in Substance Dependence
Dr. Myroslava K. Romach, Howard L. Kaplan, Ph.D., Gail Somer, M.A., Edward M. Sellers, M.D.

NR400 Comorbidity in Drug Dependent Adoptees
Barbara M. Rohland, M.D., Remi J. Cadoret, M.D., Edward Troughton, B.A.

NR401 Depression in Drug Dependency
Mark S. Gold, M.D., Norman S. Miller, M.D., Norman G. Hoffmann, Ph.D.

NR402 Fenfluramine Treatment of Cocaine Dependence: Interim Analysis
Steven L. Batki, M.D., Mark Bradley, Mark D. Herbst, M.D., Tracy Jones, Michael Markman, Allyson Washburn, Ph.D., Peyton Jacob III, Ph.D., Reese T. Jones, M.D.

NR403 Substance Abuse: Treatment Failure Profiles
Portia P. Belden, Ph.D., Helen M. Pettinati, Ph.D., Charles Ruetsch, M.S., Fran Kaplan, B.A., Bradley D. Evans, M.D.

NR404 Growth Hormone Response to Bromocryptine in Alcoholics and Controls
Conor K. Farren, M.D., Anthony W. Clare, M.D., Faiq A. Hameedi, M.D., Douglas M. Ziedonis, M.D., Timothy G. Dinan, M.D.

NR405 Prolactin Response to d-Fenfluramine in Alcoholics and Controls
Conor K. Farren, M.D., Anthony W. Clare, M.D., Faiq A. Hammeedi, M.D., Douglas M. Ziedonis, M.D., Timothy G. Dinan, M.D.

NR406 Depression in Cocaine Abusing Opioid Addicts Treated with Buprenorphine Versus Methadone
Douglas M. Ziedonis, M.D., Conor K. Farren, M.D., Thomas R. Kosten, M.D.

NR407 Serotonergic Function During Acute and Chronic Cocaine Abstinence
Faiq A. Hameedi, M.D., Marc I. Rosen, M.D., Lawrence H. Price, M.D., Conor K. Farren, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

NR408 Substance Abuse and Psychiatric Illness: Psychosocial Correlates
Kevin L. Sloan, M.D., Gail Rowe, Ph.D.

NR409 Perceived Severity of Alcoholism and Relation to Self-Efficacy
Elaine Souder, Ph.D., Eve J. Wiseman, M.D., Patricia S. O'Sullivan, Ed.D.

NR410 Craving and Treatment Need: A Function of Denial
Eugene Somoza, M.D., R. Jeffrey Goldsmith, M.D., John Lutz, M.D., Juris P. Mezinskis, Ph.D., Sue R. Dyrenforth, Ph.D.

NR411 Factors Influencing Drug Craving Over Time
Sue R. Dyrenforth, Ph.D., Eugene C. Somoza, M.D., Juris P. Mezinskis, Ph.D., Mark W. Cohen, Ph.D.

NR412 Cocaethylene Effects in Humans
Elinore F. McCance-Katz, M.D., Lawrence H. Price, M.D., Thomas R. Kosten, M.D., Peter I. Jatlow, M.D.

NR413 Transdermal Nicotine and Drug Craving
Eve J. Wiseman, M.D., Donald E. McMillan, Ph.D., Margaret J. Briggs, L.P.N.

NR414 Measuring Alcoholism Severity: Relationship of DSM-III-R and Michigan Alcoholism Screening Test
Eve J. Wiseman, M.D., Elaine Souder, Ph.D., Patricia S. O'Sullivan, Ed.D.

NR415 The Effects of Morphine on Ethanol Consumption: Effect of Prior Ethanol Exposure
Michael F. Stromberg, Ph.D., Joseph R. Volpicelli, M.D., Barbara L. Slifer, Ph.D., Steven C. Meister, B.S., Ronald R. Ulm, Ph.D.

NR416 An Objective Measure of Nicotine Craving for Psychiatric Patients
Neil Hartman, M.D., George C. Mazzei, B.A., Sidney Gold, M.D., Shelly Wilkerson, R.N., Nicholas Caskey, Ph.D., Murray E. Jarvik, M.D.

NR417 The Wender Utah Rating Scale and Residual ADHD in Adult Substance Abusers
James J. McGough, M.D., John F. Curry, Ph.D.

NR418 Haloperidol and Smoking Behaviors in Normals
William C. Wirshing, M.D., Murray E. Jarvik, M.D., Nicholas Caskey, Ph.D., Donna Ames, M.D.

NR419 SPECT Imaging of the Dopamine Transporter During Cocaine Abstinence
Elizabeth A. Wallace, M.D., Robert T. Malison, M.D., Susan E. Best, M.D., Robert B. Innis, M.D., Thomas R. Kosten, M.D.

NR420 Low Dose of Lorazepam Increases Psychometric Performances in Healthy Volunteers
Michel Bourin, M.D., Marie C. Colombel, B.A., Myriam Malinge, M.D.

NR421 Serotonergic Mechanisms and Personality Profiles in PTSD Patients
H. Constance Bonbrest, M.D., Ramesh Arora, Ph.D., Omar Nasib, M.D., John W. Crayton, M.D.

NR422 Pilot Study of Platelet Serotonin Transporter Binding Sites in Women with Postpartum Depression
Zachary N. Stowe, M.D., Michael J. Owens, Ph.D., Charles B. Nemeroff, M.D.

NR423 HPA Axis Effects on Dopamine Activity in Man
Joel A. Posener, M.D., Alan F. Schatzberg, M.D., Joseph J. Schildkraut, M.D.

NR424 Hippocampal Lesions Enhance Vasopressin Response to Stress
Morris B. Goldman, M.D., Beth Christiansen, M.S., Mary B. Gaskill, M.S., Gary L. Robertson, M.D.

NR425 Variability of the Human Melatonin Phase Response Curve
Vance K. Bauer, M.A., Alfred J. Lewy, M.D., Katherine H. Thomas, M.D.

NR426 The D-Fenfluramine Challenge in Alcoholics
Mario Seguel, M.D., Sergio Gloger, M.D., Rodrigo Labarca, M.D., Rafael Torres, Ph.D., Sergio Valdivieso, M.D.

NR427 MRI and Neurological Soft Signs in PTSD Veterans
Tamara V. Gurvits, M.D., Martha E. Shenton, Ph.D., Hiroto Hokama, M.D., Natasha B. Lasko, Ph.D., Roger K. Pitman, M.D.

NR428 Plasma Tryptophan and Brain Serotonin Function in Patients Taking Cholesterol Lowering Drugs
Nicholas J. Delva, M.D., Philip J. Cowen, M.D., David R. Matthews, B.M.

NR429 Dopamine Enhances GABA Transmission in the Hippocampus
Stephen J. Schertzer, M.D., Liang Zhang, M.D., Peter Carlen, M.D.

NR430 Verapamil Versus Placebo for Acute Mania: Preliminary Results From a Double-Blind Study
Philip G. Janicak, M.D., Ghanshayam Pandey, Ph.D., Rajiv P. Sharma, M.D., Jim Peterson, B.S., Anne Leach, M.D., John M. Davis, M.D.

NR431 Toward a Biological Classification in Psychiatry
Erwin R. John, Ph.D., Leslie S. Prichep, Ph.D., Robert Cancro, M.D., Francis G. Mas, M.D.

NR432 Evolution of Dementia in Quantitative Electroencephalographic Subtypes of the Elderly
Leslie S. Prichep, Ph.D., Erwin R. John, Ph.D., Barry Reisberg, M.D., Steven Ferris, M.D.

NR433 Clinical Relevance of Quantitative Electroencephalogram Subtyping
Francis G. Mas, M.D., Leslie S. Prichep, Ph.D., Eric Hollander, M.D., Michael R. Liebowitz, M.D.

NR434 Regional CBF Studies in Narcolepsy
Shashidhar M. Shettar, M.D., Smruti Parikh, M.D., James Mountz, M.D., Ronald Acton, Ph.D., Chakri Inampudi, M.D., Robert O. Friedel, M.D.

NR435 Cortical Gender Dimorphism in Healthy Subjects
Thomas E. Schlaepfer, M.D., Allen Y. Tien, M.D., Patrick E. Barta, M.D., Gordon J. Harris, Ph.D., Godfrey D. Pearlson, M.D.

NR436 Correlations Between Topography of Resting Metabolism and Clinical Presentation in Schizophrenia
Ruben C. Gur, Ph.D., Raquel E. Gur, M.D., Lyn Harper-Mozley, Ph.D., P. David Mozley, M.D., Derri L. Shtasel, M.D., Abass Alavi, M.D.

NR437 Brain Function in First Episode Schizophrenia
Raquel E. Gur, M.D., Ruben C. Gur, Ph.D., Derri L. Shtasel, M.D., Fiona Gallacher, M.S., Bruce Turetsky, M.D.

NR438 Correlates of SPECT Findings in Schizophrenics
Mantosh J. Dewan, M.D., Prakash Masand, M.D., F.D. Thomas, M.D., John Tanquary, M.D., N. Szeverenyi, Ph.D., M. Lynch, Ph.D.

NR439 Do Neurologically Impaired Schizophrenics Have Abnormal SPECT Scans?
Prakash Masand, M.D., Mantosh J. Dewan, M.D., F.D. Thomas, M.D., John Tanquary, M.D., N. Szeverenyi, M.D., M. Lynch, Ph.D.

NR440 Acute Effects of Cigarette Smoking on CBF: A PET Study
Michael A. Flaum, M.D., Daniel S. O'Leary, Ph.D., Richard D. Hichwa, Ph.D.

NR441 SPECT Changes with Risperidone in the Elderly
Ileana Berman, M.D., Julia Pavlov-Rachov, M.D., Mordechai Lorberboym, M.D., Claire Schaefer, Ph.D., Michael Pontecorvo, Ph.D., Miklos F. Losonczy, M.D.

NR442 SPECT in Panic Disorder Pre- and Post-Treatment
David B. Bresnahan, M.D., Cheryl Huber, M.D., Todd Cannon, D.O., Michael J. Goldstein, Ph.D., Harold H. Harsch, M.D., Ronald Tikofsky, Ph.D.

NR443 Depression and Frontal Regional Cerebral Metabolic Rates of Glucose Correlate Inversely
Terence A. Ketter, M.D., Mark S. George, M.D., Paul J. Andreason, M.D., Barry Horwitz, Ph.D., Priti J. Parekh, B.A., Peggy J. Pazzaglia, M.D., Lauren B. Marangell, M.D., Ann M. Callahan, M.D., Robert M. Cohen, M.D., Peter Herscovitch, M.D., Robert M. Post, M.D.

NR444 Regional Cerebral Metabolic Rates of Glucose in Unipolar Versus Bipolar Depression
Terence A. Ketter, M.D., Mark S. George, M.D., Paul J. Andreason, M.D., Priti J. Parekh, B.A., Peggy J. Pazzaglia, M.D., Lauren B. Marangell, M.D., Ann M. Callahan, M.D., Robert M. Cohen, M.D., Peter Herscovitch, M.D., Robert M. Post, M.D.

NR445 CBF After ECT for Depression
Russell G. Vasile, M.D., Thomas C. Hill, M.D., Frank M. Bradley, M.D., Kerry L. Bloomingdale, M.D., Joseph J. Schildkraut, M.D.

NR446 Quantitative Morphology of the Corpus Callosum in Children and Adolescents: Effects of Age and Gender
Jay N. Giedd, M.D., Deb Kaysen, B.S., F. Xavier Castellanos, M.D.

NR447 Symptom Activation and rCBF in OCD
Benjamin D. Greenberg, M.D., Rudolf Hoehn-Saric, M.D., Mark S. George, M.D., Cheryl Rubenstein, M.A., Margaret Altemus, M.D., David Keuler, B.A., Lawrence Wang, Dennis L. Murphy, M.D.

NR448 Intravenous Clomipramine for Clomipramine-Refractory OCD
Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., Raphael Campeas, M.D., Franklin R. Schneier, M.D., Donald F. Klein, M.D., Sharon Davies, R.N.

NR449 Cognitive Activation SPECT in Memory Disorders
Philippe Robert, Octave Migneco, M.D., Michel Benoit, M.D., J. Darcourt, M.D., F. Bussiere, M.D., G. Darcourt, M.D.

NR450 Personality Traits Correlate with Resting rCBF
Mark S. George, M.D., Terence A. Ketter, M.D., Priti J. Parekh, B.A., Barry Horwitz, Ph.D., Peter Herscovitch, M.D., C. Robert Cloninger, M.D., Robert M. Post, M.D.

NR451 Magnetic Resonance Showing Basal Ganglia Volumes in Schizophrenia
Hiroto Hokama, M.D., Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

NR452 Three-Dimensional Brain Atlas From Magnetic Resonance Data
Hiroto Hokama, M.D., Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Cynthia G. Wible, Ph.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

NR453 Mood Effects on CBF Correlates with Emotional Self-Rating: $_{15}O$ Study
Frank Schneider, M.D., Ruben C. Gur, Ph.D., Raquel E. Gur, M.D., Lyn Harper-Mozley, Ph.D., Robin Smith, Ph.D., P. David Mozley, M.D., Abass Alavi, M.D.

NR454 Learned Helplessness Produces Reciprocal CBF Changes in Mammillary Bodies, Amygdala and Hippocampus: A PET $_{15}O$ Study
Frank Schneider, M.D., Ruben C. Gur, Ph.D., Raquel E. Gur, M.D., Lyn Harper-Mozley, Ph.D., Robin Smith, Ph.D., P. David Mozley, M.D., Abass Alavi, M.D., Martin E.P. Seligman, Ph.D.

NR455 Three-Dimensional Magnetic Resonance Surface Measures of Planum Temporale in Schizophrenia
Martha E. Shenton, Ph.D., Hiroto Hokama, M.D., Ron Kikinis, M.D., Michelle Ballinger, Dorothy P. Holinger, Ph.D., Robert W. McCarley, M.D.

NR456 Neuroimaging of Reaction Time Crossover with PET Reveals Cingulate Involvement
Martin A. Weiler, M.D., Dan Storzbach, M.A., William Spaulding, Ph.D., John Sunderland, Ph.D.

NR457 Neuroanatomical Correlates of Normal Human Emotion
Richard D. Lane, M.D., Eric M. Reiman, M.D., Geoffrey L. Ahern, M.D., Gary E. Schwartz, Ph.D., Richard J. Davidson, Ph.D., Beatrice Axelrod, M.S.

NR458 PET Measurement of Cerebral Metabolism with Acute Tryptophan Depletion in Remitted Major Depression
J. Douglas Bremner, M.D., Ronald Salomon, M.D., Chin K. Ng, Ph.D., John H. Krystal, M.D., Robert B. Innis, M.D., Dennis S. Charney, M.D.

NR459 Functional MRI Shows Dynamic Deployment of Neural Resources
Bruce E. Wexler, M.D., Ajay Dhankhar, Ph.D., Andrew Blamire, Ph.D., Robert G. Shulman, Ph.D.

NR460 WITHDRAWN

NR461 Cerebral Perfusion in Heroin Addicts: A Tc-99m Exametazime SPECT Study
Judith S. Rose, M.D., Marc Branchey, M.D., Kenya Chasten, ARRT, Albert Werrell, M.D., Morelly Maayan, M.D.

NR462 Three-Dimensional Brain MRI Position Standardization
Houwei Wu, M.D., Rafael Munne, M.D., Robert Bilder, Ph.D., Gail Lerner, M.S., Martin Redmond, M.S., Jeffrey A. Lieberman, M.D.

NEW RESEARCH

Wednesday, May 25, 1994, 3:00 p.m.-5:00 p.m.

New Research 12 – Poster Session – Exhibit Hall D, Street Level, Convention Center

RELIGIOUS ISSUES IN PSYCHIATRIC PRACTICE; AIDS AND HIV-RELATED DISORDERS; C/L AND EMERGENCY PSYCHIATRY; GERIATRICS; PSYCHOIMMUNOLOGY; ORGANIC MENTAL; SLEEP AND SOMATOFORM DISORDERS; VIOLENCE AND TERRORISM; AND STRESS

Moderator: Paula G. Panzer, M.D.

NR463 Religiosity in Liver Transplant Patients
Shimon S. Waldfogel, M.D., Lisa Marcucci, M.D., Michael J. Moritz, M.D., S.A. Westerberg, M.D.

NR464 Predicting Depression in HIV Disorders
J. Hampton Atkinson, M.D., Thomas L. Patterson, Ph.D., James L. Chandler, M.D., Igor Grant, M.D., Andres Sciolla, M.D., HNRC Group

NR465 Clinical Efficacy and Tolerance of Paroxetine Therapy in HIV/AIDS Patients: 12-Month Experience of an HIV/AIDS Psychiatry Clinic
Jonathan L. Worth, M.D., Mark H. Halman, M.D., Naomi M. Hamburg, B.A., Kathy M. Sanders, M.D., Anne D. Emmerich, M.D.

NR466 Pain and Psychological Distress in Intravenous Drug Users with AIDS
William Breitbart, M.D., Barry Rosenfeld, Ph.D., Steven D. Passik, Ph.D., Russell Portenoy, M.D., David Hewitt, M.D., Margaret McDonald, B.S., Kathy Grummon, M.A., Francisco Gil, M.A.

NR467 Anatomic Correlates of Cerebral Blood Flow Abnormalities in HIV
Renee M. Dupont, M.D., Terry Jernigan, Ph.D., Patrica Lehr, Ph.D., Guy Lamoureaux, M.D., Samuel Halpern, M.D., Igor Grant, M.D.

NR468 Cerebrovascular Response in HIV Infection
Renee M. Dupont, M.D., Patrica Lehr, Ph.D., David Yeung, M.D., Samuel Halpern, M.D., Guy Lamoureaux, M.D., Igor Grant, M.D.

NR469 HIV and Tuberculosis Among the Homeless Mentally Ill
Mary R. Stock, M.S.W., Mark H. Townsend, M.D., Irma J. Bland, M.D., Kathleen W. McCaffery, M.S.W.

NR470 HIV Disease and Sexual Functioning in Intravenous Drug Using Men
Heino F.L. Meyer-Bahlburg, Ph.D., Curtis L. Dolezal, Ph.D., Theresa M. Exner, Ph.D., Anke A. Ehrhardt, Ph.D., Wafaa El-Sadr, M.D., Stephan J. Sorrell, M.D.

NR471 Evaluation of Factors Related to Retention of HIV-Positive Patients in Ambulatory Psychiatric Treatment
Cheryl Ann Kennedy, M.D., Joan H. Skurnick, Ph.D., Monica M. Lintott, Ph.D.

NR472 Compliance Patterns in a Child Psychiatry Outpatient Consultation/Liaison Unit
Ilisse R. Perlmutter, M.D., Suellen Carney, Psy.D., H. Paul Gabriel, M.D., Richard Oberfield, M.D., Raul Silva, M.D.

NR473 Major Depression and Irritable Bowel Syndrome: Is There a Relationship?
Prakash Masand, M.D., David Kaplan, M.D., Sanjay Gupta, M.D., Amar N. Bhandary, M.D., George Nasra, M.D., Mark Kline, M.D.

NR474 Ovarian Cancer Risk: Adherence to Recommendations
Kathleen N. Franco, M.D., Jerome Belinson, M.D., Graham Casey, Ph.D., Marion Piedmonte, M.S., Sarah Plummer, B.S.

NR475 Medical Evaluations of Emergency Psychiatric Patients
James M. Schuster, M.D., Ole J. Thienhaus, M.D.

NR476 Alcohol Level at Head Injury and Subsequent Psychotropic Treatment During Trauma Critical Care
Peggy E. Chatham-Showalter, M.D., Wayne E. Dubov, M.D., Michael Rhodes, M.D., Maria C. Barr, Pharm.D., Jyh-Ming Sun, B.S., Thomas Wasser, M.Ed.

NR477 Psychiatric Problems in Left Ventricular Assist Device Patients
Peter A. Shapiro, M.D.

NR478 Desipramine Deaths May Be Adrenergic
Charles W. Popper, M.D.

NR478-A Fifth Case of Sudden Death in a Child Taking Desipramine
Brian Zimnitzky, M.D., Charles W. Popper, M.D.

NR479 Prediction of Psychiatric Outcome in Liver Transplantation
Marian Fireman, M.D., Roland M. Atkinson, M.D., John M. Rabkin, M.D., C. Wright Pinson, M.D.

NR480 Age, Gender and Post-Ethanol Acetate Metabolism
Thomas P. Beresford, M.D., Joseph Schwartz, M.D., Michael R. Lucey, M.D.

NR481 Correlation of Age at Onset of Dementia with Regional Cerebral Glucose Metabolism in Alzheimer's Disease
Walter W. Hong, M.D., Gene E. Alexander, Ph.D., Cheryl Grady, Ph.D., Randall R. McIntosh, Ph.D., Marc J. Mentis, M.D., P. Pietrini, M.D.

NR482 Site Variability in a Geriatric Depression Trial
Gary W. Small, M.D., Lon S. Schneider, M.D., Susan Holman, M.S., Alexander Bystritsky, M.D., Barnett S. Meyers, M.D., Charles B. Nemeroff, M.D.

NR483 Depressive Symptoms in Alzheimer's Disease and Multi-Infarct Dementia
William E. Reichman, M.D., Andrew C. Coyne, Ph.D.

NR484 Presentation of OCD in the Elderly
Robert Kohn, M.D., Robert J. Westlake, M.D., Steven A. Rasmussen, M.D., Richard T. Marsland, R.N.

NR485 Cognitive Decline and Olfaction in Older Depressives
Diane L. Amend, Ph.D., Iris R. Bell, M.D., Alfred W. Kaszniak, Ph.D., Josh Miller, Ph.D., Jacob Selhub, Ph.D.

NR486 Depression and Suicide in Old Age: A Tragedy of Neglect
Geoffrey S. Duckworth, M.D., Hazel E.A. McBride, Ph.D.

NR487 Risperidone in Elderly Psychotic Patients
Ileana Berman, M.D., Julia Pavlov-Rachov, M.D., Kammalama Duvvi, M.D., Amalia Merson, M.D., Michael Pontecorvo, Ph.D., Miklos F. Losonczy, M.D.

NR488 Late-Life Dysphoria in Nursing Home Residents
Andrew Satlin, M.D., Adam Burrows, M.D., Carl Salzman, M.D., Kenneth W. Nobel, M.D.

NR489 Impact of a Geriatric Delirium Service
Martin G. Cole, M.D., Francois J. Primeau, M.D., Robert F. Bailey, M.D., Michael J. Bonnycastle, M.D., Filippo Masciarelli, M.D., Frank Engelsmann, Ph.D.

NR490 Clinical Correlates of Postmortem Brain Serotonin Levels in Alzheimer's Disease
Brian A. Lawlor, M.D., Linda M. Bierer, M.D., Theresa M. Ryan, B.S., Vahram Haroutunian, Ph.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR491 Plasma MHPG and Clinical Symptoms in Alzheimer's Disease
Brian A. Lawlor, M.D., Linda M. Bierer, M.D., Theresa M. Ryan, B.S., Lizette L. Williams, B.A., Peter J. Knott, Ph.D., Richard C. Mohs, Ph.D.

NR492 Caregiver Assessment of Depression in Patients with Probable Alzheimer's Disease
Bernardo Arias, M.D., Miguel Alfonso, M.D., Steven Sevush, M.D.

NR493 Cortical Metabolic Deficits are Related to Subcortical Pathology in Vascular Dementia
David L. Sultzer, M.D., Jeffrey L. Cummings, M.D., Michael E. Mahler, M.D., Wilfred G. Van Gorp, Ph.D., Charles Brown, M.D., William H. Blahd, M.D.

NR494 Self-Awareness of Memory Impairment
Hilary T. Hanchuk, M.D., Andrew C. Coyne, Ph.D., William E. Reichman, M.D., Neil Cederbaum, B.S.

NR495 Agitation in Alzheimer's Disease and Vascular Dementia Patients
Enid Rockwell, M.D., Edward Jackson, M.D., Dilip V. Jeste, M.D.

NR496 Psychiatric Symptoms of Dementia: Results in a Population-Based Sample
Isabelle M. Paquette, M.D., Bernadette Ska, Ph.D., Yves JoAnette, Ph.D., Francine Giroux, M.Sc.

NR497 WITHDRAWN

NR498 Folate and Dementia
David A. Casey, M.D., Charles A. Class, M.D., Tony A. Bouldin, B.S.

NR499 Beta-Amyloid Peptide Fragment Channel Formation in the Etiology of Alzheimer's Disease
Bruce L. Kagan, Ph.D., Tajib Mirzabekov, Ph.D., Meng Chin Lin, B.S., Peter J. Marshall, B.A., Ivan Lieberburg, M.D.

NR500 Older Age and the Under Reporting of Depressive Symptoms
Jeffrey M. Lyness, M.D., Christophe Cox, Ph.D., Jennifer Curry, B.A., Yeates Conwell, M.D., Deborah A. King, Ph.D., Eric D. Caine, M.D.

NR501 Treatment of Psychosis in the Non-Demented Elderly
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.

NR502 WITHDRAWN

NR503 Temazepam 7.5mg: Sleep Effects in Elderly Insomniacs
Anthony Kales, M.D., Alexandros N. Vgontzas, M.D., Edward O. Bixler, Ph.D., David Myers, B.A., Anthony Centurione, M.A.

NR504 Managing Disruptive Behavior in the Elderly
Elaine Souder, Ph.D., Kim Heithoff, Sc.D., Patricia S. O'Sullivan, Ed.D.

NR506 Lithium Augmentation in Geriatric Major Depression
Paul A. Kettl, M.D.

NR507 Depression and Adherence to Advance Directives
David M. Smith, M.D., Melinda Lee, M.D., Linda K. Ganzini, M.D., Darien Fenn, Ph.D.

NR508 Psychiatric Medications in Chronic Elderly Inpatients
Barbara R. Sommer, M.D., Michael J. Parrella, Ph.D., Leonard White, Ph.D., Michael Davidson, M.D.

NR509 Psychiatric Predictors of Medical Readmissions
Jennifer Fetner, B.A., George Fulop, M.D., Peter Tafti, David Huertas, M.D., Karen Pasternak, James J. Strain, M.D.

NR510 Effect of ECT on Mortality and Clinical Outcome in Elderly Patients
Larry L. Richards, D.O., Robert A. Philibert, M.D., George Winokur, M.D.

NR511 Effect of Emotion on Retention in Old Age
Avraham Calev, Ph.D.

NR512 Educational and Current Reading Level in the Elderly
F.M. Baker, M.D., Janice T. Johnson, Susan A. Velli, B.A., Cynthia Wiley, B.S., Patricia Langenberg, Ph.D.

NR513 Reliability of the Geriatric Depression Scale and the Center for Epidemiologic Studies of Depression Scale in the Elderly
F.M. Baker, M.D., Cynthia Wiley, B.S., Susan A. Velli, B.A., Janice T. Johnson

NR514 Qualitative Assessment of Brain Morphology in Geriatric Depression
Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., Bernhard Bogerts, M.D., Manzar Ashtari, Ph.D., Peter Aupperle, M.D., Luis G. Allen, M.D., David Zeman, M.D., Mahendra Patel, M.D.

NR515 Hypothyroidism in Geriatric Psychiatric Patients
Irl L. Extein, M.D.

NR516 Criteria to Enroll End-Stage Dementia Patients Into a Hospice
Mark J. Alexakos, B.A., Patricia H. Hanrahan, Ph.D., Daniel J. Luchins, M.D.

NR517 Mechanisms for Outcome in Psychiatric Intervention Studies in the Medically Ill: A Reanalysis
James J. Strain, M.D., Albert Diefenbacher, M.D., Mary Eichmann, Ph.D., Mimi Fahs, Ph.D., John Lyons, Ph.D., Jeffrey S. Hammer, M.D.

NR518 Weekly Psychiatric Review of Nursing Home Patients
Suhayl J. Nasr, M.D., Lori C. Gilmore, B.A.

NR519 Effect of Naloxone on Stress-Induced Immunosuppression
Choong-Han Yoon, M.D., Byung-Hwan Yang, M.D., Kwang-Il Kim, M.D., Kim Jung-Mogg, M.D.

NR520 Immunity in Young Adults with Major Depressive Disorders
Steven J. Schleifer, M.D., Jacqueline A. Bartlett, M.D., Beverly Delaney, M.D., Diane Zeitlin, B.A., Haftan Eckholdt, Ph.D., Steven E. Keller, Ph.D.

NR521 Localization of Stem Cell Factor mRNA in Rat Brain
Ma-Li Wong, M.D., Julio Licinio, M.D.

NR522 Distribution of Interleukin-1 Receptor Type I mRNA in the Brain
Julio Licinio, M.D., Ma-Li Wong, M.D.

NR523 Aggression and Immunity
Jacqueline A. Bartlett, M.D., Steven E. Keller, Ph.D., Melissa K. Demetrikopoulos, Ph.D., Steven J. Schleifer, M.D.

NR524 Medical Status, Depressed Mood and Immune Function
Steven E. Keller, Ph.D., Steven J. Schleifer, M.D., Jacqueline A. Bartlett, M.D., Melissa K. Demetrikopoulos, Ph.D.

NR525 Temporo-Limbic Epilepsy and Dream-Like States
R. Andrew Schultz-Ross, M.D.

NR526 Psychopathology in Psychophysiological Insomnia
Silvio Scarone, M.D., Orsola Gambini, M.D., Marco Zucconi, M.D., Arturo Campana, M.D., Luigi Ferini-Strambi, M.D., Salvatore Smirne, M.D.

NR527 Long-Term Efficacy of Uvulopalatopharyngoplasty for Sleep Apnea
Edward O. Bixler, Ph.D., Alexandros N. Vgontzas, M.D., Ernest Manders, M.D., Rocco L. Manfredi, M.D., Anthony Kales, M.D.

NR528 Delta Sleep-Inducing Peptide in Normals and in Sleep Apnea and Narcolepsy
Alexandros N. Vgontzas, M.D., Theodore Friedman, M.D., George Chrousos, M.D., Edward O. Bixler, Ph.D., Antonio Vela-Bueno, M.D., Anthony Kales, M.D.

NR529 Association of Tumor Necrosis Factor Microsatellite Polymorphisms with Narcolepsy
Charles Rivers, B.S., Rodney Go, Ph.D., Shashidhar M. Shettar, M.D., Bracie Watson, Ph.D., Chotip Vanichanan, M.D., Mei-Ling Tseng, Ph.D., Yan Qui, B.S., Ronald Acton, Ph.D.

NR530 A Sleep Disorder Questionnaire Subscale for Chronic Fatigue Syndrome
Alan B. Douglass, M.D., Jon K. Zubieta, M.D., Mark A. Demitrack, M.D., N. Cary Engleberg, M.D.

NR531 More Cortisol Suppression in Depressed Cacosmics: DST Evaluation of Chemically-Sensitive Older Adults
Iris R. Bell, M.D., Diane L. Amend, Ph.D.

NR532 Memory and EEG in Chemically-Sensitive Young Adults
Gary E. Schwartz, Ph.D., Iris R. Bell, M.D., Anne M. Herring, Ph.D., Julie M. Peterson, B.S., Alfred W. Kaszniak, Ph.D.

NR533 Irritable Bowel Syndrome and Psychiatric Illness: A Family Study
Catherine L. Woodman, M.D., Kevin Breen, M.D., Russell Noyes, Jr., M.D, Carol Moss, B.A., Robert Fagerholm, R.N., Robert Summers, M.D.

NR534 High Frequency of Somatization in Benzodiazepine Dependents
Herminio Martinez-Cano, M.D., Antonio Vela-Bueno, M.D., Rolando Pomalima, M.D., Mariano Iceta, M.D.

NR535 Development of an Inventory for the Multidimensional Assessment of Sex and Aggression
Robert A. Prentky, Ph.D., Raymond A. Knight, Ph.D.

NR536 Adolescent Murderers: Follow-Up and Typology
Louis Morissette, M.D., Jean Toupin, Ph.D., Juan E. Labadie, M.D.

NR537 Machine Learning of Back-Ward Violence Patterns
Cheryl K. Cantrell, M.D., David A. Pensak, Ph.D.

NR538 Atypical Violence Patterns in Back-Ward Patients
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D., D. Erik Everhart, B.A.

NR539 Training and Experience of Psychiatric House Staff with Domestic Violence Identification
Glenn W. Currier, M.D.

NR540 Adjunctive Propranolol and Nadolol in Aggression and Akathisia
Edward R. Allan, M.D., Murray Alpert, Ph.D., Gabriel Laury, M.D., Cecile E. Sison, Ph.D.

NR541 Deployment and Dysfunction
Ronald Koshes, M.D., Joseph M. Rothberg, Ph.D., John Shanahan, Ed.D., Karl Christman, M.Ed.

NR542 Negative Symptoms and Serotonin in PTSD
Christopher G. Fichtner, M.D., Francine L. O'Connor, R.N., Hock C. Yeoh, B.S., Muhammad O. Nasib, M.B., Ramesh C. Arora, Ph.D., John W. Crayton, M.D.

NR543 Sleep Disturbance Related to Hurricane Andrew
Thomas A. Mellman, M.D., Daniella David, M.D., Renee Kulick-Bell, B.A., Joanne R. Hebding, Psg.T., Bruce Nolan, M.D.

NR544 Trauma as a Predictor of Dual Diagnosis
Juris P. Mezinskis, Ph.D., Eugene C. Somoza, M.D., Mark W. Cohen, Ph.D., Sue R. Dyrenforth, Ph.D.

NR545 Trauma Related Symptoms in Bosnian Refugees
Stevan M. Weine, M.D., Daniel F. Becker, M.D., Thomas H. McGlashan, M.D., Dori Laub, M.D., Steve Lazrove, M.D., Dolores Vojvoda, M.D.

NR546 Evoked Response Indicators of Attention in Disaster Survivers With and Without PTSD
Svein Blomhoff, M.D., Ivar Reinvang, Ph.D., Ulrik F. Malt, M.D., C. Nielsen

NR547 Are Long Delayed Traumatic Memories Accurate: An Independently Varifiable Case
Susan Mirow, M.D.

NR548 Biases in Mixed Models for Analysis of Clinical Trials
Zhengyu Wang, M.S., John M. Davis, M.D.

NR549 Outcome of Inpatient Psychiatric Care Over Time
Charles J. Rabiner, M.D., William B. Hawthorne, Ph.D., Michele W. Chadwick, Ph.D., Daniel C. Cohen, M.S.W.

NR550 Predictors of Abstract Publication
Robert G. Stern, M.D., Lora K. Heisler, M.S., Idan Sharon, M.D.

NR551 Methodological Issues in Clinical Drug Trials in Schizophrenia
Robert G. Stern, M.D., Michael Davidson, M.D., James Schmeidler, Ph.D.

NEW RESEARCH

Thursday, May 26, 1994, 9:00 a.m.-10:30 a.m.

New Research 13 – Oral/Slide Session – Exhibit Hall D, Street Level, Convention Center

INFANT AND CHILDHOOD, ALCOHOL AND SUBSTANCE ABUSE, ANXIETY, AND EATING DISORDERS

Chp.: George E. Woody, M.D.

NR552 WITHDRAWN

NR553 Does Alcoholic Liver Disease Indicate Alcohol Dependence?
Thomas P. Beresford, M.D., Michael R. Lucey, M.D.

NR554 Evaluation of Bupropion Versus Placebo for Treatment of Nicotine Dependence
Linda H. Ferry, M.D., Raoul J. Burchette, M.A.

NR555 Predictors of Response to Paroxetine Therapy in OCD
Martin Steiner, Ph.D., Rosemary Oakes, M.S., Ivan P. Gergel, M.D., David E. Wheadon, M.D.

NR556 Effect of Cognitive/Behavioral Therapy on Twenty-Four Hour Food Intake in Bulimia Nervosa
Theodore E. Weltzin, M.D., Lee-Keung G. Hsu, M.D., Madelyn Fernstrom, Ph.D., Burt Bolton, B.S., Walter H. Kaye, M.D.

NR557 A Four-Year Follow-Up Study of Eating Disorders and Medical Complications in Young Women with Insulin-Dependent Diabetes Mellitus
Anne C. Rydall, B.Sc., Gary M. Rodin, M.D., Marion P. Olmsted, Ph.D., Robert G. Devenyi, M.D., Denis Daneman, M.B.

NEW RESEARCH

Thursday, May 26, 1994, 9:00 a.m.-10:30 a.m.

New Research 14 – Oral/Slide Session – Exhibit Hall D, Street Level, Convention Center

MOOD DISORDERS AND PSYCHOPHARMACOLOGY

Chp.: Sally R. Szymanski, M.D.

NR558 Optimal Phase Advancement for Resolution of SAD
Katherine H. Thomas, M.D., Alfred J. Lewy, M.D., Vance K. Bauer, M.A.

NR559 Paroxetine Dose: Experience in Clinical Practice
Ivan P. Gergel, M.D., David E. Wheadon, M.D., James P. McCafferty, B.S.

NR560 The Pharmacology of Antidepressants: Characteristics of the Ideal Drug
Elliott Richelson, M.D.

NR561 Fluoxetine Versus Placebo: Long-Term Treatment of Major Depressive Disorder
Patrick McGrath, M.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D., Jay D. Amsterdam, M.D., Jan A. Fawcett, M.D., Frederick Reimberr, M.D.

NR562 Imipramine Plasma Levels: Response Curves in Panic
Matig R. Mavissakalian, M.D., James M. Perel, Ph.D.

NR563 Estrogen Plus Fluoxetine for Geriatric Depression
Gary W. Small, M.D., Lon S. Schneider, M.D., Susan Holman, M.S., Alexander Brystritsky, M.D., Barnett S. Meyers, M.D., Charles B. Nemeroff, M.D.

NEW RESEARCH

Thursday, May 26, 1994, 12:00 noon-2:00 p.m.

New Research 15 – Poster Session – Exhibit Hall D, Street Level, Convention Center

ECONOMIC ISSUES; INFANT AND CHILDHOOD DISORDERS; CHILD AND ADOLESCENT PSYCHIATRY; PSYCHOPHARMACOLOGY AND OTHER SOMATIC THERAPIES; EATING DISORDERS; DIAGNOSTIC ISSUES; EPIDEMIOLOGY; PSYCHIATRIC EDUCATION; STIGMA; SOCIAL PSYCHIATRY; RESIDENT AND MEDICAL STUDENT, AND GENDER ISSUES; PRESIDENTIAL THEME: OUR HERITAGE, OUR FUTURE; COUPLE AND FAMILY, AND BEHAVIOR AND COGNITIVE THERAPIES; FORENSIC, AND COMMUNITY PSYCHIATRY

Moderator: Wade H. Berrettini, M.D.

NR564 Clinical Psychopharmacologic Trials: Cost of Patient Recruitment
Naresh P. Emmanuel, M.D., Michael R. Ware, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

NR565 Factors That Influence the Length-of-Stay on an Inpatient Psychiatric Unit
James M. Schuster, M.D., Ester Mandelker, Ph.D., Kenneth L. Goetz, M.D.

NR566 Biopsychosocial Traits of General Hospital Patients
Gail A. Mallory, Ph.D., Jeremy S. Musher, M.D., Jess D. Amchin, M.D.

NR567 Do Nice Patients Drive Out Difficult Cases?
Alex Richman, M.D., Cyril Nair, M.A., Leonard MacLean, Ph.D.

NR568 Efficacy of Drugs Used in Psychiatry Versus Internal Medicine
John M. Davis, M.D.

NR569 Inhibited and Uninhibited Temperament at Age Two: Psychophysiology and Behavior Twelve Years Later
Carl E. Schwartz, M.D., Jerome Kagan, Ph.D., Joseph J. Schildkraut, M.D., Rachel J. Kramer, Ph.D., Nancy Snidman, Ph.D.

NR570 Effect of Methylphenidate on Signal Detection Indices in Behavior Disordered Adolescent Inpatients
Daniel F. Becker, M.D., William S. Edell, Ph.D., Kenneth N. Levy, B.A., Terry Ann Fujoika, Ph.D., Thomas H. McGlashan, M.D.

NR571 Attentional and Intellectual Deficits in Unmedicated Behavior Disordered Adolescent Inpatients
Daniel F. Becker, M.D., William S. Edell, Ph.D., Terry Ann Fujioka, Ph.D., Kenneth N. Levy, B.A., Thomas H. McGlashan, M.D.

NR572 Predictors of Length-of-Stay for Children's Psychiatric Hospitalization
Dinohra Munoz-Silva, M.D., Raul Silva, M.D., Richard Perry, M.D., Christine Pappas, Sunil Khushalani, M.D.

NR573 Adolescent Attachment and Psychopathology
Diana S. Rosenstein, Ph.D., Harvey A. Horowitz, M.D.

NR574 Predisposing Factors for Epidemic Dissociation Among School Girls in Thailand
Umaporn Trangkasombat, M.D., Umpon Su-Ampun, M.D., Vera Churujikul, M.D., Orawan Nukaew, M.S., Vilailuk Haruhanpong, M.S., Kamthorn Prinksulka, M.D.

NR575 EEG and Dynamic Brain Mapping in Conduct Disorders
Atilla Turgay, M.D., Edward Gordon, M.D., Martin Vigdor, Ph.D.

NR576 Lethal Learning Problems: New Findings in Adolescent Suicide
Hazel E.A. McBride, Ph.D., Geoffrey S. Duckworth, M.D., Linda L. Siegel, Ph.D.

NR577 Atypical Depression in Suicidal Adolescents
Thomas A. Hunter, M.D., Daniel Castellanos, M.D.

NR578 Left-Right Asymmetries of Quantitative Electroencephalogram in Abused Children
Yutaka Ito, M.D., Martin H. Teicher, M.D., Carol A. Glod, R.N., Erika Ackerman, B.A.

NR579 Children on Antidepressants: Orthostatic Changes
Nancy B. Campbell, M.D., Marijo B. Tamburrino, M.D., Kathleen N. Franco, M.D., Cynthia L. Evans, M.D.

NR580 Adolescent Sexual Activity, Axis I and Personality Disorders
Roger C. Burket, M.D., Wade C. Myers, M.D.

NR581 Childhood Psychopathology in 40 Adult Bipolar Patients
Gary Sachs, M.D., Beny Lafer, M.D., Amy Thibault, M.D., Christine Truman, B.A.

NR582 Characterization of the Pregnant Adolescent
Catherine A. Martin, M.D., Kelly S. Kearfott Hill, M.D.

NR583 A Pilot Study of School-Based Mental Health Clinics in Special and Regular Education Settings
Spyros J. Monopolis, M.D., John Myhill, Ph.D., Lois Flahery, M.D., Mark Weist, Ph.D., Peggy Caltrider, L.C.S.W, Patricia Cronin, L.C.S.W

NR584 Diagnostic and Referral Patterns of School and Mental Health Services
H. Allen Handford, M.D., Dana Sanderson, M.D., Richard Mattison, M.D., Edward O. Bixler, Ph.D.

NR585 Parent and Child Agreement on DICA Diagnosis in Conduct Disordered Psychiatric Inpatients
Richard P. Malone, M.D., Krista A. Biesecker, B.A., James Luebbert, M.D., Mary White, M.D., Mary A. Delaney, M.D.

NR586 Stability of Major Depression in Child Psychiatry Inpatients
Richard P. Malone, M.D., Mary A. Delaney, M.D., Krista A. Biesecker, B.A., James Luebbert, M.D., Mary White, M.D.

NR587 The Effect of Lithium Treatment for Aggression on Measures of Cognition
Patrick W. McGuffin, Ph.D., Richard P. Malone, M.D., Cornelius Fergueson, B.A., James Luebbert, M.D., Krista A. Biesecker, B.A., Mary A. Delaney, M.D.

NR588 Which Sexually Abused Children are Recommended for Follow-Up?
Gail A. Edelsohn, M.D., Ruth P. Zager, M.D., Irena C. Haughton, M.D.

NR589 Aggression in Child Psychiatric Hospitalization
Stuart L. Kaplan, M.D., Joan Busner, Ph.D., Timothy Skahen, M.A.

NR590 Family Assessment in Adolescent Inpatients
Susan R. Borgaro, M.A., David L. Pogge, Ph.D., John M. Stokes, Ph.D.

NR591 Adolescent Health Promotion in Central Texas
Jack D. Burke, Jr., M.D., Kimberly C. Burke, M.S., Jenny Hurt, B.S., M. Kay Psencik, Ed.D.

NR592 Comorbidity in Conduct Disordered Adolescents
Dwain C. Fehon, Psy.D., Daniel F. Becker, M.D., Kenneth N. Levy, B.A., Carlos M. Grilo, Ph.D., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR593 Outcome of 18 Months of Clozapine Treatment for 100 State Hospital Patients
William H. Wilson, M.D.

NR594 Addition of Lithium to Haloperidol in Nonaffective Antipsychotic Nonresponsive Schizophrenia
William H. Wilson, M.D., Arvilla M. Claussen, M.S.

NR595 CSF Predictors of Clozapine Response
Samuel Craig Risch, M.D., C.A. Haden, Jane Caudle, R.R.J. Lewine, Ph.D.

NR596 Acetazolamide in Bipolar Affective Disorders
Stephen G. Hayes, M.D.

NR597 A Placebo Controlled Double-Blind Study of Naltrexone for Trichotillomania
Gary A. Christenson, M.D., Scott J. Crow, M.D., Thomas B. Mackenzie, M.D., Ross D. Crosby, Ph.D., James E. Mitchell, M.D.

NR598 Startle and Alprazolam in PTSD and Panic Disorder
Arieh Y. Shalev, M.D., Tuvia Peri, M.A., Genia Gelpin, M.D., Eitan Gur, M.D., Leonid Oumanski, M.D., Miki Bloch, M.D.

NR599 Safety of Combination Clozapine and ECT Therapy
Betty Patterson, Ph.D.

NR600 A Double Blind Study Comparing Idazoxan to Bupropion
Fred Grossman, D.O., William Z. Potter, M.D., Elizabeth Brown, M.Ed., Merry Ann Jackson, B.S.N., Nancy Skoczalek, B.A.

NR601 Effects of Fluoxetine on Symptoms of Insomnia in Depressed Patients
Winston G. Satterlee, M.D., Douglas E. Faries, John H. Heiligenstein, M.D., Gary D. Tollefson, M.D.

NR602 Desipramine Augmentation of Selective Serotonin Reuptake Inhibitor Treatment of Refractory OCD Patients
Linda C. Barr, M.D., Wayne K. Goodman, M.D., Amit Anand, M.D., Lawrence H. Price, M.D.

NR603 Effects of Tryptophan Depletion on Mood During Fluoxetine Treatment of Healthy Subjects
Linda C. Barr, M.D., Wayne K. Goodman, M.D., George R. Heninger, M.D., Lawrence H. Price, M.D.

NR604 Neuroleptic-Induced Psychopathology
Conrad M. Swartz, M.D.

NR605 Increased Risk of Periodic Leg Movements During Sleep with Use of Fluoxetine
Cynthia M. Dorsey, Ph.D., Steven L. Cunningham, R.PSG.T., Scott E. Lukas, Ph.D., John W. Winkelman, M.D.

NR606 Trial of the Novel Noradrenergic Antidepressant ABT-200
Neal R. Cutler, M.D., Jerome F. Costa, M.D., John J. Sramek, Pharm.D., Kenneth B. Kaskin, M.D., Jack A. Grebb, M.D., Sara S. Kennedy

NR607 Trial of a Cholecystokin$_B$ Antagonist in Panic Disorder
Neal R. Cutler, M.D., Jerome F. Costa, M.D., John J. Sramek, Pharm.D., Mark S. Kramer, M.D., Scott A. Reines, M.D.

NR608 Desipramine Desensitizes Platelet Adenylyl Cyclase
John J. Mooney, M.D., Jacqueline A. Samson, Ph.D., Jonathan E. Alpert, M.D., Martha Koutsos, M.D., Nancy McHale, B.S., Joseph J. Schildkraut, M.D.

NR609 Clozapine Plasma Levels and Therapeutic Response
Carol Vander Zwaag, M.D., Mark F. McGee, M.D., Joseph P. McEvoy, M.D.

NR610 Desipramine with Paroxetine or Sertraline
Jeffrey A. Alderman, Ph.D., Janet Allison, M.D., Menger Chung, Ph.D., Wilma Harrison, M.D., David J. Greenblatt, M.D.

NR611 Use of Lamotrigine in the Treatment of Bipolar Disorder
Richard H. Weisler, M.D., Marcus E. Risner, Ph.D., John A. Ascher, M.D., Trisha L. Houser, B.A.

NR612 Kindling with Clozapine
Duane Denney, M.D., Janice R. Stevens, M.D.

NR613 Male Sexual Dysfunction Induced by Buproprion Sustained Release
Mark D. Fossey, M.D., Mark B. Hamner, M.D.

NR614 Risperidone: A One-Year Open-Label Study
Alan I. Green, M.D., Risperidone Study Group

NR615 Lithium in the Treatment of Bipolar Depression
Simavi Vahip, M.D., Alp Ayan, M.D., Isil Vahip, M.D., Inci Doganer, M.D., Bekir Ozkan, M.D., Serdar Korukoglu, Ph.D., Isik Tuglular, M.D.

NR616 Serotonin Depletion in Paroxetine: Treated Panic Disorder Patients
Pedro L. Delgado, M.D., Alan J. Gelenberg, M.D., Linda Bologna, R.N.

NR617 Risperidone in the Treatment of Neuroleptic-Refractory Schizophrenic Patients
Jean-Pierre Lindenmayer, M.D., George M. Simpson, M.D.

NR618 Clinical Efficacy of Risperidone in a Patient with Severe Tardive Dyskinesia
Christian L. Shriqui, M.D., Philippe Nobecourt, M.D., Francois Rousseau, M.D., Wendy Arnott, Pharm.D.

NR619 Alexithymia, Depression and Treatment Outcome in Bulimia Nervosa
Janet M. de Groot, M.D., Gary M. Rodin, M.D., Marion P. Olmsted, Ph.D.

NR620 Fluvoxamine Treatment of Binge Eating Disorder: A Multicenter, Placebo-Controlled Trial
James I. Hudson, M.D., Susan L. McElroy, M.D., Nancy C. Raymond, M.D., Scott Crow, M.D., Paul E. Keck, Jr., M.D., Jeffrey M. Jonas, M.D.

NR621 m-chlorophenylpiperazine Challenge in Bulimia Nervosa
Robert D. Levitan, M.D., Allan S. Kaplan, M.D., Anthony J. Levitt, M.D., Russel T. Joffe, M.D.

NR622 Child Sex Abuse and Bulimia Nervosa in the United States, Austria and Brazil
Harrison G. Pope, Jr., M.D., Barbara Mangweth, M.A., Andre B. Negrao, M.D., James I. Hudson, M.D., Taki A. Cordas, M.D.

NR623 Serotonin Function in Bulimia Nervosa
David C. Jimerson, M.D., Barbara E. Wolfe, M.S.N., Eran D. Metzger, M.D., Jeffrey M. Levine, M.D.

NR624 Body Dysmorphic Disorder: Comorbidity Study
Olga Brawman-Mintzer, M.D., R. Bruce Lydiard, M.D., Naresh P. Emmanuel, M.D., Violetta D. Czepowicz, M.D., Gerardo Villarreal, M.D., James C. Ballenger, M.D.

NR625 The Effect of Naloxone on Twenty-Four Hour Luteinizing Hormone Secretion in Bulimia Nervosa
Theodore E. Weltzin, M.D., Judith Cameron, Ph.D., Claire McConaha, R.N., Walter H. Kaye, M.D.

NR626 CSF Isatin (Purified Tribulin) in Bulimia Nervosa
Timothy D. Brewerton, M.D., Joseph J. Zealberg, M.D., R. Bruce Lydiard, M.D., V. Glover, M.D., M. Sandler, M.D., James C. Ballenger, M.D.

NR627 Do Adolescents with Anorexia Nervosa Share Alexithymia with Their Parents?
Jean-Philippe Raynaud, M.D., Cecile Dounet, M.D., Laurent Schmitt, M.D., Marc Benatia, M.D., Pierre Moron, M.D.

NR628 A Rare Case of Bulimic Purging Through Blood Donation
A. Missagh Ghadirian, M.D.

NR629 Eating Disorder and OCD Comorbidity: Analysis of SPEM Impairment
Stefano Pallanti, Ph.D., Barbara Mezzani, M.D., Stefano Massi, M.D., Gaetano Zaccara, Ph.D., Lorella Grecu, M.D., Leonardo Querciou, M.D.

NR630 Clinical Diagnoses in Community Psychiatry: Accuracy and Cost
Monica Basco, Ph.D., Dona Davies, M.S., Michael Kashner, Ph.D., Jeff Bostic, M.D., William Hendrickse, M.D., A. John Rush, M.D.

NR631 Managed Care and Global Assessment of Functioning
Sally Caldecott-Hazard, Ph.D., Richard C.W. Hall, M.D.

NR632 Psychiatric, Personality and Cognitive Factors in Mitral Valve Prolapse During Panic Disorder
Bonnie R. Aronowitz, Ph.D., Charles Swencionis, Ph.D., Eric Hollander, M.D.

NR633 Neuropsychology of OCD: Preliminary Findings
Bonnie R. Aronowitz, Ph.D., Eric Hollander, M.D., Concetta M. Decaria, M.S., Lisa Cohen, Ph.D., Dan J. Stein, M.D., Daphne Simeon, M.D.

NR634 DSM-III-R Diagnoses in Benzodiazepine Dependent Subjects
Herminio Martinez-Cano, M.D., Antonio Vela Bueno, M.D., Rolando Pomalima, M.D., Mariano Iceta, M.D.

NR635 Psychometric Characteristics of the Beck Anxiety Inventory with Adult Outpatients
John B. Jolly, Psy.D., Thomas A. Kramer, M.D., Denise Gilliam, Ph.D., Janet M. Jolly, M.D., Jeffrey N. Wherry, Ph.D.

NR636 Comparison of Depression Measures in Veterans
Kenneth J. Hoffman, M.D., William F. Page, Ph.D., Robert J. Ursano, M.D.

NR637 Severity of Medical Illnesses Diagnosed During Psychiatric Hospitalization
Peter Manu, M.D., Lynda Freedman, M.D., Joyce Fogel, M.D., Erik Nieddritis, M.D., Simcha Pollack, Ph.D., John M. Kane, M.D.

NR638 Diagnostic Interview Schedule: Development and Validation of a French Computerized Version
Denis J.B. Lepage, M.D., Francois B. Jolicoeur, Ph.D., Ellen Moulton, B.A., F. Gheysen, M.D., E. Zarfian, M.D.

NR639 Current Toxic Status, Psychological Distress and History of Psychiatric Symptoms in Alcoholic Patients
Juana L. Vainer, M.D., Juan C. Negrete, M.D.

NR640 Alert for Clinicians: Somatization Symptoms and Alcoholism
Allen Y. Tien, M.D., Thomas E. Schlaepfer, M.D., Hans U. Fisch, M.D.

NR641 Arthur Conan Doyle's Method of Observation and Deductive Reasoning in Psychiatric Evaluations
Paul A. Hriso, M.D., Emmanuel Hriso, M.D.

NR642 Evaluation of the Basic Sexual Knowledge of Advanced Medical Students
Errol M. Aksu, M.D., Edward O. Bixler, Ph.D.

NR643 Psychosocial Functioning in the Ehlers-Danlos Syndrome
Ralph Rubenstein, M.D., Mark A. Lumley, Ph.D., Margaret Jordan, Ph.D., Petros Tsipouras, M.D., Mark Evans, M.D.

NR644 Public Attitudes to the Quality of Psychiatry
Per Hamre, DDS, Alv A. Dahl, M.D., Ulrik F. Malt, M.D.

NR645 Prescription Patterns in Hospitalized Patients with Refractory Psychosis
Jean-Yves Roy, M.D., Guy Chouinard, M.D., Monique Tremblay, M.D., Claire L.I. Damecours, M.D.

NR646 Socioeconomic Drift Among Patients with Schizophrenia and Severe Affective Disorder
Hillevi M. Aro, M.D., Seppo L. Aro, M.D., Ilmo Keskimaki, M.D.

NR647 Faculty Attitudes About Abuse of Medical Students
Francis Kane, M.D., Thomas A. Kramer, M.D.

NR648 Female Psychiatric Residents: A Research Future?
Kaye L. McGinty, M.D., Catherine A. Martin, M.D., Karen L. DeMoss, Ph.D., Kelly S. Kearfott Hill, M.D.

NR649 Psychiatry Training in Internal Medicine Residencies
Mark D. Sullivan, M.D., Steven A. Cohen-Cole, M.D., Roger G. Kathol, M.D., Geoff Gordon, M.D., Steven R. Hahn, M.D.

NR650 Psychosocial Predictors of Postpartum Depressive Symptomatology
Odette Bernazzani, M.D., Jean-Francois Saucier, M.D., Helene David, D.P.S., Francois Borgeat, M.D.

NR651 Gender Differences in Axis I Comorbidity in Major Depressive Disorder
Maurizio Fava, M.D., Melissa Abraham, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Jerrold F. Rosenbaum, M.D.

NR652 Factors Associated with Sexuality Among Women with Metastatic Breast Cancer
Leslie Smithline, B.A., Julia L. Zarcone, M.A., Cheryl Koopman, Ph.D., David Spiegel, M.D.

NR653 Historical Analysis of the Evolution of American Biological Psychiatry in the 20th Century
Ross J. Baldessarini, M.D.

NR654 Influence of Family Approach in Halfway House Residence on the Rehospitalization of Schizophrenic Patients
Francis L. Ritz, M.D., Jacqueline Lalive Aubert, M.D.

NR655 Enhancement of Learning with a Floral Odor
Alan R. Hirsch, M.D., Lisa H. Johnston, M.D.

NR656 A Controlled Study of Cognitive-Behavior Therapy with Buspirone or Placebo in Panic Disorder with Agoraphobia: A One-Year Follow-Up
Jean A. Cottraux, M.D., Ivan D. Note, M.D., Charly Cungi, M.D., Patrick Legeron, M.D., Francois Heim, M.D., Laurent Chneiweiss, M.D.

NR657 Sertraline in Social Phobia: A Double-Blind, Placebo-Controlled Crossover Pilot Study
David J. Katzelnick, John H. Greist, James W. Jefferson, Kenneth A. Kobak

NR658 The Profile of Persons Hospitalized by Court Remand and the Outcome
Chitra M. Shenoy, M.D.

NR659 Housing Choice and Supported Housing for Homeless Persons Served by Assertive Community Treatment
Lisa Dixon, M.D., Nancy Krauss, M.S.W., Patrick Myers, M.A., Anthony Lehman, M.D.

NR660 Predicting Homeless Status in a Population of Chemically Dependent Veterans
Juris P. Mezinskis, Ph.D., Eugene C. Somoza, M.D., Sue R. Dyrenforth, Ph.D., Mark W. Cohen, Ph.D.

NR661 Housing the Homeless: Results of a Random Controlled Trial
Stephen M. Goldfinger, M.D., George Tolomiczenko, Ph.D., Winston Turner, Ph.D., Russell Schutt, Ph.D., Olinda Gonzalez, Ph.D., Sondra Hellman, R.N.C.S., Norma Ware, Ph.D.

NR662 Mental Alternation Test Performance and Functional Status at Discharge in the Chronically Mentally Ill
Beverly N. Jones, M.D., Geetha Jayaram, M.D., Jack F. Samuels, Ph.D., Hilary Robinson, ROT

NR1 Monday, May 23, 9:00 a.m.-10:30 a.m.

Personality Disorders in HIV Positive Persons: Association with Other Measures of Psychiatric Morbidity

Jeffrey J. Richards, M.D., Psychiatry, Wilford Hall Medical, 2200 Bergquist Drive Ste 1, Lackland AFB TX 78236; Susan E. McManis, M.D., Robert A. Zachary, Ph.D., George R. Brown, M.D.

Summary:

Objective: HIV+ military personnel were studied to examine the relationships between personality disorders and 1) Axis I diagnoses and 2) other measures of psychosocial functioning.

Method: 173 HIV-infected military patients were interviewed on two separate occasions one year apart. Axis I and II disorders were diagnosed using a modified version of the *Structured Clinical Interview for DSM-III-R.* Various interview and self-report measures were also administered.

Results: Compared to the 17 patients who did not have any personality disorder, the 37 HIV+ patients diagnosed with a personality disorder on both occasions had significantly higher mean scores on 14/15 psychosocial measures indicating distress at time 1 and 15/15 measures at time 2 (all ps $\leq$ .05). Current major depression and being unmarried were also significantly associated with an Axis II diagnosis, but not other current and past Axis I disorders. The remaining 119 HIV+ patients represent a group which on one occasion presented with an Axis II diagnosis, traits, or no Axis II diagnosis, but on the second occasion presented differently. Although eliminated from this study which looks at diagnostically "clean" populations, this "mixed" population merits further analysis.

Conclusions: HIV+ persons with an Axis II diagnosis could represent a population vulnerable to major depression, as well as symptoms of dysphoric mood, anxiety, and loneliness, therefore requiring earlier or more intensive interventions.

NR2 Monday, May 23, 9:00 a.m.-10:30 a.m.

Gender Differences in AIDS-Related Bereavement

Jacquelyn Summers, Psychiatry, University of Calf. SD, 2760 5th Avenue #200, San Diego CA 92103; Andres Sciolla, M.D., Sidney Zisook, M.D., J. Hampton Atkinson, M.D., Janet Chandler, M.D., Igor Grant, M.D.

Summary:

Objective: To compare grief reactions in HIV-seropositive men and women, since gender differences has been reported in non-HIV samples.

Methods: In a longitudinal cohort study (n = 549), mood, grief response, and quality of well-being were examined using the Structured Clinical Interview for DSM-III-R (SCID), Hamilton Rating Scales for Depression and Anxiety (HRSD and HRSA), Texas Revised Inventory of Grief (TRIG-R), and Quality of Well Being (QWB) in 243 men and 23 women who had been bereaved in the preceding 12 months.

Results: Women had more unresolved grief (30.4% vs., 9.7%, $p < .002$) and higher mean scores for TRIG-R items: not able to keep up activities (2.2 vs. 1.6, $p < .04$); difficulty sleeping (2.7 vs. 2.0, $p < .01$); cry at thought of deceased (2.7 vs. 2.0, $p < .002$); and upset at thought of deceased (3.4 vs. 2.6, $p < .01$). QWB mean scores were lower for women (.63 vs. .71, $p < .02$). One year prevalence of major depression was higher in women (60% vs. 31.5%, $p < .01$), but current rates and ratings did not differ.

Conclusion: HIV-bereaved women may have worse grief symptomatology and life quality than their male counterparts. Longitudinal studies need to evaluate whether these differences may influence the course of the HIV illness.

NR3 Monday, May 23, 9:00 a.m.-10:30 a.m.

Suicidality and HIV Status

Stephan F. Baum, M.D., Psychiatry, University of N. Carolina, Campus Box 7160, Chapel Hill NC 27599; Diana O. Perkins, M.D., Carol E. Murphy, M.P.H., Robert N. Golden, M.D., Dwight L. Evans, M.D.

Summary:

Objective: Persons with AIDS are at increased risk for suicide. However, studies are inconclusive in determining if suicidal ideation and suicidal attempts are more common in asymptomatic HIV-infected individuals. We studied HIV-positive asymptomatic and HIV-negative gay men to determine the relationship between HIV status, suicidal ideation, and suicide attempts. We also examined factors that may be predictive of suicidal attempts.

Methods: Subjects were studied at three six-month intervals. At initial visit we studied 108 HIV-positive and 73 HIV-negative gay men. Eighteen-month follow-up data were available for 80 HIV-positive and 56 HIV-negative subjects. Strict inclusion criteria were used to eliminate confounding factors. At each visit subjects were assessed with the SCID-RDC, Brief Symptom Index, and the Modified Life II to determine psychiatric diagnosis, extent of suicidal ideation, suicide attempts, and seriousness of attempts. At the initial visit these factors were assessed retrospectively for the subjects lifetime.

Results: No significant difference was found for lifetime suicidal ideation or seriousness of intent by serostatus ($p = 0.44$, $p = 0.096$). Although thoughts of death and dying were significantly greater in HIV-positive subjects ($p = .026$), thoughts of ending their lives were not significantly greater ($p = 0.29$). Lifetime suicide attempters did not significantly differ by HIV status ($p = 0.11$). In the eight subjects who made attempts during the study, serostatus was not significant ($p = 0.57$). The presence of a personality disorder was significantly greater in attempters compared to non-attempters ($p = 0.05$). The presence of lifetime major depression was not significantly greater in the attempter group as a whole ($p = 0.1$), but was significant in HIV-positive attempters ($p = 0.04$). The mean age of attempters during the study was significantly younger than nonattempters ($p = .005$).

Conclusion: Risk factors that were found to be significant in predicting suicide attempts in gay men include younger age, the presence of lifetime major depression in combination with HIV-positive status, and the presence of a personality disorder. No significant correlation was found between HIV status and lifetime suicidal ideation, seriousness of intent, or presence of a suicide attempt. HIV-positive status by itself in asymptomatic gay men does not appear to significantly influence attempted suicide.

NR4 Monday, May 23, 9:00 a.m.-10:30 a.m.

Apathy and Psychomotor Functioning in A-Symptomatic HIV-Seropositive Gay Men

Stephan F. Baum, M.D., Psychiatry, University of N. Carolina, Campus Box 7160, Chapel Hill NC 27599; Susan G. Silva, Ph.D. Robert A. Stern, Ph.D., Nicole Chaisson, B.A., Robert N. Golden, M.D., Dwight L. Evans, M.D.

Summary:

Recent studies indicate that subtle cognitive and motor disturbances observed in early asymptomatic HIV infection cannot be attributed to depression. However, it remains to be determined whether these early neurobehavioral changes are associated with the symptom of apathy, which has both psychiatric and neurologic etiologies. We evaluated apathy level and psychomotor function in 37 asymptomatic HIV-seropositive (HIV+) and 17 HIV-seronegative (HIV–) gay men. Strict exclusion criteria were used to preclude confounding effects of substance abuse, head injury, CNS disorder, learning disability, or psychiatric illness. Apathetic behav-

ior was measured using the Apathy Evaluation Scale (AES); depression was assessed using the 17-item Hamilton Rating Scale (HamD). A psychomotor score, derived from a principal components analysis of neuropsychological test scores, was used to evaluate psychomotor speed. Psychomotor functioning was further examined using processing and efficiency scores derived from the 2 and 7 Selective Attention Test. Between-group differences were not detected on any psychiatric (t tests) or neurobehavioral (ANCOVAs) measures. Among the HIV+ subjects significant spearman correlations (r_s = .37 to .45, $p \leq .05$) were found between AES score and psychomotor speed, efficiency and processing variables. Greater apathy was associated with psychomotor slowing and a decrease in parallel processing in the HIV+ group, but not in the HIV- group. No significant correlations between HamD and psychomotor performance existed in either group.

The results suggest that early HIV infection produces subtle CNS changes that enhance interactions between neurobehavioral processes mediating apathy and psychomotor functioning. These findings are consistent with previous studies indicating that early HIV infection results in subcortical and/or frontal system dysfunction.

NR4A Monday, May 23, 9:00 a.m.-10:30 a.m.

Attitudes and Preferences Regarding Treatment Among AIDS Patients: Minority Issues

Kenneth B. Ashley, M.D., NYU, Bellevue Hospital, Department of Psychiatry, 1st Avenue and 27th Street, 19W19, New York, NY 10016; Joel J. Wallack, M.D., Murray Alpert, Ph.D.

Summary:

Psychiatric morbidity, attitudes, and preferences towards treatment, and specific issues in treatment among HIV-infected African Americans and Latinos have not been extensively studied. We conducted a pilot study under the auspices of the APA Psychiatric Minority Research Training Program utilizing two outpatient AIDS clinics in Manhattan. Patients were given original demographic and attitude/preference questionnaires and four self-report scales—the Millon Clinical Multiaxial Inventory (MCMI-II), the Bleck Depression Inventory (BDI), the Symptom Checklist-90-Revised (SCL-90-R), and the Zung Self-Rating Anxiety Scale (SAS). The MCMI-II revealed 82% of patients met criteria for a personality disorder and 35% a diagnosis of substance abuse. The BDI revealed 20% of patients met criteria for moderate-severe depression, with the Zung SAS identifying anxiety in 21% of patients. Of the first 32 patients, preliminary results revealed that if referred for psychotherapy 80.6% preferred individual supportive/exploratory therapy, and 54.8% expressed opposition to referral for group psychotherapy.

The goal of this continuing study will be to make recommendations regarding the design and implementation of intervention and treatment strategies specific for these subpopulations infected with the AIDS virus.

NR5 Monday, May 23, 9:00 a.m.-10:30 a.m.

Diazepam Loading: A Novel Technique for Alcohol Detoxification

Todd R. Cheever, M.D., Psychiatry, VA Medical Center, 2250 Leestown Road, Lexington KY 40511; Mark C. Hyatt, M.D., William Fisher, M.D.

Summary:

Objective: The authors' goal was to evaluate the efficacy and safety of an alcohol detoxification technique employing diazepam loading where drug administration was based on the level of diazepam induced intoxication, not alcohol withdrawal symptoms.

Method: Twenty-five male veterans presenting to the hospital for alcohol detoxification were administered 20 mg p.o. of diazepam at the first sign of alcohol withdrawal. Withdrawal and intoxication assessments were done hourly for the next 12 hours. Subjects were administered additional 20 mg p.o. doses of diazepam every one to two hours in order to maintain a specified level of intoxication. After the initial 12hour diazepam loading period, additional diazepam was administered only upon the emergence of prominent alcohol withdrawal symptoms.

Results: The mean period of diazepam administration was 8.7 hours (SD: 2.8). The mean dose of diazepam was 152 mg (SD: 51). None of the subjects required diazepam beyond the 12hour loading period. There were no diazepam intoxication or alcohol withdrawal related complications noted with this technique.

Conclusion: The results suggest that this technique provides an effective, safe, and timely detoxification from alcohol that will decrease detoxifying drug administration time and hence, shorten hospitalization.

NR6 Monday, May 23, 9:00 a.m.-10:30 a.m.

Substance Use and Psychiatric Disorders in Adolescents

Deborah Deas-Nesmith, M.D., Psychiatry, Med. Univ of South Carol., 171 Ashley Avenue, Charleston SC 29425; Kathleen Brady, M.D., Mark Wagner, M.D., Sallie Campbell, M.S.W.

Summary:

Few studies have investigated the co-existence of substance use disorders, and psychiatric disorders in adolescents. To expand the knowledge base in this area, we assessed adolescents presenting for treatment to an inpatient substance abuse treatment facility (SUH), an inpatient psychiatric facility (IPH), and a community based psychiatric facility (CMHC) for comorbid substance use and psychiatric diagnoses. Thirty subjects from each facility (total n = 90) were interviewed using the revised Child Schedule for Affective Disorders and Schizophrenia (K-SADS), and the Structured Clinical Interview *DSM-III-R* (SCID-R) for substance use diagnoses. The average age of subjects at the SUH was 15.3; 14.9 at the CMHC; and 15.4 at the IPH. 90% (27/30) of the adolescents in the SUH had a comorbid psychiatric and substance use disorder. 30% (9/30) of the CMHC, and 27% (8/30) of the IPH adolescents had a comorbid substance use and psychiatric disorder. The average age of onset for substance use was 13.1 CMHC, 12.7 SUH, and 13.0 IPH respectively. There were significantly ($p \leq .01$) more anxiety disorders in both inpatient groups when compared to the outpatient group. Social phobia appeared significantly ($p \leq .01$) more in the inpatient groups. 62% of adolescents in the IPH group with social phobia had a comorbid substance use diagnosis, and 40% of adolescents at the SUH had social phobia. There was no difference in the number of affective disorders between the groups. There was a trend ($p \leq .10$) toward more disruptive disorders in the inpatient groups. Both CMHC and IPH had significantly ($p \leq .05$) more past psychiatric hospitalization than SUH. There was no difference in past medical hospitalization, or trauma (physical and/or sexual) between the groups. The IPH group had significantly ($p \leq .01$) more past suicide attempts than both CMHC and SUH. Surprisingly, both the IPH and CMHC groups had significantly ($p \leq .05$) more family substance use histories than the SUH groups. There was a trend ($p \leq .10$) toward more family medical history in the CMHC and IPH groups. Comorbidity among adolescents presenting in different treatment settings warrants further investigation.

NR7 Monday, May 23, 9:00 a.m.-10:30 a.m.

A New Method to Screen for Anabolic Steroid Abuse

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Summary:

Anabolic steroids may precipitate major mood syndromes, violent behavior, and possibly substance dependence. However, steroid users are often secretive and may not reveal their history to the clinician. We report a simple method by which a clinician can test whether an athlete's muscularity falls within the naturally attainable range, or whether it exceeds that which could be expected without pharmacological assistance.

In an examination of 157 athletes, comprising 83 (53%) steroid users and 74 (47%) non-users, lean body mass index (LBMI) was calculated on the basis of height, weight, and body fat from skinfold measurements, then normalized to the height of a 1.8 meter athlete. Each athlete's history of steroid use was obtained by detailed personal interview, supplemented by urine testing. Urine test results were consistent with verbal history for all subjects. Height and percent body fat did not differ significantly between the two groups, but the steroid group was dramatically heavier in weight and LBMI ($p < .0001$ for both comparisons). Normalized LBMI values for non-users all fell below a sharp limit of 25.0, whereas 37 (45%) of the users exceeded this limit. Thus, an LBMI of greater than 25.0 strongly suggests surreptitious steroid abuse.

NR8 Monday, May 23, 9:00 a.m.-10:30 a.m.

Comparison of Sleep Architecture for Stimulant and Alcohol Abusers in Acute Withdrawal

Peter M. Thompson, M.D., Psychiatry, UCSD VAMC, 9500 Gilman Drive 0603, La Jolla CA 92037; Shahrokh Golshan, Ph.D., Michael R. Irwin, M.D., Christian J. Gillin, M.D.

Summary:

Purpose: Is the phenomenology of withdrawal similar in alcoholics and stimulant abusers? We compared polygraphic sleep measures in primary alcoholics and stimulant abusers. We hypothesized that stimulant abusers would sleep more than alcoholics during relatively acute withdrawal.

Methods: We compared the sleep EEG patterns for 14 stimulant abusers (7 cocaine, 4 amphetamine, 3 with both) and 16 age-matched primary alcoholics. All subjects were inpatients and were studied in an independent group design between one to nine days after last drug use (Phase 1: 8 stimulant abusers, 7 alcoholics) or 10 to 14 days after last drug use (Phase 2: 6 stimulant abusers, 9 alcoholics). Data were analyzed by a two-way ANOVA.

Results: Four statistically significant interaction effects were found: consistent with our hypothesis, compared with alcoholics, stimulant abusers showed greater total sleep, Stage 2, and sleep efficiency at Phase 1 and less at Phase 2. In all measures, however, values for patients were less than in normal controls. In contrast, duration of the first REM period tended to be greater than normal in all patients; from Phase 1 to Phase 2, it decreased in alcoholics and increased in stimulant abusers.

Conclusions: Our data on sleep support the hypothesis that withdrawal differs in alcoholics compared with stimulant abusers. Different physiological mechanisms may underlie withdrawal in these two substances.

NR9 Monday, May 23, 9:00 a.m.-10:30 a.m.

Alcoholics in General Hospital Evaluation and Treatment

Cecelia P. Kane, M.D., Psychiatry, Emory University, 490 Peachtree Street 561-C, Atlanta GA 30308; Francis J. Kane, M.D.

Summary:

Objective: This study reports a retrospective evaluation of general hospital patients hospitalized with alcohol related medical disorders.

Methodology: 1993 admissions with alcohol related disorders were reviewed in three Atlanta General Hospitals (pancreatitis, cardiomyopathy, hepatitis, etc.). Charts were evaluated for (1) presence of alcohol diagnosis, (2) mental status evaluation, (3) psychiatric consult, (4) referral, (5) counseling re-alcohol therapies, (6) therapy for withdrawal state. The initial hospital sample reviewed all possible diagnoses that a hospitalized alcoholic might have. The other two samples took those with known diagnoses.

Results: Our initial sample showed that 10 of 40 patients admitted with alcohol related problems did not have an alcohol related diagnosis on discharge. Only 17% had an evaluation of mental status, while 15% had psychiatric consultation. 17% of charts mentioned referral to treatment. 22% mentioned counseling, most of which represented telling the patient not to drink. 16/31 received needed detox, in six of whom it was judged to be poorly done. 29 had multiple admissions for the same problem. The other hospital samples were not significantly different.

Our data confirm prior reports of under-diagnosis and under-treatment of alcoholic patients, probably related to poor training in recognizing and treating psychiatric disorders during specialty training.

NR10 Monday, May 23, 9:00 a.m.-10:30 a.m.

Substance Abuse/Dependence in Pregnancy: New Jersey Obstetrical Deliveries, 1984-1988

Mary Elizabeth Witt, M.D., Child Psychiatry, UMDNJ-RBT Wood John, 24 New Street, South River NJ 08882; Mary B. Breckenridge, Ph.D.

Summary:

Objective: To gain information about the statewide prevalence of substance abuse/dependence (SA/D) in pregnancy over a five-year period.

Method: Hospital claims data for all obstetrical deliveries in New Jersey, 1984–1988 (N = 515,200) were analyzed in collaboration with the Peer Review Organization of New Jersey.

Results: ICD-9-CM code 648.3 (drug dependence in pregnancy) and/or specific codes for SA/D (291–2,303–5) were found in 2,717 women (0.5%). Of these, 696 or 25.6% were also coded for mental disorders in pregnancy (648.4), a code which includes drug-related diagnoses as well as psychiatric disorders, or were coded for a specific mental disorder. Mental disorders in pregnancy (648.4) without a code for SA/D was found in an additional 1277 women.

Although coding for opioid use increased slightly over the five years, cocaine showed a prominent rise, and was the most common substance recorded. Age-specific rates of SA/D were highest in the 20–24 year age group.

Women with codes for drug dependence or specific drug abuse had more than three times the rate of complicated cesarean deliveries (14.8%) and more than twice the rate of complicated vaginal deliveries (11.1%) in comparison with women without SA/D codes. Also fetal distress was reported in 13.3%, premature labor in 18.5%, cord complications in 18.5%, and placental abruption in 2.1%.

Conclusions: Hospital claims data may be a useful source of statewide information about the prevalence and delivery characteristics of women with substance abuse/dependence.

NR11 Monday, May 23, 9:00 a.m.-10:30 a.m.

Disulfiram Improves Quality of Life in Alcoholics

Maria Gerber, Psychiatrische Univ, Murten Strasse 21, Poliklinik, Bern CH 3010, Switzerland; Peter Widler, M.D., Richard Joyce, Ph.D., Hans-Ulrich Fisch, M.D.

Summary:

Background: Alcoholism has a major impact on aspects of life relevant to individual QoL. Perceived increase of QoL during treatment may encourage the patient to further abstinence, but the effect of treatment on QoL in alcoholism has apparently not been previously studied.

Material and Methods: The administration of disulfiram (3 × 400mg/week) to 20 consecutive outpatients with alcoholism of longer than five years and moderate alcoholic liver disease was supervised by a trustee, in collaboration with the family physician. QoL was measured with the Schedule for Evaluation of Individual Quality of Life (SEIQoL) [1,2]. QoL and liver function were assessed at baseline and after six months. QoL was also assessed in 20 volunteers matched for sex, age, education, and social status.

Results: For patients and volunteers, respectively, SEIQoL scores were 59 ± 12 (73 ± 10) at baseline and 70 ± 10 (74 ± 7) after six months: at baseline, but not after six months, patient QoL was significantly lower than that of volunteers (ANOVA $p < 0.01$). Patient bilirubin, GGT, ASAT, and MCV all returned to normal in this period.

Conclusions: Supportive treatment of ambulatory alcoholics with disulfiram improved the individual perception of QoL and liver function. QoL may be an important, relevant, and sensitive criterion for the assessment of treatment efficacy in alcoholism.

NR12 Monday, May 23, 9:00 a.m.-10:30 a.m.

Early Penetrating Sexual Abuse and Early Intravenous Drug Users

William C. Holmes, M.D., 170 Idris Road, Merion PA 19066; Barbara C. Bix, M.D.

Summary:

Objective: To examine if initiation of IPSUD in HIV seropositive and at-risk, seronegative individuals, occurs earlier in those with a history of early PSA.

Methods: 103 HIV-seropositive and 43 seronegative, at-risk—history of HIV risk behavior as defined by 1987 CDC criteria—enrolled in a psychiatric prevalence study. All subjects were male. An intake interview was done to obtain subjects' sociodemographic characteristics and histories of early PSA—forced engagement of a subject in penetrating sexual activity during childhood. Childhood was defined as age less than 11 years. Presence of IPSUD in subject's lifetime was determined using the Structured Clinical Interview for DSM-III-R (SCID-NP-HIV). Early IPSUD defined as beginning before age of 20 years.

Results: Cohort characteristics are: mean age, 38.8 years; 123/146 (84%) gay; 46/146 (32%) nonwhite; 61/146 (42%) below the poverty level; and 23/146 (16%) less than 12 years education. Also, 21/146 (14%) subjects were forceably engaged in early PSA. Compared with other subjects, early PSA subjects were more likely to be gay ($p = 0.024$), nonwhite ($p = 0.006$) and below poverty level ($p = 0.003$). There was no association between HIV seropositivity and early PSA ($p = 0.26$). A greater proportion of early PSA subjects—7/21 (33%) vs. 7/125 (6%)—had a history of early IPSUD ($p < 0.001$). Mean age of IPSUD initiation was 16.2 years (S.D.-2.7) for all early IPSUD subjects—early PSA subjects didn't initiate IPSUD at a significantly lesser age. The odds ratio for early IPSUD in early PSA subjects compared with all other subjects is 8.4 (95% CI – 2.4 to 30.2).

Discussion: Prevalence of early PSA is high in HIV-seropositive and at-risk individuals. There is a significant association between a history of early PSA and early IPSUD. Future research, incorporating qualitative methods, is needed to further define the psychological impact of early PSA as it relates to the subsequent development of early IPSUD. Results could effect HIV risk reduction interventions in this group.

NR13 Monday, May 23, 9:00 a.m.-10:30 a.m.

Outpatient Benzodiazepine Detoxification Using Clonazepam in Methadone Patients

Todd I. Muneses, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Robert P. Schwartz, M.D., Jeannette L. Johnson, Ph.D., Leroy C. Bell, M.D., Nicole E. Posner, B.A.

Summary:

Benzodiazepine dependence is a problem in methadone patients. Clonazepam seems promising for outpatient benzodiazepine detoxification in these patients because of its long half-life, anticonvulsant properties, and relatively low abuse potential. However, there is scant literature on its use in methadone patients. We initiated outpatient benzodiazepine detoxification in six benzodiazepine-dependent methadone patients.

All patients were Caucasian, with a mean age of 37. Five were women. Their mean methadone dose was 70 mg. Four were dependent on a mean of 3 mg alprazolam, and two on a mean of 10 mg clonazepam.

Before detoxification, all patients were administered the State/Trait Anxiety Inventory (STAI) and the Beck Depression Inventory (BDI). The detoxification protocol began with an initial clonazepam dose that was equal to their reported dose of either clonazepam or alprazolam.

This initial clonazepam dose was decreased weekly by 1 mg until reaching 2 mg, and by 0.5 mg thereafter. Patients were seen weekly for repeat BDI, urine drug test, withdrawal symptom checklist, and dose adjustments.

Four of six patients scored above eight on the BDI, indicating moderate to severe depression. All but one scored high (greater than 92 percentile) on the STAI. These high levels of depression and anxiety must be addressed for comprehensive treatment during outpatient benzodiazepine detoxification.

NR14 Monday, May 23, 9:00 a.m.-10:30 a.m.

One-Year Outcome of Early and Late Onset Alcoholics

Sanaa Helmi, M.D., Psychiatry, University Kansas Med Ctr, 3901 Rainbow Blvd., Kansas City KS 66160; Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Elizabeth J. Nickel, M.A., Mikel H. Thomas, M.D., Barry J. Liskow, M.D.

Summary:

In a prospective, one-year outcome study, 360 male alcoholic patients admitted to a VA inpatient alcoholism treatment unit were subdivided into two groups according to the age of onset of problem drinking: early onset ≤ 24 years (N = 197) and late onset ≥ 25 years (N = 163). The two subgroups were compared on multiple dimensions at intake and one year later. At intake, the early-onset group reported a significantly higher incidence of familial alcoholism and other family psychiatric disorder; a more severe alcoholism course, with greater medical and social sequelae; increased prevalence of comorbid psychiatric disorder among probands; higher scores on current and lifetime measures of psycho-

pathology and emotional distress; and greater psychosocial dysfunction. One year later, the early- and late-onset groups showed marked improvement in many areas of functioning, including alcoholism severity that was reduced by 50 percent in both groups. Differences between the early- and late-onset groups were much less striking at outcome, although early-onset alcoholics continued to show somewhat greater sociopersonal impairment and abusive drinking after 12 months. Contrary to expectation, age-of-alcoholism-onset proved to be a relatively poor *predictor* of one-year outcomes despite its efficacy as a powerful *postdictor* of clinical history. Our results support recent findings suggesting that alcoholism typologies based upon a single dimension, such as age of onset, are probably of limited utility to clinicians because they do not accurately predict the future course of abusive drinking.

NR15 Monday, May 23, 9:00 a.m.-10:30 a.m.

Neuroanatomical Studies of Addiction

Herbert W. Harris, M.D., Psychiatry, Yale University, 34 Park Street Room 323E, New Haven CT 06519; Eric J. Nestler, M.D.

Summary:

Inbred Lewis (LEW) and Fischer (F344) rat strains have served as models of mechanisms of addiction. LEW rats show greater inherent preference for opiates, cocaine, cannabinoids, and alcohol than do F344 rats. In comparison to F344 rats, LEW rats also have higher levels of tyrosine hydroxylase (TH) and lower levels of neurofilament proteins in the ventral tegmental area (VTA); and higher levels of the cAMP pathway and lower levels of TH in the nucleus accumbens (NAc). To investigate structural correlates of these biochemical changes, immunohistochemical studies of VTA dopaminergic neurons in these strains were undertaken. Results show that the density of TH-positive neurons in the VTA in LEW rats is about 50% of that found in F344 rats ($n = 6$, $p < 0.01$). In contrast, examination of substantia nigra in the same sections revealed no differences in the density of TH-positive cells between these strains. These anatomical findings shed new light on the functional differences between LEW and F344 rats that may be associated with drug preference. The observation of lower numbers of TH-positive VTA neurons in the LEW strain is consistent with a model of addiction in which dopaminergic VTA neurons play a central role in the drug-preferring state.

NR16 Monday, May 23, 9:00 a.m.-10:30 a.m.

Role of Parkinsonism and Antiparkinsonian Therapy in the Subsequent Development of Tardive Dyskinesia

Kelly Elliott, B.S., Psychiatry, Univ of Florida Sch Med., 500 South Preston, Louisville KY 40292; Rif S. El-Mallakh, M.D., Susan Lewis, Ph.D., Stephen W. Looney, Ph.D., Robert Caudill, M.D., Teresita Bacani-Oropilla, M.D.

Summary:

Tardive dyskinesia (TD) is a side effect of prolonged neuroleptic treatment involving abnormal involuntary movements. This troublesome disorder occurs in only 15% to 30% of patients taking neuroleptics, suggesting that these individuals are physiologically distinct as to be predisposed. This study analyzed possible factors contributing to TD development. Fifty patients on depot neuroleptics for more than 7.1 years were examined for TD and drug-induced parkinsonism (DIP) using the Smith-Trims rating scale for an average of five years. The patients were assessed for the severity of the movement and if the movement increased or decreased with respect to neuroleptic dosage, anticholinergic dosage, parkinsonism, and other related factors. Both the TD and DIP increased over time (TD 4.94, $p < 0.001$, DIP 4.895, $p < 0.001$). In the patients whose dose of neuroleptic decreased, the increase in TD ratings was not significant (1.01). Using a forward step-wise regression DIP was found to increase as TD worsened but did not appear to predict subsequent TD development ($p < 0.01$). Although anticholinergic treatment was also related to the worsening of TD, its correlation with the change in TD ($p < 0.01$) was less significant and is probably a reflection of progressive DIP. These results have implications for the management of combined TD and DIP presentation.

NR17 Monday, May 23, 9:00 a.m.-10:30 a.m.

Treatment and Predictive Factors of Catatonia

Harold W. Goforth, M.A., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus OH 43210; Brendan T. Carroll, M.D.

Summary:

Catatonia is a syndrome of motor signs including mutism, immobility, withdrawal, and others. This syndrome has historically been subtyped under the diagnosis of schizophrenia but primarily appears in affective illness.

Thirty patients were identified in a retrospective case study using four different sets of diagnostic criteria. The criteria used were those defined by Kahlbaum, Rosebush, Lohr, and Wisniewski, and *DSM-IV* respectively, with twenty-six patients satisfying at least one of the three more stringent sets. Catatonia was secondary to medical illness, in three of the 30 cases.

Treatment options were generally limited to lorazepam therapy, neuroleptic therapy and/or ECT. Significant findings include: 1) failure of lorazepam therapy predicts a positive response to electroconvulsive therapy; 2) a statistically significant number of patients responded to ECT as defined by a 50% reduction in signs. This trend was not seen in those receiving neuroleptics or lorazepam; and 3) specific diagnostic criteria failed to predict treatment response.

These findings suggest that lorazepam may be used initially in catatonia as both a therapeutic device and a predictor of response. Stringent criteria carried no greater predictive capacity than *DSM-IV* criteria and supports current diagnostic nosology.

NR18 Monday, May 23, 9:00 a.m.-10:30 a.m.

Symptomatic Change After One Week of Treatment and Response to Clozapine in Schizophrenia

Robert G. Stern, M.D., Psychiatry, Mount Sinai Hospital, Box 1228 One Gustave Levy Pl., New York NY 10029; Rene S. Kahn, M.D., Michael Davidson, M.D., Rena M. Nora, M.D., Kenneth L. Davis, M.D.

Summary:

Forty treatment-refractory chronic schizophrenic inpatients (mean age ± SD: 39.1 ± 6.3) completed this five-week clozapine treatment (up to maximum 600 mg p.o/day) study after having given written informed consent. At the end of the five weeks, 18 patients were classified as treatment responders and 22 as non-responders according to a priori established criteria.

A significant reduction in total BPRS ($t = 2.62$; $df = 1,17$; $p < 0.05$), and specific BPRS subscale scores (psychosis: $t = 2.48$; $df = 1,17$; $p < 0.05$; tension: $t = 3.38$; $DF = 1,17$; $p < 0.005$) was found after only one week of clozapine treatment in the eventual responders. In contrast eventual non-responders showed a significant symptomatic worsening after the first week of treatment. Higher BPRS scores at baseline and larger improvements in BPRS scores after the first week were predictive of favorable outcome after five weeks of treatment, and yielded 75% classification accuracy.

The findings of a significant reduction in BPRS scores within the first week of clozapine treatment and of a predictive value to the BPRS baseline and week 1 change scores are consistent with previous studies (1,2).

Thus, the assessment of baseline symptom severity and of symptom changes after the first week of treatment might be helpful when deciding whether the risk of clozapine continuation (in particular the risk for agranulocytosis) is outweighed by the treatment's potential benefits.

NR19 Monday, May 23, 9:00 a.m.-10:30 a.m.

Entorhinal Cortex Volume in Schizophrenia: A Controlled MRI Study

Sarita K. Sharma, B.S., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus OH 43210; Henry A. Nasrallah, M.D., Marla N. Kemmerer, B.S., Robert Martin, Stephen C. Olson, M.D., Mary B. Lynn, M.A.

Summary:

Abnormalities of the entorhinal cortex have been reported in postmortem studies of the brains of schizophrenic subjects. The pathology described includes both gross hypoplasia and histopathologic changes suggestive of impairment in neurodevelopmental processes. We report here the first *in vivo* study of the volume of the entorhinal cortex in schizophrenic patients using MRI scans. We hypothesized that the entorhinal cortex, like other limbic temporal structures, may be hypoplastic in schizophrenia.

DSM-III-R schizophrenic (N = 57, mean age = 32.6 7.1, duration of illness = 9.8 6.1 years) and health volunteer subjects (N = 35, mean age = 29.3 ± 7.6 years) consented to participate in the study. All received brain MRI scans (GE 1.5 Tesla, TI = 800 MS, TR = 1500 MS). Consecutive coronal sections in which the entorhinal cortex appears were traced on a computer image analysis system and the volume calculated on the right and left.

Schizophrenic and control groups were compared using ANOVA and the effect of diagnosis, gender, side, and duration of illness examined.

There were no differences in the mean volumes of the entorhinal cortex between mean schizophrenia (2.218.015) and controls (2.208 ± .018). No effect by any of the parameters considered were noted except for a trend for schizophrenic females to be larger than control females (P = .078).

The data suggest that although there may be morphological or histological abnormalities in the entorhinal cortex in schizophrenia, there may be no significant differences in volume.

NR20 Monday, May 23, 9:00 a.m.-10:30 a.m.

Increased Hippocampal Volume in Bipolar Disorder

Marla N. Kemmerer, B.S., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus OH 43210; Henry A. Nasrallah, M.D., Sarita K. Sharma, B.S., Robert Martin, Stephen C. Olson, M.D., Mary B. Lynn, M.A.

Summary:

Bipolar disorder has been associated with structural brain abnormalities similar to those found in schizophrenia. These include ventricular enlargement, sulcal widening as well as cerebral and cerebellar hypoplasia. However, there have been no studies of the volume of the hippocampus in bipolar disorder, although several studies describe a reduced size of the hippocampus in schizophrenia. Here we report a controlled study of hippocampal volume in bipolar disorder. We hypothesized that limbic structural hypoplasia may also be observed in bipolar disorder. *DSM-III-R* bipolar patients (N = 29, mean age = 32.7 ± 6.3, duration of illness 10.1 ± 7.8 years) and healthy volunteer subjects (N = 35, mean age = 29.3 ± 7.6 years) consented to participate in the study. All received brain MRI scans (GE 1.5 Tesla, TI = 800 MS, TR = 1500 MS). Consecutive coronal sections in which the hippocampus appears were traced on a computer image-analysis system and the volume calculated on the right and left. Bipolar and control groups were compared using ANOVA and the effects of diagnosis, side, age, and duration of illness were examined.

There was a significant effect of diagnosis on hippocampal volume in bipolar (343.9 mm^3) and control (221.4 mm^3) groups ($p = .031$). The left hippocampal was significantly larger than the right across samples ($p = .028$). No effect of gender, age or duration of illness were observed. The data suggest that in contrast to what has been reported in schizophrenia, hippocampal volume is *increased* in bipolar disorder. The possibility that such a limbic abnormality may account for differences in clinical pathology in bipolar disorder vs schizophrenia are discussed.

NR21 Monday, May 23, 9:00 a.m.-10:30 a.m.

Short- and Long-Term Outcome in First-Episode and Chronic Schizophrenia

Fiona Gallacher, M.S., Psychiatry, Univ of Penn. 10th Flr., 3400 Spruce Street Gates Bldg, Philadelphia PA 19104; Derri L. Shtasel, M.D., Roland J. Erwin, Ph.D., Bruce Turetsky, M.D., Kimberly A. Hambrose, R.N., Raquel E. Gur, M.D.

Summary:

Objective: Previous studies reported that first-episode patients with schizophrenia have better treatment outcomes than chronic patients. It was hypothesized that first-episode patients have poorer treatment outcomes early in the course of illness.

Methods: Subjects were 18 first-episode (FE) neuroleptic naive patients and 12 chronic (CS) previously medicated patients (off medications for at least two weeks at intake). Symptoms and functioning were assessed using the Brief Psychiatric Rating Scale (BPRS), and the Strauss-Carpenter Level of Function Scale (LEV) during an acute state (intake), short-term follow-up (six months), and long-term follow-up (two to five years).

Results: Clinical profiles of FE and CS patients were contrasted using LEV and BPRS change scores for short- and long-term follow-up. FE patients showed less improvement in level of function at short-term follow-up ($F(1,28) = 4.64$, $p < .04$). No significant differences in BPRS measures across groups were obtained. However, there was a positive relationship between FE patients' BPRS and LEV scores at intake ($r = .70$, $p < .001$).

Conclusion: These results suggest that FE patients take time to resolve functioning and that FE patients with high pre-morbid level of function present with more severe symptoms at intake. Both patterns may relate to lack of adaptation to illness.

NR22 Monday, May 23, 9:00 a.m.-10:30 a.m.

Effects of Naltrexone on Stereotypic Behaviors

Julia A. Becker, M.D., Psychiatry, University of Chicago, 4841 S. Maryland Avenue MC3077, Chicago IL 60637; Morris B. Goldman, M.D., Daniel J. Luchins, M.D., Mohammed Y. Alam, M.D.

Summary:

Objective: To determine if the opiate antagonist naltrexone diminishes the severity of polydipsia and other stereotypic behaviors in chronic schizophrenics.

Method: Eight polydipsic male chronic schizophrenics on an inpatient psychiatry research unit received naltrexone 25mg po BID for six weeks in an open label trial, following a two-week baseline. Patients were maintained on a stable dose of neuroleptics throughout the study. The frequency of six stereotypies (hoarding, pica, polydipsia, pacing, bulimia, and mannerisms), plasma osmolality, and AM and PM urine dilution were determined

three times weekly. Ratings were based on eight-hour observations and were performed by trained staff. Positive and negative symptoms scale (PANSS) ratings were performed weekly.

Results: Total repetitive behaviors declined over the six weeks of treatment from a level of moderately severe to moderate (random effects regression linear trend $z = 2.65$, $p < .008$). Polydipsia declined slightly from its moderate baseline levels (linear trend $z = 2.43$, $p < .013$), and diurnal weight gain fell from 5.0 ± 4.9 lb to 3.0 ± 6.3 lb at the study's end (linear trend $z = 3.38$, $p < .001$), but neither plasma osmolality nor urine dilution changed. PANSS ratings were unchanged.

Conclusion: Opiate antagonists appear to diminish stereotypic behaviors, and maximal effects may require more than six weeks. Water balance may subtly improve, but the clinical significance is unclear. Placebo-controlled studies are warranted to verify these impressions.

NR23 Monday, May 23, 9:00 a.m.-10:30 a.m.

Executive and Motor Impairments in Schizophrenia: Relation to Increased Spread of Activation in Semantic Networks

John H. Poole, Ph.D., VA Medical Center 116W, 4150 Clement Street, San Francisco CA 94121; Sophia Vinogradov, M.D., Emily Marton, B.A., Beth A. Ober, Ph.D., Gregory K. Shenaut, Ph.D.

Summary:

The present study compared executive and motor abilities to linguistic information processing in 23 unmedicated *DSM-III-R* schizophrenic outpatients and 21 demographically and IQ-matched normal controls. Subjects were administered the Wisconsin Card Sort Test (WCST, a measure of cognitive flexibility), an operationalized neurological examination of fine-motor and executive-motor abilities (related to frontal lobe function), and a semantic priming task (measuring facilitation of word recognition by presentation of categorically related words). Schizophrenic subjects showed significantly more perseverative errors on the WCST and more frequent motoric soft signs than controls. However, heterogeneity was evident among schizophrenics, prompting their division into a Normative Group (unimpaired WCST and motor exam, $n = 9$) and a Deficit Group (impaired WCST and/or motor exam, $n = 14$) for further analyses. The two groups differed significantly in semantic-priming effects: The Deficit Group showed normal or hyper-priming of automatic semantic information processing, with diminished priming in the controlled realm. The Normative Group showed a trend toward subnormal priming of automatic processing, with normal or increased priming of controlled processing. These preliminary findings suggest that the presence of executive and motor deficits in schizophrenia may be related to increased automatic spread of semantic activation immediately following linguistic input. Schizophrenics with unimpaired executive and motor abilities appear to have different abnormalities in the processing of linguistic stimuli. Clinical profiles characterizing these two groups will also be presented.

NR24 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Impact of Self-Medication on the Knowledge of Discharge Medications in the Psychotic Patient

Douglas N. Shaffer, M.D., Psychiatry, Univ of North Carolina, 805 B6 Park Ridge Road, Durham NC 27713; Avni Cirpili, M.S.N., John H. Gilmore, M.D., Diana O. Perkins, M.D.

Summary:

Objectives: Medication awareness is essential to patients with psychotic disorders with ramifications upon compliance, relapse, and optimal functioning. In a retrospective study, we examined the impact of "self-medications" upon the ability to list prescribed medications upon discharge from an acute psychiatric hospitalization.

Methods: 27 patients (mean age = 28 ± 9; male 60%, female 40%) with *ICD-9* diagnoses of schizophrenia, schizoaffective disorder, or psychotic disorder NOS were asked to list their prescribed medications. All patients received education about their illness and medications in both group and individual settings. Twelve patients (44%) were placed on "self-medication"—designated to self-administer their medication under nursing supervision.

Results: Patients placed on "self-medication" knew a greater percentage of their discharge psychotropic medications compared to those not on "self-medication" (97% and 81%, respectively, $p = 0.058$). Similarly, more patients on "self-medication" knew all of their psychotropic medications (92% and 63%, respectively, $p = 0.08$). There were trends for other factors, including lower age, lesser number of medications, and female gender to be associated with greater ability to list discharge medications.

Conclusions: "Self-medication" during hospitalization is associated with improved ability to list discharge medications. Further prospective studies are needed to examine the impact of "self-medication" on medication knowledge and compliance in patients with chronic psychotic disorders.

NR25 Monday, May 23, 9:00 a.m.-10:30 a.m.

Neuroleptic Response at the Onset of Psychosis

Russell E. Scheffer, M.D., Psychiatry, D.D.E. Army Med Center, Fort Gordon GA 30905; Elizabeth Correnti, M.D., Sukdeb Mukherjee, M.D.

Summary:

There is evidence that duration of psychosis prior to initiation of neuroleptic treatment influences the quality of therapeutic response. We therefore undertook a study of response to naturalistic neuroleptic treatment in patients admitted at the D.D. Eisenhower Army Medical Center for a first episode of psychosis. All 16 patients had a very short duration of psychosis (mean duration 4.8 ± 2.5 days; range 2–10) at the time of admission. The Brief Psychiatric Rating Scale was used to measure clinical change. There was a significant decrease from baseline to week 3 in BPRS total score ($p = .02$) and positive symptom score ($p = .003$), but not in negative symptom score ($p = .45$); with no further change from week 3 to week 6 in any of the measures ($p > .60$ for all). Positive and negative symptom scores were significantly correlated at baseline ($p < .01$), but their changes were not correlated at any time point. Thus, close to the onset of psychosis, therapeutic effects of neuroleptic treatment occur uniformly and rapidly for positive symptoms, but not for negative symptoms. This is consonant with positive and negative symptoms reflecting discrete dimensions of pathology.

NR26 Monday, May 23, 9:00 a.m.-10:30 a.m.

Serotonin Function in Drug Naive Schizophrenics

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Summary:

A role for serotonin dysregulation in psychosis has been proposed, and appears to be supported by the efficacy of atypical neuroleptics. Platelet imipramine binding sites, a model of presynaptic serotonin reuptake sites, may be useful as a peripheral marker of central serotonin function. We undertook a study of tritiated imipramine binding in platelets from 13 drug-naive, first-episode, schizophrenic patients and nine matched normal con-

trols. Patients were studied at baseline and after three weeks of naturalistic neuroleptic treatment, and were unique in their very short duration of psychosis (4.6 ± 2.6 days) at admission to D.D. Eisenhower Army Medical Center. Baseline Bmax and Kd were significantly lower in patients than in normal controls ($p < .01$ for both), but did not show a significant change after three weeks of treatment ($p > .60$ for both). There was a trend for Bmax to be correlated with plasma homovanillic acid levels ($p = .06$) at baseline, but not with BPRS positive or negative symptom scores. However, increase in Bmax was correlated ($p < .05$) with decrease in positive symptom scores after treatment. These are consonant with a role for serotonergic function in psychosis and response of positive symptoms to neuroleptic treatment.

NR27 Monday, May 23, 9:00 a.m.-10:30 a.m.

Reduced Left Hemisphere Dominance for Language in Schizophrenia: Relation to Positive Symptoms

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Summary:

Objective: Given recent reports of left temporal lobe deficits in schizophrenia, this study investigated the relationship of cerebral dominance for language and positive vs. negative patient symptomatology on the PANSS (Kay, Opler, & Fishbein, 1992). A secondary aim examined neuroleptic effects on task performance.

Method: Subjects included 25 psychotic patients (22 schizophrenic/paranoid, three schizoaffective/bipolar) from the Schizophrenia Research Unit at New York State Psychiatric Institute (NYSPI), 65 nonpsychotic depressed patients from an outpatient Depression Evaluation Service at NYSPI, and 85 normal subjects. Research diagnoses were determined using clinical and semi-structured interviews by trained raters and consensus with senior clinicians. Psychotic patients, either on 10–15 mg. of haloperidol or four-week medication withdrawn, were tested on the Fused Rhymed Word test (Wexler et al., 1991) in which words differing in the initial consonant were simultaneously presented to both ears. The number of correctly identified right- or left-ear words provided a laterality index.

Results: Mean left hemisphere dominance differentiated schizophrenics from both depressives ($p < .05$) and controls ($p < .01$). Reduced left hemisphere dominance was associated with positive, but not negative symptoms of schizophrenia ($p < .025$). Medication status proved insignificant.

Conclusion: These findings are consistent with recent neuroimaging and electrophysiologic evidence of left temporal lobe deficits in schizophrenics with predominant positive symptoms.

NR28 Monday, May 23, 9:00 a.m.-10:30 a.m.

Blood-Brain Barrier Permeability in Schizophrenia

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Summary:

Objective: A number of studies of psychotic subjects (most of whom were schizophrenic) indicate that a significant subgroup of these patients have evidence of increased blood-brain barrier (BBB) permeability as determined by measurement of the cerebrospinal fluid (CSF)/serum albumin ratio. The goal of this study was to determine whether single photon emission tomography (SPECT) using the radioligand technetium (Tc-99m) gluceptate is a viable method with which to assess the functional integrity of the BBB in schizophrenic patients.

Method: In a university hospital setting, all subjects underwent the Structured Clinical Interview for the DSM-III-R. Ten medicated schizophrenic and 10 matched normal controls were selected, and underwent a SPECT scan. Tc-99m gluceptate was administered intravenously, and SPECT imaging was performed at 5 minutes, at 30 minutes, and at 60 minutes post injection. SPECT at 5 minutes was used as a baseline, and the amount of radioactivity leaked into the brain parenchyma was quantitated at 30 and 60 minutes after subtraction of radioactivity within the scalp, skull, and vascular structures.

Results: Preliminary data analysis does not reveal differences between schizophrenic and normal subjects in brain parenchymal radioactivity.

Conclusions: First, the hypothesis that in schizophrenic subjects elevated CSF/serum albumin ratios are due to increased BBB permeability may not be correct. Second, if the hypothesis is correct and there is increased BBB permeability in schizophrenia, SPECT using Tc-99m gluceptate does not appear to be a sufficiently sensitive tool with which to measure it.

NR29 Monday, May 23, 9:00 a.m.-10:30 a.m.

Early Weight Gain During Clozapine Treatment as Predictor of Response

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Summary:

Clozapine-induced weight gain has been reported to correlate with treatment response. We hypothesized that early weight gain might be a useful clinical predictor of eventual response to clozapine.

Methods: In 69 patients weekly weights during the first eight weeks of open clozapine treatment were compared (repeated measure ANOVA) between responders and nonresponders for the whole group and for those 31 patients classified as responders/nonresponders only after at least 10 weeks of treatment ("late" response group). In the latter group the sensitivity and predictive power of weight gains of more than 10%, 15% and 20% by week 6, 7, and 8 to identify later responders were calculated. Psychopathology was assessed with BPRS and CGI.

Results: In both groups responders showed greater mean absolute and relative (%) weight gain. However, differences were not statistically significant. In the "late" response group a weight gain of 15% or more by weeks 6, 7, or 8 identified significantly more responders than nonresponders, while BPRS scores did not yet differ. While the predictive value was high, sensitivity was modest.

Conclusion: In patients without early response considerable early weight gain may predict later response. A weight gain of 15% or more by week 6 is a better predictor of later response than the BPRS score at that time.

NR30 Monday, May 23, 9:00 a.m.-10:30 a.m.

Suicidality in Recent Onset Schizophrenia

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Summary:

Objective: Approximately 10% of individuals with schizophrenia die by suicide, and the period of greatest risk is the first decade of illness. While anxiety and depression are increased in schizophrenia, their temporal interaction with suicidality is poorly understood. This is a study of the temporal course of suicidality and of the interrelationship among suicidality, anxiety, and depression in a population with recent-onset schizophrenia.

Method: This study was part of an intensive longitudinal project examining neuropsychological measures, symptoms, and medication effects in recent-onset schizophrenics. Subjects were rated every two weeks for one year using the Brief Psychiatric Rating Scale, which was augmented to assess suicidality.

Results: Suicidal behavior was less frequent than in most epidemiologic studies. Most suicidal subjects had at least one occurence of significant anxiety and depression during the year; however, many subjects with significant anxiety and depression never became suicidal. The severity of suicidality changed rapidly, and the temporal interrelationship among suicidality, anxiety and depression was complex.

Conclusions: The severity of suicidal ideation and behavior can change rapidly in individuals with recent-onset schizophrenia. Even with biweekly assessment, sudden increases in suicidality make it difficult to predict clinically significant suicidality.

NR31 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Effects of Caffeine and Nicotine on Smooth Pursuit Eye Movements in Schizophrenic Patients

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Summary:

One of the most reported applications of smooth eye movement dysfunction (SPEMD) studies is in the potential use as a phenotypic marker for a gene that increases the susceptability to schizophrenia. We hypothesized that both caffeine and nicotine would have effects on SPEMD based both on their pharmacology and previously reported studies.

Twelve subjects, who were moderate to heavy users of both caffeine and/or nicotine, were examined with regard to their smooth pursuit eye movements. Smooth pursuit gain was measured using an infra-red reflectance method as the subjects tracked a sinusoidally moving target. Measurements of gain were made when the subjects were in acute withdrawal following a 12-hour period of abstinence from both caffeine and nicotine (baseline), and after receiving a test dose of caffeine and again after chewing nicotine resin gum.

A statistically significant decrease in gain from baseline ($p < 0.002$) was seen for schizophrenics, but not controls, after nicotine administration. This caused an increased chance of a subject being classified as having SPEMD. Nonschizophrenic subjects showed a nonsignificant increase in gain in response to nicotine. All nonschizophrenic subjects responded to caffeine with a small but statistically significant increase in gain ($p < 0.01$). Schizophrenic subjects had inconsistent responses to caffeine. The effects of caffeine and nicotine were different between the two groups and this difference is masked if aggregate data were examined.

NR32 Monday, May 23, 9:00 a.m.-10:30 a.m.

Prolactin Level and Clinical Response to Clozapine

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Summary:

The release of prolactin is under tonic inhibitory control of dopamine in the tubero-infundibular area of the brain. While typical neuroleptic drugs routinely elevate serum prolactin levels through antagonism of the D_2 receptor, the atypical neuroleptic clozapine, which produces a weak D_2 blockade, has been reported to have only modest effects on serum prolactin level.

Objective: In a study of 17 treatment-resistant/treatment-intolerant schizophrenic patients treated with clozapine, we evaluated the relationship between changes in serum prolactin level during treatment with clozapine and clinical response to the drug.

Method: Following a 2 1/2- to 6-week drug-free period (benzodiazepines allowed), clozapine was titrated to a therapeutic level of 500–550 mg/day, or to the highest tolerated dose. Symptom assessments were made at drug-free baseline and weekly for 12 weeks with the Brief Psychiatric Rating Scale (BPRS); serum levels of prolactin were evaluated on the same schedule. Clinical response was expressed as percent change in BPRS from baseline to the average score of weeks 12 and 13; change in prolactin level was expressed as the difference between baseline and the average values of weeks 4–12.

Results: In the total group of 17 subjects, mean values of serum prolactin did not change during the study. Nine subjects showed a > 30% decrease in BPRS during treatment (responders); eight subjects had a less favorable response. In the nine responders, six had an increase in serum prolactin level during treatment, whereas in the eight nonresponders, only one patient showed such an increase (Fisher's Exact Test; $p < .05$).

Conclusions: This preliminary study suggests that those patients whose prolactin level increased during clozapine treatment were more likely to respond to clozapine than were those patients whose prolactin level did not increase.

NR33 Monday, May 23, 9:00 a.m.-10:30 a.m.

Detrusor Hyperreflexia in Schizophrenic Patients with Incontinence

David R. Hunter, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52242 William W. Bonney, M.D., Sanjay Gupta, M.D., Stephan Arndt, Ph.D., Nancy C. Andreasen, M.D.

Summary:

This study demonstrates that detrusor hyperreflexia is present in a subset of schizophrenic patients with urinary incontinence.

We previously proposed incontinence as a neurobiological correlate of schizophrenia. Brain imaging studies have shown ventriculomegaly, neural tissue loss, and dopamine dysregulation—abnormalities similar to those seen in normal pressure hydrocephalus, Parkinson's disease and other conditions associated with incontinence and detrusor hyperreflexia on a neurogenic basis.

In a previously reported demographic study we compared hospitalized schizophrenic and mood disorder patients in regard to urological symptoms. Urinary urge incontinence, bed wetting and incontinence of any type were significantly more prevalent in the schizophrenic group, controlling for age, sex, and duration of illness.

In the present study we performed urodynamic studies on 11 schizophrenic patients who presented for evaluation and treatment of troublesome urinary incontinence. Of the 11 patients, eight had detrusor hyperreflexia, involuntary high pressure bladder contractions as the bladder filled. Six leaked with these contractions.

All of these findings support our concept of urinary incontinence as a neurobiological correlate in a subset of schizophrenic patients. Now in progress are controlled studies designed to test the relationships among schizophrenia, urinary function brain abnormalities, and potential confounding variables such as neuroleptic medication.

NR34 Monday, May 23, 9:00 a.m.-10:30 a.m.

Atypical Antipsychotics, Serotonin and Weight Gain

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Harmon, Andrew Berisford, M.A., William C. Wirshing, M.D., Stephen R. Marder, M.D.

Summary:

Objective: Risperidone and clozapine are atypical antipsychotic medications. Their efficacy and lack of extrapyramidal side effects are thought to be due to their ability to block serotonin receptors, particularly serotonin$_2$ receptors. Serotonin$_2$ receptor blockade may account for the weight gain that has been reported in patients treated with these agents.

Method: Weight changes of 21 patients with schizophrenia treated with either clozapine or risperidone and 24 patients with schizophrenia treated with haloperidol deconoate were examined retrospectively. Regression analyses were used to predict total weight gained (the difference between end weight and beginning weight) and maximum weight gained (the difference between the maximum and the minimum weights). Sampling bias was controlled by covarying demographic variables in the regression equation.

Results: A priori selected predictors, drug group and duration of drug treatment, resulted in a significant predictive model for total weight gained ($p = .026$) and maximum weight gained ($p = .012$). Follow-up tests determined that clozapine/risperidone patients gained significantly more weight ($p = .045$) compared with the haloperidol deconoate patients. The duration of treatment was predictive of maximum weight gained ($p = .029$).

Conclusions: Our data are consistent with a serotonergic mechanism as a cause of weight gain in risperidone- and clozapine-treated patients.

NR35 Monday, May 23, 9:00 a.m.-10:30 a.m.

Neurologic Deficits, Tardive Dyskinesia and Medication Status

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Summary:

Objective: Neurologic deficits in schizophrenia may be indicative of either a neurodevelopmental or neurodegenerative etiology. This study was designed to examine the role that medication may play in the development of these abnormalities.

Method: Neurologic soft signs (NSS) were evaluated in 79 schizophrenics and 60 normal controls using a modified version of Heinrich's and Buchanan's neurologic evaluation scale (NES).

Results: The instrument was very sensitive, it detected minor abnormalities in control patients at a rate of 91%. We found that 54% of normals had one rating of 2 or higher, whereas 98% of schizophrenics had a rating of 2 or higher. Schizophrenic subjects had much more severe deficits in terms of overall total score on the NES. There was no relationship between tardive dyskinesia and total NES score ($F = 3.28$, $p < .085$). Nor was there a relationship between medication status and total NES score ($F = .297$, $p < .587$).

Conclusions: Medication status and tardive dyskinesia status appear to be unrelated to neurologic abnormalities assessed using the modified NES. This may indicate that these deficits are neurodevelopmental or possibly neurodegenerative in origin and should be studied over time. The data also demonstrate differences between the relative effect of atypical and conventional antipsychotic medications on the presence of neurologic soft signs.

NR36 Monday, May 23, 9:00 a.m.-10:30 a.m.

Withdrawal-Emergent Dyskinesia in Patients with Schizophrenia During Antipsychotic Discontinuation

Susan K. Schultz, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52242; Steve Ziebell, B.S., Delwyn Miller, M.D., Nancy C. Andreasen, M.D.

Summary:

Tardive dyskinesia, a disorder of abnormal involuntary movements, has been associated with use of antipsychotic medication. Unfortunately, treatment of TD has had disappointing results. If one could use a preventive approach by identifying those individuals vulnerable to the development of TD, this would be of great clinical utility.

Objective: This study investigated withdrawal-emergent dyskinesia (WE-D) as a possible indicator of vulnerability to the development of TD. It is our hypothesis that WE-D represents an early phase of receptor dysregulation leading to persistent TD. We expect the clinical characteristics of this group to resemble those with persistent TD.

Methods: Eighty patients with schizophrenia participated in medication discontinuation. Those with WE-D were compared with those with no dyskinesia, and to those with persistent TD across the following variables: neurologic soft signs, negative symptoms, neuropsychological testing, duration of illness, and antipsychotic exposure. ANOVA was used to compare the groups.

Results: In terms of soft signs, there was no difference between the WE-D and TD group, and a trend for difference from the non-TD group. The WE-D and TD groups were also similar in terms of duration of illness as compared with the non-TD group. Interestingly, the WE-D group did not differ from either group in terms of antipsychotic exposure, but had a longer mean duration than the non-TD group and a shorter duration than the TD group. The TD group did differ from the non-TD group in duration of antipsychotic exposure. We are in the process of a longitudinal follow-up of the WE-D patients to assess subsequent development of TD.

Conclusion: Those persons who do not have TD, but develop dyskinesias on withdrawal of medications, have similar clinical characteristics to those who have persistent TD, and possibly represent a group vulnerable to the development of TD.

NR37 Monday, May 23 9:00 a.m.-10:30 a.m.

Evidence for a Neuroprotective Effect of Benzodiazepines in an Animal Model of Psychosis

Rona J. Hu, M.D., Psychiatry, University of Calif., 401 Parnassus Avenue #0984, San Francisco CA 94143; S. Paul Berger, M.D.

Summary:

Objective: Benzodiazepines have been shown in clinical studies to be useful adjuncts in treatment of schizophrenia and psychosis, and in animal models to be neuroprotective in ischemia. Olney and others suggest that the ability of potent psychotomimetic phencyclidine (PCP) to injure cingulate cortex may be relevant to schizophrenia. We have therefore examined whether benzodiazepines are neuroprotective against PCP-induced injury in animals.

Method: Male Sprague-Dawley rats (N-33) were used. Experiments included low and high doses of diazepam (5mg/kg and 40mg/kg), alprazolam (4mg/kg, 10mg/kg, and 100mg/kg), and lorazepam (8mg/kg). For each dose, half the animals were pretreated with benzodiazepine 30 minutes before receiving PCP 50mg/kg IP. Half were controls, receiving PCP only. All animals were sacrificed 24 hours later, paraformaldehyde perfused, and their fixed brain sections stained using monoclonal antibodies to HSP-70 (heat-shock protein.)

Results: 100% of control animals expressed HSP-70 in neurons of the anterior and posterior cingulate and retrosplenial cortex.

None of the animals pretreated with alprazolam or lorazepam, and only 25% (one of four) of animals pretreated with high-dose diazepam, showed any cortical or subcortical staining.

Conclusions: As heat-shock protein is a powerful marker for neuronal injury, these results suggest that the therapeutic effects of benzodiazepines in psychosis may be related to a protective effect against cortical neuronal injury.

NR38 Monday, May 23, 9:00 a.m.-10:30 a.m.

Working Memory Dysfunction in Schizophrenia

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Summary:

The concept of working memory (WM) has received attention recently as a heuristically useful model in elucidating neuropsychological dysfunction in patients with schizophrenia (SC). This model involves a "central executive," which is responsible for the overall coordination of information processing and two peripheral "slave" systems—the phonologic loop, and the visuospatial scratch-pad—specialized for the short-term retention of phonological and visual information, respectively. We have conducted three separate studies to assess the functioning of each of the WM components in patients with schizophrenia (SC) and normal controls (NC). To investigate the central executive we utilized a modified version of the Brown-Peterson (SC = 15, NC = 13) and found that SC patients exhibited a diminution in overall processing resources. Next, we assessed the visuospatial scratchpad via a spatial-delay task, visual span, and line orientation (SC = 32, NC = 18). The results intimate that whenever memory is necessitated in spatial tasks, SCs perform poorly. Lastly, the integrity of the phonologic loop was investigated with tests of phonological suppression, word length, and phonologic similarity. Results suggested that while the level of performance of this subsystem is deficient, the response to manipulations was lawful (SC = 17, NC = 17). Overall, SCs exhibited impairments in the central executive, and to a lesser degree, in the slave systems.

NR39 Monday, May 23, 9:00 a.m.-10:30 a.m.

Psychosocial Correlates of Chronic Fatigue

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Summary:

Chronic fatigue syndrome (CFS) is a debilitating condition which is presumed to be multifactorial in origin, though its precipitating cause(s) and modifying co-morbid influences are poorly understood. Since CFS bears phenomenologic similarity to certain psychiatric illnesses, the specific role of psychiatric disorders in the onset and course of CFS has become a principal focus for research. Clinical observation provides compelling evidence that, like depressive patients, CFS patients report an unusually high burden of stressful events preceding the onset of their illness, and a subsequent disruption in the quality of their interpersonal relationships. Few studies have used validated measures of psychosocial stress and interpersonal function to confirm these observations.

In this study, we employed previously validated assessment techniques examining several specific domains of psychosocial function: major life events, resources and deficiencies in social relationships, and personal vulnerability based on developmental history. *DSM-III-R* diagnoses were established in all subjects using the SCID. Twenty-nine consecutive subjects seeking treatment at a tertiary care infectious disease clinic for chronic, debilitating fatigue were recruited for study. Comparison groups were age- and sex-matched, and included inpatients with major depression (n = 29), primary care outpatients with chronic fatigue as their presenting symptom either with (n = 29) or without (n = 29) a psychiatric illness history, and primary care outpatients (n = 29) with no history of either fatigue or a psychiatric illness.

Our interview results confirm previous observations that CFS and several psychiatric illnesses have a high degree of comorbidity. Indeed, 62% of our tertiary care fatigue sample had a history of major depression. The specific domains of psychosocial stress in patients with CFS were contrasted with depressed patients. Comparison of fatigued subjects in tertiary and primary care settings addressed the role of selection bias in the symptomatic expression of CFS.

We suggest that an increased lifetime burden of psychological stress and the persistence of disturbances in current social relationships may both enhance the vulnerability to develop CFS, and at the same time, aggravate its longitudinal course by increasing the likelihood of abnormal illness behaviors during the recuperative period.

NR40 Monday, May 23, 9:00 a.m.-10:30 a.m.

Low Platelet MAO Activity in Spanish Bullfighters

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Summary:

Sensation seeking is a highly heritable personality trait associated with extroverted and risky behaviors. High sensation seeking levels have been reported in association with several electrophysiological and biochemical measures, including low concentrations of platelet monoamineoxidase (MAO).

To test the possibility that low platelet MAO has a direct influence on major aspects of human behavior, we have studied this marker in three different professional groups. Sixteen full-time bullfighters and 29 explosive experts, thought to be sensation seekers, and 25 medical doctors were investigated. MAO activity was measured by means of an isotopic technique using C14-benzylamine as substrate. Personality traits were assessed by using the Zuckerman's Sensation Seeking Scale, the Eysenck's Personality Inventory, and the Cloninger's Tridimensional Personality Questionnaire.

As expected, bullfighters showed significantly higher degrees of thrill and adventure seeking and extroversion ($p < 0.001$) but explosive experts did not so. Platelet MAO in bullfighters was significantly lower than in both other groups ($p < 0.01$). MAO concentrations were negatively correlated with sensation seeking scores ($p < 0.05$).

As a conclusion, low platelet MAO activity might participate significantly in the career orientation of bullfighters.

NR41 Monday, May 23, 9:00 a.m.-10:30 a.m.

Prolactin Response to Buspirone Challenge in the Presence of Dopaminergic Blockade

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Summary:

Objective: Buspirone-stimulated prolactin release has recently been employed as an indirect measure of central serotonin activity. However, it remains unclear whether serotonergic or dopaminergic systems are responsible for this response. The following study was therefore designed to shed further light on this mechanism

by studying the prolactin response to buspirone in the presence of maximal dopaminergic receptor blockade.

Method: Following the production of dopaminergic blockade with an intravenous bolus and steady infusion of metoclopramide, eight healthy male volunteers were given an oral dose of buspirone 60 mg under placebo-controlled, double-blind conditions. Plasma prolactin levels were then assayed over half-hour intervals for three hours, and compared in the two study conditions using a two-way repeated measures ANOVA.

Results: The prolactin response to buspirone in the presence of metoclopramide was not statistically different from that to placebo under the same conditions. Further prolactin release by a bolus of TRH in a third trial excluded the possibility of pituitary prolactin depletion by metoclopramide.

Conclusions: These results lend further support to a dopaminergic mechanism in Buspirone-induced prolactin secretion; further caution is therefore warranted in interpreting the results of this challenge test as a measure of serotonergic activity in the brain.

NR42 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Effects of Desipramine on Serotonin Function in Depressed Patients and Healthy Subjects

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Summary:

The effects of norepinephrine (NE) reuptake inhibitors on serotonergic (5-HT) function are unclear. Several studies have reported enhanced 5-HT function, as assessed by various indirect measures, while others have described down-regulation of 5-HT receptors following exposure to NE reuptake inhibitors. We applied a neuroendocrine challenge paradigm, the "clomipramine (CMI) challenge test," in studies of the effects of the NE reuptake inhibitor desipramine (DMI) on 5-HT systems in healthy subjects and depressed patients.

We measured the prolactin response to CMI challenge in 14 carefully screened healthy volunteers before and after two-week, double-blind exposure to either DMI (titrated to 150 mg/day) or placebo. The prolactin response to CMI decreased significantly in the DMI group (signed rank, $p = 0.05$), but not in the placebo group ($p = 0.6$).

Twenty-five patients meeting DSM-III-R criteria for major depression received CMI challenge before and after six weeks treatment with DMI. In the 12 patients who responded to DMI treatment, there was a significant decrease in the prolactin response to CMI challenge (signed rank, $p = 0.02$). There was no significant change in the prolactin response to CMI challenge in the 13 patients who were nonresponders (signed rank, $p = 0.20$).

These findings suggest that DMI does not enhance 5-HT function, as measured by the prolactin response to CMI challenge. Further, the blunted prolactin response to CMI that has been described in depressed patients may represent a trait marker, which persists after clinical response to DMI pharmacotherapy.

This work was supported in part by PHS grants MH-42145, MH-33127, MH-19111, and RR-00046.

NR43 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Role of Serotonin$_3$ Receptors in the Psychobiological Response to the Clomipramine Challenge Test

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Summary:

The prolactin response to central serotonergic stimulation by pharmacological challenge agents has been utilized as an indirect measure of 5-HT function. Unfortunately, 5-HT stimulation can elicit nausea in some subjects, which in itself can stimulate prolactin release, thereby confounding the interpretation of the results. The specific 5-HT receptors that mediate the prolactin and nausea responses to 5-HT challenge have not been clearly identified. We tested the hypothesis that 5-HT$_3$ receptors mediate the nausea associated with 5-HT challenge, but not the prolactin response. Under double-blind conditions, healthy volunteers received i.v. infusion of either the 5-HT$_3$ receptor antagonist ondansetron or placebo, followed by a standard clomipramine (CMI) challenge test. Plasma prolactin concentrations were measured with radioimmunoassay, and nausea was quantified using 100 mm self-report lines.

In the 12 subjects studied to date, there was no significant difference in the prolactin responses to CMI challenge in the ondansetron vs. placebo pretreatment groups (rank sum: $p = 0.60$). In contrast, pretreatment with ondansetron led to significantly less nausea associated with CMI challenge, compared with placebo pretreatment (rank sum: $p = 0.05$). These preliminary results suggest that 5-HT$_3$ receptors may play a role in mediating the nausea response to 5-HT stimulation.

This work was supported in part by PHS grants MH-42145, MH-33127, MH-19111, and RR-00046.

NR44 Monday, May 23, 9:00 a.m.-10:30 a.m.

Orthostatic Response in Panic and Depressed Patients

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Summary:

Autonomic disturbances have been reported for panic disorder (PD). Stein et al, found that in comparison to normal controls and social phobics PD's had greater heart rates (HR's) to an orthostatic challenge. This work attempts to replicate these findings and compares PD with major depression (MD).

Twelve PD and 12 MD (DSM-III-R) outpatients were age matched for the orthostatic challenge. All were physically healthy and medication free for six weeks. Monitoring for mean arterial pressure (MAP) and HR occurred via an automated unit (Dinamap-Plus). Subjects were supine for 30 min. and subsequently stood up. MAP and HR were monitored every 5 min. while supine and at .5, and 3 min. after standing.

To compare the two groups response over time an RM ANOVA was conducted for MAP and HR separately. Orthostatic changes in HRs were similar in the two groups ($F = 1.042$, $p = .318$). Both groups had a similar response over time ($F = 43.272$, $p = .0001$; group × time, $F = 0.132$, $p = .877$). However, while resting MAP did not differentiate the groups, the PDs had a significantly different orthostatic response over time compared with the MDs (group × time: $F = 3.494$, $p = .039$). This suggests an increased autonomic responsivity in PD. These findings add to the physiological differences between PD and MD and may have cardiovascular implications.

NR45 Monday, May 23, 9:00 a.m.-10:30 a.m.

Clozapine Response in Chronic Schizophrenia and Brain Morphology on MRI: A Preliminary Report

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Pollack, Ph.D., Robert Bilder, Ph.D., John M. Kane, M.D., Allan Safferman, M.D.

Summary:

Clozapine, an atypical antipsychotic agent with demonstrated efficacy in treatment resistant and treatment intolerant schizophrenic populations, may be related to morphologic abnormalities in lateral frontal and prefrontal cortices as measured on CT (Friedman 1991; Honer 1993) and MRI (Breier 1993). Eighteen chronic schizophrenics (DSM-III-R) (mean age 27, 89% male) receiving standardized treatment with clozapine (mean treatment duration = 30 months ± 19.43), underwent assessments for psychopathology (BPRS, CGI, SANS) and MRI brain morphology. Using a Siemens-Magneton (1.0 tesla) system, MRIs were analyzed under blind conditions using quantitative (brain volume, interhemispheric fissure volume) and qualitative (evaluation of sulcal prominence, cerebral cortex, lateral ventricles, third ventricle, medial temporal lobe structures) measures. Data analyses examined the relationship between brain morphologic variables and measures of psychopathology at baseline and during clozapine treatment. Preliminary analyses found no significant associations between the specific morphologic variables and treatment outcome. Mean severity of psychopathology at baseline was associated with increased interhemispheric fissure volume ($r = 0.54$, $p = 0.02$), mainly reflecting positive symptom factors on the BPRS. These results do not replicate previous findings of abnormal brain morphology being associated with poorer clozapine response. Reasons may include differences in patient samples and the limited number of patients studied. Findings will be reexamined using a larger patient sample as data emerge.

NR46 Monday, May 23, 9:00 a.m.-10:30 a.m.

PET Changes in OCD Versus Depression with Paroxetine Treatment: Preliminary Data

Sanjaya Saxena, M.D., Psychiatry, UCLA NPI, 760 Westwood Plaza, Los Angeles CA 90024; Arthur J. Brody, M.D., Mark Colgan, M.E., Lewis R. Baxter, M.D.

Summary:

PET studies of OCD have shown that improvement in obsessive and compulsive symptoms correlates with a decrease in caudate metabolic rate, while studies in depression have demonstrated that improvement in depressive symptoms correlates with an increase in caudate metabolic rate.

In this study, we compare patients with OCD to patients with unipolar depression treated with the same agent, paroxetine (20–40 mg/day for six to eight weeks), using FDG-PET to determine whether the changes in glucose metabolism are the same or different in these disorders. To date, we have studied seven OCD patients (of whom two responded, one worsened, and four were unchanged) and three depressed patients (of whom two responded and one was unchanged).

Preliminary analysis using PET-PET subtraction techniques of pre- and post-treatment images suggests that the depressed patients who responded had an increase in caudate metabolism with treatment, while the nonresponder had no apparent change. In OCD, the patient who worsened had an increase in caudate metabolism, while in responders, no clear pattern has emerged thus far. The direction of these changes was in concordance with previous reported results. Data from further analysis will be presented in expanded fashion.

NR47 Monday, May 23, 9:00 a.m.-10:30 a.m.

PET Study of Cerebral Activation in Normal and Schizophrenic Subjects Performing Cognitive Challenge Tests

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Summary:

Objective: To use PET to study cerebral activation in normal and schizophrenic subjects performing cognitive challenge tests known to activate frontal lobe regions.

Method: Twelve normal volunteers and eight medicated patients with SCID diagnoses of chronic schizophrenia were recruited. All subjects were males aged 21 to 45. The schizophrenic patients had a mean duration of illness of 14 years (SD = 5). PANSS scores were obtained for each patient. All subjects performed a baseline attentional task, a lexical decision task, and a semantic categorization task known to involve activation of the dorsolateral prefrontal cortex (DLPFC). 0–15 water activation PET scans were obtained for each task. PET scans were analysed using Statistical Parametric Mapping (SPM) to determine significant regional deviation from the baseline task.

Results: Scans obtained during the semantic categorization task revealed significant activation ($P < 0.0001$) of the left DLPFC in the normal group, but not in the schizophrenic group. The normal group also performed better on this task (95% accuracy) compared with the schizophrenic group (85%). The scan and performance differences were less remarkable for the cognitively less complex attentional and lexical decision tasks.

Conclusion: This finding is consistent with other investigations that have implicated dysfunction of the DLPFC in patients with schizophrenia.

NR48 Monday, May 23, 9:00 a.m.-10:30 a.m.

Normal Aging and Frontal Lobe CBF: A PET Study

Brenda S. Kirkby, M.Sc., Unit on PET, NIMH/CBDB NIH 10-4N317, 9000 Rockville Pike, Bethesda MD 20892; Giuseppe Esposito, M.D., Jill L. Ostrem, B.A., John D. Van Horn, Ph.D., Daniel R. Weinberger, M.D., Karen F. Berman, M.D.

Summary:

Results from previous studies of normal aging, although not uncontested, indicate that regional cerebral blood flow (rCBF) declines with age, with some studies demonstrating a disproportionate decrease in frontal regions. Diminished performance on cognitive tasks that involve the frontal lobes has also been reported with increased age. To investigate further the relation between aging, CBF, and cognition, we measured rCBF using the oxygen-15 water PET method in 31 normal adults (15 females, 16 males; mean age 33.6, age range 18–67) during four tasks: The Wisconsin Card Sorting Test (WCS), a test of frontal lobe integrity; Raven's Progressive Matrices (RPM), a nonverbal intelligence test found by our lab to involve more posterior brain regions; and two sensorimotor control tasks. Subjects were screened for major medical and psychiatric illness. Absolute CBF (ml/min/100g) was determined with a least squares fit to the Kety model. Regions of interest were individually drawn on each subject's coplanar MRI scan and then applied to 1) the absolute rCBF scans and 2) the rCBF data after pixel-by-pixel normalization (as a percentage of the whole brain mean). Mean global CBF values decreased significantly with age in all four tasks (Pearson r values between −.47 and −.61; $p < .001$), but did not correlate with performance on either the WCS or RPM. Consistent with the global CBF changes, analyses of absolute regional data revealed CBF decreases in most cortical regions with age; subcortical regions, including thala-

mus and basal ganglia, were relatively spared. Analyses of normalized regional data (i.e., with global changes accounted for) indicated that, in general, decreases in rCBF with age were most evident in frontal areas. Performance on the WCS declined with age ($r = -.44$, $p < .01$), whereas overall accuracy on RPM did not correlate with age. Our data confirm an association between normal aging and reduced mean global CBF, with particular decrement in frontal regions. The finding of reduced rCBF in frontal regions in the context of poor performance on a frontal task, and not on a more posterior task, highlights the effect of aging on frontal lobe neurophysiology and cognition.

NR49 Monday, May 23, 9:00 a.m.-10:30 a.m.

Monte Carlo Simulation of PET Region of Interest Data Sets

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Summary:

The search for optimal methods for the statistical analysis of positron emission tomographic (PET) data has generated much debate in the functional brain imaging literature. A particular problem has been that the large intra- and inter-individual differences in global blood flow or metabolism generally observed can obscure the more subtle regional changes produced by cognitive activation. Therefore, data transformation is often used to "correct" or "adjust" PET data for differences in global activity. While a number of normalization approaches have been taken (e.g. ratio of CBF to the whole brain mean, ANCOVA, etc.), no best method has yet been clearly established, and no manner for assessing the efficiency of the various approaches has been generally adopted. One way to inspect the behavior of these normalization methods under various conditions is to conduct Monte Carlo simulation. The effects of transformation on Type I and Type II error rates in regional t-tests performed on the data can be empirically assessed. We simulated multivariate PET data sets, varying sample size, within-subject and between-condition correlations, statistical effect size, and relative contribution of brain areas not included in regional analyses but that are used in the computation of the whole brain average. Five hundred simulated experiments were performed with each parameter configuration, and the resultant raw data sets were passed through each of several normalization procedures to produce corrected data sets. Student's t-tests were then performed on complementary ROIs from the corrected data sets. Results indicated that several of the methods had greatly inflated Type I error rates, while others had biases dependent upon the contribution of non-included brain areas. When data set correlation was low, some methods depending upon covariation with the whole brain average greatly over-estimated Type I and Type II error, but this improved as correlation and sample size increased. This work indicates that Monte Carlo methods will 1) be useful in modeling and detailing the conditions under which a given normalization procedure should perform best and 2) better indicate the optimal statistical approach for a given PET data set.

NR50 Monday, May 23, 9:00 a.m.-10:30 a.m.

Effects of Cohort Size on PET Cognitive Activation Studies

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Summary:

A number of recently published PET studies of cognitive activation have employed sample sizes as small as six or even four subjects. While an attractive approach for complex and costly research such as PET, this methodological trend may contribute to inconsistencies in the literature. This study explores the impact of sample size on the reliability of PET results using the two most popular methods of data analysis: Individual region of interest (ROI) analysis and Statistical Parametric Mapping (SPM). We took advantage of a large data set (48 normal subjects; 24 males, 24 females; mean age 25.4 years, range 18–39) obtained with the oxygen-15 water PET method for measuring regional cerebral blood flow (rCBF). Subjects were scanned during performance of 1) The Wisconsin Card Sorting Test (WCS) and 2) a sensory motor control task (WCScon). The ROI analysis identified four highly significant regions ($p < 0.0003$) for the entire group ($N = 48$) based on paired t-tests between normalized rCBF data (i.e. expressed on a pixel by pixel basis as a percentage of the whole brain mean) for WCS and WCScon. These regions were the left & right inferior frontal gyrus (LIFG, RIFG) (Brodmann's Areas [BA] 9 & 46) and left & right inferior parietal lobule (LPAR, RPAR) (BA 7 & 40). In addition, SPM analysis was performed and four highly significant pixels within these regions were determined ($p < 0.001$). Subjects were then divided into smaller independent subgroups matched for age and sex and reanalyzed as follows: eight groups of six subjects, four groups of 12, two groups of 18 and 24, and one group of 30. We then determined if the four regions from the ROI analysis or pixels from the SPM analysis remained significant in these smaller subsamples. The table below shows the ratio of the number of subgroups in which we found a significant difference between WCS and WCScon to the number of subgroups examined.

REGIONS	N = 6		N = 12		N = 18		N = 24		N = 30	
	ROI	SPM	ROI	SPM	ROI	SPM	ROI	SPM	ROI	SPM
LIFG	2/8	2/8	4/4	3/4	2/2	1/2	2/2	2/2	1/1	1/1
RIFG	1/8	4/8	1/4	3/4	1/2	2/2	1/2	2/2	1/1	1/1
LPAR	2/8	4/8	2/4	3/4	2/2	2/2	2/2	2/2	1/1	1/1
RPAR	3/8	5/8	3/4	4/4	2/2	2/2	2/2	2/2	1/1	1/1

These data suggest that sample sizes under 12 subjects contribute to inconsistent findings in PET studies and, in many cases, result in type II error particularly in studies of complex cognition. These findings may help to guide future PET methodology specifically related to the study of neuropsychological activation paradigms.

NR51 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Phenomenon of Dysautonomia in OCD

Srinivasan S. Pillay, M.B., South Belknap 3, McLean Hospital, 115 Mill Street, Belmont MA 02178; S. Nassir Ghaemi, M.D., Anthony B. Joseph, M.D., Jonathan O. Cole, M.D.

Summary:

Two patients with obsessive compulsive disorder (OCD), movement disorders (choreiform movements and parkinsonian signs), and dysautonomia (evidenced by diarrhea and urinary incontinence) are described. The authors suggest that this syndrome be included in the spectrum of obsessive compulsive disorders and note that to their knowledge, it has not been previously described. In addition they postulate that the finding of pathological dysautonomia in OCD is consistent with the serotonergic hypothesis. Alternative explanations are discussed. These include possible links between the OCD spectrum and neuropathological changes of the autonomic nervous system and basal ganglia.

NR52 Monday, May 23, 9:00 a.m.-10:30 a.m.

Complex Partial Seizures and Panic Disorders: A Truly Complex Relationship

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Summary:

Panic disorder is a common anxiety disorder with a lifetime prevalence of around 2% in the general population. It is also estimated that about 720,000 persons in the United States suffer from non-convulsive seizures, with a great majority of patients carrying the diagnosis of partial seizures with simple or complex symptoms. Even though complex partial seizures commonly present with impairment of consciousness, automatisms, and perceptual disturbances, frequently the presenting symptoms are similar to those seen in patients with panic disorder. Ten out of 13 *DSM-III-R* symptoms for panic disorder overlap with complex partial seizure symptoms. These include dizziness, palpitations, sweating, abdominal distress, depersonalization, tingling or numbness, hot flashes or chills, chest pain, and fear of dying or fear of going crazy. As clinicians, there are three possible scenarios that are encountered in practice. Scenario one—complex partial seizures may be misdiagnosed as panic disorder. Scenario two—panic disorder may be misdiagnosed as complex partial seizures, and scenario three—the patient has both panic disorder and complex partial seizures but is diagnosed as having only one. The authors describe three cases representing the above scenarios and discuss the relevant literature.

NR53 Monday, May 23, 9:00 a.m.-10:30 a.m.

Psychiatric Disorders in Epileptic Patients

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Summary:

Forty consecutive adult admissions to a neurology video-telemetry unit were examined with structured clinical interviews for *DSM-III-R* (SCID-Epilepsy) to determine current and lifetime prevalence of psychiatric diagnoses among epileptic patients and to identify psychosocial and epilepsy variables as risk factors for psychiatric comorbidity. The Mini-Mental State Exam and the Millon Clinical Multiaxial Inventory-II were also administered.

Twenty-five patients had telemetry-diagnosed epileptic seizures (ES), including complex partial seizures, complex partial seizures with secondary generalization, and/or generalized tonic/clonic seizures. Thirteen patients had non-epileptic seizures (NES). Forty-eight percent (12/25) of ES patients had lifetime SCID-derived diagnoses, including depressive disorders (N = 8), substance abuse disorders (N = 6), anxiety disorders (N = 3), and psychotic disorder (N = 1). Eighty-five percent (11/13) of the NES patients had lifetime psychiatric diagnoses, including depressive disorders (N = 5), substance abuse disorders (N = 5), and anxiety disorders (N = 4).

A significantly greater prevalence of psychiatric disorders, suicide attempts, and childhood sexual abuse was found in NES patients as compared to ES patients. Demographic, psychosocial, and epilepsy variables such as seizure type and laterality of seizure focus did not identify ES patients at risk for psychiatric comorbidity.

NR54 Monday, May 23, 9:00 a.m.-10:30 a.m.

Psychiatric Disorders and Functional Disability in Ambulatory Traumatic Brain Injured Patients

Jesse R. Fann, M.D., Psychiatry, University of Washington, Mail Stop Rp-10, Seattle WA 98195; Wayne J. Katon, M.D.

Summary:

Objective: To examine psychiatric sequelae of traumatic brain injuries (TBI) in outpatients and their relationship to functional disability.

Method: 50 consecutive outpatients with TBI presenting to a brain injury rehabilitation clinic for initial evaluation were examined for *DSM-III-R* diagnoses using the Diagnostic Interview Schedule (DIS). Patients completed the Medical Outcome Study Health Survey (SF-36) to assess functional disability and a questionnaire to assess post-concussional symptoms and self-perceptions of TBI severity and cognitive functioning.

Results: 13 (26%) had a current major depression (four with concomitant Generalized Anxiety Disorder) and an additional 14 (28%) reported a first-onset major depressive episode after the injury that had resolved. Eight (16%) had current generalized anxiety disorder without major depression and four (8%) reported current substance abuse. The depressed and/or anxious group was significantly more impaired on the SF-36 measures of emotional role functioning, mental health, and general health perceptions. Depressed patients reported significantly more post-concussional symptoms that were increasing in severity. The depressed and/or anxious group rated their injury as significantly more severe and their cognitive functioning as significantly worse, despite no significant differences in objective measures of injury severity and Mini-mental State Exam scores.

Conclusions: Depression and anxiety are common in ambulatory TBI patients. Those with psychiatric disorders are more functionally disabled and depressed patients report more post-concussional symptoms that are increasing in severity. Depressed and anxious patients also perceive their injury and cognitive impairment as more severe.

NR55 Monday, May 23, 9:00 a.m.-10:30 a.m.

Excited Catatonia: Prevalence and Phenomenology

George Bush, M.D., Psychiatry, University Hospital, HSC T-10, Stony Brook NY 11794; Georgios Petrides, M.D., Andrew Francis, M.D.

Summary:

Objectives: Since the catatonic syndrome was first described by Kahlbaum, there has been no empirical delineation of catatonic subtypes, nor prospective studies of patients described as excited catatonics. In this study, we sought to detect catatonia in patients presenting to the psychiatric ER, in order to define clustering of catatonic signs with or without concomitant excitement.

Methods: In a pilot phase, we informally screened admissions to the ER. We determined the presence of agitation-excitement using the Yudofsky Overt Aggression Scale and two BPRS items; and catatonia with the 23-item Bush-Francis Catatonia Rating Scale [BFCRS]. An ongoing formal study is systematically screening consecutive ER admissions.

Results: Of 160 cases evaluated to date, we identified 53/160 as agitated-excited and 14/160 as catatonic (≥2 signs on the BFCRS). There was a trend toward greater prevalence of catatonia among agitated-excited patients (11.3%) vs. nonagitated-excited patients (7.5%). Excited catatonics displayed more signs of catatonia than nonagitated cases (means of 8.5 vs. 3.5 signs, $p < .04$).

Conclusions: The data to date suggest that catatonia is more common among agitated patients, that excited catatonia can be empirically identified, and that it is characterized by a greater

number and variety of catatonic signs. The empirical identification of catatonic subtypes (e.g., excited/retarded) will aid systematic study of phenomenology, biology, and treatment of catatonia.

NR56 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Immune Effects of a Medical Stressor

JoAnn Difede, Ph.D., Psychiatry, Cornell Medical College, 445 East 68th Street #3-K, New York NY 10021; Lawrence B. Jacobsberg, M.D., Dana Bovbjerg, Ph.D., Daniel Goodman, M.D., Samuel W. Perry III, M.D.

Summary:

Numerous studies have documented that a range of stressful life events are associated with alterations in immune function. In the present study, we sought to determine if a stressful medical procedure (i.e., HIV testing for HIV seronegative gay/bisexual males and CD4 count assessment for HIV seropositive gay/bisexual males) would also be associated with immune alterations.

The Stress group consisted of those subjects who were scheduled for their biannual HIV testing (at-risk seronegatives) or CD4 count assessment (seropositives) as part of an ongoing longitudinal HIV testing and counseling study. The No Stress comparison group consisted of the HIV study participants who were not scheduled for their biannual testing, but who accepted an offer to have a free influenza vaccination. (Those in the Stress group also received the influenza vaccination). All subjects completed two psychological measures (the Profile of Mood States (POMS) and Brief Symptom Inventory (BSI)) and blood was drawn for the immune assays (T1). Follow-up psychoimmune assessments were scheduled at seven (T2) and 14 (T3) days following the medical procedures.

Mitogen response decreased for the Stress group between notification of serostatus or CD4 count (T2) and the 14-day follow-up (T3) and did not change for the No Stress group ($F(2,51) = 3.6$, $p < .03$). Among HIV-positive participants, those in the Stress group showed reduced mitogenic response one week after notification of CD4 count (T3) compared with those in the No Stress group ($F(1,23) = 8.0$, $p < .01$). Among HIV-negative participants, those in the Stress group showed reduced mitogenic response one week after notification of serostatus (T3) compared with those in the No Stress group. There was a trend toward a difference in psychological distress between the two groups as measured by the POMS ($F(1,74) = 3.0$, $p < .08$) and the BSI ($F(1,74) = 2.8$, $p < .10$).

These results suggest that a stressor with clear medical significance (HIV testing/CD4 assessment) was associated with a decrease in mitogenesis, a measure of cellular immune response. Interestingly, despite being immunocompromised, the immune response of HIV+ participants was sensitive to stress.

NR57 Monday, May 23, 9:00 a.m.-10:30 a.m.

Interleukin-6 in Depression and Schizophrenia

Ulrich H. Frommberger, M.D., Psychiatry, University Clinic, Hauptstr 5, Freiburg 75104, Germany; P. Haselbauer, A. Fraulin, J. Bauer, M.D., M. Berger, M.D.

Summary:

Objective: Serum levels of the cytokine interleukin-6 (IL-6) has been reported to be elevated in remitted schizophrenic patients (Shitani et al. 1991) and as a result of stress (LeMay et al. 1990). It was our intention to extend these studies.

Method: We measured IL-6 serum concentrations during the acute and remitted state of inpatients with either a major depression ($n = 13$) or schizophrenia ($n = 33$) compared with healthy controls ($n = 12$). Patients were diagnosed according to DSM-III-R by the Structured Clinical Interview (SCID). IL-6 concentrations (Units/ml) were determined in serum using a bioassay with the IL-6-dependent hybridoma cell line B9. Patients with acute allergic conditions, chronic systemic diseases, or any significant inflammatory process were excluded.

Results: In the acute state, drug-free depressed and drug-free schizophrenic patients exhibited a significant elevation of their IL-6 concentrations ($p \leq 0.05$ and $p \leq 0.04$, resp.) when compared with controls. This difference remained significant both in depressed and schizophrenic patients ($p \leq 0.07$ and $p \leq 0.03$, resp.) after drug treatment had been induced. In the remitted state, IL-6 serum concentrations had significantly decreased, and no differences were found between depressed and schizophrenic patients compared with controls.

Conclusions: IL-6 serum levels appear to be elevated during the acute state of affective disorder and schizophrenia.

NR58 Monday, May 23, 9:00 a.m.-10:30 a.m.

Does Clozapine Cause OCD?

S. Nassir Ghaemi, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Carlos A. Zarate, Jr., M.D., Anand P. Popli, M.D., Srinivasan S. Pillay, M.B., Jonathan O. Cole, M.D.

Summary:

Background: Emergence of obsessive compulsive symptoms during clozapine treatment has been reported in recent case studies, yet the incidence and significance of this finding is still unclear since larger descriptive studies have yet to be performed.

Method: We conducted a retrospective review of the medical record of 140 random inpatients treated with clozapine before 1992.

Results: Two patients (1.4%) were identified with obsessive compulsive symptoms that seemed to be temporally associated with clozapine treatment. Both cases involved exacerbation of pretreatment obsessive compulsive symptoms. Neither involved emergence of de novo symptoms of obsessive compulsive disorder. No statistical differences were found in age, sex, dose, or duration of clozapine treatment between the groups with and without obsessive compulsive symptoms.

Conclusion: This incidence rate is one-tenth that expected from a prior study; that sample consisted of more patients with chronic schizophrenia, in which obsessive compulsive symptoms are often part of the natural history, and involved greater dosage and duration of clozapine treatment.

While clozapine may be associated with obsessive compulsive symptoms, this effect is more likely to occur in patients with pretreatment obsessive compulsive symptoms or with schizophrenia, and occurs more often with greater dose and duration of treatment.

NR59 Monday, May 23, 9:00 a.m.-10:30 a.m.

Lack of Potentiation of Neuroleptic Action by Clonidine in Psychosis

Scott T. Hedges, M.D., Psychiatry, University of Louis, Louisville KY 40292; Rif S. El-Mallakh, M.D.

Summary:

Introduction: Clonidine is a centrally acting antihypertensive and has been used widely for over 20 years. Because it decreases central norepinephrine activity, clonidine has been investigated for many psychiatric uses. Soon after its introduction, clonidine was tested as an antipsychotic in psychotic patients. In most of the preliminary studies, clonidine was tested as the sole antipsychotic agent. We set out to evaluate whether clonidine in combination with neuroleptics would potentiate the antipsychotic effects.

Methods: We performed a double-blind, placebo-controlled, crossover design to compare placebo/neuroleptic to clonidine/

neuroleptic in a group of 16 psychotic patients. Of these 16, three dropped out secondary to side effects of the clonidine and one was lost to follow-up. Clonidine dosage varied from 0.2 μgs to 0.6 μgs per day. Concurrent neuroleptic was one of the following: haloperidol, thiothixene, thioridazine, mesoridazine, or fluphenazine at an average dose of 34 mg per day of haloperidol equivalents. Symptoms were monitored using the Psychiatric Symptoms Assessment Scale (PSAS), a derivation of the Brief Psychiatric Ratings Scale (BPRS).

Results and Implications: The data (mean PSAS score 1.74 ± SE 0.257 vs. 2.09 ± 0.369 in placebo vs active, respectively; paired t = 1.185, df = 11, p = 0.261) provided evidence that clonidine does not significantly potentiate the antipsychotic effects of neuroleptics. These data suggest that the central norepinephrine activity of neuroleptics maximizes the neurotransmitter system, and additional antagonism from clonidine does not potentiate the system.

NR60 Monday, May 23, 9:00 a.m.-10:30 a.m.

Sertraline Pharmacotherapy in Patients with Social Phobia

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Summary:

Social phobia is characterized by excessive shyness in public that often results in phobic-avoidance and occupational dysfunction. Pharmacotherapy with antidepressants such as the TCAs and MAOIs can be effective, but often are associated with substantial side effects; anxiolytics such as the benzodiazepines can be associated with tolerance, dependence, or withdrawal effects. The antidepressant, sertraline, has relatively limited side effects and has been reported to possess some anxiolytic effects. With these issues in mind, we completed an open six-week trial of sertraline (50 mg/day) in non-depressed patients (10 females, 4 males; mean age, 35 ± 2 yr.; mean duration of illness 18 ± 2 years; baseline Ham-D, 8.2 ± 1.8) who met primary *DSM-III-R* criteria for social phobia. At baseline, each patient scored at least a 20 on a standardized rating scale for social phobia, the Duke Brief Social Phobia Scale (mean baseline BSPS ± SEM, 40.9 ± 2.7). Patients were serially evaluated by rating scales, including the BSPS throughout the study. Sertraline was well tolerated and a repeated measures ANOVA revealed a significant treatment (sertraline) effect over time [$F(1,3) = 9.05$, $P < 0.001$] as measured by the BSPS. The mean BSPS score was significantly reduced from baseline at week 4 (−12.6 ± 3.0, $P < 0.005$) and at week 6 (−13.5 ± 2.7, $P < 0.005$) of sertraline administration. These preliminary results suggest that sertraline may represent a safe and effective treatment for patients with social phobia, even in the absence of depression.

NR61 Monday, May 23, 9:00 a.m.-10:30 a.m.

Clinical Implications of Adjunctive Valproic Acid Use in Clozapine Treated Psychiatric Patients

Lance P. Longo, M.D., Mass Mental Health Center, 74 Fenwood Road, Boston MA 02115; Carl Salzman, M.D. Alan I. Green, M.D.

Summary:

Objective: Adjunctive use of valproic acid (VPA) for seizure prophylaxis in high dose clozapine-treated patients is common standard of care. As part of an ongoing study of risks and benefits of concomitant VPA-clozapine use we evaluated changes in clinical rating scale scores, blood level changes, and side effect profiles pre-and-post VPA addition to patients on high doses of clozapine (>500 mg/d).

Methods: Eight schizoprenic patients were studied. After baseline rating scale scores and serologic measures (clozapine blood levels, LFT's, CBC's), VPA was added (intended for seizure prophylaxis). After approximately one month at therapeutic range (50-100 μg/ml, mean 62μg/ml), the above parameters were reassessed. Clozapine dose was fixed during this time (mean daily dose 610 mg. range 500–900, blood level 353 μg/ml), and no other medication changes occurred.

Results: There were no significant changes in clinical ratings (BPRS, CGI), LFT's or CBC's; side effects were negligible. Clozapine blood level changes were modestly but significantly decreased $p = .05$; norclozapine levels were markedly decreased (mean pre-post t test $p = .04$; 3/4 had greater than 50% reduction.

Conclusion: VPA, unexpectedly, decreased clozapine blood levels but did not result in worsening of clinical status, nor significant side effects or toxicity. Norclozapine levels, however, were markedly reduced. Recent data suggest that norclozapine is substantially more toxic to hematopoietic stem cells (in vitro) than is clozapine. These preliminary data suggest that VPA may offer protection against agranulocytosis (as well as prophylaxis against seizures) with no decrement in therapeutic effect or toxicity.

NR62 Monday, May 23, 9:00 a.m.-10:30 a.m.

Clozapine Use in the Dually Diagnosed Mentally Retarded: Three Case Studies

Lance P. Longo, M.D., Psychopharm, Mass Mental Health Center, 74 Fenwood Road, Boston MA 02115; Mark J. Hauser, M.D. Michael L. Commons, Ph.D.

Summary:

Patients with concomitant psychiatric illness and mental retardation present difficult diagnostic and pharmacologic treatment challenges to clinicians. Clozapine was used to treat three clients with chronic psychotic illnesses who had previously not responded adequately to multiple trials of typical neuroleptics and polypharmacy. The reported cases are clients in a longterm residential facility who were monitored carefully via several clinical and behavioral rating scales which tracked aberrant target behaviors, psychiatric symptoms, and global impressions. In two of the three cases studied, the patients derived substantial benefit from clozapine, as reported in case vignettes and data tables. In the third case, the patient experienced an alleviation of several symptoms while on clozapine, but needed to discontinue because of medical side effects. Target symptoms which are especially problematic in this population, including self-abusive, assaultive, and destructive behaviors, showed statistically significant reductions. Clozapine's increased antipsychotic efficacy, effects on impulsivity, aggression, and cognition, and lesser risk of causing tardive dyskinesia, support clozapine's potential for use in this population. Risks and benefits exemplified by these case reports may guide clinicians in their future management of this difficult and under-served population.

NR63 Monday, May 23, 9:00 a.m.-10:30 a.m.

Idazoxan Effects on Attention in Normal Volunteers

Annick Vincent, M.D., ETB/SCP, NIMH RM 2D46, 9000 Rockville Pike, Bethesda MD 20892; Robert Risinger, M.D. Mark Schmidt, M.D. Philippe Baruch, M.D. Sophie Lemelin, Bps William Z. Potter, M.D.

Summary:

Introduction: Idazoxan (IDX) is a selective alpha-2 adrenergic antagonist. Functional brain imaging measures following acute intravenous IDX indicate a significant central effect of IDX; con-

comitantly plasma norepinephrine increases. IDX therefore shows promise as a probe to explore the role of alpha-2 receptor regulation and norepinephrine in attentional processes in humans.

Methods: 11 healthy volunteers (4F, 7M; mean age; 30 ± 10 y.o.) were tested in a singleblind, placebo-controlled protocol. Training was provided before testing. Volunteers received a placebo (PBO) infusion on the first day and an infusion of IDX, 200 mcg/kg over 30 minutes on the second day. Digit span (forward and backward) and a computerized battery assessing simple reaction time (SRT), choice reaction time (CRT), selective (Stroop task and a visuo-spatial interference task), and divided attention were performed 30 minutes after each infusion. Differences between PBO and IDX effects on these parameters were tested by paired t-test of group means. A difference was considered significant when $p < 0.05$.

Results: Compared to PBO, IDX improved two of four CRT (quadrant task and arrow task) and two of two selective attention tasks but failed to affect digit span or SRT. IDX improved the last of three divided attention task series with no effect on the first two.

Discussion: IDX appears to improve specific aspects of attention in normal humans. Further studies are needed to assess the relationships between IDX effects and task complexity, performance under stressful condition or fatigue and capacity to inhibit distractors.

NR64 Monday, May 23, 9:00 a.m.-10:30 a.m.

Trimethapham for Blood Pressure Control During ECT

Georgios Petrides, M.D., Psychiatry, SUNY at Stony Brook, HSC T10, Stony Brook NY 11794; Farrokh Maneksha, M.D. Iannis Zervas, M.D. Andrew Francis, M.D.

Summary:

Trimethaphan (Arfonad) is a short-acting hypotensive agent that does not cross the blood-brain barrier. It is used for short-term hypertension control during surgery as a continuous IV drip at the rate of 3–4 mg/min. It is also used to control hypertension and tachycardia during ECT (Maneksha, 1991). Because of the short duration of ECT, trimethaphan bolus administration are not established.

We carried a double-blind, within-subject study to determine the optimal dose during ECT. Thirteen patients classified as ASA 1 or 2 for physical health without cardiovascular illness received placebo, 5, 10 or 15 mg. of trimethaphan during their second to fifth treatments in a random sequence. Blood pressure and heart rate were recorded every 30″ by automated oscillometric recorder (Dynamap). Recordings before administration, during seizure, five and 20 minutes after seizure were analyzed.

All doses of trimethaphan ameliorated the usual BP and pulse rate increases during the seizure. The 10 and 15 mg. doses elicited a faster return to baseline readings than 5 mg. and placebo (15 greater than 10). No rebound hypertension, prolonged hypotension, or other side effects were noted. Trimethaphan did not alter seizure duration.

NR65 Monday, May 23, 9:00 a.m.-10:30 a.m.

The Estrogen Antagonist Tamoxifen Causes Treatment Resistance to Antidepressants

Jacqueline Quak, M.D., Psychiatry, SUNY at Buffalo, 462 Grider Clinical Ctr. BB170, Buffalo NY 14215; Susanna Goldstein, M.D. Uriel Halbreich, M.D.

Summary:

Tamoxifen, an estrogen antagonist, is widely used as a treatment or adjuvant therapy for breast cancer in women. It is also studied in a nationwide trial as a prevention therapy for healthy women with a high risk to develop breast cancer.

Two patients with a life history of repeated depressive episodes that had responded well to treatment with antidepressants, were diagnosed as having breast cancer. After surgery and chemotherapy they started treatment with Tamoxifen. Within 12 months they became depressed, presenting symptoms similar to their previous depressive episodes. Treatment with antidepressants to which they responded in past episodes was ineffective. Several alternative treatments were unsuccessful. One was unsuccessfully treated with a MAOI. She had high platelet monoamine oxidase (MAO) activity so the MAOI dosage was increased with a good response. When she was taken off Tamoxifen, severe side effects appeared and MAOI was decreased. Subsequently Tamoxifen was reintroduced and the patient again developed a depressive episode requiring an increase of the dosage of MAOI.

Estrogen antagonists might turn depressives to non-responders to antidepressants in usual dosages. Increase in MAO might be one of the mechanisms that cause the non-response, but some other possible mechanisms should also be investigated.

NR66 Monday, May 23, 9:00 a.m.-10:30 a.m.

Double-Blind Randomized Trial Comparing the Efficacy and Tolerability of Medifoxamine and Imipramine in Major Depressive Disorder

Andre J. Galinowski, M.D., Sainte Anne Hospital, 1 Rue Cabanis, Paris 75014; Jean P. Olie, M.D. P. Lehert, Ph.D. F. Lemonnier, M.D. H. Loo, M.D.

Summary:

Medifoxamine (Cledial TM), an original new generation antidepressant with a serotonergic and dopaminergic profile, was compared to imipramine in a multicenter, doubleblind trial. Patients (n = 94) suffering from *DSM-III-R* major depression were included with a minimum MADRS score of 25 and received flexible doses of either drug (≥ 100 mg after 2 weeks of treatment). No associated treatment was permitted except for lorazepam 2 to 5 mg per day mean dose.

In the medifoxamine group (164 mg daily for 28 days) improvement in MADRS scores, number of patients with a MADRS improvement of at least 50%, and a final MADRS score < 8, were not significantly different from the imipramine group (mean dose:161 mg at day 28). No more difference appeared when several clinical variables were analyzed, in particular the *DSM-III-R* melancholic, the Newcastle endogenous subtypes and the in-or outpatient status. These intention to treat analyses were corroborated by on treatment analyses of the subgroup who could be assessed at all the assessment times. Medifoxamine appeared as better tolerated than imipramine, especially for anticholinergic symptoms.

Combining efficacy and tolerance, patients were classified according to MADRS and CGI scores: 57% of medifoxamine patients belonged to the success group vs 39% for the imipramine patients ($p < 0.04$). Medifoxamine appears as well tolerated and efficacious in severe forms of depression.

NR67 Monday, May 23, 9:00 a.m.-10:30 a.m.

Evaluation of Neuroleptic-Induced Hyperprolactinemia

David M. Klahr, M.D., Psychiatry, Columbia University, 710 West 168th Street 6th Flr, New York NY 10032; Lewis A. Opler, M.D. Nereida Correa, M.D. Andrew G. Frantz, M.D. Paul Michael Ramirez, Ph. D. Michael Y. Hwang, M.D.

Summary:

Goals: Although neuroleptic-induced hyperprolactinemia (NIH) is a well-recognized side effect and has been associated with a myriad of physical and psychological effects, there are no studies that have attempted to define the syndrome in a systematic manner. The Evaluation of Neuroendocrine Side Effects (ENSE) was devised for this reason.

Methods: There are three major parts to the scale: physical exam of the breast, questionnaire about side effects putatively associated with NIH (specific to gender), and serum prolactin level. The three subscales were assessed for correlation with each other. N = 10 men, 5 women.

Results: Preliminary data show no correlation between prolactin level and reported or observed side effects. There is also no correlation between neuroleptic dose and prolactin level. Reported side effects is correlated with observed side effects. As measured by our scale, NIH does not have clinically significant effects in men.

Conclusions: Our results show that more objective tests (e.g., nocturnal penile tumescence) may be necessary to determine clinical effects of NIH in men. Prolactin levels are not reliable predictors of clinical ramifications of NIH.

NR68 Monday, May 23, 9:00 a.m.-10:30 a.m.

Are Spine Films Medically Necessary Prior to ECT?

Miguel A. Perez, M.D., Psychiatry, University of Miami, 4300 Alton Road 3 Warner, Miami Beach FL 33140; Jose E. Ribas, M.D. David Loewenstein, Ph.D.

Summary:

Despite current recommendations that spine films no longer be performed prior to ECT they are required by most hospitals. This study sought to examine: (1) the incidence of pre-existing fractures; (2) do complications develop related to the fractures; (3) does medical justification exist for the risks and costs of pre-ECT spine films? The records of 228 consecutive inpatients treated with ECT (January 1988-June 1993) were reviewed regarding multiple variables including spine film results, number of ECT treatments, complications, and medication dosages. Patients were divided into three groups: (1) normal films (N = 100); (2) abnormal film without fracture (N = 88); (3) fracture (n = 22). Statistical analyses were performed utilizing Anova and student-Neumann-Keuls test for multiple comparisons.

No complications attributable to any spine film abnormalities developed. The groups differed with respect to age (with the fracture group being older; P 0.0001) but not gender or total number of treatments/dosage of succinyl choline used.

Compression fractures are commonly found prior to ECT, especially in the elderly. Despite no difference in number of treatments/dose of succinyl choline used, no patient developed complications related to fractures or other abnormalities on spine films. These findings support the recommendation that spine films are no longer medically necessary prior to ECT.

NR69 Monday, May 23, 9:00 a.m.-10:30 a.m.

Seizures During an Inpatient Psychiatric Hospitalization

Anand P. Popli, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Judith C. Kando, Pharm.D. Srinivasan S. Pillay, M.B. Mauricio Tohen, M.D. Jonathan O. Cole, M.D.

Summary:

Seizures are relatively rare but serious adverse events associated with psychotropic medications. The higher incidence of seizures associated with the newer agents like bupropion and clozapine have made clinicians more aware of this adverse drug reaction. During a period of two and a half years, there were over 10,000 admissions at a large psychiatric hospital. All patients referred to the internal medicine department for adverse drug reactions were screened by a quality assurance nurse for probable drug related seizures. These were reviewed by a clinical pharmacist. The charts of 27 patients who experienced seizures while on psychotropics were reviewed retrospectively.

Results: Nineteen (70%) had pre-existing seizure disorder and eight had new onset seizures. Psychotropics were implicated in five of eight in the new onset group and three of the 19 in the pre-existing seizure group. Noncompliance with sub-therapeutic blood levels and pseudoseizures accounted for 32% and 26% of the pre-existing group, respectively. Benzodiazepines withdrawal and alcohol withdrawal seizures together were a factor in 26% of the total cases.

Conclusions: Seizures were relatively rare events during an inpatient psychiatric hospitalization and occurred mostly in patients with a pre-existing seizure disorder. Noncompliance, benzodiazepine and alcohol withdrawal, and polypharmacy were important associated factors.

NR70 Monday, May 23, 9:00 a.m.-10:30 a.m.

The McLean Hospital First-Episode Psychoses Family Study

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Bruce Cohen, M.D. Mauricio Tohen, M.D. James Heggarty, M.D. Franca Centorrino, M.D. Michelle Weiss, M.S.

Summary:

Objective: To determine the morbid risk for psychiatric disorders in first-degree relatives of probands with a first episode of psychosis.

Methods: This is a preliminary report on an ongoing longitudinal family study of the first-degree relatives of probands recruited for the first-episode McLean Project. The first-degree relatives (N = 156) of probands with first-episode psychosis (N = 32) were either interviewed in person with the Diagnostic Interview for Genetic Studies (DIGS) and/or the Family Interview for Genetic Studies (FIGS) by a rater who was blind the probands diagnosis, treatment, and outcome.

Results: Probands were divided into two groups, affective psychoses (AP): bipolar disorder (BD), major depressive disorder (MDD); and non-affective psychoses (NAP): schizophrenia (SZ), schizoaffective disorder (SAD), schizophreniform (SZP), delusional disorder (DD), and psychosis NOS (Pnos). In probands with AP, the morbid risk in relatives was: SZ 2.82 ± 0.028, MDD 32.65 ± 0.067, BD 21.15 ± 0.027, Pnos 1.54 ± 0.0015. In probands with NAP, the morbid risk in relatives was: SZ 3.05 ± 0.021, MDD 23.53 ± 0.084, and BD 4.0 ± 0.039. BD was more common in relatives of probands with an AP compared to probands with a NAP (X^2 = 4. 13, p = .041). The morbid risk for other psychiatric disorders did not differ significantly between the relatives of probands with an AP vs. NAP.

Conclusions: Relatives of probands with a psychotic affective disorder had a higher risk for bipolar disorder.

NR71 Monday, May 23, 9:00 a.m.-10:30 a.m.

Liver Function Tests and Anticonvulsants

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Mauricio Tohen, M.D., German Baraibar, M.D., Jong-Won Kim, M.D., Jose Castillo-Ruiz, M.D., Judith Kando, Pharm. D.

Summary:

Objective: To determine the incidence of liver function test abnormalities associated with the psychiatric use of carbamazepine (CBZ) and valproate (VPA). Method: Abnormal liver function tests were divided into either moderate or marked abnormalities and were as follows: alanine aminotransferase (ALT,SGPT) counts of 50–100 IU/L (moderate), or more than 100 IU/L (marked), aspartate aminotransferase (AST,SGOT) counts of 50–100 IU/L (moderate), or more than 100 IU/L (marked), lactate dehydrogenase (LDH) counts of 250–350 IU/L (moderate), or more than 350 IU/L (marked) were identified in a population of 1,628 cases at risk among 7,941 patients admitted to McLean Hospital in a recent three year period. Cases included patients receiving CBZ or VPA, whose liver test abnormality was not associated with relevant medical condition or hepatotoxic agents.

Results: The incidence of any abnormal liver function test with both CBZ and VPA, of 26% (14/54) was significantly higher than the 3.3% (23/703) incidence with CBZ (^{2} = 55.36, p = .0000, and the 2.8% (26/925) with VPA (^{2} = 69.56, p = .0000).

Conclusions: the incidence of abnormal liver function tests with either CBZ or VPA alone was low. The authors will discuss the findings, as well as offer guidelines in monitoring of liver function tests.

NR72 Monday, May 23, 9:00 a.m.-10:30 a.m.

Demographic Characteristics of Patients Referred to the University of Miami/Jackson Memorial Hospital Adult Outpatient Psychiatric Clinic

Eusebio G. Hernandez, M.D., Psychiatry, Univ of Miami JMH D29, 1611 NW 12th Avenue, Miami FL 33136; Seana Shaw, M.D.

Summary:

Introduction: The University of Miami/Jackson Memorial Hospital Psychiatric Outpatient Clinic accommodates 5,000–6,000 patient visits a year and is centered in an urban, multicultural, multilingual community. Miami is a city that has endured a major natural disaster (Hurricane Andrew in August 1992) and significant population changes due to immigration. The study will compare variables before and after the hurricane as well as the three-year period from January 1, 1991 to December 31, 1993.

Method: This is a retrospective study that uses data collected from computerized records of visits to the outpatient clinic of a large university teaching hospital in Miami, Florida from 1991–3. The data were analyzed comparatively in terms of race, gender, language spoken, diagnosis, number of patients, and number of clinic visits per year for 1991, 1992, and 1993. The impact of Hurricane Andrew was studied by comparing the above variables pre and post hurricane in respect to number of visits and shift in diagnosis.

Results: The outpatient clinic racial and ethnic composition mirrors that of Miami as reported in 1990 population studies. Affective disorders account for the 30%–33% of the total and Psychotic disorders 23%. The number of visits and monthly pattern of visits show no change related to Hurricane Andrew. There has not been a shift of diagnosis or increase of depression or stress related disorders. The clinic population reflects the ethnic composition of Miami. Caucasians comprise 30%, Hispanic 49%, and Blacks 20% of the clinic population.

Conclusions: An outpatient data base is an essential research tool that can be used to explore questions about outpatient psychiatric service delivery. While we found no change in our utilization patterns, there may be factors not studied to account for this finding, such as relocation of hurricane victims or utilization of services closer to the victimized population.

NR73 Monday, May 23, 1:00 p.m.-2:30 p.m.

Personality Dimensions and Anxiety Disorders

Vladan Starcevic, M.D., Psychiatry, Medical College of Pennsylvania, 3300 Henry Avenue, Philadelphia, PA 19129; Eberhard H. Uhlenhuth, M.D., Brian A. Roberts, M.D., Stephanie Fallon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize there is no significant personality-related differences between SP and GAD.

Summary:

Objective: Comparison of the Tridimensional Personality Questionnaire (TPQ)-derived personality dimensions (PDs) in social phobia (SP) and generalized anxiety disorder (GAD).

Method: 50 patients with SP and 49 patients with GAD were administered the TPQ, which assesses three main PDs: novelty seeking (NS), harm avoidance (HA), and reward dependence (RD). The score on each of these PDs is a sum of scores on four lower-order PDs

Results: Although scores on HA were substantially elevated in both groups when compared with the U.S. normative data, patients with SP scored significantly lower than GAD patients. There were no significant differences on NS and RD. As for lower-order PDs, patients with SP scored higher on shyness with strangers (HA3), and GAD patients scored higher on fatiguability and asthenia (HA4) and anticipatory worry and pessimism (HA1).

Conclusions: There are no significant, personality-related differences between SP and GAD, which is in agreement with the research findings using categories of personality disorders. The scores on HA and its subscales (HA1, HA3, and HA4) appear to reflect current state of anxiety. The validity of the HA1, HA3, and HA4 constructs is supported by the findings of the expected differences in scores on respective subscales; thus, social/interpersonal anxiety, as measured by the HA3 subscale, was more prominent in SP than in GAD.

References:

1. Cloninger CR, Przybeck TR, Svrakic DM: The Tridimensional Personality Questionnaire: U.S. normative data. *Psychol Rep* 69:1047–1057, 1991.

2. Joffe RT, Bagby RM, Levitt AJ, Regan JJ, Parker JDA: The Tridimensional Personality Questionnaire in major depression. *Am J Psychiatry* 150:959–960, 1993.

3. Kleifield EI, Sunday S, Hurt S, Halmi KA: Psychometric validation of the Tridimensional Personality Questionnaire: Application to subgroups of eating disorders. *Compr Psychiatry* 34:249–253, 1993.

NR74 Monday, May 23, 1:00 p.m.-2:30 p.m.

Craniofacial Anomalies in Schizophrenia: Clues to the Timing of Developmental Disturbance

Abbie Lane, M.B., Psychiatry, Cluain Mhuire, Newtown Park Avenue Blackrock, Co Dublin Ireland, Ireland; Anthony Kinsella, FIS, Patrice Murphy, M.B., John L. Waddington, D.Sc., Conall Larkin, M.B., Eadbhard O'Callaghn, M.B.

Educational Objectives:

To recognize that the prenatal development of patients with schizophrenia has been disturbed and that the period of gestation (8th to 22nd weeks) is critical to the development of schizophrenia, which is in keeping with the neuropathological findings, but is the first clinical evidence of timing.

Summary:

Objective: Evidence suggests that schizophrenia results from disturbed prenatal development, yet information regarding the timing of this disruption is sparse. Minor physical anomalies (MPAs) reflect developmental disturbance, such that patterns or clustering of MPAs could be clues to the timing of prenatal disruption in schizophrenia.

Method: Using a new scale, based on quantitative measurements 174 patients with *DSM-III-R* schizophrenia and 80 age- and sex-matched non-psychiatric controls were examined for MPAs.

Results: Patients displayed significantly more anomalies than controls. These included anomalies of the eyes (epicanthus, $P = 0.003$), ears (widened helices, $P < 0.001$; hypoplastic lobes, $P = 0.007$) and mouth (high and narrow palates $P < 0.001$). Using logistic regression, the anomalies that best differentiated patients from controls included: skull base width ($P = 0.003$), lower facial height ($P = 0.04$), biocular diameter ($P = 0.001$), mouth width ($P = 0.01$), ear protrusion ($P < 0.001$), supraorbital ridge ($P < 0.001$), epicanthus ($P = 0.003$), bifid tongue ($P = 0.002$), palatal ridges ($P < 0.001$) and palatal height ($P = 0.004$).

Conclusion: These anomalies of the craniofacial area, are related to the developing brain and central nervous system and result from disturbance, by genetic and/or environmental factors acting between the 8th and 22nd weeks of gestation. These findings suggest that this period may be critical to the aetiology of schizophrenia.

References:

1. Jones, K.L. Smith's recognizable patterns of human malformation. W.B. Saunder Company, 1988.

2. O'Callaghan, E., Larkin, C., Kinsella, A.., and Waddington, J. Familial, obstetric and other clinical correlates of minor physical anomalies in schizophrenia. Am Psych 4:479–483, 1991.

NR75 Monday, May 23, 1:00 p.m.-2:30 p.m.

A Computer Simulation of the HPA Axis

Joseph M. Gonzalez-Heydrich, M.D., Psychiatry, Children's Hospital, Fegan 8, 300 Longwood Avenue, Boston MA 02115; Ronald J. Steingard, M.D., Issac Kohane, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the experimental manipulations needed to decide between competing hypothesis of the pathophysiology of the HPA axis in depression.

Summary:

This paper describes the construction of a computer model that simulates the hypothalamic-pituitary-adrenal axis (HPA axis) regulation of cortisol. The model is built from components representing the integration of continuous secretion and degradation of cortisol, adrenocorticotropic hormone (ACTH), and corticotropin releasing hormone (CRH). These components are linked into a network of physiological relations based on the current knowledge of their mutual interactions. Rate constants, half lives, and receptor affinities are assigned from values derived from the experimental literature. At its current level of development the model is able to accurately simulate the timing, magnitude, and decay of the ACTH and cortisol concentration peaks resulting from the ovine-CRH stimulation test in normal and hyper-cortisolemic patients. The model will be used to predict the effects on time course of cortisol and ACTH levels of lesions in different components of the HPA axis in an effort to better understand the hypercortisolimia of depression. It is hoped that the model will help clarify the experimental manipulations needed to decide between competing hypothesis of the pathophysiology of the HPA axis in depression. Efforts are currently underway to extend the model deeper into the central nervous system.

References:

1. Debold RC, et al: Effects of ovine corticotropin-releasing hormone on ACTH secretion in the absence of olucocorticoid feedback inhibition in man. *J Clin Endocrinol Metab* 68: 431, 1989.

NR76 Monday, May 23, 1:00 p.m.-2:30 p.m.

Regulation of Early Gene Expression in the CNS by Antipsychotics

Patrick J. Rogue, M.D., UPR 416 CNRS, Center Neurochemist., 5 Rue Blaise Pascal, Strasbourg 67084, France; Guy Vincendon, M.D.

Educational Objectives:

To contribute to the understanding of the neurobiological basis of cerebral plasticity and and the long-term effects of antipsychotic drugs in the CNS.

Summary:

Dopamine D_2 receptors regulate the expression of a specific set of immediate early genes (IEG) in the rat striatum. A single injection I.P. of haloperidol (2 mg/kg) or sulpiride (100 mg/kg) produces a rapid and transient increase in c-*fosc-jun jun* B and zif268 mRNA, but has no influence on the expression of ETR1 or *jun* D (Brain Res Bull *29,* 469). These inductions are specifically blocked by pretreatment with a D_2 agonist (1 mg/kg quinelorane). We have further studied the effect of clozapine and dopamine D_2 receptor antagonists on IEG expression in different regions of the CNS by northern analysis and ISH. Both clozapine (20 mg/kg) and haloperidol (2 mg/kg) induce zif268, *c-fos,* and *jun* B in the nucleus accumbens. However, only haloperidol induces all of these proto-oncogenes in the striatum, whereas in the frontal cortex clozapine induces c-fos but not zif268. The effects of these compounds on the expression of CREB and CREM mRNAs, as well as the effects of prolonged administration, will also be presented. The significance of these specific IEG activation patterns for the mode of action of antipsychotics will be discussed.

References:

1. Rogue P, Vincendon G Do pamine D2 receptor antagonists induce immediate early genes in the rat striatum *Brain Res Bull* 29:469–472, 1992.

2. Rogus P, Malviya AN Neuroleptics differentially induce *jun* family genes in the rat striatum. *Neuro Report* (in press).

NR77 Monday, May 23, 1:00 p.m.-2:30 p.m.

Striatal Dopamine Receptor Binding in Epileptic Psychoses

Howard A. Ring, M.B., Neuropsychiatry, Institute of Neurology, Queen Squarr, London WC1N3BG, England; Michael R. Trimble, M.D., Durval O. Costa, John Moriarty, M.B., Paul Verhoeff, M.D., Peter Ell, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the straital dopamine receptor binding in epileptic psychoses.

Summary:

In order to study the nature of dopaminergic activity in epileptic psychoses we investigated striatal dopamine receptor binding in 14 patients with epilepsy. Seven of the patients were acutely psychotic when studied, having recently developed a perictal schizophreniform psychosis. The remaining patients were not psy-

chotic. All patients were scanned using single photon emission tomography (SPET) with ^{123}I-IBZM, a specific dopamine D2 receptor ligand. A region of interest analysis was performed. Comparison of mean basal ganglia to occipital cortex activity ratios in the two groups demonstrated significantly reduced specific binding of ^{123}I-IBZM to striatal D2 receptors in the psychotic patients compared to those without psychosis.

References:

1. Adamec RE: Does kindling model anything clinically relevant? *Biol Psychiatry* 27:249–279, 1990.

2. Csernansky JG et al. Mesolimbic dopaminergic supersensitivity following electrical kindling of the amygdala. Biol Psychiatry 23:285–294, 1988.

NR78 Monday, May 23, 1:00 p.m.-2:30 p.m.

Apoliporotein E-4 Allele Frequency in Two Different Populations of Patients with Alzheimer's Disease

Debby W. Tsuang, M.D., Psychiatry, University of WA, VAMC 182B 1660 S Columbian Way, Seattle WA 98108; Walter A. Kukull, Ph.D., Elaine Peskind, M.D., Gerald D. Schellenberg, Ph.D., Murray A. Raskind, M.D., Steve Edland, M.S.

Summary:

Objective: The University of Washington Alzheimer's Disease Research Center has two different populations of patients with the diagnosis of probable Alzheimer's disease (AD) by NINCDS/ADRDA criteria. Recent studies report apolipoprotein E (apoE) allele type 4 as a risk factor for late-onset AD. We investigated whether these two AD populations differ in apo-E4 allele frequency.

Method: One sample consists of newly diagnosed cases recruited through the local health maintenance organization (Group Health Cooperative). They represent the spectrum of probable AD patients and are primarily sporadic and late-onset (n = 166). The second sample comes from the general population (Core-C) and subjects are selected for their good general health in addition to a diagnosis of probable AD. Subjects include both early and late-onset as well as familial and sporadic cases (n = 119). We obtained blood samples for genotype for a majority of the patients.

Results: Within patients with sporadic AD, apo-E4 allele frequency in Core-C patients (0.48) is almost twice as high as in the Group Health patients (0.26). Core C patients are one-and-a-half times as likely to have one apo-E4 allele than Group Health patients (50% versus 35%, $p < 0.01$). Core-C patients are almost three times as likely to have two apo-E4 alleles than the Group Health patients (22% versus 8%, $p < 0.005$). Core-C patients are younger at age of onset (mean = 62.7 yrs.) than Group Health patients (mean = 76.5 yrs.) and they have a longer duration of symptoms prior to diagnosis (6.9 yrs. versus 2.8 yrs.).

Conclusion: We conclude that apo-E4 allele frequency is significantly different between these two groups of patients with AD. Selection bias may contribute to the differences in apo-E4 allele frequencies.

References:

1. Saunders AM, Strittmatter WJ, Schmechel D, St George-Hyslop PH, Pericak-vance MA, Joo SH, Rosi BI, Gusella JF, Crapper-Maclachian DR, Alberts MJ, Hulette C, Crain B, Goldgaber D, Roses AD. Association of apolipo-protein-E allele epsilon-4 with late-onset familial and sporadic Alzheimer's disease. Neurology 43:1467–1472; 1993.

2. Yu CE, Payami H, Olson J, Boehnke M, Wijsman E, Orr H, Kukull W, Goddard K, Nemens E, White J, Alonso ME, Taylor TD, Ball MJ, Kaye J, Morris J, Chui H, Sadovnick AD, Martin GM, Larson EB, Heston LL, Bird TD, Schellenberg GD. The apolipoprotein E/CI/CII gene cluster and late-onset Alzheimer's disease. Genomics (in press).

NR79 Monday, May 23, 1:00 p.m.-2:30 p.m.

Prescribing Patterns of Newer Antidepressants in a Resident Outpatient Psychiatry Clinic

Amar N. Bhandary, M.D., Psychiatry, SUNY HSC, 750 E. Adams Street, Syracuse NY 13210; Joe Medicis, M.D., Prakash Masand, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the most common side effects and that 78% of patients showed improvement in symptoms.

Summary:

The newest class of antidepressants represent a frequently prescribed group of drugs in the outpatient population. Our objective was to access prescribing habits and patient outcome in outpatient clinic. Data were collected retrospectively in adult outpatients who presented to clinic. The following variables were evaluated: the choice of agent (fluoxetine, sertraline, bupropion, and paroxetine), indications for use, dosage utilized, dosage adjustment, adequacy of trial, duration of maintenance therapy, contraindications, and outcome. Sixty-seven patients were enrolled: seven were excluded due to possible investigator bias. Fluoxetine was clearly the agent used most often (60%), followed by sertraline (23%), paroxetine (12%), and bupropion (5%). The indication for use was documented in all (100%) of the 60 patients enrolled. A trial of greater than four weeks on adequate dosage was utilized in 78% of patients before changing to or adding an augmentation strategy. The duration of therapy was less than 12 months in 73% of patients. Of thos 27% whose duration of therapy was greater than 12 months, 63% had a recurrence. A physical exam was noted to have been performed in 60% of the patients. Side effects occurred in 58% of all patients. The most common side effects included nausea and insomnia. Outcome was documented in 95% of all patients. Seventy-eight percent of patients showed improvement in symptoms.

References:

1. Keller MB. Klerman GL. Lavori PW. et al: Treatment received by depressed patients. *JAMA* 248:1848–1855, 1982.

2. Weismann MM, Klerman GL: The chronic depressive in the community unrecognized and untreated. *Compr. Psychiatry* 13:523–532, 1977.

NR80 Monday, May 23, 1:00 p.m.-2:30 p.m.

Is Childhood Sexual or Physical Abuse a Risk Factor for Psychotic Depression?

Adele C. Viguera, M.D., Psychiatry, McLean Hospital, 115 Mill Street Higginson 247, Belmont MA 02178; Anthony J. Rothschild, M.D.

Educational Objectives:

1) Participants will appreciate differences between psychotic depressed and nonpsychotic depressed patients on reported histories of childhood physical and sexual abuse; 2) Participants will learn about underdiagnosis of psychotic depression in patients with PTSD.

Summary:

Objective: Abused children admitted to an inpatient facility have been reported to be more likely to develop psychotic depression following a history of sexual abuse than after physical abuse. The purpose of the present study was to determine whether there were

differences between psychotic depressed (PD) and nonpsychotic depressed (NPD) adult patients on reported histories of childhood physical and sexual abuse.

Methods: We retrospectively reviewed 100 consecutive McLean Hospital admissions (1992–1993) with DSM-III-R chart diagnosis of major depression (N = 50) or major depression with psychotic features (N = 50). Evidence of abuse in childhood was gathered from records of clinical assessments from physicians, nurses, and social workers. Chart review revealed that five of the patients diagnosed as NPD actually met criteria for PD, making the correct number of patients with NPD 45 vs. 55 with PD.

Findings: Risk of psychosis in subjects with sexual (7/16 = 44%) or physical abuse (13/25 = 52%) was similar (both NS by χ^2; $p > 0.5$). Childhood abuse was strongly (6.5 fold) associated with comorbidity for probably PTSD (16/33 = 48.5% with, vs. 5/67 = 7.5% without abuse; $\chi^2 = 20.0$ $p < 0.00001$). Of the five PD patients with a chart diagnosis of NPD, four did not receive combined antipsychotic-antidepressant treatment or ECT, and three were considered to have PTSD.

Conclusion: These findings do not support the prediction that a history of childhood sexual abuse is a risk factor for the later development of adult PD. Though early abuse was strongly associated with PTSD, this may reflect diagnostic bias. Finally, we suggest that lack of differentiation pf PTSD and psychotic features in depressed adults may result in suboptimal pharmacologic treatment.

References:

1. Livingston R: Sexually and physically abused children. *J. Amer. Acad. Child Adol. Psychiat.* 26.3:413–415. 1987.

2. Schatzberg AF. Rothschild AJ: Psychotic (delusional) major depression: should it be included as a distinct syndrome in DSM-IV? *Am J Psychiatry* 149:733–745, 1992.

NR81 Monday, May 23, 1:00 p.m.-2:30 p.m.

Gender Differences Among Psychiatric Inpatients with Comorbid Cocaine and Alcohol Use Disorders

Ihsan M. Salloum, M.D., University of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213; Dennis Daley, M.S.W.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize gender related differences in hospitalized psychiatric patients with comorbid cocaine and alcohol use disorders.

Summary:

The aim of this study is to elucidate gender-related differences in hospitalized psychiatric patients with comorbid cocaine and alcohol use disorders. Fifty-five males and 52 females selected from 153 consecutive admissions to a dual-diagnosis unit were comparatively examined on demographic and clinical variables. The results indicated that males were more likely to be single ($P < 0.04$), employed ($P < 0.03$), report longer duration of alcohol and cocaine use, and have higher rates of intravenous drug use ($P < 0.008$). They had higher rates of bipolar disorder ($P < 0.08$), antisocial personality disorder ($P < 0.001$), and narcissistic personality disorder ($P < 0.008$). Males also reported higher rates of homicidal thoughts on admission ($P < 0.04$) and of history of violent acts ($P < 0.02$). Females, on the other hand, were more frequently diagnosed with depressive disorder, and had higher rates of sexually transmitted diseases ($P < 0.02$). Further analysis of gender difference within and across specific substance abuse groups revealed that female alcoholics were significantly older ($P < 0.01$) and had an older age of onset of alcohol use ($P < 0.0005$) than male alcoholics. They were also older than females who coabused alcohol and cocaine or cocaine only ($P < 0.00005$). They had lower functioning than male alcoholics ($P < 0.0001$) and other dually diagnosed females ($P < 0.004$) as well. On the other hand, female patients who abused both alcohol and cocaine had earlier age of onset of psychiatric disorders when compared with male coabusers ($P < 0.05$) or with females who abused only alcohol or cocaine ($P < 0.02$). They also differed from the latter female group by having earlier age of onset of alcohol and cocaine abuse. Furthermore, males in the coabuse group were rated lower than the other males on levels of functioning currently ($P < 0.006$) and on best functioning during the past year ($P < 0.002$). The results document relevant gender-specific differences and highlight the importance of exploring gender effects in studying dually diagnosed patients. These results warrant further studies exploring gender-related vulnerability to comorbid psychiatric disorders among substance abusers.

References:

1. Carroll KM, Rounsaville BJ, Bryant KJ: Alcoholism in treatment-seeking cocaine abusers: clinical and prognostic significance. *J. Stud. Alcohol* 54:199–208, 1993.

2. Theuds AK, Brady KT, Grice D, et al: A comparison of psychopathology in cocaine and alcohol dependence. *American Journal on Addictions.* 2:279–286, 1993.

NR82 Monday, May 23, 1:00 p.m.-2:30 p.m.

Retinal Effects of Chronic Lithium Use

Suzanne M. Allain, M.D., Psychiatry, McKellar General Hospital, 325 Archibald Street, Thunder Bay ON P7E 1G6, Canada; Raymond W. Lam, M.D.

Educational Objectives:

1) List some acute effects of lithium on the eye; 2) State chronic retinal effects of lithium?

Summary:

Objective: Chronic lithium has not been associated with clinical changes in vision. However, animal studies of lithium use have demonstrated structural changes within the retina and potentiation of light-induced retinal damage. In humans, acute administration of lithium is associated with changes in retinal electrophysiological function. Our objectives was to determine whether similar retinal changes occur with chronic use of lithium.

Method: We studied 23 stable bipolar patients and 20 age-1 and sex-matched control subjects. Patients were euthymic, taking lithium for at least two years, and not on neuroleptic drugs. Control subjects were drug-free and had no history of psychiatric disorder. All subjects received a detailed ophthalmologic examination followed by electroretinography (ERG) and electrooculography (EOG). ERG and EOG are noninvasive, objective, clinical electrophysiologic tests of retinal function. Data from the ERG and EOG were analyzed using repeated measures MANOVA.

Results: The patients had been taking lithium for an average of 7.6 ± 4.3 years at a current dose of 980 ± 280 mg/day and a serum of 0.8 ± 0.2 meq/l. On the ERG, there were no significant differences in b-wave amplitude or b-wave implicit time between patients and controls. Similarly, the EOG ratios were not significantly different between groups.

Conclusions: Chronic lithium use is not associated with retinal electrophysiological changes when patients are compared to a normal control group. These electrophysiologic data support previous clinical studies suggesting that any retinal effects of lithium are not of clinical significance. However, it is still possible that the retinal effects of lithium are state-dependent and/or related to the mechanism of action of lithium.

References:

1. Kaufman, P. A., et al: Ocular Effects of Oral Lithium is Humans *Acta Opthalmogica* 63:327–332, 1985.

2. Hiroz, C. A., et al: Les effets secondaires du Lithium en opthalmologie. *L'Encephale*, VII: 123–128, 1981.

NR83 Monday, May 23, 1:00 p.m.-2:30 p.m.

Untoward Effects of Lithium Treatment in Very Young Hospitalized Children

Owen R. Hagino, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus OH 43210; Elizabeth B. Weller, M.D., Mary Fristad, Ph.D., Douglas Washing, B.A., Ronald A. Weller, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the potential risks of lithium treatment of preschool-age children, including the relationship of side effects to dose.

Summary:

Purpose: The present study reports on the untoward or toxic effects of lithium in the treatment of children ages 4 through 6 years.

Subjects: Fifteen preschool-age, extremely aggressive, hospitalized children with comorbid mood disorder and disruptive behavior disorder(s) in addition to family history of mood disorder, aggression, or psychosis were studied.

Method: The investigators reviewed clinical and research records of 15 children treated with lithium according to an established impatient protocol. Side effects as reported by psychiatric staff were categorized by organ system affected and severity.

Results: A majority of the children ($n = 9$, 60%) manifested one or more types of side effects, most commonly central nervous system ($n = 7$, 47%) and gastrointestinal effects ($n = 5$, 33%). Side effects were seen at doses of 25.8 to 52.1 mg/kd/day. Serum levels drawn shortly after the onset of side effects ranged from 0.65 to 1.37 mEq/L. The maximum lithium doses and maximum lithium serum levels were significantly higher for those children who experienced side effects compared with those children who reported no side effects. Two children manifested serious side effects (confusion, slurred speech, and ataxia) on maximum doses of lithium, which were significantly greater than those given to the children with less serious side effects ($M \pm S.D. = 51.9 \pm 0.2$ vs. 42.3 ± 5.3 mg/kg/day, $t = -2.46$, $p < 0.04$).

References:

1. Campbell M, Silva R.R., Kafantaris V., et al: Predictors of side effects associated with lithium administration in children. *Psychopharmacol. Bull.*, 27(3):373–380

2. Silva R.R., Campbell M, Golden R.R., et al: Side effects associated with lithium and placebo administration in aggressive children. *Psychopharmacol. Bull.*, 28(3):319–326, 1992.

NR84 Monday, May 23, 1:00 p.m.-2:30 p.m.

Acute Psychiatric Response to the Explosion at the World Trade Center

JoAnn Difede, Ph.D., Psychiatry, Cornell Medical College, 445 68th Street 3-K, New York NY 10021; William J. Apfeldorf, M.D., Lisa Spielman, Ph.D., Marylene Cloitre, Ph.D., Samuel W. Perry III, M.D.

Summary:

Few empirical studies have addressed the acute mental health effects of terrorism. This is not surprising given the methodologic difficulties in locating and assessing victims of civil violence. The purpose of this report is to describe the results of a comprehensive assessment of a small group of the survivors of the explosion at the World Trade Center. Six women and four men with a mean age of 33 years (± 6.7 years) presented for evaluation at our anxiety disorders clinic four weeks after the incident. The evaluation consisted of a structured clinical interview, the SCID-ADIS, and self-report questionnaires (the Impact of Events Scale (IES), the Anxiety Sensitivity Index (ASI), and the Beck Depression Inventory (BSI)). Of those evaluated, six received a primary Axis I diagnosis of PTSD; two received a primary diagnosis of major depression; one a diagnosis of panic disorder; and one had no Axis I diagnosis. Of the six patients diagnosed with PTSD, one had a comorbid GAD. The mean IES-Intrusion score of 20.4 (± 10.7) compared to the IES-Avoidance score of 12.4 (± 9.0) suggests that intrusive symptoms were more characteristic of this sample. The mean Anxiety Sensitivity Index and the mean Beck Depression Inventory scores were not within the clinically significant range.

Perhaps not surprisingly, most of our subjects had PTSD. Although no conclusions can be drawn about rates of acute psychiatric disorders following terrorist incidents because our sample was small, self-referred, and treatment-seeking, it is noteworthy that the pattern of psychiatric disorders presented following this terrorist incident was similar to that of other catastrophic events. Those interviewed presented either with PTSD, another anxiety disorder, or major depression. Second, although most of those assessed received a diagnosis of PTSD, the symptomatology of PTSD did not capture the subjective experience of these trauma survivors. Those who had a diagnosis of PTSD reported a heightened sense of vulnerability, fear, and a sense of helplessness as their chief complaints; although they generally had severe intrusive symptoms (e.g., flashbacks), they did not report being especially distressed by them. It is also interesting that the three people who had a psychiatric history experienced a recrudescence of those symptoms, not PTSD, as their primary problem.

NR85 Monday, May 23, 3:00 p.m.-5:00 p.m.

Sexual Abuse in Female Psychiatric Outpatients

Sylvie Lombardo, B.A., c/o Robert Pohl, University Psych Center, 2751 E. Jefferson Suite 200, Detroit MI 48207, Robert Pohl, M.D.

Summary:

Objective: To explore the relationship between sexual abuse (SA) history and adult psychopathology. We hypothesized that a history of SA would be associated with multiple Axis I diagnoses, with anxiety disorders, and with PTSD or subsyndromal symptoms of PTSD. Method—A structured interview, based on four previously used instruments by Kilpatrick, Wyatt, Saunders, and Jehu, was used to collect the SA history in 40 adult female nonpsychotic outpatients, and the severity of any SA history was rated on a fivepoint scale. The SCID, the Davidson PTSD Scale, and the Life Environment Questionnaire were also administered.

Results: A history of SA was common (70%). Patients with a primary diagnosis of an anxiety disorder (n = 19) were more likely than those with an affective disorder (n = 18) to have a history of SA (p = 0.01). Patients with either a primary or secondary anxiety disorder (n = 28) were more likely than other patients to have a history of SA (p = 0.04), and the abuse was more severe (3.5 ± 1.5 vs. 2.1 ± 1.6, p = 0.04). There was no significant relationship between SA history and the number of Axis I diagnoses, diagnosis of PTSD, or PTSD symptoms. Conclusions—History of SA is common among adult female psychiatric outpatients and is associated with non-PTSD anxiety disorders.

NR86 Monday, May 23, 3:00 p.m.-5:00 p.m.

Cognitive Distortions in Various Anxiety Disorders

Vladan Starcevic, M.D., Psychiatry, University of New Mexico, 2400 Tucker NE, Albuquerque NM 87131, Eberhard H. Uhlenhuth, M.D., William Matuzas, M.D. Dorothy Pathak, Ph.D.

Summary:

Objective: Comparison of cognitive distortions in panic disorder (PD) and generalized anxiety disorder (GAD).

Method: Seventy-four PD patients and 49 GAD patients were administered The Anxious Thoughts and Tendencies Scale, which assesses three cognitive distortions: catastrophizing (CAT), selectivity (SEL), and intrusions (INT).

Results: The mean scores on CAT, SEL, and INT were almost identical in PD patients without agoraphobia and PD patients with mild agoraphobia. Therefore, these patients were combined into one group, "pure" PD (PPD), and compared with patients with GAD and PD with moderate and severe agoraphobia (PDAG): the latter two groups scored higher, and significantly so on SEL and INT. There was no significant difference between patients with GAD and PDAG.

Conclusions: The degree of cognitive distortions contributes to the distinction between PPD on one hand, and GAD and PDAG, on the other. The association between cognitive distortions and GAD and PDAG, may be etiologically relevant, in contradistinction to PPD, where such association appears weaker, supporting the notion that PPD is characterized mainly by biological dysfunction. A much higher score on INT in GAD patients may indicate that pathological worry in GAD has an intrusive quality.

NR87 Monday, May 23, 3:00 p.m.-5:00 p.m.

OCD in College Students: Presentation, Impairment and Treatment

Lacramioara Spetie, M.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus OH 43210, Brendan T. Carroll, M.D.

Summary:

This study gives special attention to the presentation, impairment, and treatment of college students with obsessive compulsion disorder (OCD).

From a total of 92 college students seen over a five-month period for an initial psychiatric evaluation in the outpatient service of the Student Health Service of the Ohio State University, seven (7.6%) met the *DSM-III-R* criteria for obsessive compulsive disorder (OCD). Four of them had significant academic or occupational impairment. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was used to rate the severity of OCD before and after four weeks of treatment. All patients received psychotherapy, medication, or both. Four of them showed a greater than 50% reduction in the Y-BOCS scores.

The findings of this case series suggest that OCD is frequently seen in college students attending mental health clinics and that college students with OCD may greatly benefit from treatment in these settings.

NR88 Monday, May 23, 3:00 p.m.-5:00 p.m.

Carbon Dioxide Sensitivity Following Tryptophan Depletion in Patients with Panic Disorder

Justine M. Kent, M.D., Psychobiology, NYS Psychiatric Inst., 722 West 168th Street Unit 92, New York NY 10032; Jose Martinez, M.A., Laszlo A. Papp. M.D., Jack M. Gorman, M.D.

Summary:

Objective: To investigate the hypothesis that panic disorder patients have respiratory hypersensitivity related to decreased serotonin function.

Methods: Three patients with a *DSM-III-R* diagnosis of panic disorder and seven controls were studied under two conditions; at baseline and following tryptophan depletion. Tryptophan depletion, verfied by plasma levels, was accomplished by administering an enriched amino acid drink lacking tryptophan after 24 hours of a low-tryptophan diet. Respiratory and anxious responses to room air breathing, hyperventilation, and 5% CO2 inhalation were measured. Anxiety levels were assessed by the Acute Panic Inventory (API).

Results: No patients panicked to hyperventilation; however two of the three patients panicked to 5% CO2 inhalation at baseline and all three *panicked* after tryptophan depletion. At baseline, patients showed a trend of greater respiratory frequency ($p < .06$) and minute ventilation ($p < .09$) during 5% CO2 inhalation than controls. This group difference was significant for frequency after tryptophan depletion ($p < .04$). Subjects demonstrated a trend toward increased total API scores after tryptophan depletion. This result was significant for controls ($p < .02$).

Conclusions: This pilot study suggests tryptophan depletion augments the respiratory and anxious responses to CO2 inhalation in panic disorder patients, supporting the hypothesis that decreased serotonin function is linked to respiratory hypersensitivity.

NR89 Monday, May 23, 3:00 p.m.-5:00 p.m.

PTSD and Severe Motor Vehicle Accidents

Josie C. Ramos, M.D., Psychiatry, University of Miami, 1400 NW 10th D-79 RM 304-A, Miami FL 33136; Daniella David, M.D., Thomas A. Mellman, M.D., Diane Gonzalez, R.N., Jeffrey Augenstein, M.D.

Summary:

As many as one-third of individuals exposed to life threatening events develope post-traumatic stress disorder (PTSD) and related morbidity. Motor vehicle accidents (MVA) are common life threatening events, yet little is known about psychiatric morbidity related to MVA.

We are investigating psychiatric sequelae of MVA in patients admitted to a regional trauma center. Consecutive patients recruited for a department of transportation "crash study" who were willing to be interviewed and were screened to not have gross cognitive impairment, participated ($n = 16$, M-11, F-5, age 35.4 ± 12.1). All subjects had multiple injuries and none had prolonged unconsciousness. Subjects received a structured diagnostic interview and self-report instruments within one to three weeks of the accident.

Seven of the 16 subjects (44%) had laboratory findings documenting alcohol use, two of the seven were also positive for drugs. Six (3 with alcohol) had limited or no recall of the accident. Two of the 16 (12%) had full acute PTSD and five (31%) were positive for two of three symptom clusters. The three with amnesia related to alcohol were negative for PTSD and the three with amnesia unrelated to alcohol were all positive for PTSD symptoms. Follow-up of available subjects at one to two months revealed worsening in three subjects, improvement in one and another remained asymptomatic.

Psychiatric sequelae of MVA including the influence of intoxication, recall and longitudinal course require further study.

NR90 Monday, May 23, 3:00 p.m.-5:00 p.m.

Psychiatric Morbidity Following Hurricane Andrew

Daniella David, M.D., Psychiatry, University of Miami, 1400 NW 10th D-79 RM 304-A, Miami FL 33136; Thomas A. Mellman, M.D., Lourdes M. Mendoza, M.D., Renee Kulick-Bell, B.A., Gail Ironson, M.D., Neil Schneiderman, Ph.D.

Summary:

Literature on natural disasters documents psychological sequelae and emphasizes post-traumatic stress disorder (PTSD). The purpose of this study is to characterize the range of psychiatric

morbidity related to a natural disaster and associations with premorbid and trauma-related risk factors.

Subjects were recruited who experienced threat, damage, and/or loss from Hurricane Andrew. Subjects were included if they had been free of a psychiatric disorder in the six months prior to the hurricane (n = 61; 47F, age 40.4 ± 12.3). Evaluations, done six months to one year post-hurricane, included structured assessments of current, lifetime, and familial mood, anxiety, and substance use disorders, and histories of hurricane-related and past traumatic events.

Fifty-one percent (31/61) met criteria for a new-onset disorder, including PTSD in 36%, major depression (MD) in 30%, other anxiety disorders in 20%, and alcohol dependence in 2%. An additional 26% (n = 16) had PTSD or MD symptoms not meeting full disorder criteria, that were associated with distress and dysfunction. Thirty-four subjects (56%) had significant symptoms persisting beyond six months.

Relationships of risk factors to categories of post-Hurricane psychiatric morbidity were explored by chi-square and multiple regression analysis. Positive past personal and family histories and having had "severe damage" were associated with positive morbidity. "Severe damage" was also specifically associated with PTSD and with morbidity persisting at six months.

Our data underscore the range and multiple determinants of psychiatric morbidity related to a natural disaster.

NR91 Monday, May 23, 3:00 p.m.-5:00 p.m.

Social Phobia Subtyping: Correlates to Severity

Lisa B. Shea, M.D., Psychiatry, Brown University, 345 Blackstone Boulevard, Providence RI 02906; Michele T. Pato, M.D.

Summary:

Recent research demonstrates the presence of at least four social phobia subtyping schemes [1,2]. The purpose of this study was to examine which of these schemes was able to discriminate severity of illness in a social phobic sample. Precise subtype delineation may facilitate research of the disorder [1].

We reviewed the medical records of 37 patients who had participated in pharmacological studies of social phobia. These patients were independently subtyped by the two investigators according to four subtyping models: (1) Number of Feared Situations; (2) Type of Situation Feared; (3) Pervasiveness of the Phobia; and (4) Number and Quality of Feared Situations [1]. We compared each system against three measures of severity: the Clinical Impression of Severity (CIS), the Sheehan Disability Scale (SDS), and the Duke Brief Social Phobia Scale (BSPS).

Preliminary results using the CIS indicated that Models 1 and 2 were not able to discriminate severity in our rather ill sample. Models 3 and 4 were both significantly and positively correlated to the CIS ($p = 0.034$, $p = 0.004$ using non-parametric analysis). Models 3 and 4 did not classify all subjects the same (kappa = −0.173). A comparison of these two models indicated that Model 4 may be better at predicting severity than Model 3. Comparisons of these models using the SDS and BSPS will also be presented.

NR92 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Rollback Phenomenon in Major Depression

John J. Worthington III, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114, Maurizio Fava, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Katharine G. Davidson, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

Background: Detre and Jarecki (1971) have proposed the concept of the rollback phenomenon applied to major depressive disorder. According to their theory, as the illness remits, it progressively recapitulates, albeit in reverse order, many of the stages and symptoms that were seen during the time it developed. We decided to undertake the first empirical investigation of this phenomenon.

Methods: Eligible subjects were depressed outpatients meeting *DSM-III-R* criteria for major depressive disorder, as established by the use of the SCID-P. By using the SCID-P, we were able to identify the sequence of appearance of depressive symptoms amongst our patients. Patients were then followed and changes in their symptoms were monitored by administering the 31-item HAM-D scale. By assessing the order of clinical improvement, symptoms were classified as early onset-early offset, early onset-late offset, late onset-late offset, or late onset-early offset. The chi-square goodness-of-fit test was used to evaluate the significance of the changes in each symptom.

Results: In the fifteen subjects whose data are currently available, no statistically significant patterns have been observed. Our tentative conclusion is that the rollback phenomenon has yet to be supported by empirical data. As our data collection is ongoing, statistical analyses concerning a larger sample will be presented.

NR93 Monday, May 23, 3:00 p.m.-5:00 p.m.

Panic Disorder in Emergency Ward Patients with Chest Pain

John J. Worthington III, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114, Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Thomas Lee, M.D., Susan A. Sabatino, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

Background: Recognition of psychiatric disorders in medical settings is crucial to facilitate appropriate diagnosis and render cost effective care. Because of recent reports suggesting high rates of panic disorder (PD) in patients presenting with atypical chest pain (CP), we sought to assess the prevalence of PD in patients presenting to the emergency ward (EW) with CP and examine its effect on outcome and disposition.

Methods: We administered a screening questionnaire for PD to 160 consecutive patients presenting to the EW with CP. Patients were then followed up by phone with the Structured Clinical Interview for *DSM-III-R* (SCID) to confirm psychiatric diagnoses.

Results: 43% of the first 44 patients contacted met criteria for PD (42% of these with agoraphobia). Information will be presented correlating the results of the screening instrument with the structured interviews and the association of diagnosis with medical outcome and disposition.

Discussion: Findings from this preliminary study suggest a high rate of PD in patients presenting to the EW with CP. Self-report may provide a rapid and accurate method of diagnosing PD in the EW. Recognition of PD in the EW may result in more appropriate disposition and more efficient utilization of medical resources.

NR94 Monday, May 23, 3:00 p.m.-5:00 p.m.

Reaction Times and Event-Related Brain Potentials to Traumatic Words in PTSD

Linda J. Metzger, Ph.D., VA Research Service, 228 Maple Street, Manchester NH 03103; Scott P. Orr, Ph.D., Lawrence A. Farwell, Ph.D., Roger K. Pitman, M.D.

Summary:

This study investigated reaction times and event related potentials to colored word stimuli in post-traumatic stress disorder

(PTSD). Words in three categories (personal traumatic, personal positive, standard neutral, 40 each) were prepared during interview for nine PTSD and 13 non-PTSD subjects. Words were presented one at a time on a computer screen in either red or blue. Subjects were instructed to press a key indicating word color. Analysis of variance of reaction times revealed a significant diagnosis effect ($F(1,20) = 15.1$, $p < .001$), Word effect ($F(2,40) = 20.0$, $p < .0001$) and Diagnosis x Word interaction ($F(2,40) = 13.3$, $p < .0001$), with PTSD subjects taking longer to make color responses, especially for traumatic words. These findings are consistent with previous work demonstrating the existence of a modified Stroop interference effect exerted by traumatic words in PTSD subjects. This has been explained as a consequence of priming of trauma-related information in this disorder. Analysis of the electrophysiologic correlates of delayed reaction time to traumatic words and priming in PTSD is under way and will be presented at the poster session.

NR95 Monday, May 23, 3:00 p.m.-5:00 p.m

Sertraline in Social Phobia

Violetta D. Czepowicz, M.D., Psychiatry, Medical University, 171 Ashley Avenue, Charleston SC 29425; Michael R. Johnson, M.D., Naresh P. Emmanuel, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

Summary:

Ojective: Social phobia is an illness characterized by extreme fearfulness of situations involving scrutiny by others. It is estimated to affect 2% of the population and for most people, the symptoms of social phobia are chronic, unremitting, and result in significant long-term social disability and emotional distress. The only pharmacologic treatments which have been demonstrated in controlled trials to be effective are the monoamine oxidase inhibitors and the benzodiazepine clonazepam. Both treatments are associated with potential risks and side effects. Recent evidence suggests serotonin reuptake inhibitors may be effective alternative treatments for some patients with social phobia. We will report on our experience using an open trial of sertraline.

Method: The series consists of 11 patients treated in the anxiety disorders clinic between June 1992 and June 1993. All patients were evaluated by clinicians using the structured Clinical Interview for *DSM-III-R* and met criteria for a primary diagnosis of social phobia, generalized type. Ratings of clinical global impression of clinical severity and improvement were used. Doses of sertraline ranged from 50-200mg a day.

Results: Sertraline led to an improvement in seven of eleven patients-63% (much and very much improved).

Conclusion: The results suggest that sertaline might be useful in treatment of social phobia and raise the possibility that abnormalities in serotonin function may be involved in the pathogenesis of social phobia.

NR96 Monday, May 23, 3:00 p.m.-5:00 p.m.

Attributional Style in Social Phobia: Comparison with Major Depression

Gerardo Villarreal, M.D., Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425; Michael R. Johnson, M.D., Naresh P. Emmanuel, M.D., Violetta D. Czepowicz, M.D., Mark Walsh, M.D., Olga Brawman Mintzer, M.D.

Summary:

A number of studies have identified abnormal cognitive patterns in patients with social phobia. One measure of cognitive function, the Attributional Style Questionnaire (ASQ), has been used to demostrate cognitive abnormalities in patients with depression. These patients tend to overattribute negative events to internal causes. We hypothesized a similar pattern in patients with social phobia without depression. To investigate this hypothesis we gave the ASQ to 48 patients with social phobia, 25 patients with major depression, and 12 normal controls. All subjects underwent the Structured Clinical Interview for DSM-III-R (SCID). A factorial ANOVA for attribution of negative events revealed a significant interaction by diagnosis ($F = 9.64$, $p = 0.0002$), with both patient groups rating negative events more internally than controls. The opposite pattern was revealed for positive events, with both patient groups attributing positive events more externally than controls ($F = 4.76$, $p = 0.01$). We concluded that patients with social phobia without depression have an attributional style similar to patients with depression. Both groups tend to attribute negative events internally and positive events externally. The implications of this finding will be discussed.

NR97 Monday, May 23, 3:00 p.m.-5:00 p.m

Differences Between Subtypes in Panic Disorders

Ulrich H. Frommberger, M.D., Psychiatry, University Clinic, Hauptstr 5 Freiburg 75104, Germany; Raimund Buller, M.D., Christoph Kappler, Ph.D., Otto Benkert, M.D.

Summary:

Objective: Patients with panic disorder often present with one of the following subtypes: panic disorder with cardiac anxiety (Maier et al., 1986) or with dizziness (Frommberger et al., 1993). In order to identify differences between these two subtypes, we compared two groups of patients with panic disorder, 26 with cardiac anxiety, and 23 with dizziness with respect to sociodemographic data, symptoms, diagnoses, comorbidity, and personality.

Method: Patients in both samples were assessed by the SCID, SCL-90 and Cattell-16-PF.

Results: Both groups of patients did not differ in age, gender, marital status, or age of onset of the panic attacks. Patients with cardiac anxiety subtype of panic attacks more often reported a syndrome of agoraphobia ($p \leq 0.01$), preoccupation with fear ($p \leq 0.01$), showed more symptoms during a panic attack ($p \leq 0.01$), and were more often treated as inpatients ($p \leq 0.001$). They more often experienced symptoms of dyspnea ($p \leq 0.001$), choking ($p \leq 0.05$), chest pain or discomfort ($p \leq 0.01$), and fear of dying ($p \leq 0.001$) than patients of the subtype with dizziness. Cardiac-anxiety patients reported significantly more "phobic anxiety" on the SCL-90 subscale ($p \leq 0.05$). Cardiac-anxiety patients scored less on Cattell-16-PF-Factor 'dominance' ($p \leq 0.01$).

Conclusion: The cardiac-anxiety subtype is the more severe and disabling syndrome compared with the dizziness subtype.

NR98 Monday, May 23, 3:00 p.m.-5:00 p.m.

Self-Mutilation, Dissociative Experiences and Alexithymia

Caron Zlotnick, Ph.D., Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Teri Pearlstein, M.D., Elizabeth Simpson, M.D., Ann Begin, Ph.D., Ellen Costello, Ph.D.

Summary:

Objective: Self-mutilation has been associated with dissociative symptomatology especially in women with histories of childhood abuse. This study examined the relationship between dissociative experiences, alexithymia, and multiple patterns of self-mutilative behaviors in a sample of sexually abused patients.

Method: 50 women consecutively admitted to a women's psychiatric treatment unit who reported a history of abuse completed the following self-reports measures: Dissociative Experience Scale

(DES), Toronto Alexithymia Scale (TAS), Self-injury Survey, and Sexual Trauma Questionnaire.

Results: A multiple regression found that a greater variety of self-mutilative behaviors in the last three months was significantly related to scores on the DES (p = .0001), and accounted for 33% of the variance in the model. Scores on the TAS accounted for 4% of the variance (p = .07).

Conclusion: These findings suggest that sexually abused women who have elevated levels of dissociation use multiple forms of self-mutilative behavior. A better understanding of the mechanism of self-mutilation could be guided by examining the temporal relationship between self-mutilation and dissociation.

NR99 Monday, May 23, 3:00 p.m.-5:00 p.m

Dissociative Experiences, Psychopathology and Maladaptive Schemas

Caron Zlotnick, Ph.D., Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Ann Begin, Ph.D., M. Tracie Shea, Ph.D., Teri Pearlstein, M.D., Elizabeth Simpson, M.D., Ellen Costello, Ph.D.

Summary:

Objective: The aim of this study was to determine whether in a sample of sexually abused patients those with elevated levels of dissociative symptoms report higher levels of psychopathology and more maladaptive schemas.

Method: 68 women consecutively admitted to a women's psychiatric treatment unit who reported a history of abuse completed the following self-reports measures: Dissociative Experience Scale (DES), PTSD MMPI, Symptom Checklist Revised (SCL-90-R), Social Adjustment Scale Self-Report (SAS-SR), Schema Questionnaire (SQ), and Sexual Trauma Questionnaire.

Results: Comparing subjects with high DES scores to the subjects with low DES scores, high dissociators had significantly greater psychopathology on all measures. A regression found maladaptive schemas to be significantly related to dissociative experiences independent of psychiatric distress and a history of revictimization. This model accounted for a substantial proportion of the variance (51%).

Conclusion: The study provides preliminary support for the concept of a continuum of dissociative experiences with increasing psychopathology. Our study confirmed clinical impressions that maladaptive schemas are characteristic of women with histories of sexual abuse who report dissociative symptomatology.

NR100 Monday, May 23, 3:00 p.m.-5:00 p.m

Dissociative Experiences and Self-Mutilation in BPD

Beth Brodsky, M.A., Psychology, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Rebecca A. Dulit, M.D., Marylene Cloitre, Ph.D.

Summary:

This study documents the prevalence of dissociative experiences in female inpatients with borderline personality disorder (BPD), and explores the relationship between dissociation and (1) childhood abuse history and (2) self-mutilation. The Dissociative Experiences Scale (DES), the Sexual Experiences Questionnaire, the Hamilton Depression Scale, and a treatment history interview were administered to 60 consecutive female inpatients with BPD as diagnosed by the SCID-II. Fifty percent received a score of 15 or more on the DES, suggesting pathological levels of dissociation. Sixty percent reported a history of childhood physical and/or sexual abuse and 52% reported a history of self-mutilation. Subjects who dissociated were more likely than non-dissociators (1) to report a history of childhood abuse, and (2) to self-mutilate. They also had higher levels of current depressive symptomatology as well as past psychiatric treatment. A multivariate analysis demonstrated that each of the above variables were independently predictive of dissociation, and that self-mutilation was the most powerful predictor of dissociation. Clinical implications are that female BPD's who dissociate may represent a sizeable subgroup of borderlines who are at especially high risk for depression, self-mutilation and utilization of psychiatric treatment. Clinicians should carefully evaluate BPD patients for dissociation, and be alert to depressive symptomatology as well as the possibility of childhood abuse history and propensity to self-mutilate in this population.

NR101 Monday, May 23, 3:00 p.m–5:m.-5:00 p.m

Characteristics of Abuse in Psychiatric Outpatients

Deborah S. Lipschitz, M.D., Psychiatry, Montefiore Medical Center, 111 East 210th Street, Bronx NY 10467; Margaret L. Kaplan, Ph.D., Gregory M. Asnis, M.D.

Summary:

Objective: To assess the prevalence and characteristics of childhood sexual and physical abuse and adult assaults in a general psychiatric outpatient population.

Method: Psychiatric outpatients registering for treatment on three random days completed the Traumatic Events Questionnaire (TEQ), a 49-item questionnaire that surveyed past and current histories of sexual and physical abuse. Charts were reviewed for demographic characteristics and psychiatric diagnoses.

Results: The Traumatic Events Questionnaire was given to 144 patients, with 83% completing the survey. Of the total study sample (n–120; 86 females, 34 males), 34% of subjects reported childhood physical abuse and 44% reported childhood sexual abuse; 25% reported combined abuse in childhood. Childhood sexual abuse was strongly associated with later adult physical and sexual assaults. Sexually abused patients had the highest prevalence of affective disorders, whereas the physically abused had the highest prevalence of anxiety disorders.

Conclusions: The rates of abuse in this outpatient setting were comparable to the high rates reported in inpatient populations and the majority of the abuse for females was severe in nature. Childhood sexual abuse places individuals at greater risk for abusive experiences in adulthood. A direct and detailed self-report questionnaire appears to be a viable means of routinely assessing abuse in a busy outpatient setting.

NR102 Monday, May 23, 3:00 p.m.-5:00 p.m.

Dissociative Symptomatology and Characteristics of Childhood Abuse

Deborah S. Lipschitz, M.D., Psychiatry, Montefiore Medical Ctr., 111 East 210th Street, Bronx NY 10467; Margaret L. Kaplan, Ph.D., Gregory M. Asnis, M.D., Gianni L. Faedda, M.D., Jodie Sorkenn, C.S.W., Alessandra Scalmati, M.D.

Summary:

Objective: To determine the prevalence of dissociative symptoms and their relationship to histories of childhood sexual and physical abuse among general psychiatric outpatients.

Method: 144 patients registering for treatment during three random days in one month completed self-report questionnaires on measures of dissociation (Dissociative Experience Scale, DES), demographic details, and histories of past and current sexual and physical abuse (Traumatic Events Questionnaire, TEQ). A high dissociative group, those scoring above 25 on the DES scale (n = 29), was compared to a low dissociative group with scores below 5 (n = 23) on demographic and abuse variables.

Results: 15 subjects (31 men and 84 women) completed both forms with 34% and 44% subjects reporting childhood physical and sexual abuse, respectively. The mean DES score for the

sample was 17.3 and 25% of subjects had DES scores above 25. Physical abuse alone was not associated with greater dissociative symptomatology, but subjects with childhood sexual abuse and particularly those with combined abuse had significantly greater dissociative symptomatology than nonabused subjects($p = 0.01$; $p < 0.001$). Childhood abuse, but not adult abuse was significantly related to dissociative symptomatology ($p = 0.03$). DES scores were highest in subjects with childhood rape experiences and repeated physical beatings. There were no demographic differences between the high and low dissociators, but 59% compared to 9% reported childhood physical abuse, 76% compared to 22% reported sexual abuse, and 48% compared to 4% experienced combined abuse.

Conclusion: Childhood sexual and physical abuse histories are extremely prevalent in psychiatric patients. Dissociative symptomatology is common and related to the form and combination of childhood abuse experienced.

NR103 Monday, May 23, 3:00 p.m.-5:00 p.m

Trauma and Dissociation in Two Populations

Howard C. Wetsman, M.D., Psychiatry, Naval Medical Center, Portsmouth VA 23708; Elizabeth David, M.D., Edward Morse, Ph.D.

Summary:

The authors previously reported a high prevalence of dissociative symptoms statistically unrelated to histories of child abuse in indigent psychiatric patients. To test the hypothesis that traumas other than physical or sexual abuse may account for that finding, The Dissociative Experiences Scale (DES) and the Childhood Trauma Experiences Scale (CTES) were given to 23 indigent psychiatric inpatients and a comparison group of 39 military psychiatric inpatients. The CTES, a 36-item, self-administered instrument measuring childhood exposure to 12 classes of psychological trauma, and the DES revealed significantly more childhood trauma and more current dissociative symptoms in the indigent sample. Despite the higher dissociation scores in the indigent sample, the groups did not differ in the rates of childhood physical and sexual abuse. In the indigent sample there was no relationship between reported abuse and DES score; the military population showed a trend toward a relationship between sexual abuse and DES score. No scale in either sample varied significantly with age, race, or gender. In both samples DES and CTES were significantly and positively correlated. These data suggest that the high frequency of traumas other than child abuse may cause the high prevalence of dissociative symptoms in indigent patients.

NR104 Monday, May 23, 3:00 p.m.-5:00 p.m.

A Comparison of DSM-III-R Versus DSM-IV Criteria for Melancholic Depression

Beny Lafer, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114; Maurizio Fava, M.D., Andrew A. Nierenberg, M.D., Madeleine Carey, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: The *DSM-IV* proposed criteria for melancholia is but the latest in a long series of attempts to identify a particular subgroup of severely depressed patients Our aim was to compare the *DSM-III-R* versus *DSM-IV* criteria for melancholia in a consecutive series of 176 drug-free unipolar major depressive outpatients.

Methods: A structured interview (SCID-P) was used to assess diagnosis. Additional questions about specific symptoms and course of illness were added to confirm the *DSM-III-R* and *DSM-IV* diagnosis of melancholic subtype. To assess symptom severity and functional impairment, we used the 17-item Hamilton Depression Rating Scale (HDRS), the Beck Depression Inventory (BDI) and the dysfunctional attitude scale (DAS).

Results: Out of 176 outpatients with unipolar depression, 40 met the *DSM-III-R* criteria but only 29 met the *DSM-IV* criteria for melancholia. Patients with *DSM-IV* melancholia had higher mean scores on the HDRS (23.1 vs 19.7, $p = 0.01$), BDI (28.6 vs. 21.3, $p = 0.05$), and on the DAS (159.4 vs 123.8, $p = 0.05$) when compared to patients who met *DSM-III-R* but not *DSM-IV* criteria.

Conclusions: Our results suggest that the criteria for melancholia proposed in the *DSM-IV* is more stringent and defines and a more severely depressed population than the *DSM-III-R*. The potential utility of *DSM-IV* melancholia as a predictor of treatment outcome should be examined in the future.

NR105 Monday, May 23, 3:00 p.m.-5:00 p.m.

Effects of Thiopental Dose on ECT-Induced Cardiovascular Physiological Changes

Rama Prayaga, M.D., Psychiatry, East Orange VAMC, Riverview Garden 9I, North Arlington NJ 07031; Cheng-Jen Chen, M.D.

Summary:

ECT is a low-risk procedure. However, it can increase PR, BP, and result in cardiovascular complications. Thiopental is one of the most used anesthetic agents in ECT. It can lower blood pressure through direct depression of myocardial contraction and/or dilation of blood vessels. The effects of thiopental on ECT-induced cardiovascular physiological changes, especially dose related effects, have rarely been reported. Here we demonstrated the relationship between doses of thiopental and DRPP (postECt systolic BP × postECT PR-PR—preEct systolic BP x preECT PR), ECT-induced systolic BP changes (DSYS), pulse rate changes (DPR), postECT systolic pressure (postSYS), and PR (postPR). Eight depressed patients underwent bitemporal ECT. A total of 47 treatments that used "90%" on Thymatron-percent energy dial were included for data analysis. The SAS statistical package was used for correlation and multiple regression tests.

The dose of thiopental was negatively correlated to all cardiophysiological changes, while age and succinylocholine were positively correlated to the changes. However, by the use of multiple regression analysis, only thiopental could significantly predict DRPP ($F = 18.13$, $P = 0.0001$), DSYS ($F = 7.67$, $P = 0.0083$), DPR ($F = 9.29$, $P = 0.0040$), post-SYS ($F = 17.59$, $P = 0.0001$) and post-PR ($F = 5.53$, $P = .023$)¾.

Clinical implications of the dose effect of thiopental on cardiovascular physiological changes at ECT will be discussed.

NR106 Monday, May 23, 3:00 p.m.-5:00 p.m.

Comorbid Panic Disorder in a Bipolar Family Study

Dean F. Mac Kinnon, M.D., Psychiatry, Johns Hopkins University, 600 N. Wolfe St Meyer 3–181, Baltimore MD 21287; Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., J. Raymond De Paulo, Jr., M.D.

Summary:

Objective: Patients with recurrent major affective disorders of both bipolar and unipolar types are at high risk for other psychiatric disorders. The data on the relationship of affective disorders to anxiety disorders have been inconclusive.

Method: We have conducted a preliminary analysis of the clinical data obtained from 238 SADS-L interviews on the affected family members (41 BP I, 117 BP II, four schizoaffective-manic type, and 76 recurrent unipolar disorders) of bipolar probands ascertained for a genetic linkage study of bipolar disorder. Chi-square analysis was performed on the frequency of comorbid panic disorder in bipolar and unipolar subjects. For this analysis

the diagnosis of panic disorder was applied if subject's symptoms met RDC inclusion criteria, whether or not there was concurrent depression.

Results: A significantly higher proportion of subjects with a bipolar disorder also had panic disorder compared with subjects with recurrent unipolar disorder (14.8% versus 2.6%, chi-square = 7.89, df = 1, $p < .005$)

Conclusions: The finding suggests a relationship between familial bipolar phenotypes (BP I or II) and panic disorder symptoms. Whether this relationship is specific to a subset of bipolar families and why bipolar rather than unipolar family members are at greater risk merits further study.

NR107 Monday, May 23, 3:00 p.m.-5:00 p.m.

Treatment of Chronic Major Depression with Desipramine

Nina L. Miller, M.A., Payne Whitney, New York Hospital, 525 East 68th Street, New York NY 10021; James H. Kocsis, M.D.

Summary:

Introduction: We investigated response to desipramine given to outpatients having a DSM-III-R diagnosis of major depression, chronic type (current episode lasting at least two years). Outcome was assessed after both a 10-week acute phase and a 16–20 week continuation phase of a treatment study for chronic depression. Remission rates as well as demographic and clinical characteristics of this cohort will be compared with groups of patients from the same study who met DSM-III-R criteria for dysthymia with or without current major depression, i.e. both "double-depressives" and "pure dysthymics."

Methods: The SCIDs of 118 patients entering the above trial were reviewed. Fourteen met criteria for chronic major depression. Of 104 patients with dysthymia, 61 had a concurrent major depression and 43 did not. Response was measured using study clinicians' ratings of the 24-item version of the Hamilton Depression Scale (HAM) and the Global Assessment Scale (GAS).

Results: Of 14 patients with chronic major depression, 10 completed the acute phase of the study. Four were full remitters, three were partial remitters, and three were nonresponders. The full and partial remitters completed continuation therapy on the same medication at the same final dose reached during the acute phase. During continuation treatment, two of three full remitters remained in full remission, 1 became a partial remitter, and three of three partial remitters remained partial remitters. Thus, 70% achieved at least a partial response and 85% sustained this improvement during continuation treatment. Of 43 pure dysthymics, 33 completed the acute phase, with a remission rate of 70% (15 FR, 8 PR). Fifty of 61 patients with double depression completed the acute phase, with a rate of remission of 54% (19 FR, 8 PR). Differences in remission rates between groups were not statistically significant.

Discussion: Although based on a small sample size, this preliminary analysis suggested that the efficacy of a tricyclic antidepressant for chronic major depression is comparable to the outcome demonstrated for dysthymia, with or without major depression. The data on the stability of remission provide evidence that longer-term treatment benefits these chronically ill patients.

NR108 Monday, May 23, 3:00 p.m.-5:00 p.m.

Does Succinylcholine Affect ECT-Induced Seizure Duration?

Luis M. Del Rio, M.D., Psychiatry, East Orange VAMC, 725 Joralemon Street #164, Belleville NJ 07109; Cheng-Jen Chen, M.D.

Summary:

The seizure is the primary therapeutic modality of ECT, and seizure duration is one of the important factors in seizure adequacy. Barbiturates, age, and other factors are known to shorten ECT-induced seizure duration. The role of succinylcholine remains unclear. Two previous reports have shown an inverse relationship between ECT-induced seizure duration and doses of succinylcholine (1). Succinylcholine does not cross the BBB. BBB disruption does not enhance the cerebral-stimulating effects of i.v. succinylcholine (2). We thought the previously reported relationship between ECT-induced seizure duration and succinylcholine dose is determined by factors other than succinylcholine. Eight male patients underwent bitemporal ECT. Fifty-one treatments that used "90%" on the Thymatron percent-energy dial were selected for data analysis. The SAS statistical package was used.

Positive correlation ($r = 0.28$ $p = 0.0046$) was found between succinylcholine dose and seizure duration. Age ($r = 0.40$ $p = 0.0048$) and pentothal ($r = -0.68$ $p = 0.001$) were negatively correlated with seizure duration. After adjusting the age and thiopental, the significant correlation between succinylcholine dose and seizure duration became nonsignificant. Based on the findings of this study, we suggest succinylcholine should only be used as a muscle relaxant and not for manipulation of seizure duration.

NR109 Monday, May 23, 3:00 p.m.-5:00 p.m.

Compliance with Pharmacological Treatment in Patients with Mania

Sean P. Stanton, B.S., Psychiatry, University of Cincinnati, 231 Bethesda Avenue, Cincinnati OH 45267; Jerry A. Bennett, Pharm. D., Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D., Karen C. Tugrul, B.S.N., Stephen M. Strakowski, M.D.

Summary:

Introduction: Patients with manic symptoms often have poor pharmacological compliance, and noncompliance has been associated with the recurrence of mania or hypomania. The purpose of this study is to examine the causes of pharmacologic noncompliance and whether clinical factors (age, gender, race, socioeconomic status, education, and diagnosis) are associated with noncompliance.

Methods: Patients were recruited over one year as part of the University of Cincinnati Mania Project. All patients admitted to University of Cincinnati Medical Center's psychiatry inpatient units with manic symptoms, aged 12 and above who provided informed consent, were entered into the study. Patients were diagnosed using the SCID-P, performed by psychiatrists with high interrater reliability (kappa = 0.94). History of pharmacological treatment was obtained from direct interview and review of medical record. Patients were questioned regarding reasons for noncompliance. Effects of age, sex, race, socioeconomic status, education, and diagnosis (bipolar manic, bipolar mixed, and schizoaffective disorder) were analyzed.

Results: Patients ($N = 40$) displayed a high rate of pharmacological noncompliance (67.5%). Primary reasons for noncompliance included: lack of insight (25.8%), intolerable side effects (19.8%), prescription lapsed or lost (12.9%), and the belief of no longer needing medication (12.9%). Age (median = 22), gender (50% male), race (57.5% white, 40% African American, and 2.5% Asian), socioeconomic status (70% unemployed or unskilled), education (median = 12), and diagnosis (bipolar manic 42.5%, bipolar mixed 35%, and schizoaffective disorder 22.5%) showed no statistically significant effect on the rate of noncompliance.

Conclusion: The main causes of pharmacological treatment noncompliance were lack of insight, intolerable side effects, prescription problems, and the belief of no longer needing medication. Our center often admits patients from low socioeconomic status, a group that may be experiencing more severe symptoms. Age,

gender, and race had no direct effect on pharmacological noncompliance. Factors that may improve compliance include: education about the necessity of compliance limiting medication side effects; organizing prescription schedules; and building support networks for monitoring symptoms.

NR110 Monday, May 23, 3:00 p.m.-5:00 p.m.

Geropsychiatric Effects of Mild Subclinical Hypothyroidism

Sharon M. Esposito, M.D., 1521 East Franklin St. #B104, Chapel Hill NC 27514; John J. Haggerty, Jr., M.D., Robert A. Stern, Ph.D., Mark E. Williams, M.D., George A. Mason, Ph.D., Arthur J. Prange, Jr., M.D., Michael A. Senger, M.A.

Summary:

Objective: The objective of this study was to measure the prevalence of subclinical hypothyroidism (SCH) in a geriatric clinic population, and to examine its influence in the elderly on the occurrence of depression and neurocognitive dysfunction.

Method: We examined routinely obtained laboratory data on 163 patients (117 F, 46 M) older than 65 years who were being followed in a geriatric medical evaluation clinic. Of these, 15 (9%) had TSH and FTI findings consistent with a diagnosis of SCH. Eight of the patients with SCH and 11 clinic patients of similar age and sex distribution who were euthyroid (EU) were then blindly assessed with confirmatory thyroid function—testing, SCID diagnostic interview, and a comprehensive neuropsychological testing battery.

Results: The lifetime prevalence of DSM-III-R major depression was significantly higher in clinic patients with SCH (6/8, 75%) than in those who were major euthyroid (2/11, 18%) ($p = .02$). SCH and EU subjects did not differ in any consistently meaningful way on neurocognitive measures.

Conclusions: Among geriatric outpatients, subclinical hypothyroidism is common and appears to be associated with a substantially increased lifetime prevalence of depression. Thus, elderly individuals may be even more vulnerable to the neuropsychiatric effects of subclinical hypothyroidism than has been reported in younger populations

NR111 Monday, May 23, 3:00 p.m.-5:00 p.m.

Attention Deficit in Mixed and Pure Mania

Kenji W. Sax, M.S., Psychiatry, University of Cincinnati, 231 Bethesda Avenue ML559, Cincinnati OH 45267; Stephen M. Strakowski, M.D., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Scott A. West, M.D., Sean P. Stanton, B.S.

Summary:

Impaired sustained attention has long been a robust indicator of cognitive dysfunction in schizophrenia (Nuechterlein et al., 1991), yet relatively little is known about this deficit in bipolar illness. The Continuous Performance Test (CPT) has been used to assess sustained attention in studies of schizophrenia and is widely recognized as a reliable marker of the disorder. To date, no study has compared CPT performance between patients with mixed and pure mania. While a number of clinical characteristics distinguish the two (McElroy et al, in press), differences in cognitive functioning have not been evaluated. The present study was designed to examine sustained attention performance in patients with mixed and pure mania.

Hospitalized pure manic ($n = 10$) and mixed manic ($n = 7$) subjects meeting DSM-III-R (SCID) criteria, and healthy control subjects ($n = 10$) were compared on the degraded stimulus CPT. Performance was assessed on admission (pretreatment) and again just prior to discharge (posttreatment). Controls were assessed twice over the span of two months to control for practice effects.

At admission, both the pure manic group ($p < .05$) and mixed manic group ($p < .005$) performed significantly worse than controls. A trend was noted in the comparison between the two manic groups, with the mixed performing more poorly than the pure manic group ($p < .06$). At discharge, the control and pure manic groups did not significantly differ, while differences remained between the mixed group and controls ($p < .005$). Although the mixed group performed more poorly than the pure group, this difference did not reach significance. These results are part of an ongoing longitudinal study.

These results suggest that subtypes of mania, as with schizophrenia, contain important neuropsychological differences that warrant further evaluation.

NR112 Monday, May 23, 3:00 p.m.-5:00 p.m.

Comorbidity of ADHD in Adolescent Mania

Scott A. West, M.D., Psychiatry, University of Cincinnati, 231 Bethesda Avenue ML 559, Cincinnati OH 45267; Susan L. McElroy, M.D., Stephen M. Strakowski, M.D., Paul E. Keck, Jr., M.D., Brian J. Mc Conville, M.D.

Summary:

The purpose of this study was to determine the rate of ADHD in adolescents with bipolar disorder presenting for treatment of acute mania, and to explore the potential effects of comorbid ADHD on the phenomenology and outcome on adolescent mania.

Patients 12 to 18 years old hospitalized for mania were recruited for study. The diagnosis of bipolar disorder was determined using the Structured Clinical Interview for DSM-III-R (SCID-P); the diagnosis of ADHD was made using the Schedule of Affective Disorders & Schizophrenia for School-Age Children (K-SADS-IIIR). Ratings were done weekly by persons blind to diagnoses, and included the YMRS, SICH-AD, and SAPS.

Of 14 adolescent bipolar patients with mania, eight also had a history of ADHD. Patients with comorbid ADHD were significantly more likely to be male, Caucasian, and to have mixed rather than pure mania. Also, there was a trend for patients with ADHD to have a higher mean YMRS score (23.1±) compared with patients with bipolar disorder alone (13.3±) ($P < 0.08$, R-squared 0.236).

Although preliminary, these results suggest that histories of ADHD, or ADHD symptoms, may be common in adolescents hospitalized for mania, and that patients with both disorders may be more likely to have mixed rather than nonmixed mania and more severe manic symptoms than patients with mania alone.

NR113 Monday, May 23, 3:00 p.m.-5:00 p.m.

Transitional Objects and Borderline Personality

William Cardasis, M.D., Psych UH-9C9150-0120, University of Michigian, 1500 East Medical Center Drive, Ann Arbor MI 48109-0120; Jamie Hochman, B.A., Kenneth R. Silk, M.D.

Summary:

Patients with borderline personality disorder (BPD) are said to function at the level of transitional object relationships. Despite this long-standing assumption, little empirical research on BPD and concrete manifestations of transitional objects has been conducted. On an adult general inpatient psychiatry unit, it was noted that a subset of patients brought teddy bears, pillows, or other cherished objects from home, and a preliminary investigation was performed to examine the relationship of patients who brought these objects with them during their inpatient stay and a possible diagnosis of borderline or other personality disorder. Sequential patients (except those with overt psychosis or organic brain syndrome) who were admitted to the unit were asked (via a semi-

structured interview) if they possessed objects of a special (i.e. transitional) nature that were (1) brought to the hospital, (2) kept at home, and/or (3) recalled as being important during childhood. To be classified as a transitional object, (a) the object was employed to calm the patient's anxiety and/or (b) separation from the object caused significant anxiety. BPD and other personality diagnoses were determined by (1) the MCMI, (2) a *DSM-III-R* BPD checklist that was filled out shortly after admission, and (3) discharge diagnoses. To date, 48 subjects (10 men, 38 women; age range 18–69) have participated. Significantly more patients who were borderline by the checklist ($X^2 = 8.95$, $p = .003$), by the MCMI ($X^2 = 3.80$, $p = .05$) and by discharge diagnosis ($X^2 = 4.22$, $p = .04$) endorsed transitional objects during adulthood. Borderlines (diagnosed by scoring > 85 on the MCMI on admission) more frequently endorsed having transitional objects at home ($X^2 = 8.39$, $p = .004$) but did not necessarily bring a transitional object to the hospital ($X^2 = 0.45$, p = NS). Patients who were diagnosed BPD *(DSM-III-R)* at discharge were more likely to have brought a transitional object with them to the hospital ($X^2 = 4.34$, $p = .04$). This ongoing research project will be updated at the time of presentation and implications of the results will be discussed.

NR114 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Utility of SCID-II for Diagnosing Personality Disorders

Joshua McDavid, M.D., Psychiatry, Western Psychiatric, 3811 O'Hara Street, Pittsburgh PA 15213; Suzan Clark, M.Ed., Paul A. Pilkonis, Ph.D., Brian Neighbors, M.A., Kathy Reilly, M.A., Joe Proletti, M.S.

Summary:

The SCID-II is a structured interview designed to diagnose personality disorders. Despite its relatively wide acceptance, its efficiency as a screening instrument has only been examined in a handful of studies. The operating characteristics of the SCID-II and whether total scores are useful ways of scoring the instrument have not yet been evaluated.

Objectives: To determine if 1) in a clinical population the SCID-II is a useful and efficient screening instrument for determining a personality disorder diagnosis; 2) taking a dimensional approach to the SCID-II proffers any advantages over categorical scoring approaches.

Subjects and Methods: 36 patients who have been diagnosed using a LEAD standard and followed for 21 months and then re-evaluated with the SCID-II by raters blind to the diagnoses.

Results and Conclusions: The SCID-II is a useful screening instrument (using total scores) for detecting the presence (yes/no) of a personality disorder, but not as useful for detecting individual diagnoses. Total SCID-II scores are more valid and reliable as measures of clinical personality pathology than individual diagnoses.

NR115 Monday, May 23, 3:00 p.m.-5:00 p.m.

Concomitant Personality Disorders in Patients with Social Phobia

Billinda Dubbert, M.S.N., Psychiatry, Georgetown University MC, 3750 Reservoir Road NW, Washington DC 20007; Teresa A. Pigott, M.D., Suzanne Bernstein, B.S., Eduina A. Martins, M.D., Brian B. Doyle, M.D., Laurel Northup, M.D., Vinita Leslie, B.S., Virginia M. Smolka

Summary:

Social phobia is characterized by excessive shyness in public that often results in phobic avoidance and occupational dysfunction. Data concerning the prevalence of concomitant personality disorder (PD) in patients with social phobia are limited. In the present study, 25 patients meeting DSM-III-R criteria for social phobia (16 males, nine females; mean age ± SEM, 38.0 ± 1.8 yrs.; mean duration of illness, 22.9 ± 1.9 yrs.) were administered the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II). Each patient scored ≥ 20 on the Duke Brief Social Phobia Scale (mean BSPS ± SEM, 40.9 ± 1.8). None of the patients met current criteria for a major depressive disorder (mean Ham-D, 7.3 ± 1.9). The patients with social phobia met criteria for avoidant PD (88%) or obsessive compulsive (84%) (OCPD) significantly more frequently than any other PD diagnosis. Six (24%) of the patients met the diagnostic criteria for only one PD diagnosis, and 28% met criteria for a diagnosis of mixed personality disorder. Diagnoses from cluster C, relevant to fearful or anxious behavior, were significantly more common in comparison to cluster A (40%) or cluster B (52%) PD categories. The predominance of avoidant PD could be predicted *a priori* based on the diagnostic group affiliation. However, these findings suggest that concomitant PD, especially OCPD, is common in nondepressed patients with social phobia. Further data concerning the potential link between OCPD and social phobia will also be presented.

NR116 Monday, May 23, 3:00 p.m.-5:00 p.m.

Gender Differences in Personality Disorders

Mayana Golomb, M.D., Psychiatry, Mass General Hosp., ACC 815 PPC 15 Parkman Street, Boston MA 02114; Maurizio Fava, M.D., Melissa Abraham, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: The aim of our study was to assess gender differences in personality disorders among a population of patients with a primary diagnosis of major depressive disorder (MDD), as heterogeneity in Axis I diagnoses could conceivably affect the assessment of Axis II diagnoses.

Methods: Axis II disorders were assessed with a self-rating measure, the PDQ-R (Hyler et al, 1987) on 288 patients with MDD. The SCID-II (Spitzer et al, 1990), a clinician-rated instrument, was also administered to 117 subjects, with an additional 95 subjects receiving the SCID-II for the Cluster B diagnoses only.

Results: The mean HAM-D-17 score in 108 men (mean age: 39.28 ± 9.06) was 19.0 ± 3.8 and 19.6 ± 6.9 in 208 women (mean age: 39.11 ± 11.24). On the PDQ-R, men were significantly more likely than women to meet criteria for schizotypal, narcissistic, antisocial, and obsessive-compulsive personality disorders. On the SCID-II, men were significantly more likely than women to meet criteria for narcissistic and obsessive-compulsive personality disorders.

Conclusions: Our findings are consistent with those of previous studies showing a greater prevalence of antisocial and narcissistic personality disorders in men. However, in contrast with other investigations, neither the PDQ-R nor the SCID-II revealed a higher prevelance of any personality disorder in women.

NR117 Monday, May 23, 3:00 p.m.-5:00 p.m.

Temperament and Character Inventory Predicted Probability of Personality Disorder Changes with Treatment of Depression

Kevin John Black, M.D., Psychiatry, Washington University, 4940 Children's Place Box 8134, St. Louis MO 63110; Yvette I. Sheline, M.D.

Summary:

Cloninger's Temperament and Character Inventory questionnaire (TCI) predicts presence or absence of personality disorder in psychiatric inpatients. We hypothesized that treating major depression would reduce TCI evidence of personality disorder. We

are testing our hypothesis in outpatients with DSM-III-R major depression who are receiving either an SSRI or placebo, but no psychotherapy. The full sample of 25 patients has not yet completed the trial, but to date, an abbreviated TCI has been administered to 19 patients at the beginning of treatment and to nine patients at the end of treatment, including seven who took the TCI at both time points (median, nine weeks apart). In these seven patients, the median TCI-predicted probability of personality disorder (PROB) dropped from 53% to 28% during treatment ($p < 0.02$). This finding remained significant when all 28 TCI administrations were analyzed ($p < 0.001$). Change in PROB was correlated with change in Ham-D scores ($r = 0.85$) in the seven subjects with repeat TCIs, and PROB was correlated with Ham-D scores ($r = 0.49$) in all 28 TCIs. The drop in PROB was due to improvement in the Self-Directedness (SD) scale. Data on further completers will be presented in poster form. These findings suggest that personality difficulties associated with major depression can improve when depression remits with pharmacotherapy.

NR118 Monday, May 23, 3:00 p.m.-5:00 p.m.

Alexithymia: Relationship to Personality Disorders

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Summary:

Previous studies suggested an association of alexithymia with other personality models as well as with various psychiatric syndromes. However, with regard to current diagnostic systems, the clinical validity of alexithymia remains to be established. In a sample of 182 psychiatric outpatients (mean age 40.3 years), the lifetime prevalence of DSM-III-R Axis I disorders was determined by SCID-interviews. In addition, DSM-III-R personality disorders were assessed using the PDQ-R. Alexithymia was assessed by the 26-items Toronto Alexithymia Scale (TAS). On the TAS, 17% of our sample scored in the alexithymic range. A series of stepwise multiple regression analyses were run, exhibiting no relationship between alexithymia (expressed as TAS global scores and four TAS subfactors) and any of the DSM-III-R Axis I lifetime diagnoses. In contrast, schizotypal ($p < 0.001$), dependent ($p < 0.01$), and avoidant ($p < 0.05$) personality dimensions as well as a lack of histrionic features ($p < 0.001$) emerged as significant predictors, which further supports the conceptualization of alexithymia as a personality dimension.

NR119 Monday, May 23, 3:00 p.m.-5:00 p.m.

Day Treatment: Patients at Risk for Relapse

Nuchanart Venbrux, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Richard Fonte, M.D., Edward O. Bixler, Ph.D., Pat Taksen, M.S.W., Thomas C. Lillis, M.Ed.

Summary:

Introduction: The objective of this study is to identify demographic factors and other characteristics associated with re-hospitalization of patients who participated in our day treatment program. Results from this study will be of value to clinicians for identifying patients who are likely to relapse and to make the appropriate follow-up planning and intervention.

Method: Questionnaires were sent to 189 patients who were hospitalized in our day program between a two-year period. Patients were categorized based on whether they were re-hospitalized after discharge. Questions included demographic data, past and present psychiatric treatment, diagnosis, type of medications, ability to handle stress, social relationships, family support, self-concept, work satisfaction, medical insurance coverage, geographic location, level of education, and the Beck Depression Inventory scores during hospitalization and at the time of discharge. Individual charts were also reviewed for information not provided by the patient and for accuracy of answers.

Result: We found a significant difference between the re-hospitalized patients and those who were not re-hospitalized in their ability to handle stress ($p = .008$) and in their social relationships($p = .003$). Demographic data and other factors were not significantly different. The Beck Depression Inventory scores at the time of discharge were significantly higher in the re-hospitalized group regardless of diagnosis($p = .003$).

Conclusion: Our findings emphasize the importance of social relationships and stress management as two factors contributing to how well the patients do after their hospitalization. Furthermore, the Beck Depression Inventory score at the time of discharge appears to be helpful in identifying patients who are likely to relapse. Based on this finding, we recommend that the Beck Depression Inventory be given to all patients at the time of discharge as well as during the hospitalization.

NR120 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Role of Discussion on Television Effects on Children

Nuchanart Venbrux, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Paul A. Kettl, M.D., Edward O. Bixler, Ph.D., Errin W. Crowell, B.S., James Douglas, B.S.

Summary:

Objective: Television plays a key role in the development of our children's lives and is a major source of influence on their behavior, attitudes, and perception. In recent years, television is increasingly being perceived as having a negative impact on the mental and physical health of children. Knowing that there is a direct correlation between TV watching time and aggressive behavior in children as suggested by previous research studies, any factors that may be helpful in reducing the negative effect of television would be of vital importance to clinicians and parents. This study investigates the effect of parental discussion of TV programs on the aggressive behavior seen in children.

Method: Questionnaires containing (1) The Pediatric Behavior Scale (PBS) on conduct, (2) parental discussion of TV programs and (3) time spent watching TV were sent to 1,409 elementary school children.

Result: Overall, we received 81% return. The number of hours children viewed TV did not differ significantly between homes where parents discussed the shows and those who did not. Parental education level and work type (blue collar versus white collar) were not significant factors in determining whether the shows were discussed. The TV programs were discussed in most homes. There was a greater correlation between conduct problems as indicated by the PBS scores and the number of hours spent watching TV in homes without discussion ($r = .5288$, $r = .1370$ respectively).

Conclusion: This study supports previous research findings that parent-child discussion of TV programs is helpful in reducing negative effects on children in particularly aggressive behavior. Whether the shows were discussed did not affect the viewing hours. Furthermore, it emphasized the importance of parental involvement in children's TV viewing habits.

NR121 Monday, May 23, 3:00 p.m.-5.00 p.m.

Sleep/Wake Patterns in Abused Children

Carol A. Glod, M.S.N., McLean Hospital, 115 Mill Street, Belmont MA 02178; Martin H. Teicher, M.D., Carol Hartman, D.N.S., Thomas Harakal.

Summary:

Childhood abuse has been associated with a variety of psychiatric sequelae, including PTSD. Studies suggest that sleep disturbance may be a hallmark of PTSD in adults.

Objective: The purpose of this study was to ascertain whether children with documented abuse have impairments in sleep continuity. Thirty children will comprise the total sample. To date, 14 prepubertal subjects have participated (seven normal controls [mean age 7.7 yrs], seven with substantiated physical and:shor sexual abuse [mean age 9 yrs]).

Method: All children were medication-free and were assessed via structured diagnostic interview (K-SADS-E). Sleep continuity was obtained from 72 hours of minute-to-minute actigraph data. Sleep parameters were derived using an algorithm developed by Sadeh et al. (1989), that closely agrees with polysomnography.

Results: Abused children spent nearly fourfold more time awake after sleep onset than controls (46.7 ± 39 min. vs. 12.0 ± 4.6 min.; $F[1,12] = 5.47$, $p < .04$). Abused patients also had decreased sleep efficiencies compared with controls; 87.8 ± 9.2% vs. 95.7 ± 3.1% ($F[1,12] = 4.69$, $p = .05$). There were no significant differences between groups in total sleep time or sleep latency.

Conclusions: These preliminary findings indicate that childhood abuse may be associated with a quantifiable disturbance in sleep maintenance.

NR122 Monday, May 23, 3:00 p.m.-5:00 p.m.

Untoward Effects and Their Clinical Management in Young Autistic Children Treated with Clomipramine

Laura E. Sanchez, M.D., Psychiatry, New York Univ Med Ctr, 550 First Avenue, New York NY 10016; Jeanette E. Cueva, M.D., Jorge L. Armenteros, M.D., Magda Campbell, M.D.

Summary:

Objective: To report on the untoward effects associated with clomipramine (CMI) and their management in young autistic children, all inpatients. Reports on CMI in autistic disorder involve older outpatients, ages 6 to 33 years (Gordon, et al., 1992, 1993; McDougle, et al., 1992).

Methods: The eight subjects, ages 3.5 to 8.7 years, met *DSM-III-R* criteria for autistic disorder and functioned on a moderate to severely retarded level. All were inpatients enrolled in an ongoing pilot study of CMI. Following a one-week placebo baseline, they were treated with CMI for five weeks. Untoward effects, orthostatic blood pressure and pulse rates, sleep pattern, and appetite were monitored daily; weight was recorded weekly and EKG's were obtained serially.

Results: On therapeutic doses, the first four children developed constipation and one of these, a 3.5 year old male, developed acute urinary retention (50 mg:shd or 3.149 mg:shkg:shd). No child developed urinary retention or constipation after the protocol was modified to include a high fiber diet, Metamucil, and encourage fluid intake.

Conclusions: Urinary and bowel habits must be monitored daily in young autistic children during baseline and throughout CMI treatment and measures taken to prevent the above untoward effects, which may be more common in young autistic children than in older patients.

NR123 Monday, May 23, 3:00 p.m.-5:00 p.m.

Patient Knowledge of Medication at Discharge

Michael R. Lavin, M.D., Psychiatry, Hillside Hospital, 193-41 McLaughlin Avenue, Holliswood NY 11423; Steven Budoff, D.O., Barbara Galkowski, C.S.W., Simcha Pollack, Ph.D., Michael H. Kronig, M.D.

Summary:

Previous research suggests an alarming lack of understanding of medication by patients. In this study we sought to assess patient knowledge of medication at discharge and impact on short-term compliance. We report on a pilot study in which a questionaire was administered to 31 consecutive planned discharges from an inpatient schizophrenia and psychosis unit. The mean number of separate psychiatric medications and daily doses for each patient was 2.7 and 6.8, respectively. Forty-nine percent of patients received three or more psychiatric medications. While patients named 87% of their psychiatric medications, they named only 43% of their nonpsychiatric medications. Overall, 55% of patients were able to provide the correct name, dose, and purpose of their psychiatric medications. Despite most patients having several previous hospital stays 38% indicated they were unsure how long to continue their medications or had decided to use them no more than six months after discharge. We will provide additional data including initial follow-up rates. As lengths of stays continue to shorten, greater emphasis on patient understanding of medication may help to reduce relapse rates.

NR124 Monday, May 23, 3:00 p.m.-5:00 p.m.

Homelessness and Substance Use in Severe Mentally Ill Patients

Deborah White, B.A., Psychiatry, University of Maryland, 914 Crest Park Drive, Silver Spring MD 20903; Lisa Dixon, M.D., Anthony F. Lehman, M.D., John Belcher, Ph.D.

Summary:

Objective: The purpose of this study was to examine the relationship between homelessness and substance abuse in homeless persons with severe mental illness (HPSMI) and substance abuse disorders. We hypothesized that a subgroup of "stressor" model patients used substances due to the stresses of homelessness, and a subgroup of "non-stressor" model patients had substance abuse disorders that primarily led to homelessness.

Method: Therapists of 52 dually diagnosed patients receiving services from a PACT model assertive community treatment team prospectively reported patients' drug use, current stressors (housing, financial, social, psychiatric) and consequences of drug use. Patients were then classified as having one of the following models of use: "definite stressor," "possible stressor," "definite non-stressor," "possible non-stressor," or "other."

Results: Only two (4%) patients were "definite stressor," 17 (33%) were "possible stressor," five (10%) were "definite non-stressor," 13 (25%) were "possible non-stressor," and 15 (30%) were "other" model users. No demographic characteristics distinguished patients in these groups. Most patients frequently experienced multiple stresses.

Conclusions: We found that a simple stressor:shnonstressor model was inadequate to understand the relationship between homelessness and substance abuse in HPSMI. This difficulty reflects the complicated and interdependent nature of some of the identified characteristics of homeless, dually diagnosed individuals. Stresses seemed to be important influences on behavior, regardless of whether patients were identified as using substances in relation to these stresses. This finding supports the value of providing integrated and comprehensive services to dually diagnosed homeless individuals. We present case studies detailing the characteristics associated with different models.

NR125 Monday, May 23, 3:00 p.m.-5:00 p.m.

Transfers of Hospitalized Psychiatric Patients to a General Hospital Emergency Service for Adverse Drug Reactions

Anand P. Popli, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; James Hegarty, M.D., Arthur J. Segal,

M.D., Judith C. Kando, Pharm. D., Mauricio Tohen, M.D., Ross J. Baldessarini, M.D.

Summary:

Objective: To evaluate transfers of psychiatric patients to a general hospital due to adverse drug reactions (ADRs).

Method: In a 2.5 year period in 1990–1993, of all admissions to McLean Hospital, transfers to a general hospital emergency service were identified as possibly ADR-related by a specially trained nurse, verified by a clinical pharmacist, and reviewed in detail for this study; those related to a primary medical condition were excluded.

Results: Among 10,994 admissions, 29 medical transfers met criteria as probably ADR-related (0.26% incidence); mean ± SD age was 42.7 ± 18.1 years; 16 were women. Most cases (22; 75.9%) involved neurological syndromes (delirium [36.4%] > seizures > presyncope > extrapyramidal syndromes [EPS]; none involved neuroleptic malignant syndrome, serotonin syndrome, or agranulocytosis (risk < 0.01%). Non-EPS neurological ADR cases tended to be older (47 ± 16 vs. 36 ± 19 years) and to be more prevalent in women (71% vs. 57% risk). Low-potency antipsychotics were most frequently implicated (48% of cases; followed by: other antipsychotics > anticholinergics = antidepressants > benzodiazepines = anticonvulsants > lithium). Most ADRs were of moderate severity, but eight cases (27.6%) required medical admission (0.073% incidence).

Conclusions: ADRs leading to transfer of hospitalized psychiatric patients to a general medical facility were infrequent (< 3:sh1,000 admissions), commonly involved delirium or other neurotoxic events associated with antipsychotic or anticholinergic drugs, and rarely led to medical hospitalization (< 1:sh1,000 admissions).

NR126 Monday, May 23, 3:00 p.m.-5:00 p.m.

Psychiatric Interview and Psychometric Predictors of Survival in Cardiac Transplant

Jennifer G. Gotto, M.D., Psychiatry, Baylor College of Med., One Baylor Plaza, Houston TX 77030; Ranjit Chacko, M.D., Robert G. Harper, Ph.D., James Young, M.D.

Summary:

This investigation reports on 94 heart transplant patients, all of whom were evaluated prior to transplant with psychiatric interview involving psychiatric and psychosocial assessment, and psychometric testing. Psychometric measures included the Mini Mental Status Examination, Beck Depression Inventory, Psychosocial Adjustment to Illness Questionnaire, Millon Behavioral Health Inventory, and Health Status Questionnaire. Statistical comparisons between the 66 survivors and 28 nonsurvivors showed no group differences in terms of sex, age, race, or etiology of cardiac failure. Survivors and nonsurvivors were significantly different ($p < .05$ or less) regarding pretransplant compliance, three-point interview classification of pretransplant social support and coping (poor, marginal, good), and Axis II diagnosis. Psychometric measures of behavioral health coping (Millon Behavioral Health Inventory) and psychosocial adjustment (Psychosocial adjustment to Illness Scale) also differentiated outcome groups on measures of coping style, chronic tension, vulnerability to stress, orientation to health care intervention, family, and other psychosocial support. Logistic regression analyses using selected psychometric variables and pretransplant compliance, correctly classified over 75% of survivors and nonsurvivors, prediction being primarily accurate for survivorship (90%+ accuracy for survivors; 40% for nonsurvivors). The implications of these findings are discussed in terms of the need to understand both psychiatric and medical contributions to longterm outcome of cardiac transplant.

NR127 Monday, May 23, 3:00 p.m.-5:00 p.m.

Assessment of Personality Disorders in Patients with Reflex Sympathetic Dystrophy

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Summary:

Objective: As many as 64% of RSD patients require psychiatric consultation.[1] Some have argued that RSD is largely a psychiatric entity, yet there are few studies available to support or refute this idea.[2] The purpose of this pilot study was to determine if RSD-patients are psychiatrically different from other chronic pain patients, with a focus on personality disorders.

Methods: 25 RSD patients were randomly selected from Thomas Jefferson University Hospital Neurology Clinic, a major referral center for RSD. A control group of 25 patients with low-back disc radiculopathy were matched clinically and demographically. The Structured Clinical Interview for *DSM-III-R* (SCID) was used to screen for axis I disorders. If none were present, participants were administered the SCID-II for personality disorders.

Results: 24% of RSD patients and 21% of radiculopathy patients had axis I disorders, most notably major depression. Of those who did not, 50% of the RSD patients and 66% of the radiculopathy patients had at least one personality disorder.

Conclusions: While both groups had a high incidence of personality disorders, RSD patients had less. Therefore, RSD should not be considered due more to personality disorders than other chronic pain syndromes.

NR128 Monday, May 23, 3:00 p.m.-5:00 p.m.

The Provider-Patient Relationship in Young Adults with Type I Diabetes Mellitus

Ramona Dvorak, M.D., Psychiatry, Joslin Diabetes Ctr, One Joslin Place, Boston MA 02215; Allen Jacobson, M.D., Stuart T. Hauser, M.D., Robert S. Lagos, B.S., Charlotte Cole, Ed.D.

Summary:

Objective: Young adults with a chronic medical illness are at risk for medical difficulties. This group is not well studied and little is known about how they experience their relationships with health care providers. This relationship has been shown to significantly influence health outcomes. The objective of this project is to better understand provider-patient relationships of this population, and this may serve to improve patient care.

Method: In this study, we evaluate the experiences of individuals aged 18–26 with Type I diabetes mellitus. Audiotaped semistructured interviews are used to examine the patients' experiences with their providers. A 50-item Q-sort was developed for the study to analyze the interview data. Each item describes a conceptually relevant aspect of the provider-patient relationship. The items are rated on a scale of one to nine, which is least to most characteristic of the relationship. In initial testing of the instrument, four trained raters achieved good inter-rater reliability (Cronbach's alpha = .82). Two subscales of the Q-sort items have been constructed: The Therapeutic Alliance Scale (Cronbach's Alpha = .92) measures the extent the patient feels supported by the provider; the Socioemotional Scale (Cronbach's Alpha = .77) measures the importance of interpersonal aspects of the relationship to the patient. Construct validation of the Q-sort is in progress, using independently obtained concurrent psychological measures.

Results: We present preliminary data analysis of 40 subjects studied to date. We have found no significant correlations between gender or age and patient-reported experience of the relationship. Preliminary analysis, however, does reveal moderate correlations between the two Q-sort subscales and selected psychological measures. The Socioemotional Scale is related to variables denot-

ing interpersonal psychological characteristics (for example several subscales of Shaver's Love Experience Questionnaire: Trust: $r = .62$, $p < .001$; Friendship $r = .55$, $p < .001$; Happiness $r = .51$, $p < .002$). In contrast, the Therapeutic Alliance subscale is not related to these affective variables. This subscale tends to be associated with cognitive factors (for example, the Intelligence subscale of Harter's Self Perception scale, $r = .30$, $p < .10$).

Conclusions: These preliminary results suggest that important determinants of the provider-patient experience in this group of young adults are shaped by individual interpersonal and cognitive processes.

NR129 Monday, May 23, 3:00 p.m.-5:00 p.m.

MMPI-2 and Ethnicity in the Basic Trainees of the United States Air Force

Curtis H. Holder, M.D., Psychiatry, Wilford Hall Med. Center, 2200 Bergquist Drive Suite 1, San Antonio TX 78236; Edna Fiedler, Ph.D.

Summary:

Purpose: Study MMPI-2 coping styles of basic trainees in relation to ethnicity.

Procedure: 848 basic trainees took the MMPI-2 as part of an outpatient evaluation in 1993: 705 Caucasian (C), 76 African American (AA), 16 Asian (A), 30 Hispanic (H), and 20 "other" (O). Composite T-scores were used to develop profiles of each of the major MMPI-2 scales for ethnicity and clinician recommendation.

Results: Oneway analysis of variance (ANOVA) showed AA to have higher K and L scores than C, while C had higher Si scores than AA trainees. C, AA, and H trainees all had lower Hy scores than O trainees. Increased scores in F, Hs, D, Hy, Pd, Pa, Pt, Sc, Ma, and Si and a decrease in K were found for Cs recommended for discharge (DISCH) vs those Returned To Duty (RTD). Hospitalized H trainees had higher scores in Pa than H who were RTD or DISCH. Above results are significant at the .05 level.

Conclusions: Differences among groups could arise for multiple reasons. Elevated K and L scores for the AA compared to C could be because of different socioeconomic backgrounds, ego strength, or motivation to "look good" in the testing situation. The higher Si of C's may indicate more difficulty in social interaction or less difficulty in impulse control. The O's may represent trainees using somatic dysfunction as a "default" language of distress. The high Pa elevation for hospitalized H was also noteworthy.

NR130 Monday, May 23, 3:00 p.m.-5:00 p.m.

Suicide in the Elderly Cuban-American Population of Dade County Florida: 1990–1993

Yolanda B. Zarate, M.D., Psychiatry, University of Miami, 4300 Alton Road 3 Warner, Miami Beach FL 33140; Maria D. Llorente, M.D., David Loewenstein, Ph.D.

Summary:

There is a paucity of information about suicide in elderly Cuban Americans, despite this group's having the highest suicide rate and lowest age-adjusted mortality among hispanic subgroups (D2). The purpose of this study was to determine the risk factors for and rate of suicide among Cuban-Americans over age 65.

All files of completed suicides over age 65 between January 1990 and June 1993 from the Dade County medical examiners' office were reviewed. Data were gathered regarding multiple variables, including country of origin and then analyzed utilizing chi-square with statistical significance at $P < 0.05$. A total of 306 persons > 65 completed suicide (118 Cuban American, 100 white nonhispanic and 88 some other origin). The suicide rate for Cuban American males was 26.6:sh100,000 and for white nonhispanic males 23.4:sh100,000. Cubans were statistically more likely to commit suicide by hanging, having a lower education level, and have a support system. Other variables did not differ.

Elderly Cuban males in Dade County have a comparable rate of suicide to white nonhispanic males. Despite having support systems, Cubans still completed suicide and did so via hanging. These findings emphasize the important contribution of cultural diversity. Known risk factors for suicide in one segment of the population (i.e. lack of support system), may not be so for another.

NR131 Monday, May 23, 3:00 p.m.-5:00 p.m.

Alcohol Use Among Undergraduate Asian-Americans

Edward Ma, B.S., Psych. c/o Dr. H. Chung, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Henry Chung, M.,D., Jean Mueller, Ph.D., John C. Mahler, M.D., James Hull, Ph.D.

Summary:

Objective: To identify risk factors associated with and protective factors mitigating against heavy alcohol use in Asian-American college students.

Methods: An anonymous 80-item survey of drinking behavior that included sociocultural variables (e.g. ethnic group, generational status, religious affiliation), physiologic responses to alcohol use (e.g. fast flushing), and alcohol-related behaviors (DUI, violence) was administered to Asian-American undergraduate students (n = 430) at Cornell University. Individual risk and protective factors were assessed using t-tests and chi-squared analyses.

Results: Korean Americans and American-born subjects were most likely to binge drink. Korean Americans who drank had a higher frequency of physiologic (nausea/vomiting, passing out) and behavioral-manifestations of problem drinking. "Fast flushers" (subjects who flushed with one drink) were more likely to describe themselves as abstainers and the least likely to binge drink, compared with nonflushers and slow flushers. Asian Americans belonging to religious organizations were much more likely to abstain than those belonging to fraternities. The relative importance of variable clusters will be demonstrated using a model-building strategy employing logistic regression approaches.

Conclusions: Drinking practices among Asian-American college students vary significantly with ethnicity, generational status, gender, and peer-group affiliation. Primary prevention of problem drinking among Asian Americans should take note of these specific risk and protective factors.

NR132 Monday, May 23, 3:00 p.m.-5:00 p.m.

Mental Disorders in Black Nursing Home Residents

Luis G. Allen, M.D., Psychiatry, Hillside Hospital, PO Box 38 Lowenstein Res. Bldg, Glen Oaks NY 11004; Blaine S. Greenwald, M.D., Ronald Brenner, M.D., Richard Hodder, M.D., Arthur Risbrook, M.D.

Summary:

Both the absolute numbers of blacks in nursing homes and the percent of the elderly black population who reside in nursing homes are increasing. Although several recent reports address the epidemiology of mental disturbances in nursing homes, only limited information exists on the frequency of psychiatric disorders among black nursing home residents.

Objective: To determine the prevalence of psychiatric disorders among blacks in nursing homes.

Methods: A pilot survey was conducted with 50 randomly selected black residents of four diverse NYC-area nursing homes. Major geropsychiatric diagnoses were evaluated via a composite of (1) resident interviews based upon relevant extracted items from standardized psychiatric interviews and diagnostic schemas (e.g. SCID, DSM-III-R, CARE, Psychogeriatric Dependency Rat-

ing Scale), (2) nursing staff consultation, and (3) chart review. Interviews and supporting chart reviews were conducted by a psychiatric resident (LGA) with extensive geropsychiatric experience.

Results: Mean age of black nursing home residents screened was 82.3 ± 8.7 years. 36 women and 14 men were evaluated. A total of 88% of residents had a psychiatric diagnosis. Diagnostic breakdown was as follows: major depression: 0%; dementia: 80% (AD = 43%, MID = 35%, other = 22%); delirium: 0%; schizophrenia: 2%; other late-life psychoses: 4%; alcoholism: 6% no psychiatric diagnosis: 12%. Behavioral problems (regardless of diagnosis) were present in 62% of residents, with over 60% demonstrating three or more disturbances; 20% of residents had been seen by a psychiatrist in the past three months, and 16% of residents were prescribed a psychotropic.

Conclusions: Findings approximate overall rates of psychiatric disorders and behavioral disturbances reported in general nursing home populations. This suggests that at least on this basis, mental health service delivery strategies for blacks in nursing homes need not be specialized. Despite high rates of psychiatric/behavioral problems, only one-fifth of residents had recently seen a psychiatrist. Whether this represents discriminatory practices awaits evaluation of psychiatric visits among white and other non-black populations.

NR133 Monday, May 23, 3:00 p.m.-5:00 p.m.

Delusions of Theft in Probable Alzheimer's Disease

Jesus Rivero, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue Ste 702, Miami FL 33136; Steven Sevush, M.D.

Summary:

Delusions of theft (DF) are common in probable Alzheimer's disease (PAD) but the mechanism underlying their production is not known. Possibilities include: a) DF result from memory loss combined with unawareness of deficit; b) DF result from an interaction of memory loss with general paranoia. We examined these possibilities by assessing memory, awareness of deficit, and general paranoia in 21 PAD patients with prominent DF and 29 PAD patients with little or no DF. Memory was assessed with a nine-item quantitative caregiver questionnaire; awareness of deficit was rated by the examiner according to a six-point scale; general paranoia was assessed with the Washington Paranoia Scale. Means were compared between groups by analysis of covariance controlled for duration of illness and severity of non-memory cognitive impairment. Patients with DF had greater memory impairment ($F = 6.70$, $p = .013$) and more general paranoia ($F = 10.50$, $p = .0024$) than did patients without DF, but awareness of deficit was not different between groups ($F = 0.54$, $p = .46$). These results support the thesis that DF in PAD results from an interaction of memory impairment and generalized paranoia but is independent of the patient's awareness of deficit.

NR134 Monday, May 23, 3:00 p.m.-5:00 p.m.

Tridimensional Personality Characteristics of Mentally Ill Offenders and Non-Offenders

Barry J. Mills, M.D., Psychiatry, University of Texas, 9207 Points Edge, San Antonio TX 78250; E. Ross Taylor, M.D., John A. Chiles, M.D., Jeff S. Seward, M.D.

Summary:

We compared personality characteristics of mentally ill offenders (MIO) and mentally ill nonoffenders (MIN). Cloninger's tridimensional model proposes three traits of novelty seeking (NS), harm avoidance (HA), and reward dependence (RD). Evidence links these traits to the brain systems for activation (dopamine), inhibition (serotonin), and maintenence (norepinephrine), respectively. We proposed MIOs would disclose a profile of high NS, low HA, and low RD. We gave the tridimensional personality questionaire (TPQ) to 76 patients in a county dental health clinic. The MIOs ($n = 38$) were consecutive conditional releases to a criminal forensic clinic. The MINs ($n = 38$) were randomly selected from a medication clinic. The groups did not differ significantly by age, race, gender, medications, or diagnosis, nor by NS ($p = .86$) and HA ($p = .27$). The MIO group scored significantly lower on RD ($p = .01$). These findings indicate low RD is a distinguishing personality characteristic of MIOs. Conditional release treatment may be improved by facilitation of paired association learning and resistance to extinction of previously rewarded behavior. Future studies are needed to investigate linkages between noradrenergic function, reward dependence, and criminality.

NR135 Monday, May 23, 3:00 p.m.-5:00 p.m.

Pseudopsychopathy and Conditional Release Failure in Mentally Ill Offenders

Barry J. Mills, M.D., Psychiatry, University of Texas, 9207 Points Edge, San Antonio TX 78250; E. Ross Taylor, M.D., John A. Chiles, M.D.

Summary:

Prediction of conditional release failure (CRF) in mentally ill offenders (MIOs) traditionally relies on psychosis, sociopathy, and aggression. "Pseudopsychopathy" is an executive syndrome of the orbital aspects of the frontal lobe with impulsivity, belligerence, and social inappropriateness. We propose that CRFs in executively impaired MIOs are disproportionally represented by "pseudopsychopathic" subjects. We studied 33 consecutive admissions for criminal court ordered treatment to a forensic clinic. Subjects were rated on the Brief Psychiatric Rating Scale (BPRS), Hare Psychopathy Checklist (PCL-R), Yudofsky Overt Aggression Scale (YAG), Executive Interview (EXIT), and the Qualitative Evaluation of Dementia (QED). The QED is a novel instrument that identifies the "pseudopsychopathic" type of executive syndrome. On admission 24(73%) subjects demonstrated significant executive impairment ($EXIT \geq 10$). Over 1.5 years eight(24%) subjects were revoked, all executively impaired. The revoked (RV) and active (AC) groups did not differ significantly by BPRS, PCL-R, YAG, age, race, gender, education, or diagnosis. The groups differed significantly on the QED ($p = .005$). This study indicates presence and type of executive impairment has important prognostic value. The identification of a "pseudopsychopathic" type of executive syndrome was a significant predictor of conditional release failure.

NR136 Monday, May 23, 3:00 p.m.-5:00 p.m.

Understanding Firearms and the Mentally Ill

Nicole F. Wolfe, M.D., Mental Health Division, Federal Correctional Inst, Box 1000 Old Oxford Hwy 75, Butner NC 27509

Summary:

Objective: Firearms were involved in over 12,000 murders and over 12,000 suicides in the U.S. in 1992. Federal gun control laws have since 1968 prohibitted possession of firearms by persons previously committed to a mental institution. Gun control laws for convicted felons vary by state. The purpose of this study is to determine mental health professionals' knowledge of firearm laws and their level of inquiry into their patients owning firearms.

Method: Data from a newly constructed questionnaire were obtained on mental health professionals practicing in inpatient and outpatient settings.

Results: Over 90% of those surveyed were unaware of laws prohibiting previously committed individuals from owning firearms,

including rifles and shotguns. A majority of mental health professionals treated former criminals and committed patients and seldom inquired about whether their patients owned firearms.

Conclusion: Even though laws exist to help prevent firearms-associated violence by the mentally ill and criminals, mental health professionals are frequently unaware of them. Future studies would be required to determine if more consistent enforcement of these laws would contribute to reduced fatalities by firearms.

NR137 Monday, May 23, 3:00 p.m.-5:00 p.m.

Committing the Patient Who Doesn't Meet Criteria

Mitchell H. Dunn, M.D., Psychiatry, UNC Hospitals, 101 Manning Drive CB#7160, Chapel Hill NC 27514;

Summary:

Evaluation of patients for involuntary commitment is a task performed frequently by psychiatrists in the public hospital setting. Theoretically, the patient must meet certain commitment criteria in order to be involuntarily held in the hospital prior to a hearing. In North Carolina, as in many states, these criteria (for the nonmentally retarded) are that the patient be mentally ill or a substance abuser, and dangerous to self or others. Brief interviews were conducted with the physicians who evaluated 100 consecutive patients presenting on involuntary commitment papers at a state psychiatric hospital. These interviews indicate that there is a significant minority of cases in which the evaluating physician proceeds with involuntary commitment despite the fact the he or she does not truly feel that the patient meets commitment criteria. Physician reasoning for this nonadherence to commitment statute is examined.

NR138 Monday, May 23, 3:00 p.m.-5:00 p.m.

Psychiatric Consultations in Persons 80 Years of Age and Older: Is There a Difference?

Tarak Vasavada, M.D., 109 Governors Dr., Huntsville AL 35801; Prakash Masand, M.D., Pushpi Chaudhary, M.D.

Summary:

Amongst "geriatric" individuals, those 80 years and older represent the fastest growing segment of the population. Very few studies in psychiatry have studied this latter group. We studied psychiatric consultations done in very old (80 years or older) medically/surgically ill patients to see if there were any differences as compared to the not so very old (65 to 70 years).

Method: The authors retrospectively reviewed the charts of patients seen by psychiatric consult service between January 1, 1989, through December 31, 1992. The patients were divided into a study group which comprised those who were 80 years and older (N = 38) and a comparison group of those who were between the ages of 65 and 70 (N = 38). The social, demographic, and clinical variables, reasons for consult, length of hospitalization, psychotropics prescribed, and psychiatric diagnosis were assessed.

Result: The very old patients were significantly more likely to be evaluated for competency and be diagnosed with organic mental syndromes. Very old patients were also consulted upon later during the course of their hospital stay. There were no differences in the two groups on other variables, including psychotropics prescribed and length of hospitalization.

NR139 Monday, May 23, 3:00 p.m.-5:00 p.m.

Incidence of Post-ECT Delirium in Geriatric Patients

Amaryllis Sanchez, B.A., Psychiatry, Penn. State Hershey, 800 S. Washington St. #D-106, Alexandria VA 22314; Paul A. Kettl, M.D.

Summary:

Little data are available regarding ECT in older patients in whom it appears to be particularly effective. This study determined the incidence of ECT-induced delirium in geriatric patients admitted to a university-based geriatic psychiatry unit.

We prospectively evaluated 33 patients for the presence of post-ECT delirium, which was defined by the presence of *DSM-III-R* criteria for delirium as well as a drop of at least four points in the MMSE score. Chi square statistics were used to analyze our data.

A total of 33 patients aged 65–86 (mean = 74) were studied: 24 were female and nine were male. Of these, 29 suffered from major depression and four from bipolar disorder. All were antidepressant medication failures.

Thirteen patients (39%) became delirious and of these, seven had interruptions in their ECT course due to delirium leading to a longer hospital stay. Significant factors leading to delirium included age greater than 80, longer length of peripheral seizure, and the presence of GI pathology. Non-significant trends leading to more delirium included the presence of Parkinson's Disease, higher numbers of ECT treatments, and the use of antipsychotic medication before or during ECT.

Of the 33 patients, 28 returned to their premorbid baseline, four showed significant improvement, and one did not improve.

Although ECT-induced delirium in geriatric patients is relatively common, it did not pose a significant threat, and should not be a reason to deprive patients of this treatment.

NR140 Monday, May 23, 3:00 p.m.-5:00 p.m.

Instrumental Assessment of Psychomotor Slowing

Mary E. Wylie, M.D., Western Psychiatric Inst, 3811 O'Hara Street, Pittsburgh PA 15213; Robert Sweet, M.D., Robert Nebes, Ph.D., Bruce Pollock, M.D., Edythe Halligan, M.A.

Summary:

Objective: Psychomotor slowing is a cardinal symptom of depression that may be predictive of response to treatment. Separating the cognitive and motor components of psychomotor slowing may help distinguish depressed elderly patients from those with Alzheimer's disease. Use of electromechanical techniques in conjunction with traditional psychological testing may permit this assessment. Method: We examined measures of cognitive and motor slowing in twenty-two subjects: seven normal elderly (NE), six depressed elderly outpatients (DE), six outpatients with Alzheimer's disease (AD), and three normal young (NY). All subjects performed rapid ballistic flexing movements of the wrist with wrist displacement encoded by a potentiometer and digitized to calculate peak ballistic velocities. The five fastest values for each subject's right and left hands were utilized. Concurrently subjects performed a dot enumeration task (DOT) which generates both an indirect estimate of cognitive speed (the slope), as well as an indirect estimate of response time, one of whose components is motor speed (the intercept). Result: Average velocities of right (AVR) and left (AVL) hands were highly correlated ($r = 0.80$), $p < 0.001$). AVR across all diagnostic groups was significantly correlated with DOT intercept, a function representing motor and sensory components ($r = -0.49$, $= 0.02$). For AVL this was ($r = -0.39$, $p = 0.08$). There was no correlation between either hand velocity and DOT slope, (AVR, $r = -0.07$; AVL, $r = 0.03$) suggesting a dissociation between motoric and cognitive processing speeds. Conclusions: Cognitive and motor slowing represent separate processes which are amenable to discrete assessments. Ongoing studies will include more severely depressed patients and patients in the earlier phases of dementia.

NR141 Monday, May 23, 3:00 p.m.-5:00 p.m.

A Prospective Study of Factors Associated with Discharge From Hospitalization Among Older Psychiatric Inpatients

Raymond L. Ownby, M.D., Psychiatry, University of Miami, 330 Kentucky Avenue, Ft. Lauderdale FL 33312

Summary:

Background: Older patients may comprise an increasing percentage of patients in public psychiatric hospitals due to the greater difficulty in finding community placements for them. Better understanding of the factors associated with their discharge from these facilities might allow better allocation of and tailoring of treatment programs.

Objective: To assess the relations of psychopathological, social skills, and demographic variables to discharge from a public hospital among older (age > 40 years) chronic inpatients.

Design: Prospective longitudinal with an initial cohort over 3 and 1/2 years; a second cohort was followed for the final one-year period.

Analysis: Survival analysis using the Cox proportional hazards model.

Results: For the entire group (N = 167), five variables were significantly related to discharge: positive psychotic symptoms, gender, number of prior hospitalizations, capacity to use community resources, and aggressive behaviors. Subgroup analyses showed slightly different models for more vs. less chronic patients, with psychopathology being relatively more important among less chronic patients and social skills being relatively more important among more chronic patients.

Conclusions: This study confirms the close relations of psychopathologic, demographic, and social skills variables to patients' eventual discharge from chronic psychiatric care. Subgroup analyses suggest potentially important differences between more vs. less chronic patients which may be relevant for treatment planning.

NR142 Monday, May 23, 3:00 p.m.-5:00 p.m.

Fluoxetine Treatment for Elderly Patients with Dysthymic Disorder: A Pilot Study

Mitchell S. Nobler, M.D., Biological Psychiatry, NY State Psychiatric Inst, 722 West 168th Street, Unit 72, New York NY 10032; D.P. Devanand, M.D., Tara M. Singer, B.A., Steven P. Roose, M.D., Harold A. Sackeim, Ph.D.

Summary:

Dysthymia is often unrecognized in the elderly. We report on a pilot study of fluoxetine in this population.

Method: Of 224 consecutive patients evaluated in a Late Life Depression Clinic, 40 (17.9%) met *DSM III-R* criteria for primary dysthymic disorder (mean age = 67.8 years, SD = 6.1). Twenty-one patients entered and 12 have completed a 13-week, single-blind study of fluoxetine (two-week placebo run-in, then active medication 20–40 mg/d).

Results: At baseline, mean (±SD) Hamilton Depression scores (24 item) were 14.33 (3.98). Following seven weeks of fluoxetine, mean Hamilton was 8.42 (5.48), and at the end of the study was 6.67 (4.31). Using response criteria of a 50% reduction in Hamilton score from baseline and a Clinical Global Impression score of 1 or 2 (normal or mildly ill), nine patients (75%) were responders. Overall, fluoxetine was well tolerated; side effects were mild, and included insomnia, drowsiness, and mild nausea. One striking side effect reported by 50% of patients was excessive yawning in the absence of sedation.

Conclusions: These preliminary findings indicate that fluoxetine is a safe and effective treatment in elderly patients with dysthymia.

NR143 Monday, May 23, 3:00 p.m.-5:00 p.m

Age of Onset and the Rate of Cerebral Degeneration in Alzheimer's Disease: Magnetic Resonance-Based Volumetric Study

Ju Han Kim, M.D., Psychiatry, S.N.U. Hospital, 28 Yongon-Dong, Chongro-Gu, Seoul 110744, Korea, Dong Soo Shin, M.D., Jin Hyeong Jhoo, M.D., Dong Young Lee, M.D., Jung Hie Lee, M.D., Jong Inn Woo, M.D.

Summary:

Objective: To investigate the correlation between the age of onset and cerebral degeneration in Alzheimer's disease

Method: Using MR-based volumetry through boundary tracing, image digitizing, and pixel counting, the authors measured the cortical and the cerebral(cortical and ventricular) atrophy in 28 Alzheimer patients (Age: 72.1 ± 6.84) according to NINCDS-ADRDA criteria and 22 normal control subjects (Age: 71.4 ± 5.36).

Results: In normal elderly subjects, the cerebral atropy was significantly correlated with the age ($r = 0.65$, $p < 0.005$). Alzheimer patients exhibited significantly greater cerebral atrophy than normal controls($p < 0.05$) after the age adjustment by ANCOVA. In Alzheimer patients, the age of onset was negatively correlated with the rate of disease-related cerebral degeneration [(observed atrophy—atrophy in normal aging calculated by the regression equation derived from the control group)/(duration of illness)] ($r = -0.629$, $p < 0.0005$). Multiple regression with interaction analysis based on these findings demonstrated that age, age of onset, and their interaction successfully explained cerebral($R^2 = 0.532$, $p < 0.05$) and cortical($R^2 = 0.643$, $p < 0.05$) atrophy in 16 probable Alzheimer patients.

Conclusions: Age of onset appears to highly predict the rate of disease-related cerebral degeneration in Alzheimer's disease, and our results suggest that controlling age and age of onset is essential in the volumetric study of Alzheimer's disease.

NR144 Withdrawn

NR145 Monday, May 23, 3:00 p.m.-5:00 p.m

The Treatment of Depression in Dementia Patients

Linda D. Lewis, MN, Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425; Sharon R. Burnside, M.D., Jacobo E. Mintzer, M.D., William Wellborn, Ph.D., L.R. Waid, Ph.D., Kerry Herman, B.A.

Summary:

Objective: The goal of this study was to evaluate the response to oral antidepressant pharmacological treatment of cognitively impaired elderly patients suffering from DSM-III-R diagnoses of major depression.

Methods: Subjects: 31 patients consecutively admitted to a geriatric psychiatric impatient unit with diagnosis of major depression and neuropsychological evidence of cognitive impairment were included in this study. Procedure: Level of depression was measured at baseline and upon discharge using the Cornell Scale for Depression and Dementia (CDD). In addition, Mini-Mental Score (MMS), University of Washington Paranoia Scale (WPS), and complete neurological, psychiatric, and medical evaluations were recorded at baseline to evaluate cognitive impairment, symptoms of paranoia, and diagnosis of dementia, respectively. Patients were rated to evaluate level of depression using the CDD at baseline and discharge by a blind rater. Patients were treated with oral antidepressants according to clinical judgment of a psychiatrist blind to the purpose of the study. Patients showing at discharge a decrease in CDD of 25% or more were considered responders.

Results: Nine subjects were male and 22 females. Mean age was 80 (Stdv 5.52). Baseline evaluation showed CDD 16.81 (Stdv 5.45); MMS 16.63 (Stdv 5.54); WPS 1 (Stdv 2.46). 27 subjects had DSM-III-R diagnosis of dementia (multi-infarct dementia 4, Alzheimer disease 9, and mixed type dementia 9), and 8 cognitive impairment without dementia. Twenty-four subjects were considered responders and seven nonresponders. No significant differences in gender, diagnosis of dementia or WPS, were found between responders and nonresponders. Significant differences were found between responders and nonresponders on MMS (18.08 vs 10.83, $p < 0.002$), CDD at baseline (18.21 vs 12.00, $p < 0.006$) and length of stay (19.71 vs 41.43, $p < 0.001$).

Conclusion: Oral antidepressants appear to be effective in 77% of cognitively impaired elderly patients diagnosed as suffering from major depression regardless of diagnosis of dementia. Respondents to oral antidepressive treatment appear to be significantly less cognitively impaired, have a longer hospital stay and to be more severely depressed at baseline that nonresponders.

NR146 Monday, May 23, 3:00 p.m.-5:00 p.m.

Plasma Homovanillic Acid and Cognition in Geriatric Depression

Olurotimi L. Bajulaiye, M.D., Psychiatry, NY Hosp Cornell Med Ctr, 21 Bloomingdale Road, White Plains NY 10605; George S. Alexopoulos, M.D., Robert C. Young, M.D.

Summary:

The syndrome of geriatric major depression consists of a broad range of signs and symptoms and includes cognitive dysfunction. Because brain dopamine dysfunction has been implicated in major depression and dementia, we have began to study related measures in geriatric depression. We postulated the hypothesis that cognitive impairment in geriatric depression is associated with low plasma concentrations of the dopamine metabolite homovanillic acid (pHVA).

Symptomatic geriatric inpatients with major depression (N = 12, mean age = 75.8) were studied. Cognitive functioning was assessed with the Mini-Mental State Examination (MMSE), behavioral dysfunction with the Haycox Scale, and severity of depression with Geriatric Depression Scale (GDS). pHVA was determined by high performance liquid chromatography with electrochemical detection. pHVA concentration was positively associated with MMSE ($r = .77$, $p = .003$) and negatively associated with degree of behavioral dysfunction on the Haycox Scale ($r = .73$, $p = .006$). It was not significantly associated with severity of depression as measured with GDS.

NR147 Monday, May 23, 3:00 p.m.-5:00 p.m

Religion and the HIV-Positive Patient

Mark A. McClurg, M.D., Psychiatry, Jefferson Med. College, 1201 Chestnut St. 14th Flr., Philadelphia PA 19107; Shimon S. Waldfogel, M.D., Stephan Hauptman, D.O., Roberta A. Benjamin, B.S.N.

Summary:

Background: Religiosity has been shown to have an impact on the patient's response to illness. There have been few studies that have focussed on the religiosity of the HIV positive patient. The understanding of the role of religiosity in the coping of the HIV positive patient may lead to a more comprehensive approach to care.

Objective: To ascertain the role that the various dimensions of religion play in the subjective well being and life satisfaction of HIV positive patients.

Methods: A questionnaire consisting of questions about the belief, ritual, social, experiential, and consequential dimensions of religion was completed by 33 patients in an outpatient HIV clinic at a large urban university hospital. The patients' responses to Diener's Satisfaction With Life Scale (SWLS) and the Medical Outcomes Study (MOS) Short Form Health Survey were correlated with the various dimensions of religiosity.

Results: Of the 33 patients, 26 agreed that they believed in God. Fewer of the patients indicated that religious ritual was important. Of the six that had contact with clergy regarding their illness, all were satisfied with the interaction. Sixteen of the 33 patients felt their religion to be important. Most patients do not believe that their illness is the will of God and most indicated satisfaction with their lives. Full correlational data will be presented.

Conclusions: Our preliminary findings in a healthy population of HIV positive patients indicate that religiosity plays a minimal role in the subjective assessment of well being and satisfaction with life. Following these patients as their illness progresses may lead to changes in the role religiosity plays in their coping.

NR148 Monday, May 23, 3:00 p.m.-5:00 p.m

A Study on PTSD in China: Clinical Features and Crisis Intervention of 64 Cases

Yalin Zhang, M.D., Psychiatry, Harbor UCLA Med. Center, 1124 West Carson St. B-4 South, Torrance CA 90502; Suizhen Chen, Xiaoyin Huang

Summary:

Sixty-four Chinese patients with PTSD were studied in Mainland China. The clinical features were investigated and all cases randomly assgned to either a routine therapy (medication plus general psychological support; RT) or a comprehensive biopsycho social intervention (CI). It was found that: (1) the common stressors of PTSD in China were acute and severe sickness, wound accident or death of a close family member, infidelity of spouse, severe interpersonal conflict, involvement in lawsuits, and raped; (2) based on the Eysenck Personality Questionnaire, of all cases studied, 25% were introversive, 20.3% neurotic, 6.2% extroversive; (3) 57.8% onset immediately after impact of the stressor, 32.8% within one week, and 9.4% after a week; (4) common symptoms were flashback, insomnia, nightmare, weeping, suicide ideation, fear, and irritability; (5) coping behaviors included enduring (the fact (46.9%), despairing (29.7%), looking for other way out (12.5%), ignoring (6.3%), and violence (4.7%). The effectiveness of treatments for these two groups were assessed using Zung's Anxiety (SAS) and Depression Scal (SDS), and Global Assessment Scale (GAS). One month follow-up reevaluation shows that the scores of the three scales in CI group had better improvement compared with RT group; scores in SDS were statistically significant ($P < 0.05$).

NR149 Monday, May 23, 3:00 p.m.-5:00 p.m

PTSD Symptomatology in Children: The Columbus Day School Bus Accident

Stephanie D. Young-Azan, M.D., Child Psychiatry, University of Miami, 1611 NW 12th Avenue Room 18B, Miami FL 33136; Jon A. Shaw, M.D.

Summary:

The objective is to study the course and outcome of post-traumatic symptomatology (PTS) in 42 (28 boys, 14 girls) children ages 9–10 years in a school bus accident, Columbus Day 1991, in which two classmates and a teacher died. Thirty-one children were on the affected bus (ON) and nine were not directly exposed to the accident (OFF).

Method: PTSD section of the DICA was administered at seven weeks and at 13 months. A self-selected group of 11 children were seen in group therapy 1/wk × 8 weeks.

Results: Both groups had comparable PTS at seven weeks and at 13 months (OFF, 9.2; ON, 9.0) At 13 months those on the bus had significantly higher PTS (4.9) than those off the bus (1.2). PTS was significantly higher in girls (11.8) compared to boys (8.0) at seven weeks and 13 months (girls: 6.1; boys: 3.4). PTS were not related to proximity to the front of the bus at the time of the accident, but were at 13 months. PTS did not significantly diminish with group therapy. Discussion: Initially PTS was comparable in children ON or OFF the bus suggesting a contagion effect. But proximity to the zone of impact predicted PTS at 13 months. Children with most severe PTS, were more likely to select therapy, but showed little improvement at 13 months, suggesting the enduring effects of trauma.

NR150 Monday, May 23, 3:00 p.m.-5:00 p.m

Why Do Clinicians Miss Past Suicidal Behavior?

Katalin Szanto, M.D., Labs of Neuro., Western Psych Inst., 3811 O'Hara Street, Pittsburgh PA 15213; Kevin M. Malone, M.D. Elizabeth Corbitt, Ph.D., J. John Mann, M.D.

Summary:

Introduction: Overt suicidal behavior is the most robust predictor of future suicidal behavior. Therefore, we examined how effectively routine inpatient clinical assessments detected a history of overt suicidal behavior in 50 suicide attempter inpatients with a major depressive episode, compared to a systematic research screening.

Method: Hospital records were reviewed to assess reporting at admission and discharge of: number of lifetime attempts, suicidal ideation, objective planning behavior for a suicide attempt, and degree of medical damage caused by the most lethal and recent attempts. These parameters of suicidal behavior were compared with a separate comprehensive research assessment gathered concurrently.

Results: Clinicians failed to document that 24% of the patients ($Chi^2 = 15.21$, $p = 0.0001$) at admission and 28% ($Chi^2 = 12.97$, $p = 0.0003$) at discharge were past suicide attempters. Moreover, clinicians reported fewer total lifetime suicide attempts compared to research data assessments (1.92 vs 2.96, $t = -3.59$, $p = 0.001$). Composite accuracy scores computed for admission and discharge suicide assessments improved when patients had made a more recent suicide attempt or had fewer past hospitalizations. Greater medical damage of suicide attempts increased accuracy only on admission assessments.

Conclusions: A significant degree of past suicidal behavior is not recorded during routine clinical assessment. Using semi-structured screening instruments may improve detection of past suicidal behavior.

NR151 Monday, May 23, 3:00 p.m.-5:00 p.m.

Suicidal Behavior, Axis II Disorder and Major Depression

Elizabeth Corbitt, Ph.D., Lab of Neuropharm. Rm E81, WPIC, 3811 O'Hara Street, Pittsburgh PA 15213; Kevin M. Malone, M.D., Gretchen L. Haas, Ph.D., J. John Mann, M.D.

Summary:

Introduction: Patients with major depression have a relatively high likelihood of suicidal thoughts and acts. Comorbidity of personality disorders (PDs) with MDD is associated with a higher risk of suicidal behavior, but the specific nature of this association has not been established.

Methods: We investigated the effect of a mixture of comorbid IPDE-diagnosed Axis II DSM-III-R psychiatric disturbances in a sample of 44 male and 55 female patients meeting DSM-III-R criteria for a major depressive episode. Approximately half (57%) the patients had a history of previous suicide attempts.

Results: Dimensional analyses indicated that the number of borderline PD criteria was correlated with more suicide attempts ($r = .53$, $p < 0.001$), a younger age at first suicide attempt ($r = -.53$, $p < 0.001$), younger age at first psychiatric hospitalization ($r = -.36$, $p < 0.01$), more previous psychiatric hospitalizations ($r = .24$, $p < 0.05$), and more suicidal ideation prior to hospitalization and on admission ($r = .33$, $p < 0.01$ and $r = .47$, $p < 0.001$, respectively). Although other PDs were also related to suicidal behavior, semi-partial correlations removing the variance in suicidal behavior due to borderline criteria were found to be nonsignificant.

Conclusions: Borderline PD pathology may be the most critical Axis II risk factor for suicidal behavior among inpatients with MDD.

NR152 Monday, May 23, 3:00 p.m.-5:00 p.m.

Suicide Risk Factors Among Asian Patients

Raymond D. Tam, M.D., Psychiatry, Elmhurst Hospital, 7901 Broadway, Elmhurst NY 11373; Joana Law, C.S.W., John M. Herrera, Ph.D.

Summary:

The goal of this study is to determine the extent to which Asian patients are at risk to attempt suicide. A questionnaire with 16 suicide risk factors that were derived from a literature review was constructed. This questionnaire was then used by four clinicians to conduct a retrospective chart review of all enrolled patients (n = 99) in an Asian outpatient clinic in a large municipal hospital. This group includes Chinese and Korean adult patients with DSM-III-R Axis I diagnoses. Analyses revealed that a relatively large number of patients have high-risk factors of language barrier, unemployment, isolation, noncompliance and/or poor compliance to treatment. Other risk factors significant to this population include physical disability(ies), history of suicide attempt(s), loss of loved ones and substance abuse (alcohol among Korean patients). Asian patients are at relatively high risk to attempt suicide, and there is a need for more attention in the treatment process, especially for those patients who have a combination of several risk factors. Clinicians should be cautious in the assessment of those situations that may put the patients at risk.

NR153 Monday, May 23, 3:00 p.m.-5:00 p.m.

Communal Ties Mediating Violence and Its Effects

Karyn J. Horowitz, B.A., Psychiatry, Yale University, 367 Cedar Street, New Haven CT 06510; Stevan M. Weine, M.D., James F. Jekel, M.D.

Summary:

Objective: To determine whether communal ties mediate exposure to violence and development of PTSD symptoms in female urban adolescents.

Method: A self-report questionnaire was developed to gather data on demographics, exposure to violent events, PTSD symptoms, and communal ties (three variables on a Likert Scale measuring aspects of the person's involvement with communal institutions of family, school, and peers). The questionnaire was completed by a sample of African-American (81%) and Hispanic (13%) female urban adolescents (n = 79; mean age = 15.8 years).

Results: T-tests showed that persons who met *DSM-III-R* criteria for PTSD symptoms had lower scores for communal ties in the areas of family ($p = 0.0047$), school ($p = 0.0025$), and peers ($p = 0.023$). Pearson Correlations showed increased trauma exposure correlated with lower scored for communal ties in the areas of family ($r = 0.33$, $p = 0.0044$), school ($r = 0.37$, $p = 0.001$), and peers ($r = 0.49$, $p = 0.0001$).

Conclusions: Weaker ties to communal institutions of family, school, and peers, are associated with increased violence exposure and PTSD symptoms. When violence is endogenous to a community, the person's involvement with communal institutions is a critical element in both the etiology of violence exposure and the pathogenesis of PTSD.

NR154 Monday, May 23, 3:00 p.m.-5:00 p.m.

PTSD Symptoms Profiles in Female Urban Adolescents

Karyn J. Horowitz, B.A., Psychiatry, Yale University, 367 Cedar Street, New Haven CT 06510; Stevan M. Weine, M.D., James F. Jekel, M.D.

Summary:

Objective: To describe exposure to domestic and community violence and the profile of PTSD symptoms in a sample of female urban adolescents.

Method: A self-report questionnaire was developed to gather data on demographics, exposure to violent events, and PTSD symptoms. The questionnaire was completed by a sample of African-American (81%) and Hispanic (13%) female urban adolescents (n = 79; mean age = 15.8 years).

Results: The adolescents experienced at least eight different types of domestic and community violence events occurring both before and after the age of 13 (mean frequency of events = 28; s.d. = 10). The percent of subjects who met *DSM-III-R* criteria in each of the PTSD symptom clusters includes: hyperarousal (89.9%), reexperiencing (88. 6%), avoidance (79.7%), and all three (67.1%).

Conclusions: These female urban adolescents have experienced multiple types of violent events, occurring repeatedly and contemporaneously, throughout childhood and adolescence. There was a high percentage of PTSD symptoms reported across all three symptom clusters. Efforts to quell hyperarousal and re-experiencing symptoms by avoidance may be undermined by exposure to new violent events, resulting in persistent high levels of each symptom cluster.

NR155 Monday, May 23, 3:00 p.m.-5:00 p.m.

Gender and Medical Comorbidities of Recurrent Depression in Older Inpatients

Daniel P. Chapman, Ph.D., Aging Branch, Ctrs for Disease Ctrl, 4770 Buford Hwy NE MS K 51, Atlanta GA 30341; Joan K. Miller, Donald K. Blackman, Ph.D.

Summary:

While previous research has indicated depression is a common sequela experienced by inpatients hospitalized with myocardial infarction, stroke, and multi-infarct dementia, little is known about the demographic variables and medical comorbidities characterizing older adults hospitalized with the primary diagnosis of recurrent depression. We contrasted comorbidities associated with hospitalization for recurrent depression with those associated with hospitalization for single-episode depression or other nondepressive illness in a random 5% sample of all claims of eligible Medicare enrollees aged 65 years or older in 1991 (N = 1.34 million). While comprising approximately 60% of the sample investigated, nearly 70% of the 3,204 older patients hospitalized with any primary diagnosis of depression were women ($p < .001$), who were more likely than older men to receive the primary diagnosis of recurrent depression ($p < .001$). Older inpatients hospitalized with a primary diagnosis of depression manifested a greater number and variety of comorbidities than did inpatients with a primary diagnosis other than depression. Moreover, patients with recurrent depression had an even greater number of comorbidities than single-episode inpatients ($p < .001$). Relative to inpatients with the primary diagnosis of single-episode depression, higher rates of respiratory disorders were observed in men hospitalized with recurrent depression ($p < .001$), while women inpatients with recurrent depression manifested more frequent diagnosis of circulatory comorbidities ($p < .001$).

NR156 Monday, May 23 3:00 p.m.-5:00 p.m.

Patients Who Request a Female Therapist

Melinda Fudge, M.D., Jefferson Psych Assoc., Jefferson Medical, 1201 Chestnut St. Ste 1400, Philadelphia PA 19107; Timothy Smith, M.D., Salman Akhtar, M.D., Steven E. Samuel, Ph.D.

Summary:

Objective: The authors investigate demographic and clinical characteristics of patients who request a female therapist. The effect of granting such a request on treatment drop out was then examined.

Methods: Patients who spontaneously voiced a preference for a female therapist were compared with controls on the demographic variables of age, sex, race, marital and financial status, and the clinical characteristics of diagnosis, history of sexual abuse, sexual orientation overt presence of sexual or social difficulties, history of prior treatment, gender of the previous therapist, and dropout rate.

Results: Patients voicing a request for a female therapist were more often white, young, or to have voiced sexual or social difficulties in their chief complaint. The dropout rate of study patients whose request was granted was greater than control patients who received a female therapist.

Conclusions: The request for a female therapist may be reflective of a demographics-based (age or race) comfort in expressing preference or of specific presenting complaints in the realm of sexual or social relationships. Granting such a request without a better understanding of this significance may result in premature termination of treatment.

NR157 Monday, May 23 3:00 p.m.-5:00 p.m.

Body Dysmorphic Disorder in Atypical Depression

Katharine A. Phillips, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Summary:

Body dysmorphic disorder (BDD), an often-secret preoccupation with an imagined or slight defect in appearance, has received little empirical attention. In particular, its prevalence and associated clinical features among patients with other psychiatric disorders are unknown.

Methods: 80 consecutive subjects with atypical major depression were assessed with a reliable diagnostic module for BDD, the SCID, the Hamilton Depression Rating Scale, the Atypical Depression Diagnosis Scale, and the Clinical Global Impression Scale (CGI).

Results: 11 subjects (13.8%) met criteria for BDD (95% CI of 6.2% to 21.4%). BDD was nearly as prevalent as eating disorders (16.3%) and more than twice as prevalent as OCD (6.3%). However, no subjects volunteered the presence of BDD symptoms; in all cases, use of the diagnostic module was necessary to make the diagnosis. The six men and five women had a mean age of 36.2 ± 8.6 years; only one was married. Compared with the 69 subjects who had atypical major depression without BDD, those with atypical major depression plus BDD had a significantly earlier age of onset of major depression, longer duration of the current depressive episode, briefer intimate relationships, and higher

(more severely ill) CGI scores. Subjects with BDD were also more likely to have comorbid OCD. However, the two groups did not differ significantly in terms of total Hamilton score.

Conclusions: These preliminary data suggest that BDD can coexist with depression, but that it often goes undiagnosed. In addition, the presence of BDD is associated with several important clinical features, including earlier onset and longer duration of major depression, and greater overall severity of illness.

NR158 Monday, May 23 3:00 p.m.-5:00 p.m.

Skin Picking: A Symptom of Body Dysmorphic Disorder

Katharine A. Phillips, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Sarah L. Taub, B.A., Katherine D. Atala, M.D.

Summary:

Background: Compulsive skin picking has received little empirical attention. In addition, its association with body dysmorphic disorder (BDD; a preoccupation with an imagined or slight defect in appearance) has not been recognized.

Method: 117 subjects with DSM-III-R BDD or its delusional variant were assessed with a semistructured interview, the SCID, and the Y-BOCS modified for BDD. The 32 subjects who picked their skin were compared with the 85 subjects who did not pick.

Results: The 32 BDD subjects who picked their skin had a mean age of 31 ± 8 years; 59% (N = 19) were female and 69% (N = 22) were single. Nearly all subjects (97%, N = 31) had BDD preoccupations involving the skin. Impairments in social (97%, N = 31) and occupational (84%, N = 27) functioning were common. Also 31% (N = 9) had made at least one suicide attempt, and 48% (N = 15) had been psychiatrically hospitalized. A total 47% (N = 15) had a lifetime psychotic disorder (usually attributable to delusional BDD); 91% (N = 29), a mood disorder; and 59% (N = 19), an anxiety disorder. In addition, 47% (N = 15) had received dermatologic treatment, which was generally ineffective. Twelve of 25 (48%) trials with a serotonin-reuptake inhibitor (SRI) resulted in significant improvement compared with only three of 39 trials (8%) with other medications. Compared with BDD subjects who did not pick, those who picked were significantly more likely to have actual minimal physical defects (as opposed to none), to be preoccupied with their skin, to engage in excessive grooming and camouflaging behaviors, and to have received dermatologic treatment

Conclusion: Compulsive skin picking is an underrecognized problem that commonly occurs as a symptom of BDD. Because it is associated with significant impairment and appears to respond often to psychiatric treatment (SRIs), it is important that the picking and underlying BDD be recognized and treated.

NR158A Monday, May 23, 3:00 p.m.-5:00 p.m.

Quality of Life in Women with Metastatic Cancer

Tim Gendron, Department of Psychiatry, Mayo Clinic, 200 First Street, S.W., Desk West-11A, Rochester, MN 55905; Teresa A. Rummans, M.D., Michelle Taylor, Ph.D., Roger Evans, Ph.D., Paul Novotny, Ruth Johnson, M.D., Lynn Hartmann, M.D., Ann Marie Dose, R.N., Marilyn Stiles, Ph.D.

Summary:

To determine how quality of life issues including age and stage of life, psychological and spiritual state, social supports, and financial status as well as health status vary in women with metastatic breast and gynecological cancer, we surveyed women in a large outpatient tertiary care center. The patients with breast and gynecological cancer were stratified according to stage of illness. Approximately 50 consecutive females with metastatic breast cancer and 50 consecutive females with metestatic gynecological cancer were asked about basic demographic information, personal and family concerns, employment and financial concerns, spiritual resources, as well as open-ended questions about further concerns or comments they would like to make. In addition to these questions, patients were asked to complete three standard assessment tools including the Brief Symptom Inventory (BSI), Cancer Rehabilitation Evaluation System—Short Form (CARES-SF), and the Health Status Questionnaire (HSQ).

The average age was 60 years for both groups. The majority were married and had at least a high school education. Although no statistically significant differences were found between the two groups with regards to areas of concerns and outcomes of assessment tools, each group was noted to have psychological and physical distress. Of this population, 30% endorsed significant pain. Yet many identify spiritual and social supports.

Identifying specific concerns helps one tailor one's interventions. At the same time, identifying potential untapped areas of strength may aid in improving one's quality of life.

NR159 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Heritability of Irritable Aggression: A Twin Study

Emil F. Coccaro, M.D., Psychiatry, Med. Col. of PA EPPI, 3200 Henry Avenue, Philadelphia PA 19129; C.S. Bergeman, Ph.D., Richard J. Kavoussi, M.D.

Educational Objectives:

To identify the extent of influence that genetic factors and environmental factors may play in irritability and in various forms of aggressive behavior.

Summary:

An inverse relationship between indices of central serotonin (5-HT) system function and of trait measures of impulsive aggressive behavior (both of which appear to manifest high temporal stability) has been demonstrated repeatedly in humans over the past 15 years. Moreover, preliminary evidence of an increased frequency of impulsive aggressive behaviors in family members of individuals with indices of reduced central 5-HT system function suggests that an abnormality in central 5-HT and impulsive aggression may be heritable in humans. In order to test this latter hypothesis, we sent Buss-Durkee Hostility Inventory (BDHI) questionnaires by mail to 1200 male twins through the Vietnam-Era Twin (VET) Registry. From this survey, data were available from 182 MZ and 118 DZ twin pairs (n = 600 individuals in total). All four of the BDHI subscales examined demonstrated significant heritability estimates of a nonadditive nature. ICC values for the twin correlations were as follows: Irritability—MZ: 0.39 vs. DZ: 0.06; Direct Assault—MZ: 0.50 vs. DZ:0.19; Indirect Assault—MZ: 0.42 vs. DZ: 0.02; Verbal Assault—MZ: 0.28 vs. DZ: 0.07. Model-fitting procedures confirmed this finding with heritability estimates ranging from 27% (Verbal Assault) to 40% (Direct Assault). Non-Shared, *but not* Shared, Environment made a significant contribution to explaining the variance in the model (range:53% for Direct Assault to 72% for Verbal Assault). These data suggest that irritability and various forms of aggressive behavior, as self-reported, are heritable. It is possible that the type of "impulsive aggression" previously shown to correlate with indices of reduced central 5-HT system function is heritable in humans.

References:

1. Coccaro EF, Bergeman CS, McClearn G: Heritability of irritable impulsiveness: a study of twins reared together and apart. Psychiatry Research 48:229–242, 1993.

2. Plomin R, Nitz K, Rowe DC: Behavioral genetics and aggressive behavior in childhood. In: M. Lewis & S.M. Miller (eds), *Handbook of Developmental Psychopathology*, pp. 119–133, 1990.

NR160 Tuesday, May 24, 9:00 p.m.-10:30 a.m.

Decreased Hippocampal Volume Over Time in Schizophrenia: Evidence of Neurodegeneration

Henry A. Nasrallah, M.D., Psychiatry, Ohio State University, 473 W. 12th Avenue, Columbus OH 43210; Marla Ketterer, B.S., Sarita K. Sharma, B.S., Stephen C. Olson, M.D., Robert Martin, Mary B. Lynn, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the reduced size of the hippocampus in schizophrenia may not be a static neurodevelopmental hypoplasia, but perhaps a progressive neuro-degeneration that may explain the downhill course of schizophrenia.

Summary:

Several MRI and postmortem studies have reported a decrease in hippocampal volume in schizophrenia. This volume loss has been attributed to neurodevelopmental hypoplasia or dysplasia. Here we report on neurodegeneration as a possible mechanism of decreased hippocampal volume in schizophrenia.

DSM-III-R schizophrenic (N = 57, mean age 32.6 ± 7.1, duration of illness 9.8 ± 6.1 years) and healthy volunteer subjects (N = 35, mean age 29.3 ± 7.6 years) consented to participate in the study. All received brain MRI scans (GE 1.5 Tesla, TI = 800 ms, TR = 1500 ms). Consecutive coronal sections in which the hippocampus appears were traced on a computer image-analysis system and the volume calculated. Schizophrenic and control samples were compared using ANOVA, and the effect of duration of illness and/or age on hippocampal volume in each group were examined.

There were no diagnosis, gender, or laterality effects on hippocampal volume in schizophrenia (227.9 mm^3) vs. controls (221.4 mm^3). However, there was a significant inverse correlation between hippocampal volume and the duration of illness within the schizophrenic sample (Pearson r = –0.196, P = .036). Yet no effects of age were found in either the schizophrenic or control groups. These data suggest that while there was no difference in hippocampal volume in schizophrenic patients vs. controls, there was a significant relationship between the decrement of hippocampal volume and the duration of illness (but not age) in schizophrenia.

It could be speculated that this may be a neurotoxic effect of repeated psychotic episodes. There are some studies that show gliosis in the hippocampus on postmortem histopathology, which would be consistent with progressive atrophy rather than static hypoplasia in schizophrenia.

References:

1. Nasrallah HA: Neurodevelopmental pathogenesis in schizophrenia. *Psychiatric Clinics of North America* 16:269–280, 1993.

2. Stevens JR: Neuropathology of schizophrenia. *Archives of General Psychiatry* 39:1131–1139, 1982.

NR161 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Cognitive Impairment in Geriatric Schizophrenic Patients: Clinico-pathological Studies

Michael Davidson, M.D., Psychiatry, Mt. Sinai School Med., 130 W. Kingsbridge Road, Bronx NY 10468; Vahram Haroutunian, Ph.D., Steven Gabriel, Philip D. Harvey, Ph.D., Peter Powchik, M.D., Julia A. Golier, M.D., Kenneth L. Davis, M.D.

Educational Objectives:

To help the listener understand the phenomenology and potential biological substrates of cognitive impairment in geriatric schizophrenia.

Summary:

The outcome of schizophrenia in old age remains among the most debated topics in schizophrenia research. The debate between the Kraepelinian pronouncement that outcome is invariably bleak and the view that outcome of schizophrenia in old age is variable focuses on schizophrenic cognitive capacities in old age and not on psychosis, which for many patients ameliorates. To try to address this debate, this study has assessed cognitive functions and symptoms in 400 institutionalized schizophrenic patients, between ages 25 and 85. To investigate the biological substrate for the cognitive impairment in geriatric schizophrenics, some of them had been followed until death and autopsy. Results indicated that more than half of the institutionalized geriatric schizophrenic patients experienced severe-cognitive impairment. Less than 15% of cognitively impaired schizophrenic patients on whom autopsy was available met definite neurohistological criteria for AD. Schizophrenic patients demonstrated reductions in neuropeptide Y and somatostatin, which were more pronounced in temporal and frontal lobes. A discriminant function analysis of cortical concentrations of neuropeptide Y, somatostatin, and CRF in brains of elderly controls, schizophrenics, and AD patients, correctly identified 100% of schizophrenic patients, underscoring the relevance of this abnormality to schizophrenia. We are currently measuring synaptophysin immunoreactivity and peptide concentration in several cortical layers to investigate whether the decreased peptide concentrations in the cortices of schizophrenic patients reflect neuronal degeneration, decreased neuronal production of peptide, or arrest of early migration of peptide-producing neurons.

References:

1. Carpenter W, Kirkpatrick B: The heterogeneity of the long term course of schizophrenia, *Schiz Bull;* 14(4) 645–652. 1988.

2. Purchit D, Davidson M, Perl D, et al: Severe cognitive impairment in elderly schizophrenic patients: A clinico pathological study, *Biol Psychiatry* 32:255–260. 1993.

NR162 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Gender Differences in Regional Cortical Glucose Metabolism in Schizophrenia

Benjamin V. Siegel, M.D., Psychiatry, Bronx VAMC, 130 W. Kingsbridge Rd Rte 116A, Bronx NY 10468; Monte S. Buchsbaum, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize gender differences in cortical glucose metabolic activity and how these differ in schizophrenics and normal controls. Also, the participant should know how these findings relate to gender differences in the course and phenomenology of schizophrenia.

Summary:

Sixty-nine/unmedicated schizophrenics (62 male, seven female) and 47 age- and handedness-matched normal controls (30 male, 17 female) underwent 18-fluoro-2-deoxyglucose positron emission tomography while performing a degraded stimulus, continuous performance test. Schizophrenics showed a different gender effect for lateralization of relative cortical cortical metabolism from controls. Schizophrenic females showed a more profound right-greater-than-left difference (6%) than males (2%), but both male and female normal controls showed a right-greater-than-left difference of 3%. Male normals showed higher metabolism than females in some anterior (frontal and parietal) cortical regions, while females showed higher metabolism in posterior (temporal and occipital) cortex. Schizophrenic males showed higher metabolism in some left frontal and parietal cortical regions than females, while females showed higher metabolism in some right frontal

and temporal areas. These findings may relate to the different course and phenomenology of schizophrenia in males and females and may be consistent with gender differences in lateralization in dopamine ligand binding and in ventricular volume demonstrated by other investigators.

References:

1. Andreasen NC, et al: Ventricular enlargement in schizophrenia evaluated with CT scanning. *Arch Gen Psychiatry* 1990; 47:1008–1015.

2. Rodriguez G, et al: Sex differences in regional cerebral blood flow. *J Cereb Blood Flow Metab* 1988; 8:783–789.

NR163 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Linkage on the 11q21–22 Region in a Severe Form of Schizophrenia

Michel Maziade, M.D., Univ Ctr De Recherche, Laval Robert Giffard, 2601 De La Canardiere, Beauport Quebec G1J2G3, Canada; Maria Martinez, Ph.D., Denis Cliche, M.D., Jean-Pierre Fournier, M.D., Yvon Garneau, M.D., Chantal Merette, Ph.D.

Educational Objectives:

To learn about the heterogeneity of schizophrenia and the relationship between a very severe and unremitting subform of schizophrenia and a particular region of the genome in linkage analysis; how to combine epidemiological methods and genetic linkage analysis in order to deal with heterogeneity.

Summary:

The 11q21–22 region was surveyed by linkage analysis in foor DSM-III-R schizophrenia (SZ) and six bipolar (BP) densely affected, multigenerational pedigrees (N = 218) selected from 3 systematic ascertainment in a large area of Eastern Quebec and Northern New Brunswick. These pedigrees are still being extended. The phenotypic features of one large SZ pedigree (pedigree 255) with a positive linkage trend were compared to that of the SZ pedigrees showing no linkage.

Ascertainment, assessments and genotyping: All available family members were administered the same *"consensus best-estimate diagnosis procedure"* (DSM-III-R criteria) blind to probands and relatives' diagnosis and to pedigree assignment (SZ or BP). Extended clinical quantitative measures about the lifetime presence of symptoms, severity, and clinical course were also taken. For linkage analysis, 10 microsatellite polymorphism (CA repeat) markers, located at 11q21–22, and comprising DRD2, were genotyped.

Results: Results show a linkage trend (lod score 2.86 to 3.31) at the D11S35 locus in one large family, pedigree 255. When compared with the other SZ pedigrees and with a sample of SZ familial cases, our measures indicate that the DSM-III-R SZ cases of pedigree 255 have a distinctive phenotypic pattern corresponding to a more severe, unremitting, nonresponsive form of schizophrenia corresponding to the original concept described by Kraepelin.

Conclusions: More extensive phenotyping of SZ cases during linkage analysis might be fruitful to disentangle heterogeneity. Despite recent negative findings on 11q21–22, our results suggest that this region should remain an area of future investigation for a subform for DSM-III-R of SZ made up of very severe and chronic cases. Implications for replication of linkage will be discussed.

References:

1. Maziade M, Roy MA, Fournier JP, et al: Reliability of best-estimate diagnosis in genetic linkage studies of major psychoses: results from the Quebec pedigree studies. *Am J Psychiatry* 149:12, 2–14: 1992.

2. Su Y, Burke J, O'Neill FA, et al: Exclusion of linkage between schizophrenia and the D_2 dopamine receptor gene region of chromosome 11q in 112 Irish multiplex families. *Arch Gen Psychiatry* 50:205–211, 1993.

NR164 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

The Diagnosis of Schizophrenia in DSM-IV: How Different?

Michael A. Flaum, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive 2887 JPP, Iowa City IA 52242

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognized the specific differences in the diagnostic criteria for schizophrenia in DSM-IV relative to DSM-III-R. The participant should also be able to delineate the primary rationale for these changes and understand how these differences are likely to effect case classification for schizophrenia.

Summary:

How do the diagnostic criteria for schizophrenia differ between DSM-IV and DSM-III-R, and how are these differences likely to affect caseness? This presentation will address these issues, using data from a multisite field trial.

A total of 462 subjects with psychotic disorders were evaluated across nine sites. Diagnoses were assigned according to DSM-III, DSM-III-R, ICD-10 and three sets of option criteria for DSM-IV. A wide variety of signs and symptoms were also rated such that the final version of the DSM-IV criteria could be retrospectively applied to each subject based on these ratings. The number of cases classified as schizophrenic by DSM-IV criteria was then compared with classifications according to DSM-III-R and other systems.

The concordance for the diagnosis of schizophrenia between DSM-III-R and DSM-IV was high (percent agreement = 91%, Kappa = 0.83). Reasons for those cases that were differentially classified included 1) requirement for longer duration of active symptoms in DSM-IV; 2) increased emphasis on negative symptoms in DSM-IV; and 3) increased emphasis on disorganized symptoms (disorganized speech and behavior) in DSM-IV.

These data suggest that case classification for schizophrenia in DSM-IV will be largely consistent with that of DSM-III-R, and that differences will be in the direction of reclassifying relatively transient psychoses and enhancing the emphasis on negative and disorganized symptoms as defining features of schizophrenia.

References:

1. Flaum M, Andreasen NC: Diagnostic criteria for schizophrenia and related disorders: options for DSM-IV. *Schizophrenia Bulletin,* 17:133–142, 1991.

2. Andreasen NC, Flaum M: Schizophrenia: the characteristic symptoms *Schizophrenia Bulletin,* 17:25–49, 1991.

NR165 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Neural Networks for Studying Psychiatric Decisions

Eugene Somoza, M.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Jon Marvel, M.S.,

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate factors to evaluate the decision to hospitalize patients.

Summary:

The decision to admit a patient to a hospital is of fundamental importance to psychiatry. However, it is also very complex, as the

factors that go into it are often not well defined. In this study neural networks were used to evaluate the decision to hospitalize patients from a psychiatric evaluation center (PEC) by either first-year residents or experienced staff. A total of 1723 patients seen by PEC staff (1158) or residents (565) over a two-year period were studied. This was done by evaluating the affect of 27 clinical variables (suicidality, total BPRS, global assessment of function, etc.) on the decision to hospitalize. A neural network with a back-propagation scheme was utilized with one or two hidden layers and up to 10 nodes per hidden layer. The net was trained on half the data (cycled up to 100 times), and then tested on the remaining data. ROC analysis was used to optimize the network, whose performance indicators included the kappa coefficient, maximum information gain, sensitivity, etc. This entire process was repeated with discriminant function analysis. Kappa coefficients were about 0.4 and specificity 0.94. Sensitivity analysis was used to determine which parameters were most important to residents and experienced staff in determining their decision to admit.

References:

1. Somoza E, Somoza J: A neural network approach to predicting admission decisions in a psychiatric emergency room. *Medical Decision Making* 13:273–280. 1993. 2.

2. Mezzich JW, Evanczuk KJ, Mathias RJ, Coffman GA: Symptoms and hospital decisions. *Am J Psychiatry* 141:764–769. 1984.

NR166 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Analgesic Profiles of Bupropion

Jeff Selph, B.S., Pharmacology, Burroughs Wellcome, 3030 Cornwallis Road, Res. Triangel Park NC 27709; Felicia R. Cochran, Ph.D., Mark A. Collins, B.S., Kwen-Jen Chang, Ph.D., Gary L. Grebe, B.S., Frank E. Soroko, B.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the rationale for future clinical studies designed to evaluate the potential efficacy of bupropion for the treatment of pain.

Summary:

Objective: Since tricyclic antidepressants are widely used to treat chronic pain, we investigated bupropion and its major metabolite, 306U73, in rodent models of analgesia.

Methods: Mechanical pressure was applied to the rat hindlimb in the trypsin hyperalgesia (THA), adjuvant arthritis hyperalgesia (AAHA), and phalanges algesic (PAA) tests. A thermal stimulus was employed in the mouse hot plate (MHP) assay. Mild analgesics such as ibuprofen are standard inhibitors of the THA, while strong analgesics such as codeine are standard inhibitors of the AAHA, PAA, and MHP assays.

Results: Bupropion and 306U73 were equipotent as orally active, mild analgesics in the THA. The potency of 306U73, however, was significantly greater than bupropion in the strong analgesia assay, e.g., AAHA, PAA, MHP. By contrast, the tricyclic antidepressants amitriptyline and imipramine, as well as the serotonin reuptake inhibitor fluoxetine, failed to elicit analgesia, even at pharmacologic doses. Although neither bupropion nor 306U73 demonstrated opiate receptor agonist activity *in vitro,* coadministration with codeine or morphine potentiated strong analgesia in the PAA apparently without enhancing respiratory depression.

Conclusions: Bupropion and its major metabolite, 306U73, are orally active analgesics in various rodent models of mild and strong algesia. Our results provide a rationale for future clinical studies designed to evaluate the potential efficacy of bupropion for the treatment of pain.

References:

1. Coquoz D, Prochet HC, Dayer P: Central analgesic effects of desipramine, fluvoxamine, and meclobemide after single oral dosing: a study in healthy volunteers. *Clin. Pharmacol. Ther.* 1993; 54:339–344.

2. Tollison CD: Antidepressant use in patients with chronic pain. *Drug Ther.* 1990; 20:50–57.

NR167 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Functional Status in Coronary Artery Disease: Biomedical and Psychosocial Correlates

Mark D. Sullivan, M.D., Psychiatry, University of Washington, Mail Stop RP-10, Seattle WA 98195; Andrea Lacroix, Ph.D., Carl Baum, M.D., Wayne J. Katon, M.D., Arthur J. Resnick, M.D., Edward Wagner, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize which psychosocial factors (depression, self-efficacy, social support) may be contributing to functional impairment in patients with clinically significant coronary artery disease.

Summary:

Purpose: To determine the relative contribution of biomedical and psychosocial factors to functional impairment in patients with documented coronary artery disease (CAD)

Method: 231 HMO members aged 45–80 with treadmill testing and cardiac catheterization demonstrating greater than 50% occlusion in a major coronary vessel were assessed for functional and psychosocial status at the time of their catheterization. Functional status was assessed through the Medical Outcomes Study SF-36, Activity Interference Scale of the Multidimensional Pain Inventory (MPI), and Sheehan's Role Interference Scales. Psychosocial assessment focused on three variables: 1) depression and anxiety, 2) CAD-related self-efficacy, and 3) enabling vs. disabling support from spouse.

Results: Results for SF-36 physical function scale are presented; results for activity interference and role dysfunction show even greater role for psychosocial variables. In the first model, number of coronary vessels stenosed > 75% was entered. This model was significant ($F(5,226) = 4.06$, $p < .001$), but accounted for only a small part of the variance ($R^2 = .08$). Then cardiac symptom severity (MPI severity scale) was added to the model ($F(6,225) = 11.50$, $p < .0001$, $R^2 = .26$). This was taken as the basic biomedical model to which each of the following psychosocial variables was added separately: depression severity (F to add = 17.30, $p < .0001$, $R^2 = .33$), anxiety severity (F to add = 11.69, $p < .001$, $R^2 = .30$), self-efficacy to control symptoms (F to add = 5.15, $p < .05$, $R^2 = 28$), self-efficacy to maintain activity (F to add = 11.42, $p < .001$, $R^2 = .31$). Preliminary analyses indicate that moderate amounts of spousal support balanced between punishing and solicitous responses to illness behavior best promotes function.

Conclusion: 1) CAD severity poorly accounts for functional status in CAD patients, 2) Depression, anxiety, self-efficacy and type of spousal support correlate significantly with function even after symptom severity is accounted for. Longitudinal data, which should clarify causal relationships, should be available by meeting time.

References:

1. Neil WA, Branch LG, DeJong G, et al.: Cardiac disability: the impact of coronary heart disease on daily activities. *Arch Intern Med* 145:1642–7, 1985.

2. Frasure-Smith N, Lesperance F, Tulajic M: Depression following myocardial infarction: impact on 6-month survival. *JAMA* 270:1819–25, 1993.

NR168 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Stress, Cortisol and Killer Lymphocytes

John M. Petitto, M.D., Psychiatry, University Florida, P.O. Box 100256, Gainesville FL 32610; Jane Leserman, Ph.D., Diana O. Perkins, M.D., Robert N. Golden, M.D., Carol E. Murphy, M.P.H., Dwight L. Evans, M.D.,

Educational Objectives:

At the conclusion of this presentation, the participant should be more informed about the field of psychoneuroimmunology, the role of endocrine factors in stress/immune relationships, especially as these relate to HIV infection.

Summary:

Objective: Our research has documented a significant relationship between severe stress and lower cytotoxic T lymphocyte counts, and natural killer cell numbers in homosexual men who are asymptomatic and infected with human immunodeficiency virus (HIV). This paper will examine how these stress/immune relationships may be mediated by endocrine variables, particularly cortisol.

Method: Data were collected on 101 asymptomatic HIV-positive subjects as part of an ongoing, longitudinal study, the Coping in Health and Illness Project. Subjects with known immune confounders were excluded. Stressful life events and difficulties were assessed by interview for the previous six months using methods developed by Brown and Harris and modified by Grant and colleagues. Cytotoxic T lymphocytes and natural killer cells were measured using multiple monoclonal antibodies and by controlling for circadian effects.

Results: In multiple regression analyses, we found significant interactions between severe stress and cortisol when predicting cytotoxic T lymphocyte counts and natural killer cell numbers, controlling for age, education, race, cigarette use, and helper cell count. In subjects with high cortisol (N = 46), severe stress was strongly associated with lower cytotoxic T lymphocyte counts (partial r = −.47, p = .002), and lower natural killer cell numbers including CD16 (partial r = −.39, p = .01), CD56 (partial r = −.51, p = .0008), and CD57 (partial r = −.62, p = .0001). For the low cortisol group (N = 47), there were no significant stress/immune relationships.

Conclusions: Our data provide evidence that stress in combination with high cortisol levels may alter the cytotoxic host defense against infection in HIV-positive men. The clinical significance of these findings is being studied further using longitudinal methods.

References:

1. Evans DL. Leserman J, Pedersen CA. et al.: Immune correlates of stress and depression. *Psychopharmacology Bulletin,* 25·3·319–324, 1989 Petitto JM, Folds JD, Ozer H. et al: Altered diurnal variation in natural killer cell phenotypes and cytotoxic activity in major depression. *American Journal of Psychiatry* 149:5,694–696, 1992.

NR169 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Stress and Immunity in Men Infected with HIV

Jane Leserman, Ph.D., Psychiatry, UNC at Chapel Hill, 4th Floor South Wing CB# 7160, Chapel Hill NC 27559; John M. Petitto, M.D., Diana O. Perkins, M.D., Robert N. Golden, M.D., Carol E. Murphy, M.P.H., Dwight L. Evans, M.D.,

Educational Objectives:

At the conclusion of this presentation, the participant should be more informed about the field of psychoneuroimmunology, especially as it relates to HIV infection. Furthermore, the presentation will provide information about important measurement issues concerning stressful life events and immune parameters.

Summary:

Objective: Previous research has documented a possible relationship of stress with cell-mediated immunity. We examined how severe stress (stressful life events and difficulties) may affect key parameters of immunity in men who are asymptomatic and infected with human immunodeficiency virus (HIV), and in men who are HIV negative.

Method: Data were collected on 169 homosexual men, including 101 asymptomatic HIV-positive and 68 HIV-negative men, as part of an ongoing, longitudinal study, the Coping in Health and Illness Project. Subjects with known immune confounders were excluded. Stressful life events and difficulties were assessed by interview for the previous six months using methods developed by Brown and Harris and modified by Grant and colleagues. Cytotoxic T lymphocytes and natural killer cells were measured using multiple monoclonal antibodies and by controlling for circadian effects.

Results: We found that in men who were HIV-positive, severe stress was significantly associated with lower cytotoxic T lymphocyte counts (partial r = −.32, p = .001), and lower natural killer cell numbers including CD16 (partial r = −.24, p = .02), CD56 (partial r = −.27, p = .01), and CD57 (partial r = −.44, p = .0001), controlling for age, education, race, cigarette use, and helper cell count. Severe stress was not significantly related to helper cell count among the HIV-positive men. Among the HIV-negative men, stress was not associated with any immune parameters.

Conclusions: Our data are among the first evidence that stress may alter the cytotoxic host defense against infection in HIV positive men. The clinical significance of stress-related changes in immunity is being studied further using longitudinal methods.

References:

1. Evans DL, Folds JD, Petitto JM, et al: Circulating natural killer cell phenotypes in males and females with major depression: relation to cytotoxic activity and severity of depression. Arch Gen Psych 49; 5:388=en395, 1992.

2. Perkins DO, Stern RA, Golden RN, et al: Mood disorders in HIV infection: prevalence & risk factors in a non-epicenter of the AIDS epidemic. *Am J Psych.* (In press).

NR170 Tuesday, May 24, 9:00 a.m.-10:30 a.m.

Cognitive Impairment Predicts Death in HIV-Positive Men

Igor Grant, M.D., Psychiatry, UCSD & VA Med. Center, 9500 Gilman Drive MC 0680, La Jolla CA 92093; Robert K. Heaton, Ph.D., J. Hampton Atkinson, M.D., Reena Deutsch, M.S., Julie Nelson, B.S., J. Allen McCutchan, M.D.,

Educational Objectives:

At the conclusion of this presentation, the participant should be able 1) to review neurocognitive disorders complicating HIV infection; 2) to demonstrate that such disorders affect survival in HIV disease

Summary:

We wished to determine whether mild neurocognitive disorders (MND), found in 5%–44% of HIV-positive (HIV+) medically asymptomatic persons and 40%–70% of persons with AIDS, were associated with more rapid disease progression and earlier death.

Subjects and Methods: 498 HIV+ men (age = 32 ± 7) were rated as impaired (MND+) or unimpaired (MND–) on the basis of comprehensive neuropsychological testing; 125 men had AIDS (CDC, 1993), and 373 were at an earlier disease stage. To explore the influence of MND at entry into study on later risk of death, Kaplan Meier plots of time to death were then developed for the MND+ (n = 221) and MND– (n = 277) groups.

Results: MND+ were more likely to die earlier than MND– (Figure). Since MND occurs more frequently in more advanced HIV

infection, we computed a Cox proportional hazards survival model, entering T4 lymphocyte count as a covariate. Although T4 count independently predicted death ($p < .0001$), persons with MND were twice as likely to die as those without MND after controlling for T4 ($P = .035$, logrank test).

Conclusions: HIV-infected persons with MND may be at risk for earlier death either because CNS infection reflects more impaired immunity, or because CNS disease itself disturbs immunoregulation or health-promoting behaviors.

References:

1. Grant. I., Martin AM: *The Neuropsychology of HIV Infection.* New York: Oxford University Press. 1994.

2. Volberding P, Jacobson MA: (Eds.) *AIDS Clinical Review 1993/1994.* New York: Marcel Dekker, Inc. 1994.

NR171 Tuesday, May 24, 12 noon-2:00 p.m.

Prevalence of Seasonal and Non-Seasonal Depression

Anthony J. Levitt, M.D., Mood Disorder, Clarke Inst. Psychiatry, 250 College Street, Toronto ON M5T 1R8, Canada; Michael H. Boyle, Ph.D.

Summary:

Objectives: This study evaluated the prevalence of major depression (MD) and its seasonal subtype (SAD) in a community sample, using a new structured diagnostic telephone interview.

Methods: Random digit dialing of 3662 phone numbers in the city of Toronto, established 1467 valid household numbers. Eligibility (i.e. one member aged 20 or older and resident in region at least three years) could be established in 867 households. Of these, 811 were eligible and 781 completed the interview (96.3% of all eligible households; female to male ratio = 1.8:1). Trained interviewers conducted the interview, which was designed to provide DSM-III-R diagnoses for both MD and SAD. Within a year, 237 randomly selected respondents were contacted again and 42 agreed to be reinterviewed in person, using the Schedule for Affective Disorders and Schizophrenia - Lifetime Version (SADS-LV), to determine the validity of the original phone interview.

Results: Correcting for gender, the prevalence of lifetime MD in the sample was 20.1%, (female:male = 1.4:1) and of lifetime SAD was 2.7% (female:male = 4.2:1). For lifetime depression, the telephone interview demonstrated excellent positive (90%) and negative predictive (94%) capacity.

Conclusions: To our knowledge, this is the largest single-site study of the prevalence of SAD and the first to use a validated structured interview to diagnose both MD and SAD by DSM-III-R criteria. We conclude that MD is a common disorder in the community and that SAD represents 13% of lifetime MD.

NR172 Tuesday, May 24, 12 noon-2:00 p.m.

Stress-Induced Alterations in Depression

Rand J. Gruen, Ph.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Raul Silva, M.D., Joshua Ehrlich, M.A., Stacey Greenwald, Jack Schweitzer, Ph.D., Arnold J. Friedhoff, M.D.

Summary:

Results from a number of studies support the idea that life stress may play an important role in the etiology and/or maintenance of unipolar depression. Disturbances in the capacity of corticosteroids to restrain stress-induced increases in noradrenergic activity may give rise to some of the primary symptoms of unipolar depression. The present study was designed to assess whether exposure to a naturalistic stressor led to disturbances in the relationship between cortisol and norepinephrine (NE) in depressed subjects.

Subjects: 28 females were recruited and divided into three groups: controls (n = 10); depression in remission subjects (n = 9); and actively depressed subjects (n = 9), ages ranged from 20 to 41 (mean, 27), all healthy and medication free for at least two weeks.

Methods: Subjects received a physical examination, a laboratory workup, and were diagnosed using the SCID. An indwelling catheter was placed in the antecubital vein at 9 a.m. Subjects were exposed to an induced-failure stressor. Blood samples and mood ratings of two self-report inventories (the Profile of Mood States and the Emotion Checklist) were obtained at baseline, immediately after the stressor and 35 minutes later. Plasma was analyzed for cortisol and NE. Change in plasma NE, cortisol, and mood was assessed using MANOVA. The relationship between cortisol and NE were assessed using correlational techniques.

Results: Forty minutes after stress exposure, plasma cortisol and NE were positively correlated in nondepressed subjects ($r = .57$; $p < .01$), negatively correlated in depressed subjects ($r = .42$; n.s.) Menstrual phase was not related to biochemical response.

Conclusions: Stress may lead to the dysregulation of the relationship between cortisol and NE in depressed subjects. These and other findings will be discussed and elaborated on.

NR173 Tuesday, May 24, 12 noon-2:00 p.m.

Antidepressant Effects of Total Versus Partial Sleep Deprivation

Martin Szuba, M.D., Psychiatry, University of Penn., 11 Gates 3400 Spruce Street, Philadelphia PA 19104; Lewis R. Baxter, M.D., Lori L. Altshuler, M.D., Barry H. Guze, M.D., Jeffrey M. Schwartz, M.D.

Summary:

Objective: Both partial (PSD) and total sleep deprivation (TSD) produce same-day, but transient, antidepressant effects. To clarify mediating factors, we compared the acute mood responses to PSD and TSD.

Method: We randomly assigned 26 inpatients with depression to one night of PSD (n = 13) or TSD (n = 13). Blind to sleep condition, raters completed a modified, validated Hamilton Depression Scale (HD) on subjects the day before and day of sleep deprivation. Subjects completed the POMS every two hours while awake.

Results: PSD and TSD subjects did not differ on demographic or clinical variables or response rate to sleep deprivation. HD percentage change from pre- to post-sleep deprivation was greater in responding PSD (62.9 ± 13.5%) and TSD subjects (50.7 ± 20.5%) than in nonresponding PSD (16.7 ± 42.6%) and TSD subjects (3.5 ± 22.2%) [$F = 5.6, p = .005$]. However, PSD responders scored better than TSD responders ($p < .05$) on POMS Vigor, Fatigue, and Anger subscales. Significant mood response to *both* procedures was not evident on the POMS until 1500 hours.

Conclusion: PSD and TSD produce acute beneficial effects in depression. As researchers work to clinically exploit these rapid antidepressant effects, the apparent greater tolerability of PSD may be particularly relevant.

NR174 Tuesday, May 24, 12 noon-2:00 p.m.

Fenfluramine Challenge Test in Mania

Lakshmi N. Yatham, M.D., Psychiatry, University Hospital, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Margaret Brock, R.N.

Summary:

Objective: Prolactin and cortisol responses to fenfluramine challenge provide an overall index of serotonin (5HT) function. Using

this strategy, 5HT function was examined in manic patients in comparison with healthy controls.

Method: Ten patients who fulfilled DSM-III-R criteria for mania and who were drug free for at least two weeks, and the same number of age- and sex-matched controls, were recruited. The severity of symptoms in manic patients was assessed by Manic State Rating Scale. After obtaining two samples for baseline prolactin and cortisol levels, 60 mg of fenfluramine was given orally to each subject, and hormonal response was measured by obtaining further blood samples over a five-hour period.

Results: The baseline prolactin or cortisol levels were not different in manic patients compared with controls. Similarly, there was no difference in hormonal responses to fenfluramine challenge between manic patients and controls. Furthermore, hormonal responses did not correlate with severity of symptoms in manic patients.

Conclusion: Results of this study do not support alteration of overall 5Ht function in mania.

NR175 Tuesday, May 24, 12 noon-2:00 p.m.

Outcome of One Versus Two Weeks Phototherapy in SAD

Lawrence A. Labbate, M.D., Psychiatry, Walter Reed, Army Medical Center, Washington DC 20307; Beny Lafer, M.D., Jerrold F. Rosenbaum, M.D., Amy Thibault, B.A., Gary S. Sachs, M.D.

Summary:

The efficacy of bright light treatment for seasonal affective disorder (SAD) has been demonstrated in over 20 controlled studies. However, the original studies and nearly all subsequent studies did not assess treatment response beyond one week. This study evaluated whether there is a change in response between one or two weeks of phototherapy. All subjects (N=26) were between ages 18 and 65 and met DSM-III-R criteria for major depression, recurrent, seasonal pattern and had a HAM-D $\geq$ 20. Eligible patients were participants in a randomized study of three different light treatment schedules of two hours of bright light (2500 lux). A rater blinded to treatment schedule and study hypothesis repeated the HAM-D-31 one and two weeks after baseline to assess treatment response. Response rate at week 1 defined by 50% reduction in HAM-D-31 was 62%. However, at week 1 only 27% attained HAM-D-31 score < 8. At week two, 65% had a 50% reduction in HAM-D-31, but 62% had a HAM-D-31 score < 8 (Chi-square = 6, p = 0.01). This suggests that one week trials of phototherapy may be too brief to assess full response of symptoms in SAD.

NR176 Tuesday, May 24, 12 noon-2:00 p.m.

The Relationship of Alprazolam and Clonazepam Dose to Steady-State Plasma Concentration

Lawrence A. Labbate, M.D., Psychiatry, Walter Reed AMC, Washington DC 20307; Mark H. Pollack, M.D., Michael W. Otto, Ph.D., George Tesar, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

This study addresses the correlation between dose and plasma concentration for both alprazolam and clonazepam. Patients were 43 participants in a six-week, double-blind, placebo-controlled study of alprazolam and clonazepam for the treatment of panic disorder. Plasma concentration at week three for clonazepam (N = 24) was linearly related with dose, measured as mg/d (R = .724, F = 24.2, p = .0001) or mg/kg/d (R = .863, F = 58.3, p = .0001). The correlation between plasma concentration and daily dose for alprazolam (N = 19) was also significant (R = .60, F = 9.5, p = .007), although the correlation between dose measured as mg/kg/d and plasma level was not significant (R = .361, F = 2.4, p = 0.14).

This replicates previous findings that for each additional mg/d dose of alprazolam there is a corresponding increase of approximately 10ng/ml in the plasma, and presents preliminary data that for each added 1mg/d dose of clonazepam there is approximately an increase of 12ng/ml in the plasma. For both drugs, however, there may be considerable variation in plasma level for a given dose. Weight-adjusted clonazepam plasma concentration of may be more predictable than weight-adjusted alprazolam plasma concentration.

NR177 Tuesday, May 24, 12 noon-2:00 p.m.

Hyposomnia as Predictor of Anticonvulsant Response in Bipolar Affective Disorder

Dale A. D'Mello, M.D., Psych. St. Lawrence Hosp, Michigan State University, 1210 W. Saginaw, Lansing MI 48915; John A. McNeil, D.O., Bhekumusa Msibi, D.O.

Summary:

Widely acknowledged predictors of anticonvulsant response in bipolar disorder include severe, psychotic, rapid cycling, and dysphoric mania. In addition, the presence of psychosensory symptomatology may favor anticonvulsant response. In a naturalistic review of 156 consecutively admitted patients with bipolar affective disorder and schizoaffective disorder, the patients who responded to anticonvulsant agents slept fewer hours than those who responded to lithium carbonate (mean sleep duration: lithium 5.5 $\pm$ 1.8 hrs, carbamazepine 4.6 $\pm$ 1.9 hrs, valproate 3.5 $\pm$ 1.5 hrs). Hyposomnia is a cardinal symptom of mania. Sleep deprivation is considered to be a precipitant of mania, and sleep loss is known to perpetuate the manic state. The severity of the sleep deficit is thought to parallel the severity of mania. Bipolar manic patients who experience profound sleeplessness may show a preferential response to anticonvulsant mood stabilizers rather, than lithium.

NR178 Tuesday, May 24, 12 noon-2:00 p.m.

Predictive Profiles of Antidepressant Response

Fabrice Duval, M.D., Psychiatry, Centre Hospitalier, 27 Rue Du 4 RSM, Rouffach 68250, France; M-Claude Mokrani, Ph.D., Martine Jautz, Psych, Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Thahn Son Diep, M.D., Eduardo De Andrade, M.D., Jean-Paul Macher, M.D.

Summary:

Objective: The purpose of this study was to determine predictive bioclinical profiles of antidepressant treatment response in depressed patients.

Methods: Fifty-seven drug-free inpatients meeting DSM-III-R criteria for major depressive episode (MDE) were treated for one month with antidepressants and were then classified as full, partial, or nonresponders according to their posttreatment Hamilton Depression Scale score. These three groups were examined for differences in clinical, psychological, and neuroendocrine (i.e. 8 A.M. and 11 P.M. TRH-TSH tests and dexamethasone suppression test (DST)) variables.

Results: Endocrine tests remained abnormal in partial responders (n = 12) and nonresponders (n = 19); they normalized in the responder group. However, at baseline the responder group showed a lower incidence of endocrine abnormalities (χ^2 = 11.6, df = 2, p < 0.003). A factorial correspondence analysis was carried out to examine differences at baseline between the three groups. Nonresponders were mainly characterized by blunted 8 AM - ΔTSH, mood-congruent psychotic features, and history of antidepressant nonresponse. Moreover they differed from responders by having increased frequency of blunted 11 P.M. - ΔTSH and

melancholic features. Responders were characterized by normal ΔΔTSH (difference between 11 P.M. and 8 A.M.-ΔTSH), absence of personality disorder, total duration of illness less than two years, presence of psychosocial stressor during the last year, DST-positive (cortisol nonsuppression), and response to serotonin reuptake inhibitors such as fluoxetine. Partial responders were characterized by increased frequency of blunted ΔΔTSH and borderline personality disorder.

Conclusion: These findings suggest that patients meeting DSM-III-R criteria for MDE are heterogeneous and that a multivariate approach combining clinical, psychological, and neuroendocrine variables may define subgroups with different prognoses.

NR179 Tuesday, May 24, 12 noon-2:00 p.m.

Depression Screening in Primary Care: A Validity Study

Marijo B. Tamburrino, M.D., Psychiatry, Medical College of Ohio, 3000 Arlington Avenue, Toledo OH 43699; Denis J. Lynch, Ph.D., Rollin Nagel, M.A., Nancy J. Stadler

Summary:

Screening instruments have been developed to help family physicians identify depression, but validity of these scales has been questioned. This study explored the validity of the eight-item MOS Depression Inventory using DIS follow-ups one week later. At a family practice training center, 566 patients completed the MOS while waiting to see their physicians. Of those, 92% agreed to participate. A total of 33.4% (N = 189) scored positive for depression on the MOS; 70% (N = 133) of those screened positive were followed up with the DIS, along with a random sample, of 62 persons who screened negatively. DIS results yielded an estimated prevalence of lifetime depression of 17.9% for the 566 sampled patients.

Among the 133 persons who scored positive on the MOS, 16.5% (N = 22)were diagnosed with major depression and 11.3% (N = 15) were diagnosed dysthymic disorder on the DIS. Those diagnosed with depression were significantly more likely to be younger, previously married, cigarette smokers, and to report increased body pain, poorer health, and stress. Estimated sensitivity for current depression on the MOS was .878 and specificity was .718. These results compare favorably with the original reports on the MOS and support this instrument's validity.

NR180 Tuesday, May 24, 12 noon-2:00 p.m.

The Effects of Gender and Age of Onset of Depression on Mortality

Robert A. Philibert, M.D., NSB, NIMH Bldg 49 RM B1EE16, 9000 Rockville Pike, Bethesda MD 20892; George Winokur, M.D., Larry L. Richards, D.O.

Summary:

Depression may have a marked negative impact on geriatric patient mortality and morbidity. The exact reasons and risk factors for these effects are not well understood. Seeking to better define these factors, we analyzed the effects of gender and age of onset of affective disorder in a retrospective, naturalistic study of 193 geriatric patients consecutively admitted to a large midwestern tertiary care facility between 1980 and 1987 for the treatment of unipolar depression. Data were analyzed by Chi square and ANOVA analysis. After controlling for age at index, patients with an onset of depression before age 40 suffered much less mortality in follow-up than those with onset after age 40. When effects of gender are examined, the effects of age of onset are most profound in women with three-fold increase in rate of death in the cohort with age of onset of depression of after 70 years of age as compared with those with onset before age 40. These and accompanying results suggest that depression in elderly women without a previous history of affective disorder are at a markedly increased risk for morbidity and mortality. Reasons for this are discussed.

NR181 Tuesday, May 24, 12 noon-2:00 p.m.

Order of Onset of Major Depression and Drug Abuse

Henry D. Abraham, M.D., Psychiatry, New England Medical, 750 Washington St. #1007, Boston MA 02111; Maurizio Fava, M.D.

Summary:

This study addressed the issue of whether drug abuse was a cause or result of major depressive disorder. A total of 375 outpatients with major depression were divided into relatively pure subgroups in nine substance categories. Subjects in each category were then compared on measures of affective disorder severity, life prevalence of drug use, and order of onset of depression with respect to drug use using a structured diagnostic instrument (SCID-P, Lifetime Ver.). The classes with the youngest age of onset of depression were polydrug and LSD users (16.3y and 17.0y, respectively). Nondrug users had the highest mean age of depression onset (25.6y). Alcohol and cocaine abuse followed the onset of first major depression by 4.4 and 6.4 years, respectively (each p = 0.005). LSD, stimulant, and cocaine users suffered the greatest number of life depressive episodes, and opiate users, nondrug users, and polyusers the fewest. LSD and cocaine abuse were significantly overrepresented among depressed outpatients compared with community samples (odds ratios of 39 and 42, respectively). The first life depressive episode in LSD users appeared to be contemporaneous with LSD use. This last finding may represent a partial answer to the rising secular trend of depression in the young.

NR182 Tuesday, May 24, 12 noon-2:00 p.m.

Social Vocational Adjustment in Mood Disorders: Episodic Major Depression, Dysthymic Disorder and Double Depression

Susan Evans, M.A., Payne Whitney, New York Hospital, 525 East 68th Street, New York NY 10021; Marylene Cloitre, Ph.D., James H. Kocsis, M.D., Daniel N. Klein, Ph.D., Charles Holzer, Ph.D., Michael B. First, M.D., Leah Gniwesch, M.A.

Summary:

A total of 430 patients participating in a DSM-IV field trial received a SCID-derived DSM-III-R diagnosis of major depressive disorder (n = 131), dysthymic disorder (n = 37) or "double depression" (n = 262), i.e., patients with current major depression and dysthymia. The purpose of this study was to compare the severity of social impairment across the three groups. Social impairment was measured using the Social Adjustment Scale-Self Report (SAS). Mean SAS scores for the major depression, dysthymia and double-depression groups were 2.51 (sd= .49), 2.34 (sd= .37) and 2.63 (sd= .50), respectively. These scores were significantly higher than those from a normal community sample ($\bar{X}$ = 1.6; sd= .4) ($p < .001$). Patients with double depression demonstrated significantly greater social morbidity than dysthymic or major depressives ($p < .001$). A regression analysis was performed to identify the strongest correlates of the high levels of social morbidity in the double depressives. Severity of illness, as measured by a depression symptom checklist predicted overall social adjustment ($p < .001$) followed by age of onset of depression ($p < .04$). An analysis of SAS subscales revealed that major depressives and double depressives were significantly more impaired than dysthymics in work outside their home ($p < .05$). Double depressives also showed greater impairment in the area of finance

than either the major depressives or dysthymics ($p < .05$). In conclusion, this investigation revealed that double depressives were more socially impaired than episodic major depressives or dysthymics.

NR183 Tuesday, May 24, 12 noon-2:00 p.m.

Are Neurovegetative Symptoms Stable in Recurrent Atypical Depressive Episodes?

Andrew A. Nierenberg, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114; Joel A. Pava, M.D., Kathy Clancy, B.A., Maurizio Fava, M.D.

Summary:

Despite extensive study of the atypical depressive syndrome, few data exist that assess the presence of patients' reversed and positive neurovegetative symptoms from one depressive episode to the next. To assess the stability of depressive symptoms across episodes in the same individual, we studied depressed patients before treatment with fluoxetine and again when patients relapsed while on either fluoxetine or placebo. We followed 74 outpatients with atypical unipolar major depression, diagnosed by the Structured Clinical Interview for DSM-III-R, who responded to fluoxetine. Patients were assessed drug free at baseline with both the Atypical Depression Diagnosis Scale (ADDS) and the extended 28-item Hamilton Depression Rating Scale (HDRS). During follow-up, patients were evaluated with the HDRS only. Thirty-two (43%) of the fluoxetine responders had a recurrence; 21 out of 32 (66%) had a predominance of either reversed or atypical neurovegetative symptoms at baseline. Nine of 10 (90%) patients with reversed symptoms at baseline had the same symptoms at time of relapse; 7 of 11 (64%) of those with positive symptoms at baseline had positive symptoms again (Fishers exact test p = .017). Overall, only 5 of 21 (24%) had changes in their sleep, appetite, or weight when they relapsed. This study therefore supports the stability of the recurrent atypical neurovegetative symptoms. A small proportion of patients had different neurovegetative symptoms during different episodes.

NR184 Tuesday, May 24, 12 noon-2:00 p.m.

Prodromal and Residual Symptoms in Bipolar Disorder

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Christine E. Ryan, Ph.D., David A. Solomon, M.D., Ivan W. Miller, Ph.D., Ellen Frank, Ph.D.

Summary:

Objective: We attempted to identify prodromal and residual symptoms of depression and mania by eliciting information from patients and their families.

Method: 70 patients with bipolar disorder were asked to describe early and residual symptoms of mania and depression. In 45 cases another adult family member also provided similar information. Three experienced clinicians classified the data into six broad categories of symptoms: behavioral cognitive, mood, neurovegetative, social, and other. Clinicians also differentiated unusual from classic symptoms.

Results: 79% of the patients reported prodromal depressive symptoms and 82% prodromal manic symptoms; more than half of the patients reported residual symptoms of depression (56%) or mania (57%). Cognitive (32%) and neurovegetative (25%) symptoms were the most frequently reported prodromal depressive symptoms, while behavioral (34%) and cognitive (27%) symptoms characterized prodromal mania. Cognitive and mood symptoms were the most common residual symptoms of both depression (45%, 19%) and mania (40%, 26%). Patients were more likely to report unusual symptoms after an illness (residual depression = 44%, residual mania = 59%) rather than preceding the illness (prodromal depression = 32%, prodromal mania = 23%). Agreement on symptoms reported between patient and family members seems particularly strong for the prodromal stage of the illness (for either depression or mania) but less so for the residual phase.

Conclusions: These preliminary results suggest that prodromal symptoms may be easier to identify than residual symptoms, and that variation and unusual symptoms are more suggestive of residual rather than prodromal effects of the illness. Awareness of prodromal symptoms by patients and family members may be important in early identification of recurrence of the illness, and awareness of residual symptoms should guide follow-up care.

NR185 Tuesday, May 24, 12 noon-2:00 p.m.

ADHD Among Adults with Major Depression

Jonathan E. Alpert, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street, Boston MA 02144; Anne B. Maddocks, B.A., Andrew A. Nierenberg, M.D., Richard L. O'Sullivan, M.D., Joel A. Pava, Ph.D., John J. Worthington, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Objective: The comorbidity of major depression with anxiety disorders, including panic disorder and social phobia, and with alcohol and substance use disorders, has been well-documented. The clinical relevance of current or past attention-deficit hyperactivity disorder (ADHD) to adults who present with depressive disorders remains to be elucidated. The goal of our study was to assess ADHD symptom history among adults with major depression in order to better define the prevalence and clinical impact of ADHD on course and treatment of depression.

Methods: Subjects were 114 adults (aged 18–65 years) consecutively enrolled in our depression research program for treatment. All individuals had a current episode of major depression on Structured Clinical Interview for DSM-III-R Diagnosis (SCID-P) and a Hamilton Depression Rating Scale Score of ≥ 16. After enrollment, prior to antidepressant treatment, subjects completed a 14-item self-rating questionnaire for ADHD and were administered the SCID module for ADHD.

Results: Of 114 subjects, seven (6.1%) had met full (≥ 8) ADHD criteria by age 7, while an additional 10 (8.8%) were subthreshold with ≥ 5 of eight criteria for ADHD (n = 9) or ≥ 8 criteria but onset in later childhood (n = 1).

Conclusions: Major depressive disorder in adults often presents in the context of other significant psychiatric conditions. The prevelance of ADHD appears to be high. Since our sample of depressed adults excluded some conditions which themselves may be comorbid with ADHD (e.g. antisocial personality disorder or active substance abuse), it is likely that the prevalence of ADHD is even higher among a more heterogeneous outpatient population of depressed adults. Data regarding gender, depression history and severity, and antidepressant treatment response of individuals with ADHD will be presented.

NR186 Tuesday, May 24, 12 noon-2:00 p.m.

Antiglucocorticoid Treatment of Depression

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Summary:

Objectives: The pathophysiologic significance of hyperadrenocorticism in psychiatric illness is uncertain, but elevated corticosteroid levels may feed back onto the central nervous system and produce certain neurobiological and behavioral changes. One new strategy to investigate the possible involvement of steroid hormones in psychopathology is to administer antiglucocorticoid medications and to observe resultant behavioral changes.

Method: In open-label pilot study 10 hypercortisolemic depressed patients received ketoconazole, a cortisol biosynthesis inhibitor, 400–800 mg per day for three to six weeks. In a subsequent ongoing double-blind trial, patients with major depression were treated in a similar manner with ketoconazole (n = 5) or placebo (n = 5) for four weeks.

Results: Seven patients completed the open-label trial and demonstrated significant decreases in 4 p.m. serum cortisol levels ($p < 0.05$) along with significant decreases in Hamilton Depression Rating Scale (HDRS) ratings ($p < 0.01$). Individual symptoms showing significant improvement included insomnia, tiredness, apathy, suicidality, and loss of appetite (all: $p < 0.05$). Ketoconazole-associated decreases in serum cortisol levels were significantly correlated with decreases in ratings of insomnia, suicidality, guilt, anxiety, and somatic symptoms (all: $p < 0.05$). Preliminary results of the double-blind trial are consistent with these pilot data: Ketoconazole, compared with placebo administration, was associated with a trend toward a significant decrease in HDRS ratings ($F = 4.66$, $p = 0.06$). Decreases in depression ratings in the ketoconazole group averaged 35%, versus 7% in the placebo group.

Conclusions: These preliminary results raise the possibility that hyperadrenocorticism may contribute to the expression of depressive symptomatology and that antiglucocorticoid medication may be effective in alleviating such symptoms.

NR187 Tuesday, May 24, 12 noon-2:00 p.m.

Thyroid Indices and Cerebral Metabolism in Mood Disorders

Lauren B. Marangell, M.D., BPB, NIMH, 9000 Rockville Pike, Bethesda MD 20892; Terence A. Ketter, M.D., Mark S. George, M.D., Peggy J. Pazzaglia, M.D., Ann M. Callahan, M.D., Paul J. Andreason, M.D., Priti J. Parekh, B.A., Barry Horowitz, M.D., Peter Herscovitch, M.D., Robert M. Post, M.D.,

Summary:

Objective: To further clarify the relationship between the thyroid axis and mood disorders, we investigated the relationship between thyroid hormones and brain glucose metabolism in affectively ill patients.

Methods: Twenty-nine affectively ill NIMH inpatients were studied medication-free with fluorine-18 deoxyglucose positron-emission tomography to measure regional brain glucose metabolism (rCMRglu). Statistical parametric mapping was used to correlate normalized rCMRglu with serum T3, T4, free T4 (FT4) and TSH (significance threshold $r > 0.43$, $p < 0.01$).

Results: Serum T3 (but not other thyroid indices) was positively correlated with anterior mesial frontal rCMRglu. Serum T3 and TSH, and to a lesser extent T4 (but not FT4), were negatively correlated with occipital rCMRglu.

Conclusions: Since frontal metabolism is decreased in depression, the positive correlation between T3 and frontal metabolism is consistent with both its antidepressant properties and the increased prevalence of depression in hypothyroidism. The potential relevance of relationships between occipital metabolism and the physiology of thyroid function and mood disorders requires further exploration.

NR188 Tuesday, May 24, 12 noon-2:00 p.m.

Cholesterol and Cerebral Metabolism in Mood Disorders

Ann M. Callahan, M.D., BPB, NIMH NIH 10/3N212, 9000 Rockville Pike, Bethesda MD 20892; Terence A. Ketter, M.D., Mark S. George, M.D., Lauren B. Marangell, M.D., Peggy J. Pazzaglia, M.D., Paul J. Andreason, M.D., Priti J. Parekh, B.S., Barry Horwitz, Ph.D., Peter Herscovitch, M.D., Robert M. Post, M.D.

Summary:

Objective: To assess relationships between regional cerebral metabolic rates of glucose (rCMRglu) and fasting total serum cholesterol levels in mood disorder patients.

Background: Epidemiological studies suggest that changes in serum cholesterol may be associated with emotional and behavioral disturbances. Cholesterol is not only a crucial structural component of neuronal membranes but also is the primary precursor of all steroids, including the recently discovered neurosteroids.

Methods: Thirty medication-free, mood-disorder inpatients (9 UP, 13 BPII, 8 BPI) had fluorine-18 deoxyglucose positron emission tomography to measure rCMRglu while performing an auditory continuous performance task. Statistical parametric mapping (SPM) was used to assess correlations between fasting total serum cholesterol levels and normalized rCMRglu.

Results: Serum cholesterol levels correlated inversely with rCMRglu in the anterior cingulate gyrus and left caudate. Cholesterol levels also had positive correlations with right inferior parietal and right temporal rCMRglu.

Conclusions: The inverse correlation between serum cholesterol levels and rCMRglu in the anterior cingulate and left caudate is consistent with prior observations of functional disturbances in these regions in mood disorders. In light of these findings, further exploration of possible links between cholesterol and behavior is indicated.

NR189 Tuesday, May 24, 12 noon-2:00 p.m.

Depression in Adolescents: Clinical Outcome in Early Adulthood

Uma Rao, M.D., Mood Disorder, Western Psychiatric, 3811 O'Hara Street, Pittsburgh PA 15213; Neal D. Ryan, M.D., Boris Birmaher, M.D., Ronald E. Dahl, M.D., Douglas E. Williamson, B.A.

Summary:

Objective: The aim of this study was to examine the longitudinal clinical course and outcome in early adulthood of adolescent onset unipolar major depressive disorder (MDD) using a prospective controlled design.

Method: Subjects were 28 adolescents systematically diagnosed with unipolar MDD and 35 group-matched normal controls. Follow-up assessments were conducted "blindly" in early adulthood using standardized clinical instruments six to eight years after the initial study in 93% of the MDD cohort and 94% normal controls. The main outcome of interest was recurrence of MDD during the interval period in the depressed cohort or new onset of MDD in normal controls. Another outcome was psychosocial adjustment in adulthood.

Results: The depressed group was at increased risk for recurrence of MDD episodes (70%) during the interval course when compared with new onset of MDD in normals (18%, $\chi^2 = 13.7$, $p \leq 0.0002$). The MDD cohort also had elevated rates of bipolar disorder (19% vs 0%, FET, $p \leq 0.01$), but there were no significant group differences in nonaffective psychopathology. Additionally, the depressed group had significant impairment in several domains of social adjustment in adulthood.

Conclusions: These findings suggest that adolescent-onset unipolar MDD predicts continued risk for recurrences with persistence of depressive episodes and psychosocial morbidity into adulthood. There is also substantial specificity in the continuation of affective disturbance.

NR190 Tuesday, May 24, 12 noon-2:00 p.m.

Recurrence of Unipolar Depression in Adolescents: Psychobiological Predictors

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Summary:

Objective: our aim was to examine the factors that predict recurrence of adolescent unipolar major depressive disorder (MDD) using a prospective controlled design.

Methods: Subjects were 28 adolescents systematically diagnosed with unipolar MDD and 35 group-matched normal controls who participated in a multidimensional psychobiological (sleep EEG and neuroendocrine) study. Standardized clinical assessments were conducted "blindly" six to eight years after the initial study in 93% of the MDD cohort and 94% controls. The sample was divided by clinical outcome into unipolar MDD subjects with and without recurrence (N = 13, 7 respectively). Normal controls were separated by no disorder (normals) and new onset of MDD (N = 24, 6 respectively). We compared these four groups on clinical and psychobiological measures performed during the initial study as potential predictors of clinical course.

Results: None of the initial clinical characteristics predicted recurrence of MDD. However, the recurrent MDD group had elevated cortisol secretion around sleep onset when compared with normals (10.8 ± 4.7 vs 6.7 ± 2.7 μg/dl, $t_{34} = 2.99$, $p \leq 0.005$), and the nonrecurrent group (10.8 ± 4.7 vs 7.3 ± 5.3, $t_{17} = 1.77$, $p \leq 0.08$). MDD subjects without recurrence did not differ from normals. Normals with new onset MDD had reduced REM latency when compared with normals without a disorder (67.3 ± 20.2 vs 104.1 ± 48.2 min., $t_{23} = 1.75$, $p \leq 0.08$).

Conclusions: Sleep onset cortisol may be helpful in predicting recurrence of adolescent unipolar MDD. Reduced REM latency may be a trait marker for MDD.

NR191 Tuesday, May 24, 12 noon-2:00 p.m.

Diurnal Plasma 3-methoxy-4-hydroxyphenylglycol, Cortisol and Autonomic Rhythms in Acute and Remitted Depression

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Summary:

Objective: Dysregulation hypotheses of depression that suggest that diurnal rhythmicities are altered in acute depression and return to normal in remission. This study evaluates diurnal data on plasma MHPG, cortisol and autonomic indices in acute and remitted male depressed patients and age-matched male normal controls.

Method: Mean, peak, variability and time-course of plasma 3-methoxy, 4-hydroxyphenylglycol (MHPG), plasma cortisol, and autonomic (mean arterial blood pressure [MAP] and heart rate [HR]) measures were examined hourly from 1000h to 1800h in 28 acutely depressed males, 14 males in remission, and 19 normal controls.

Results: Plasma MHPG peaked earlier in acute, but not remitted, depressed patients ($p < 0.02$), and had greater intra-group variability in acutely depressed, and not remitted, patients, compared with normal controls ($p < 0.02$). Acutely depressed, but not remitted, patients had higher plasma cortisol concentrations than did normal controls ($p < 0.02$). MAP tended to be lower in acutely depressed patients than in the normal controls ($p < 0.1$), and tended to increase more slowly than in the normal controls ($p < 0.1$). Acutely depressed patients began with a higher HR and converged by midday to normal HR, compared with normal controls ($p < 0.01$). A diurnal increase in the plasma MHPG/cortisol ratio was not found in acutely depressed patients as it was in the normal controls ($p < 0.03$), and remitted depressed patients demonstrated no differences from normal controls.

Conclusions: This study of diurnal plasma MHPG, cortisol, MAP, and HR in acute and remitted depression suggests peripheral manifestations of central noradrenergic and hypothalamic-pituitary axis function are abnormal in

NR192 Tuesday, May 24, 12 noon-2:00 p.m.

Changes in Folate with Antidepressant Therapy

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Summary:

Objectives: Many studies have examined the relationship between folate and mood in cross-section, but the effect of treatment for depression on folate status has received little attention. The current study examines folate status in depressed outpatients before and after five weeks of desipramine treatment.

Methods: Ninety-nine consecutive unmedicated outpatients meeting Research Diagnostic Criteria for nonpsychotic unipolar major depression had blood drawn for serum folate (SF), red cell folate (RCF), and vitamin B12 within 24h of completing the Hamilton Rating Scale for Depression (HRSD) and the Beck Depression Inventory (BDI) at the beginning and end of a five-week trial of desipramine. Vitamins were assayed using radio-immunoassay.

Results: The prevalence of low SF, RCF, and vitamin B12 at baseline was 1.4%, 8%, and 7.2% respectively. RCF was correlated negatively with BDI ($r = -.22$, $p < .005$) and HRSD ($r = -.13$, $p < .06$) and positively with age of onset of illness ($r = +.25$, $p < .05$). At week 5, percent improvement in HRSD scores was significantly correlated with percent change in RCF ($r = .20$, $p < .05$). Using t-tests, the mean (±SD) change in RCF was significantly greater in responders (16.6 ± 101.5) as compared with non responders (–26.4 ± 96; $t = 2.09$, $df = 96$, $p < .05$).

Conclusions: RCF is correlated with severity of depression and increases as depression improves. This suggests that folate may be involved in the regulation of mood in depression.

NR193 Tuesday, May 24, 12 noon-2:00 p.m.

Residual Symptoms in Major Depression: A Comparison with Normal Controls

Joel A. Pava, Ph.D., Psychiatry, Mass General Hospital, 15 Parkman St. ACC 815, Boston MA 02114; Andrew A. Nierenberg, M.D., Madeleine Carey, B.A., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Objective: Despite robustly positive outcomes following antidepressant treatment, residual symptoms frequently persist following remission from a major depressive episode. Further, the presence of depressive residual symptoms has been associated with a greater likelihood of relapse/recurrence. The current study at-

tempts to characterize residual symptoms in a sample of depressives in remission from an acute episode of major depression. In addition, the level of psychosocial functioning is compared with that observed in a normal sample of volunteers without any history of depression.

Methods: Fifty-three recovered outpatients who had met SCID-P criteria for a current episode of major depressive disorder prior to entering an acute treatment trial were assessed following eight weeks of treatment with fluoxetine 20 mg/day. Patients who met criteria for remission (HAM-D ≤ 7 for at least three weeks) were evaluated for residual symptoms on a number of psychosocial psychiatric disorders using the SCID-P.

Results: Significant differences were observed between remitted depressives and normals in their levels of 1) depressive, anxious, somatic, and total psychiatric symptoms (Symptom Questionnaire), 2) cognitive functioning (Dysfunctional Attitude Scale; Cognitions Questionnaire); 3) social adjustment (Social Adjustment Scale-SR), and 4) problem-solving ability (Problem Solving Inventory). Normal subjects demonstrated better psychosocial functioning than recovered depressives on all measures.

Conclusions: These data suggest that, in spite of significant clinical improvement following antidepressant treatment, depressed patients continue to display significant residual problems.

NR194 Tuesday, May 24, 12 noon-2:00 p.m.

Undertreatment of Chronic Depression

Michael E. Thase, M.D., Psychiatry, Western Psychiatric, 3811 O'Hara Street Room E828, Pittsburgh PA 15213; George Trapp, M.D., Charles Holzer, Ph.D., John M. Zajecka, M.D., A. John Rush, M.D., Robert Howland, M.D.

Summary:

Several lines of research conducted in the early 1980s revealed that chronic depressions were not only common in community samples, they were also, in general, poorly treated. This is unfortunate because chronic depressions, while associated with substantial psychosocial impairment and economic costs, are often responsive to adequate trials of antidepressant medications. Extensive efforts have been undertaken through the National Institute of Mental Health's Depression Awareness, Recognition and Treatment Program to address this problem through professional and public education programs.

We report data for 212 chronically depressed outpatients participating in a multicenter antidepressant trial. Included were patients with double depression (n = 123) and chronic major depression, with the current episode lasting ≥ 24 months (n = 89). Patients were treated with a SSRI (sertraline) or a TCA (imipramine) and assigned randomly in a 2:1 ratio (sertraline:imipramine). Diagnoses were made by SCID/DSM-III-R criteria and response to controlled double-blind pharmacotherapy was monitored prospectively with the Clinician's Global Impressions improvement Scale (CGI) and Hamilton Depression Rating Scale. History of antidepressant treatment, psychiatric hospitalization, and ECT will be presented. Our preliminary findings indicate that the majority of these patients had never received antidepressant medication before entering this trial. During the 12-week, acute treatment phase, the majority of patients responded to treatment with either sertraline or imipramine.

Conclusions: 1) chronic depression remains underrecognized and undertreated despite extensive educational efforts; 2) chronic depressions are responsive to antidepressant medication.

NR195 Tuesday, May 24, 12 noon-2:00 p.m.

Paroxetine in a Clinical Practice Setting

James P. McCafferty, B.S., Clinical Development, SmithKline Beecham, P.O. Box 1510, King of Prussia PA 19406; David E. Wheadon, M.D., Ivan P. Gergel, M.D.

Summary:

Placebo-controlled clinical studies have established the safety and efficacy of paroxetine in treating major depression. By design, these trials were structured with restricted criteria for patient enrollment.

Summary:

Objective: To assess the benefits and risks of paroxetine in treating depression in the clinical practice setting.

Methodology: The study was a randomized, open-label, multicenter trial of eight-weeks duration. Eligible for the study were adult outpatients with a diagnosis of major depression who in the judgment of the treating psychiatrists warranted treatment with antidepressant medication. Patients were randomized in a 4:1 ratio to receive either paroxetine or one of two comparators: fluoxetine or nortriptyline. Using a predetermined scheme, patients were randomized only after qualifying for entry. Clinicians reviewed patient progress at least biweekly for efficacy (HAMD and CGI) and tolerability.

Results: There were 1602 patients enrolled in 230 sites located throughout the continental U.S. and Puerto Rico. Approximately 2/3 were female, and the mean age for the study was 45 years. Over 80% of the patients were diagnosed with recurrent depression and 66% had previously received treatment. Across regimens, 71% of the patients completed eight weeks of therapy. Approximately 10% of paroxetine and fluoxetine patients withdrew due to an adverse event. Poor response accounted for 4% of withdrawals. Within the nortriptyline group, the rates were slightly higher (16% for adverse events and 9% for poor response). Mean changes from baseline in HAMD total scores show that all three regimens produced comparable reduction in depressive symptoms.

	Paroxetine (N = 1302)	Fluoxetine (N = 243)	Nortriptyline (N = 57)
Baseline HAMD total (± S.D.)	22.2 ± 6.9	21.5 ± 6.6	22.4 ± 6.5
Change from baseline (± S.D.)	−13.9 ± 6.6	−12.5 ± 8.2	−13.0 ± 9.9

Conclusions: These results extend data from placebo-controlled trials demonstrating that paroxetine is an effective agent when used in the clinical practice setting.

NR196 Tuesday, May 24, 12 noon-2:00 p.m.

Shortened REM Latency and ECT

Leon J. Grunhaus, M.D., Psychiatry, Sheba Hospital, Ramat-Gen Tel Hashomer; James E. Shipley, M.D., Alan Eiser, Ph.D., Anna L. Remen, M.A., Atul C. Pande, M.D., Rajiv Tandon, M.D., John F. Greden, M.D.

Summary:

Electroconvulsive therapy (ECT) is highly effective in the treatment of major depressive disorder (MDD). However, the one-year relapse rates are reported to be high and in the 30%–60% range. To test whether polysomnography (PS) can identify patients with a propensity for relapse we studied 20 patients, responders to a course of ECT with PS studies. All patients met baseline diagnostic criteria fo MDD, were treated with ECT following standardized protocols, had PS studies performed after the course of ECT in a medication-free state, received maintenance antidepressants post-ECT, and were followed periodically with phone interviews. The recurrence of depressive symptoms was determined at three and six months after discharge. Fifty-five percent of the patients were symptomatic when evaluated six months after the ECT. Sleep onset REM periods were identified in 55% of the patients. As a group, patients who had experienced a recurrence of depressive symptoms by six months after discharge had significantly shorter REM latencies after the course of ECT. A shorter REM latency after ECT identified patients who at six months demonstrated

significant depressive symptomatology. Shortened REM latency after ECT in patients with MDD appears to be a correlate of vulnerability for relapse.

NR197 Tuesday, May 24, 12 noon-2:00 p.m.

Modelling the Seizure in ECT: Critical Indicators of Therapeutic Response

James S. Lawson, Ph.D., Psychiatry, Queen's University, Kingston ON K7L3N6, Canada; Felix Juan J. Letemendia, M.D., Nicholas J. Delva, M.D., James Inglis, D.Sc., Martin Rodenburg, M.D., John J. Waldron, M.B., Dennis W. Lywood, MIEEE

Summary:

Objective: This near-threshold ECT study explores the relationship between seizure parameters and therapeutic response in three electrode placements: bitemporal (BT), right unilateral (RU) and bifrontal (BF).

Method: Forty-seven patients with major depression were randomly assigned to one of the three placements: 18 BT; 14 RU; 15 BF. Seven of the RU patients had to be changed to BT because of failure to respond.

Results: The EEG of the ECT induced seizure was modelled in terms of a simple exponential decay function: $Y = Ae^{-Bx}$ where Y is μV^2 in the frequency range 0.4–16 Hz, X is time after the cessation of the stimulus, A is the intercept parameter and B is the rate parameter. The RU nonresponders showed a very poor fit to the model with abnormally low levels of A, possibly indicating the occurrence of Jacksonian, rather then centrencephalic, seizures. When these patients were changed to BT they showed a more normal seizure profile and also improved clinically. In general good clinical response was associated with high levels of A, this effect occurring equally throughout the frequency range. The rate parameter B did not predict response for any of the treatment groups.

Conclusions: Good clinical response is associated with seizures showing a clean exponential decay profile and high initial power levels.

NR198 Tuesday, May 24, 12 noon-2:00 p.m.

Higher Levels of Cholesterol in Depressive Patients

Claudi Udina, M.D., Psychiatry, Hosp. Gral. Catalunya, Gomera SN Sant Cugat, Barcelona 08190, Spain; Josep Tresserra, M.D., Vicens Valles, M.D., Rosa Catalan, M.D.

Summary:

In the last few years, differences in the levels of plasma lipids have been reported in patients suffering from some psychiatric disorders. The object of our study is to compare the plasma levels of cholesterol, VLDL, LDL, HDL, and triglycerids in samples of healthy subjects, patients with anxiety disorders (panic disorder and generalized anxiety disorder), and patients with major depressive disorder.

We completed psychiatric diagnoses with patients directed to the psychiatric clinic by a general practitioner due to stress. Seventy patients were included (11 with generalized anxiety disorder, 11 with panic disorder, and 20 with major depressive disorder); 28 patients (also referred by a general practitioner) without any psychiatric diagnosis were included in the control group.

In our study, the plasma cholesterol level was higher in the group of patients with major depressive disorder than in the anxiety disorders and the control group, in men (ANOVA $p < 0.04$) as well as in women (ANOVA $p < 0.01$)

NR199 Tuesday, May 24, 12 noon-2:00 p.m.

Leukocyte Adhesiveness/Aggregation in Major Depression

Zvi Zemishlany, M.D., Geha Hospital, P.O. Box 102, Petah-Tikva 49100, Israel; Cynthia Klein, M.D., Dov Aizenberg, M.D., Ilan Modai, M.D., Moshe Aronson, Ph.D., Abraham Weizman, M.D.

Summary:

Objectives: The adhesive properties of leukocytes in the peripheral blood have been shown to be increased by inflammatory processes, mental and physical stress, and neuroleptic drug treatment. The objective of this study was to examine the effect of major depression (MD) and heterocyclic antidepressants on the state of leukocyte adhesiveness/aggregation (LAA).

Methods: Eighty subjects were categorized into four equal groups matched for age and sex: 1) untreated MD patients; 2) treated depressed MD patients; 3) nondepressed patients treated with antidepressants; 4) healthy controls. MD was diagnosed according to DSM-III-R criteria. A score of ≥ 15 on the Hamilton Rating Scale for Depression was required for inclusion in groups 1 and 2. LAA was defined as the percentage of leukocytes found in aggregation of three or more on a stained blood smear under a microscope.

Results: LAA values for the untreated and treated MD patients were significantly increased, $13.8 \pm 7.7\%$ and $13.5 \pm 8.6\%$, respectively, compared with groups 3 and 4 who showed LAA values of $5.4 \pm 3.9\%$ and $6.4 \pm 3.2\%$, respectively (one way ANOVA, $p < 0.001$).

Conclusion: Elevated LAA is a state-dependent phenomenon for MD and is not affected by heterocyclic antidepressants. The state of LAA may potentially serve as a useful laboratory marker for major depression.

NR200 Tuesday, May 24, 12 noon-12:00 p.m.

DST and Clinical Outcome in Elderly Depressed Patients

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Summary:

Ninety-four elderly DSM-III-R depressed patients were treated with moclobemide, nortriptyline, or placebo in a seven-week, double-blind, multicentre study. Patients were rated using the 17-item Hamilton Depression Rating Scale (HDRS), the Clinical Global Assessment of Efficacy (CGAE), and Severity (CGAS) and the Melancholia subscale (MES) of the HDRS. The DST, a putative marker of major depression (Carroll et al, 1981), was carried out at baseline and end of treatment. At baseline, there were 37 suppressors and 57 nonsuppressors, thus representing a 61% sensitivity of the test, with no relationship found between DST status and the clinical measures. At the end of the trial, 65 patients were available for DST (32 suppressors and 33 nonsuppressors). The suppressors had significantly lower mean HDRS score ($p < 0.05$), MES score ($p < 0.02$), and CGAE ($p < 0.01$) with a trend for CGAS ($p < 0.1$) than the nonsuppressors. Of the 22 patients on nortriptyline, 73% were suppressors at the end of treatment, whereas, for moclobemide and placebo the percentage was 43% and 32%, respectively ($p < 0.02$), which parallels the order of clinical efficacy of these three agents in our study. Thus, the DST may be a useful adjunct for evaluating the clinical outcome of antidepressant treatment but not for diagnostic purposes.

NR201 Tuesday, May 24, 12 noon-2:00 p.m.

Psychosocial Correlates of Postpartum Mood

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Summary:

Objective: To assess the relationship between postpartum depressive mood and several prepartum psychosocial variables.

Method: 412 healthy primiparous or secundiparous pregnant women volunteered for a longitudinal study of postpartum adjustment. At three or four months of pregnancy, prepartum mood (BDI), demographic data (social class, education, medical history, etc.), personality (locus of control, self-esteem, hopelessness, etc.), life events, marital and social support, and several attitudes towards pregnancy and parenthood were measured. Mood was assessed at two and six months postdelivery by the Hamilton Rating Scale for depression.

Results: Multiple regression analysis showed that 13 variables accounted for 27% of variance ($F = 8.09$, $p < .001$). The most significant predictors of a more depressed mood during postpartum were: value given to parenthood, negative life events preceding pregnancy, difficulty to believe one is pregnant, nausea or vomiting during first trimester, number of apprehended perinatal stressors, and number of persons accepting the woman as she is.

Conclusion: The relationship between psychosocial variables in pregnancy and postpartum mood remains modest as in previous studies. Some predictors seem to indicate an ambivalent or anxious attitude regarding pregnancy or motherhood.

NR202 Tuesday, May 24, 12 noon-2:00 p.m.

Plasma Lithium Elevation at the End of Mania

Simavi Vahip, M.D., Psychiatry, EGE University, TIP Fakultesi, Izmir 35100, Turkey; Bekir Ozkan, M.D., Alp Ayan, M.D., Serdar Korukoglu, Ph.D., Isik Tuglular, M.D.

Summary:

Clinicians frequently observe that plasma lithium levels decrease at the beginning and increase at the end of a manic episode despite unchanged doses. There are some retrospective evaluations and case reports, but this study is the first prospective and controlled investigation. Fifty-eight manic patients were followed in an inpatient unit. Probable factors that could influence the plasma levels, such as variations in sodium intake, nonsteroid antiinflammatory drugs, etc., were controlled. Plasma lithium levels were held in the range of 0.9–1.20 mEq/L. Patients were rated by CPRG-Mania scale (doctor, nurse, and patient forms) weekly. Plasma lithium levels were measured weekly. 0.20 mEq/L or more was the criterion for elevation. Despite unchanged lithium doses, elevation at the end of manic episode was found in 39.7% of patients. For this group, average elevation was 39 ± 15% of last stable level. Age, sex, age of onset, number of episodes, duration of lithium, seasonality, and rapidity of recovery were not significantly different between elevated and non-elevated group. Family history of bipolar disorder was significantly more in non-elevated groups. Elevation mostly ocurred at the end of manic episode, but tended to be a gradual process and did not predict the time for cessation of antimanic treatment.

NR203 Tuesday, May 24, 12 noon-2:00 p.m.

Outcome in Single and Dual Diagnosis Patients

Sally Caldecott-Hazard, Ph.D., Psychiatry, Florida Hospital, 601 E. Rollins Street, Orlando FL 32803; Richard C.W. Hall, M.D.

Summary:

Objective: This study compared work, social, and physical functioning and symptoms controls and two groups of psychiatric outpatients (depressed only and depressed plus an eating disorder). Variables predicting good patient outcomes were analyzed.

Method: A total of 77 controls, 36 depressed-only outpatients, and 35 depressed/eating disordered outpatients were interviewed at 1.5 years after hospital discharge. A questionnaire obtained demographics and psychiatric history was administered with the Global Assessment of Functioning scale, and anxiety symptom checklist, and the Zung Depression to GAF scores were also obtained at hospital admission and discharge. Test scores were compared between groups using Analyses of Covariance. Predictor variables were analyzed with Pearson Product Moment Correlations or Chi Square tests.

Results: GAF scores significantly improved from hospital admission to discharge, and outpatient scores did differ from discharge scores. GAF, Zung, and anxiety scores for both outpatient group were slightly (significantly) lower than control scores. Ratings of social function for depressed only outpatients did not differ from controls on five out of six measures. Predictors of posthospital improvement included high satisfaction with hospital treatment, high GAF scores at hospital admission, perceived effectiveness of outpatient therapy, younger age, and an absence of sexual abuse or prior psychiatric hospitalization.

Conclusions: Single and dual diagnosis patients who obtained outpatient therapy improved with hospital treatment and appeared relatively healthy at 1.5 years post hospitalization.

NR204 Tuesday, May 24, 12 noon-2:00 p.m.

Six-Month Clinical Outcome of Outpatients with Early-Onset Chronic Depression

Vito Agosti, M.S.W., Psychiatry, Columbia University, 722 West 168th Street Unit 35, New York NY 10003

Summary:

Objective: The author examined the six-month clinical course and social functioning of depressed outpatients who were discharged from a university based psychopharmacology research clinic.

Method: Ninety-two former patients were randomly selected to be prospectively followed by the author, who administered a brief semistructured telephone interview without knowledge of the patient's history. Information regarding symptoms, social functioning, and treatment were gathered.

Results: Patients with early-onset chronic depression, who received subsequent medication treatment, had significantly longer months ($p = .01$) of remission than those who did not enter this treatment.

Conclusions: Results from other naturalistic follow-up studies indicated that the six-month prognosis for these patients to be relatively poor. These results suggest that maintenance antidepressant medication treatment improves the prognosis for patients with early-onset chronic depression.

NR205 Tuesday, May 24, 12 noon-2:00 p.m.

Norplant Associated Major Depression and Panic Disorder

Karen D. Wagner, M.D., Psychiatry, University Texas Medical, 1014 Texas, Galveston TX 77555-0425; Abbey Berenson, M.D.

Summary:

Objective: Norplant is a long-acting subdermal implant system that is widely used for contraception. The implant releases a continuous dose of levonorgesterol, a synthetic progestin. Although

oral contraceptives are associated with depression and panic disorder, no cases have been reported of psychiatric disorders secondary to the use of Norplant.

Method: Two cases of women, ages 18 and 29, are described who developed major depression and panic disorder on Norplant.

Results: These women with no psychiatric history developed major depression and panic disorder one to two months after insertion of Norplant. The symptoms worsened over the course of a year. Following removal of Norplant, the symptoms of depression and anxiety resolved within one month.

Conclusion: The progesterone content of oral contraceptive has been linked to major depression and panic disorder. Since Norplant is a progestin-only preparation, it is likely that some women will develop these disorders. These cases illustrate the importance of careful psychiatric follow-up for adolescents and adults who select Norplant for contraception. Patients should be informed about the possible occurrence of psychiatric disorders. When evaluating new onset of depression and panic disorder in adolescent and adult women, it is important to inquire about Norplant insertion.

NR206 Tuesday, May 24, 12 noon-2:00 p.m.

Television and Growth of Major Depression in Youth

Paul A. Kettl, M.D., Psychiatry, Penn. Ketl, M.D., Psychiatry, Penn. State Hershey, P.O. Box 850, Hershey PA 17033; Michelle Sredy, M.D.

Summary:

A variety of studies over the last decade have documented an increase in major depression since World War II along with a decreased age of onset. The increase in depression in our youth corresponds with the growth of television as a social force in American society. We compared the prevalence of major depression at age 24 (1) from 1954–1984 to the social presence of television at the same period as measured by the ten-year average of the number of TV's in use per 100,000 population, the number of Nielsen TV households per 100,000, and the number of Nielsen multiple set TV households per 100,000 population (2).

Television showed dramatically high correlations with lifetime prevalence of major depression at age 24. Lifetime prevalence of major depression at age 24 at different birth cohorts correlated with the number of TV sets in use at the time ($r = 0.97$, $p = 0.03$), number of TV households ($r = 0.99$, $p = 0.01$), and multiple set TV households ($r = 0.99$, $p = 0.003$).

Thus, the social effects of television, broadcasting seven hours per day to the average American home, must be included as a possible reason for the earlier onset and growth of major depression among the young. Thousands of hours of TV viewing expose our children to repetitive acts of senseless violence and may further distance children from social contacts with peers and family leading to an increased risk of major depression.

NR207 Tuesday, May 24, 12 noon-2:00 p.m.

Affective Disorders and Seasonality in Brazil

Florence Kerr-Correa, M.D., Neurol & Psiqui, Fac Medicina UNESP, Fac Medicina Botucatu UNESP, Botucatu SP 18618-000, Brazil; Lucijane B. Sousa,

Summary:

It has already been well stablished that there is a higher incidence of depression in winter time in North Hemisphere countries. There are also few studies showing a pattern of summer depressions often accompanied by hypomania in the winter in Australia (Boyce and Parker, 1988) and a spring/summer peak in New Zealand (Mulder et al, 1990; Sayer et al, 1991).

The aim of this study was to analyze the seasonal pattern of occurence of affective disorders. For these purpose, we assessed in a 10-year period (1982–1991), all admissions in a state psychiatric hospital in Botucatu, Saõ Paulo, Brazil. There were about 1545 hospitalized patients per year (range: 1171–1872), 2/3 of whom were male ($\bar{x} = 1122$), and 1/3 female ($\bar{x}$ 423). We found 157 charts with a probable diagnosis of affective disorders (DSM-III-R criteria): 46% of them were made by the hospital psychiatrists and 54% were made by the first author through psychiatric annotation in the files (anamnesis plus psychiatric examination). The patients were bipolar-manic episode (72%), bipolar-depressive epidose (8%), and unipolar depressives (20%). Patients had a single hospitalization in 43% of the cases and four or more hospitalizations in 20% of them. We observed a seasonal pattern just in women with manic episodes, with mania occuring more frequently ($p < 0.02$) in spring and summer. No seasonal pattern occured with manic or depressive males or depressive females. It seems that, in our country, affective disorders are still underdiagnosed, and depressive episodes are tolerated by the patients, families, leading to fewer hospitalizations. More studies are needed to better assess seasonal patterns in tropical areas.

NR208 Tuesday, May 24, 12 noon-2:00 p.m.

Discrimination of Anxiety and Depression with Cognition Data

John B. Jolly, Psy.D., Psychiatry, Univ of Arkansas Med Sci, 4300 W. Markham, Little Rock AR 72203; David C. Wiesner, Ph.D., David S. McCray, M.D., Nickolaus Paal, Ph.D., J. Chris Rule, B.A., Janet M. Jolly, M.D.

Summary:

Objective: This study compared and integrated two adult methods of assessing internalizing cognitions to determine their utility in differentiating anxious and depressive symptoms in 110 inpatient adolescents.

Method: Subjects were administered a randomized packet of self-report measures that included the Automatic Thoughts Questionnaire-Negative (ATQ-N) and Positive (ATQ-P), the Cognition Checklist (CCL), and noncognitive forms of the Beck Depression (BDI) and Anxiety (BAI) Inventories.

Results: Results demonstrated that: (a) positive cognitions (ATQ-P) were related (inversely) to noncognitive depression but not anxiety, while general negative cognitions (ATQ-N), depressive cognitions (CCL-Depression), and anxiety cognitions (CCL-Anxiety) were related to both anxiety and depression; (b) hierarchical multiple regressions (accounting for ATQ-N scores) demonstrated that a combination of general negative cognitions (ATQ-N) and anxious cognitions (CCL-A) predicted anxiety symptoms, while depressive symptoms were significantly predicted by general negative cognitions, anxious cognitions, and (low) positive cognitions.

Conclusions: Results support the integration of both adult models of assessment in discriminating anxious from depressive symptoms. A cognitive assessment measure that includes primarily positive and anxious cognitions may have considerable utility in discriminating anxiety from depression in disturbed adolescents.

NR209 Tuesday, May 24, 12 noon-2:00 p.m.

Pharmacoeconomic Evaluation of Oral Therapies in the Management of Major Depressive Disorder

Thomas R. Einarson, Ph.D., Research, Health Economics, 400 Plaza Drive, Selaulus NJ 07094; Steven R. Arikian, M.D., Robert E. Lee

Summary:

A pharmacoeconomic analysis was conducted comparing four treatment regimens for major depressive disorder (MDD): The therapeutic drug classes considered for therapy of MDD include

tricyclics (TCAs), serotonin-selective reuptake inhibitors (SSRIs), heterocyclics (HCAs), and serotonin/norepinephrine reuptake inhibitors (venlafaxine). The study was performed from a cost-based payor perspective. A four-step pharmacoeconomic model was utilized that consisted of problem identification, a clinical management analysis, a pharmacoeconomic analysis, and a comprehensive sensitivity analysis. Four different decision analytic models were analyzed in this paper: inpatient brand and generic, and outpatient brand and generic. Venlafaxine proved to be the most cost-effective therapy in all but one of the models, the outpatient generic model, where it ranked second behind the HCAs.

NR210 Tuesday, May 24, 12 noon-2:00 p.m.

A Poisson-Erlang Model Analysis of Cognitive Retardation in Depression

Sophie Lemelin, BPS, Psychiatrie, Hopital Enfant-Jesus, 1401 18e Rue, Quebec G1J1Z4, Canada; Philippe Baruch, M.D., Francois Brisebois, M.Sc., Annick Vincent, M.D., James Everett, Ph.D., Louis-Paul Rivest, Ph.D.

Summary:

Slowing of reaction times (RT) is frequently observed in depression. Besides mean RT, analysis of RT distribution provides more information. Poisson-Erlang model proposes that RT distribution is generated by two states: processing and distraction. In any trial, processing time (PT) corresponds to the cognitive operations necessary to give a correct answer. PT is constant for a given task condition. PT and total distraction time (TDT) are estimated by an algorithm for each subject at each task.

Methods: Study included 24 DSM-III-R depressed untreated patients (7M & 17F) divided in two groups according to their score on the Widlöcher Psychomotor Retardation Scale (WPRS): 12 retarded patients (age: 42.17 ± 9.35; WPRS: 29.82 ± 7.63) and 12 nonretarded patients (age: 40.50 ± 9.10; WPRS: 13.75 ± 6.59). Twenty comparable controls participated in the study (3M & 17F; age: 38.45 ± 6.85). All subjects were assessed twice using a computerized Stroop test (first session for training). The results of the second evaluation are presented.

Results: On Color series, when compared with nonretarded patients and controls, retarded patients presented an increased mean RT ($p < .0009$) and an increased TDT ($p < .0005$) with a normal PT. On the Color-Word series, retarded patients showed again longer mean RT ($p < .0001$) and longer TDT ($p < .02$), but PT was increased for all patients ($p < .0001$).

Conclusions: Slowing of RT appears to be typical of retarded depressives and mainly due to an increased distraction time. This result underlines the importance of disentangling the psychomotor retardation assessed clinically from its cognitive aspect. Compared to mean analysis, analysis of distribution using Poisson-Erlang model is a potent tool to assess distractibility in depression.

NR211 Tuesday, May 24, 12 noon-2:00 p.m.

Predictors of Response to Cognitive Therapy

Jacqueline A. Samson, Ph.D., Dep. Research FAC, McLean Hospital, 115 Mill Street, Belmont MA 02178; Martha T. Dewitt, Ph.D., Joseph J. Schildkraut, M.D., Alan F. Schatzberg, M.D., Jonathan O. Cole, M.D.

Summary:

Objective: Levels of urinary MHPG predict response to at least one antidepressant drug treatment (Garvey et al, 1990). Thus, we initiated a study to examine urinary catecholamine output as a predictor of response to cognitive-behavioral therapy (CBT). We also examined a number of additional psychosocial measures including the Personal Style Inventory (PSI) which has been associated with good medication response (Peselow et al, 1992).

Method: Subjects were 12 outpatients (Seven male, five female) with unipolar major depressive disorder. All were free from medication, major medical disorders, and received no other form of treatment during the 16-week study. Response was measured by weekly Hamilton ratings conducted by a rater not in the treatment process.

Results: Consistent with previous reports we found significant correlations between good CBT response, lower baseline severity scores on the Beck Depression Inventory ($r = -.68$ $p = .05$), and higher social functioning ($r = .90$, $p < .001$). Patients with higher autonomy scores on the PSI showed poorer outcome ($r = -.65$, $p = .05$).

There were no significant correlations between baseline urinary catecholamine measures and CBT response. However, patients who responded to CBT showed somewhat higher initial levels of urinary MHPG (2434 ± 590 μg/24 hrs) than did nonresponders (2209 ± 476 μg/24 hrs), and showed greater reduction (measured by percent change from baseline to week 16) in MHPG levels (corrected for volume and creatinine) than did nonresponders (Kruskal-Wallis chi square = 6.53, $p = .01$).

Conclusions: Low autonomy scores and higher MHPG may identify patients who are likely to respond to CBT and fail on medication alone.

NR212 Tuesday, May 24, 12 noon-2:00 p.m.

Sertraline Administered for Eight Weeks to Depressed Patients Did Not Alter Sleep Architecture: A Preliminary Report

Andrew Winokur, M.D., Psychiatry, University of Penn., 11 Gates 3400 Spruce Street, Philadelphia PA 19104; Nedra Lexon, Kathleen Allen, Dan Reed, William Breitmeyer

Summary:

Administration of the selective serotonin reuptake inhibitors fluoxetine and paroxetine has been associated with polysomnographic (PSG) observations of disruption in sleep continuity. In a previous study examining the effects of sertraline on sleep architecture, we observed no significant alterations in measures of sleep continuity, but a robust suppressant effect on REM indices in depressed patients treated for two weeks. The present investigation assessed the effects of sertraline on sleep architecture after eight weeks of treatment.

Six MDD patients with a total score ≥ 18 on the 17-item Hamilton Depression Rating Scale (HDRS) participated in this study. Subjects were drug-free for at least two weeks prior to baseline evaluation and free of significant medical problems or primary sleep disturbance. Sleep assessment batteries, consisting of two consecutive nocturnal sleep PSG studies, were conducted at baseline and after eight to ten weeks of treatment.

Mean HDRS scores decreased significantly from 23 ± 2.8 at baseline to 5 ± 2.6 after eight weeks of treatment ($p < 0.003$), and all patients' HDRS scores decreased ≥ 50% from baseline. No significant alterations in sleep architecture were observed in association with sertraline therapy, and measures of sleep continuity, including sleep efficiency and wake time after sleep onset, were not affected.

NR213 Tuesday, May 24, 12 noon-2:00 p.m.

Discriminating Apathy and Depression Using Items From the Hamilton Rating Scale for Depression

Robert S. Marin, M.D., Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15217

Summary:

Apathy and depression are discriminable but related dimensions of behavior. The purpose of this study was to evaluate the source

of the overlap between measures of apathy and depression. We evaluated the intercorrelations between the Apathy Evaluation Scale (AES) and the Hamilton Rating Scale for Depression (HamD) in 107 subjects, aged 53–85, who met research criteria for normal aging, left or right cerebral hemisphere stroke, probable Alzheimer's disease, or major depression. We determined the correlation between the individual items on the HamD and the total scores on the AES and the HamD. The HamD items having the strongest correlations with AES total score were diminished work/interest, psychomotor retardation, anergy, and lack of insight. The correlation between AES and HamD total scores was nonsignificant when major depression subjects and those variables most closely related to apathy were excluded from consideration. These findings indicate that the convergence between HamD and AES is attributable to a subset of HamD items that are consistent with the syndrome of apathy, and the fact that major depression is associated with both apathy and depression. Clinical and research applications of these results are discussed.

NR214 Tuesday, May 24, 12 noon-2:00 p.m.

Co-Occurrence of Bipolar Disorder and Personality Disorder

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Summary:

This study examined the co-occurrence of bipolar disorder and personality disorder in a sample of 32 bipolar inpatients. Participants were administered a modified version of the Schedule For Affective Disorders and Schizophrenia and the Personality Disorder Examination. Thirty-five percent of the bipolar patients met criteria for a mixed state, 35% for bipolar disorder not otherwise specified (e.g., bipolar II), 21% for bipolar disorder depressed, and 9% for bipolar disorder, manic. Forty-four percent of the bipolar disorder subjects met criteria for at least one personality disorder diagnosis. There was no significant association between any single personality disorder or cluster and bipolar disorder subtype. Nevertheless, two trends were identified: (1) bipolar disorder, mixed and Cluster B and Cluster C personality disorders may be associated, (2) bipolar disorder not otherwise specified and Cluster B and Cluster C disorders may be associated. We expect to detect significant associations in an increased sample. Longitudinal observation is necessary to conclude whether the association of bipolar disorder and personality disorder endures in this sample and whether comorbidity impacts upon treatment. Also, the accrued cycling in bipolar illness and the marked affective instability in mixed presentations may impact upon the patients' interpersonal styles and personality organization.

NR215 Tuesday, May 24, 12 noon-2:00 p.m.

Dysthymia: Assessing Symptoms and Treatment Response with the Cornell Dysthymia Rating Scale

David J. Hellerstein, M.D., Psychiatry, Beth Israel Med. Center, First Avenue & 16th Street, New York NY 10003; Lisa W. Samstag, M.A., Suzanne Little, M.A., Philip Yanowitch, M.D.

Summary:

Objective: Despite the high prevalence for dysthymia, there is a lack of appropriate scales for measuring symptom severity and treatment response. Typically, researchers use measures (e.g. Hamilton Depression Rating Scale [HDRS]) normed on major depression samples. This study attempted to determine the value of the newly described Cornell Dysthymia Rating Scale [CDRS] in patients with DSM-III-R dysthymia.

Method: 63 patients with dysthymia, predominantly early-onset, and without coexisting major depression, were recruited for two eight-week SSRI treatment studies. Pre- and post-treatment and five-month follow-up data were collected using the CDRS, HDRS, Hopkins Symptom Checklist [SCL-58], and Clinical Global Impressions [CGI] scales. Responders and nonresponders were compared over treatment. Inter-correlations were conducted among the scales to determine the relationship between symptoms from both patient and clinician perspectives.

Results: As expected, there was a high correlation between the HDRS and CDRS. Differential results were found when the CDRS was broken into its two-factor structure, with dysthymia and anxiety/somatic subscales appearing to measure distinct phenomena. Preliminary findings suggest that clinician ratings on the CDRS may be more closely related to patient self-report of symptoms than the HDRS.

Conclusion: Results suggest the CDRS is useful in initial assessment and evaluating/psychopharmacologic treatment response of dysthymics.

NR216 Tuesday, May 24, 12 noon-2:00 p.m.

Comparison of Quality of Life in Outpatients Suffering From Affective Disorders

Patrick M. Martin, Ph.D., QOL Health Care, AMC Research Group, 50 Rue M Dassault, Boulogne 92100, France

Summary:

Affective disorders are illnesses associated with significant morbidity and mortality. Patients, affective disorders suffer from functional impairment with may be comparable to that experienced by patients with heart conditions and more severe than that associated with other chronic illnesses. Also, it appears that affective disorders are one of the most prevalent health problem.

Many epidemiological studies confirmed the frequent comorbidity between different psychiatric disorders, particularly anxiety, depression, or alcoholism. For example, the frequent comorbidities between alcoholism and anxiety and/or depression were observed.

It could be emphasized that affective disorders, comorbidities, and psychotropic therapeutics might alter the quality of life (QoL) in these patients.

Thus, we have undertaken several cross-sectional studies to investigate the sociodemographic, clinical, and therapeutic variables in patients suffering from generalized anxiety disorders (GAD), depressive disorders, or in alcoholic outpatients according to DSM-III-R criteria and treated with psychotropic treatments. Data were collected at a single point in time.

The aim of these studies was to assess the impact of these affective disorders on the psychiatric patients's quality of life (QoL). We assessed QoL using the Functional Status Questionnaire (FSQ) and RAND 36-item, health survey, which are two generic instruments that include several dimensions.

We evaluated scores of Qol and their correlations with clinical data, consumption of psychotropic drugs, comorbidities, and with the severity of the diseases.

Results indicate that

- psychological function, sexual relationships and feelings about health appear to be the most sensitive QoL dimensions ($p > 0.001$).

- a significant ($p > 0.001$) correlation among QoL dimensions and clinical outcomes scores in each population.

-Patients' QoL scores with comorbidities are significantly decreased, compared with patients without comorbidities

-Patients' QoL scores with psychiatric treatments are significantly decreased, compared with patients without psychiatric treatments.

NR217 Tuesday, May 24, 12 noon-2:00 p.m.

Effects of Buspirone and 1-PP in Animal Models of Panic Attacks

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Summary:

The panic attacks are the central pathologic feature of panic disorder and agoraphobia. Panic is characterized by unexpected anxiety attacks involving such symptoms as tachycardia, dizziness, breathlessness, chest pain, trembling, and fear of dying or losing self-control (DSM-III-R; APA, 1987)

However, panic disorders have been the focus of considerable controversy. For example, researchers disagree about whether panic disorder constitutes a homogenous clinical syndrome. During unexpected panic attacks, some patients try to join a safety-zone and others are in expectation with inhibited cognitive and behavioral processes. These two subtypes of patterns could represent two different models in the pathophysiology of panic disorder and could correspond to different biological defects.

A major focus of recent investigation into the pathophysiology of these disorders has involved the provocation of panic attacks by a variety of pharmacologic agents. On the other hand, some data have found no therapeutic benefit from buspirone in patients with panic disorders. However, the main metabolite of buspirone, 1-PP, which possesses alpha adrenoceptor antagonist properties, might exhibit a deleterious effect and induce panic attacks, in contrast to parent drug.

Using an experimental paradigm in rats, which shows homology in the behavioral modifications induced with those observed during panic, particularly in patients who experience cognitive and behavioral inhibition, we investigated the effects of buspirone and 1-PP.

Methods: On day 1, groups of rats are exposed to a briefly incontrollable situation (IS). On days 2 and 3, in the morning, rats are submitted to an avoidance task in a shuttle-box. The response required is the passage into another compartment to escape from the aversive situation. The number of or absence of passage was recorded for each group.

Drug administration: On day 1, before exposure to the IS, either H20 (control group) or well-known panicogenic substances (experimental group) were administred to rats. On day 3, 30 min. before the shuttle-box session, we administered, imipramine, phenelzine, buspirone or 1-PP to the experimental group of rats. Following results were observed:

- Experimental rats pretreated with panicogenic drugs, including 1-PP, exhibit a behavioral deficit (AP) compared with control rats or experimental rats without panicogenic treatment.

- In experimental rats pretreated with penicogenic drugs, once daily administration of buspirone, imipramine, and phenelzine reverse the behavioral deficit (AP).

In conclusion, in these experimental conditions, these results seem to indicate that the parent drug buspirone exhibits the same effects as drugs effective in panic disorder. In contrast 1-PP alone, such as lactate or caffeine, induce a behavioral deficit (AP). These effects could be supported by a "hypersensitivity" of alpha receptors in a minority of panic patients and/or by the increasing of 1-PP ratio.

NR218 Tuesday, May 24, 12 noon-2:00 p.m.

Suppressibility and Recovery of the Thyroid Axis in Major Depression

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Summary:

Studies in depressed pt's have shown abnormalities of the brain pituitary thyroid (BPT) axis that include increased plasma T4, low T3 levels, elevated plasma TSH and CSF reverse T3, decreased TSH response to TRH, and increased prevalence of anti-thyroid antibodies compared with normals (nl's). Our major aim is to assess thyroid axis suppressibility in depressed pt's by analyzing plasma TSH suppression and recovery in response to a single exogenous dose of either triiodothyronine (T3) or levothyroxine (T4). To our knowledge, no such dynamic studies have been done: depressed pt's while ill and following recovery will be compared to nl's as to this dynamic test and basal TFT's. Within 3 days of admission, 8 pt's (5M, 3F) with a DSM-III-R diagnosis of MDD received an oral a.m. dose of T4 (900, 2,000 or 3,000 mcg) or T3 (25 or 50 mcg), after basal TFT's were obtained (T3, T4, TSH). Blood samples for TFT were then obtained every 2 hours for the first 10 hours post-dose and then at 24, 48, 72, 120, and 168 hours post-dose. Selected s's had further samples drawn at 3 day intervals until 3 or 4 weeks post-dose. All samples were frozen until assayed by RIA using kits from Diagnostic Products Corp. Depressed pt's received T4 in doses of 3,000 mcg, except a few who received smaller doses. In all instances, there was a doubling of serum T4 within 10 to 24 hours post-dose and plasma T3 showed a slightly delayed 1.5 to 2× increase, usually peaking at 24 to 48 hours post-dose. T4 levels gradually returned to baseline in 9 to 12 days and T3 levels in about 4 to 15 days. Four nl's received a similar T4 dose and showed similar findings in plasma T4 and T3 to the depressed pt's. TSH levels clearly decreased in 5 nl's within 10 to 24 hours after 25 to 50 mcg of T3. Recovery occurred within 48 to 72 hours. TSH suppression was slightly slower after T4 (3,000 mcg) and persisted for nearly 3 weeks. Depressed pt's showed TSH suppression after T4 (2,000 to 3,000 mcg), which was first clearly evident at 24 hours; reaching nadir after 5 to 7 days. No clear TFT response differences were evident between nl's and depressed pt's with the limited number of studies to date.

NR219 Tuesday, May 24, 12 noon-2:00 p.m.

Fixed and Titrated Dose RUL ECT in the Elderly

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Summary:

Objective: No prior studies have directly compared the efficacy of titrated versus fixed-dose ECT. We report such an ongoing trial.

Method: We randomized 17 drug-free patients (three men, 14 women; mean age 74 ± 6 years) receiving RUL brief pulse ECT to either titrated moderately suprathreshold or high fixed-dose stimuli. Eight subjects were enrolled in the titrated condition (150% above seizure threshold), and nine in the fixed dose (403 mC). Seizure threshold was only determined at treatment #1 in the titrated group. Blind Hamilton ratings were collected before and after each ECT.

Results: The titrated and fixed-dose subjects were not different on any demographic variable. A repeated measures ANOVA showed that the titrated patients responded differently than the fixed-dose group ($f = 5.48$; $df = 1,81$; $p < 0.05$). Post-hoc t-tests show the fixed-dose group had greater improvement after ECT #2 ($t = 2.2$; $p < 0.05$), ECT #4 ($t = 3.4$; $p < 0.005$), and ECT #5 ($t = 2.6$; $p < 0.05$). Final Ham-D scores showed a trend for a greater improvement in the fixed-dose group (7.6 + 4.5) than in the titrated group (10.3 ± 4.0) (p = n.s.).

Conclusion: Elders receiving fixed-dose RUL ECT had superior early improvement compared with patients receiving titrated, mod-

erately suprathreshold ECT. Thus, fixed, high-dose RUL ECT may have a role in depressed elderly patients when speed of response is the overriding concern.

NR220 Tuesday, May 24, 12 noon-2:00 p.m.

Physiological Correlates of ECT

Veronika Solt, M.D., Psychiatry, UMDNJ, 30 Bergen Street Bldg 15 #1501, Newark NJ 07107; Cheng-Jen Chen, M.D.

Summary:

The ECT stimulus intensity is an important factor for the therapeutic effects of ECT. There is no currently available objective indicator that could serve as an index of stimulus intensity. ECT induces heart rate and blood pressure changes through electrical stimulation of the autonomic centers of the brain. We hypothesized that the ECT stimulus intensity was related to the difference of rate pressure product (DRPP = postECT PR × systolic BP preECT × systolic BP).

Eight male patients (age = 69.9 ± 2.69) with a diagnosis of recurrent major depression who were refractory to pharmacotherapy were studied. They were admitted to the East Orange VA Medical Center between January 1991 and January 1993. Patients were given eight courses of ECT treatment. PreECT BP, preECT PR, postECT BP, postECT PR, Thymatron percent-energy level, seizure duration, dosages of pentothal, and succinylcholine were recorded. DRPP highly correlated with ECT stimulus intensity ($r = 0.89$, $n = 8$, $p = 0.0031$), but did not correlate with either the seizure duration or the dose of thiopental or succinylcholine.

We suggest that DRPP may be used as a noninvasive indicator of the electrical stimulus that reaches the deep brain structures from the ECT devices and may be an objective indicator of therapeutic efficacy.

NR221 Tuesday, May 24, 12 noon-2:00 p.m.

Possible Iatrogenic Cardiovascular Risks for Older Patients Receiving ECT

Cheng-Jen Chen, M.D., Psychiatry, East Orange VAMC, EOVAMC Tremont Avenue, East Orange NJ 07019; Peter E. Stokes, M.D.

Summary:

Electroconvulsive therapy (ECT) is a low-risk procedure. However, it may be associated with significant cardiovascular morbidity and mortality (1). It has been demonstrated that stimulus energy correlates positively and pentothal doses negatively with ECT-induced cardiovascular responses. Under the current pattern of ECT practice, older patients generally receive stronger electrical stimulus energy and lower absolute doses of anesthetics during ECT treatment (2). We hypothesized that older patients are exposed to more cardiovascular risks under the current pattern of ECT practice.

A younger ($n = 4$, age = 56, 65, 67, 68 y/o) and an older ($n = 4$, age = 71, 75, 78, 79 y/o) group of patients, who were consecutively admitted to the hospital and received a full course of bitemporal ECT, were included for data analysis. The energy and pentothal used during ECT and the ECT-induced cardiovascular physiological changes were analyzed.

The results were as follows: Age was positively correlated to energy ($r = 0.52$, $n = 55$, $p = 0.0001$) and negatively correlated to pentothal ($r = -0.55$, $n = 54$, $p = 0.0001$). The older patients were given more energy ($F = -6.07$, $p = 0.0000$) and less pentothal ($F = 3.77$, $p = 0.0005$), and had more prominent cardiovascular responses ($F = -2.49$, $p = 0.016$). After adjustment for energy and pentothal, the group difference of cardiovascular responses subsided ($F = 1.53$, $p = 0.1991$).

The findings suggest that under the current ECT practice pattern, older patients are exposed to more ECT-induced cardiovascular burden, which is iatrogenic. This practice pattern needs a serious reexamination, especially for geriatric patients.

NR222 Tuesday, May 24, 12 noon-2:00 p.m.

Cerebral Blood Volume and Oxygenation During ECT

Laszlo Gyulai, M.D., Psychiatry, University of Penn., 3600 Market St. 8th Floor, Philadelphia PA 19104; Larry Lipton, Ph.D., William Ball, M.D., Chilton Alter, B.S., Britton Chance, Ph.D.,

Summary:

The goal of the study was to explore whether tissue perfusion and oxygen supply is comprised in the brain by ECT. Six depressed patients (five with major depression and one with bipolar disorder) aged 66–80 years received a total of 13 unilateral or bilateral brief pulse or bilateral sinusoidal ECT as part of their clinical care. The cerebro-cortical blood volume and hemoglobin oxygenation were monitored continuously and simultaneously during ECT in the left frontal lobe using a RunMan near-infrared spectrometer supplied with a light probe providing approximately 2 cm deep and 2 cm wide crescent-shaped light penetration in the left frontal lobe. In all patients the blood volume decreased for 12–68 seconds in the beginning of the elicited seizures and was accompanied in the majority of measurement occasions (10) by a decreased hemoglobin oxygenation. This phase was followed by a gradual increase in blood volume and reoxygenation of hemoglobin starting in most cases during seizure and reaching their maximum during the postictal phase. The decrease in cortical blood volume and hemoglobin deoxygenation suggests a mismatch between tissue perfusion and oxygen demand during electrically induced seizures in humans, although it does not necessarily indicate tissue hypoxia. This study highlights that near-infrared spectroscopy is a promising, cheap technique that can be used at bedside to monitor hemodynamics and oxygenation of the brain at rest and during activation, thus having a high potential of applicability in psychiatry.

NR223 Tuesday, May 24, 12 noon-2:00 p.m.

Identification of Markers of Mild Delirium in the Elderly

Ira R. Katz, M.D., Psychiatry, Hospital University of PA, 3600 Market Street 8th Floor, Philadelphia PA 19104; Jana Mossey, Ph.D., Luisa Skoble, M.D.,

Summary:

We conducted a prospective study of delirium in elderly residential care patients to evaluate methods for identification of milder cases. We obtained baseline assessments (updated every four months) and assessed patients during acute hospitalization with the Minimental State Examination (MMSE), level of accessibility (LOA), a test of verbal vigilance (VV) and EEG measures in occipital leads (P3-01, P2-04). Of 34 subjects with research and clinical evaluations during hospitalization, eight had definite, four had possible, and 22 had no delirium by psychiatrist's diagnosis. By one way ANOVA, delirium during hospitalization was associated with MMSE, LOA, VV, and EEG theta changes. By repeated measures ANOVA (baseline vs. hospital), there was a significant time X diagnosis interaction for LOA, VV, EEG theta, and EEG alpha. These findings suggest that the availability of baseline data can improve case recognition. Other findings using multiple in-hospital measures suggest that repeated observations in the pathological state can also improve diagnosis.

NR224 Tuesday, May 24, 12 noon-2:00 p.m.

Effective Treatment for Premenstrual Syndrome with a Gonadotropin-releasing Hormone Agonist and an Oral Contraceptive

Michael Feinberg, M.D., Mental Health, Hahnemann University, 1427 Vine St. MS 950, Philadelphia PA 19102; Mona M. Shangold, M.D.

Summary:

We assessed the effectiveness of nafarelin acetate and ethinyl estradiol/norethindrone, alone and in combination, in relieving premenstrual syndrome (PMS), and we correlated therapeutic response with endogenous hormone suppression and bleeding pattern during treatment. Eighty-seven women were screened stringently with prospective daily diaries and structured psychiatric interviews; 53 who met DSM-III-R criteria for LLPDD underwent single-blind placebo treatment for two cycles. Thirty-eight of these women met inclusion and exclusion criteria and were willing to take medication. They were randomized, double-blind, to one of four treatment groups for three consecutive cycles: (1) nafarelin acetate nasal spray (Synarel®) 200 mcg BID and ethinyl estradiol 35 mcg/norethindrone 0.5 mg (Brevicon®) daily on cycle days 6–26, (2) Synarel® and placebo pills, (3) Brevicon® and placebo nasal spray, or (4) placebo nasal spray and placebo pills. Using regression analysis, treatment with Synarel® and Brevicon® was significantly more effective than placebo ($p < 0.05$) in relieving PMS symptomatology; treatment with Synarel® alone or Brevicon® alone was not effective. Therapeutic response did not correlate with endogenous hormone suppression or bleeding pattern during treatment. We recommend combination therapy with Synarel® and Brevicon® for women with an established diagnosis of PMS.

Supported in part by a grant from Syntex Laboratories, Inc.

NR225 Tuesday, May 24, 12 noon-2:00 p.m.

Serious Suicide Attempts in Children and Adolescents

Atilla Turgay, M.D., Psychiatry, Wayne State University, 3219 Bloomfield Shore Drive, West Bloomfield MI 48323; Lillian Mok, M.D., Anne Marie D'Aloisio, M.S.W., JoAnne Sheehan, R.N.,

Summary:

This long-term prospective clinical study involved 350 children and adolescents with at least one psychiatric disorder, diagnosed according to DSM-III-R criteria, who were assessed immediately after serious suicide attempts. Clinical findings were compared with those for age- and gender-matched children and adolescents with at least one psychiatric disorder, with no history of suicidal behavior. Compared with the children and adolescents without suicide attempts, the following characteristics of the seriously suicidal children and adolescents were significantly more frequent ($p < 0.05$): 1) one or more comorbid psychiatric disorders, 2) the presence of mood disorder, especially major depression or bipolar disorder, 3) the presence of conduct disorder, 4) parental separation and divorce, 4) chronicity and treatment resistance of the psychiatric disorder(s), determined according to NIMH criteria for chronicity, 5) history of earlier suicidal attempts, 6) history of earlier psychiatric admission. Compared with children and adolescents with serious suicidal attempts, children with psychiatric disorders with no suicidal behavior presented the following characteristics, statistically more significantly ($p < 0.05$): 1) The presence of ADHD, and adjustment disorders, 2) good treatment response to psychopharmacological and psychosocial interventions, 3) intact family.

NR226 Tuesday, May 24, 12 noon-2:00 p.m.

Driven to Suicide? Adolescent Needs and Drives

Catherine A. Martin, M.D., Psychiatry, University of Kentucky, 820 South Limestone Annex 4, Lexington KY 40536; Arch G. Mainous, Ph.D., Michael J. Oler, M.D., Eric T. Richardson, M.D., Amy S. Haney, M.D.

Summary:

Objective: Adolescent suicide is a significant public health problem. A factor that has received little investigation concerns the increased biological drives or needs of puberty and how these may relate to adolescent suicidal behavior.

Method: A survey of 823 students was conducted at a public high school in a rural southern state. The questionnaire contained items on high-risk behaviors (substance abuse, sexual activity), depression (Children's Depression Inventory), and a scale focusing on adolescent bodily needs and drives (Adolescent Need Scale). Suicidal behavior was measured by an index of suicidal ideation and an indicator of a past suicide attempt.

Results: Seven percent of the respondents had attempted suicide. The Adolescent Need Scale positively correlated with suicidal behavior ($r = .38$ $p \leq 0.001$), depression, ($r = .49$, $p \leq .0001$), as well as the high-risk behaviors of cigarette ($p \leq 0.001$), alcohol ($p = 0.001$), marijuana ($p = 0.0001$), and cocaine ($p = 0.001$) use and sexual activity ($p = 0.001$).

Conclusions: The findings indicate that heightened bodily needs and drives among adolescents are related to suicidal and other high-risk behaviors. Depression and the bodily need state overlap in their relation to suicidal behavior. This suggests that a feature associated with adolescent depression, the need to satisfy a bodily drive, may be an important link in motivating adolescent suicidal behavior.

NR227 Tuesday, May 24, 12 noon-2:00 p.m.

Anger Impulsivity and Coping Styles in Suicidal Patients

Elie Lepkifker, M.D., Psychiatry, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel; Netta Horesh, Ph.D., Zipi Rolnick, M.A.

Summary:

The purpose of the study was to assess the relations between suicidal risk, anger, impulsivity, and coping styles. Thirty patients hospitalized because of suicidal risk, 30 psychiatric patients hospitalized with no sucidal risk, and 32 healthy subjects were studied. All of them were assessed by the Suicide Risk Scale (SRS), the Impulsivity Risk Scale (IRS), the Multidimension Anger Inventory (MAI), and the AECOM Coping Scale. A positive correlation was found between suicidal risk and anger and impulsivity. Nevertheless, anger differentiated only between suicidal patients and normals, while impulsivity distinguished suicidal patients from both control groups. The coping styles of suppression, blame, and substitution were positively correlated with suicidal risk, while minimization, mapping, replacement, and reversal had a negative correlation with suicidal risk. Suicidal patients had lower scores of minimization and mapping than the controls. The results indicate that impulsivity is a specific characteristic of suicidal patients. They also have high levels of anger, pessimistic approach to their problems, and difficulties in finding new solutions. It is suggested that these aspects be carefully considered in assessment and treatment of patients with suicidal risk.

NR228 Tuesday, May 24, 12 noon-2:00 p.m.

Childhood Abuse and Suicidal Behavior in Psychiatric Outpatients

Margaret L. Kaplan, Ph.D., Psychiatry ADC, Montifore Medical Center, 111 East 210th Street, Bronx NY 10467-2490; Deborah S. Lipschitz, M.D., Gregory M. Asnis, M.D.

Summary:

Objective: To examine the relationship between suicidal behaviors and childhood histories of physical and sexual abuse in a large general outpatient population.

Method: 251 outpatients registering for treatment completed the Harkavy-Asnis Suicide Survey (HASS), the Traumatic Events Questionnaire (TEQ), the SCL-90-R, and the Dissociative Experiences Questionnaire (DES).

Results: 62 patients (51 females, 11 males) reported a prior suicide attempt. Patients with a history of childhood abuse (n = 128) were significantly more likely than nonabused patients (n = 123) to report a prior suicide attempt ($p = .007$). Suicidal behavior was most prevalent among patients who experienced combined (physical and sexual) abuse in childhood. Patients with combined abuse were more likely than nonabused patients to report past suicide attempts ($p < .001$), more multiple suicide attempts ($p = .007$), more suicidal ideation at a younger age ($p = .001$), and more current suicidal ideation ($p = .01$). Specific characteristics of abuse (e.g. severity and age of onset) were also related to past and current suicidality. Among the abused patients, the suicide attempters could be distinguished from the nonattempters by significantly higher levels of specific symptoms (e.g. interpersonal sensitivity, phobic anxiety, and dissociative symptoms).

Conclusions: Our results suggest that the significant relationship between childhood abuse and subsequent suicidal behavior is mediated by the type and characteristics of the abuse. Symptom profiles may be helpful in determining those abuse patients at risk for self-destructive behavior.

NR229 Tuesday, May 24, 12 noon-2:00 p.m.

Comorbidity in Alcoholics Who Attempted Suicide

Jean-Michel Chignon, M.D., Psychiatry, Hopital Bicuat, 46 Rue Henri Huchard, Paris 75018, France; Patrick M. Martin, Ph.D., Catherine Dissoubray, M.D., Eric Souetie, M.D., Jean Ades, M.D.

Summary:

Objectives: The relationship between alcoholism and suicidal behavior has long been recognized. The present study examined the lifetime prevalence of suicide attempts in alcoholic patients and the impact of comorbidity, namely with depressive anxiety disorders and antisocial personnality disorder in alcoholic patients who attempted suicide.

Methods: In a cross-sectional design including outpatients referred for alcohol abuse or dependance according to DSM-III-R criteria, we used a specific standardized and structured interview allowing DSM-III-R diagnoses.

Results: We included 507 patients (343 males and 164 females). The mean age at the intake of the study was 43.2 (SD:9.6) years without difference between males and females. One hundred twenty-nine patients (25.4%) had attempted suicide during their lifetime. Age of onset of alcoholism was younger in suicide attempters than non ($p \leq .01$), whether in males or females. As regards lifetime comorbidity, major depression was more frequent in alcoholics who attempted suicide (74.8% vs 41.5%; $p \leq .001$). Moreover, we found a higher prevalence for panic disorder and social phobia. When comparing suicide attempt repeaters with other alcoholic suicide attempters, we found a higher prevalence for lifetime generalized anxiety disorder in repeaters (58.7% vs 37.0%; $p \leq .05$) and for antisocial personnality disorder (17.8% vs 5.7%; $p \leq .05$). Conversely, sociodemographic characteristics and lifetime rates of other comorbid disorders were found similar.

The different patterns of comorbidity in alcoholic patients who attempted suicide will be presented and discussed with logistic regression models integrating sociodemographic and clinical parameters.

NR230 Tuesday, May 24, 12 noon-2:00 p.m.

Buspirone Induced Panic: Possible Role of 1 (2-Pyrimidinyl) Piperazine

Jean-Michel Chignon, M.D., Psychiatry, Hopital Bicuat, 46 Rue Henri Huchard, Paris 75018, France; Patrick M. Martin, Ph.D., Jean-Pierre Lepine, M.D.

Summary:

Noradrenergic and serotoninergic (5HT) systems have been implicated in the pathophysiology of panic disorder (PD). Particularly, it has been suggested that a dysfunction of central α_2-adrenoceptors may exist in PD.

Buspirone, which has anxiolytic and antidepressant properties, exerts its effects through interactions with 5HT type 1A receptors. However, this compound is extensively metabolized in 1(2-pyrimidinyl)piperazine (1-PmP), which exhibited α_2 adrenoceptor antagonist effects. In animal studies, buspirone reverses helpless behavior at low and moderate doses. However, higher doses failed to reverse this behavior. In addition, we have shown in a previous study, that 1-PmP antagonizes effects of $5HT_{1A}$ agonists in the learned helplessness paradigm in rats. In humans we reported that buspirone could have panicogenic properties in some PD patients. These effects could be support by an increase of circulating 1-PmP and/or by a hypersensitivity of α_2 adrenoceptors in some PD patients. To test these hypotheses, we compared 1-PmP plasma level one hour after intake of 10 mg of buspirone in two groups of PD patients (n = 20) who panicked (n = 10) or not (n = 10) after intake of buspirone. These two groups of PD patients were matched for sex, age, and duration of current PD episode. The mean of 1-PmP plasma level was found higher in PD patients who had panic attack one hour after intake of 10 mg of buspirone ($p < .01$) suggesting a possible role of different metabolism of buspirone in PD patients.

NR231 Tuesday, May 24, 12 noon-2:00 p.m.

Catecholamine Neurons of Suicides: Ultrastructure

Marietta R. Issidorides, Ph.D., Theodo Theohari Cozzika, Foundation, Neurobiol. Resesearch Inst, Souidias 69 Athens 11521, Greece; Virginia Kriho, B.A., George D. Pappas, Ph.D.

Summary:

A large fall in noradrenaline (NA) concentration in the locus coeruleus (LC) is critically involved in mediating depression. With the potassium permanganate method for EM demonstration of catecholamines, as dense cores inside vesicles, we have shown that numerous large vesicles or globules in the human LC neurons of control brains contain a dense precipitate presumably indicating the presence of the catecholamine. This accumulation of dense core globules in man could represent a high-capacity back-up storage compartment of neurotransmitter necessary for fast NA-mediated collateral inhibition of LC cell bodies by local release, and for meeting increased demands for catecholamine to cope with unpredictable stresses. In the LC of 10 suicides with a diagnosis of major depression, we found that in the neurons the dense core globules were as numerous as into the controls, but their FM density, presumably reflecting NA concentration, was greatly reduced, suggesting a depletion of the stored neurotransmitter. Abnormalities in the ultrastructure of the limiting membranes surrounding the dense bodies, indicating increased fluidity, found in

low cholesterol, support the hypothesis that defective membrane chemistry and structure may be the cause of neurotransmitter leakage and an important biological substratum for the spectrum of dysfunctions characteristic of major depression.

NR232 Tuesday, May 24, 12 noon-2:00 p.m.

Efficacy of Alprazolam in Selective Serotonin Reuptake Inhibitor-Induced Jitteriness

Jay D. Amsterdam, M.D., Psychiatry, Depression Research Unit, 3600 Market St. 8th Fl. USC, Philadelphia PA 19104; Mady Hornig-Rohan, M.D., Greg Maislin, B.S.

Summary:

Background: Selective serotonin re-uptake inhibitors (SSRIs) have become the most widely prescribed antidepressants in the United States. The selective influence of SSRIs on serotonin neurotransmission has resulted in a specific constellation of adverse effects termed "jitteriness" syndrome which occurs in at least 30% of patients taking SSRIs. Because there have been few systematic studies examining treatment of SSRI-induced "jitteriness," we conducted a prospective study of the efficacy of adjunctive alprazolam therapy for fluoxetine-induced "jitteriness" symptoms.

Methods: 54 subjects with major depression were treated with fluoxetine 20 mg daily. Subjects experiencing an increase in "jitteriness" symptoms within two weeks of starting fluoxetine were given adjunctive alprazolam 0.5 mg to 4.0 mg daily for two weeks followed by a two week taper period.

Results: 18 of 54 (33.3%) patients experienced "jitteriness" symptoms during fluoxetine treatment. We observed a statistically significant reduction in the severity ($p = 0.0002$) and number ($p = 0.007$) of "jitteriness" symptoms with adjunctive alprazolam. Moreover, in most cases "jitteriness" symptoms did not reappear during the alprazolam taper period or after alprazolam was discontinued.

Conclusion: These observations suggest that a brief course of adjunctive alprazolam treatment may be efficacious in reducing the duration and severity of "jitteriness" symptoms resulting from antidepressants selective for serotonin.

NR233 Tuesday, May 24, 12 noon-2:00 p.m.

A High-Risk Pilot Study of Social Phobia

Michael A. van Ameringen, M.D., Psychiatry, St. Josephs Hosp 3rd Flr., 50 Charlton Ave E. Fontbonne, Hamilton ON L8N 4A6, Canada; Catherine Mancini, M.D., Peter Szatmari, M.D., Christina Fugere, B.Sc., Michael H. Boyle, Ph.D.

Summary:

Children of patients suffering from social phobia were studied to determine whether they are at increased risk for developing psychiatric disorders. Twenty-six outpatients with a primary DSM-III-R diagnosis of social phobia, and at least one child between the ages of 4 and 18, participated in the study. Information was collected from parents and from children between 12 and 18 years of age. Diagnoses in the children were made by a best-estimate method, using parent and child reports from a modified Anxiety Disorders Interview Schedule for Children, the Child Behaviour Checklist, the Current Self-Report Childhood Inhibition Scale, and the Alcohol Dependence Survey. Of the 47 children, 49% had at least one lifetime anxiety disorder diagnosis. The most common diagnoses were overanxious disorder (30%), social phobia (23%), and separation anxiety disorder (19%). Sixty-five percent meeting anxiety disorder criteria had more than one anxiety disorder diagnosis. Lifetime major depression was found in 8.5% of the children. Parents whose children met criteria for an anxiety disorder had a greater mean number of comorbid diagnoses, than did parents of unaffected children. This pilot study suggests that a substantial risk for psychiatric disorder may exist in children of social phobics. Further studies incorporating direct interviews of the children and a control group are needed.

NR234 Tuesday, May 24, 12 noon-2:00 p.m.

Serotonin Reuptake Inhibitors Are Superior to Alprazolam and Imipramine in Panic: A Meta-analysis

William F. Boyer, M.D., Psychiatry, Atlanta VAMC, 1670 Clairmont Road, Decatur GA 30033;

Summary:

The etiology and optimum treatment of panic disorder remain unclear. Imipramine and alprazolam are reasonably well-established treatments. Several reports have suggested that serotonin reuptake inhibitors may also be effective for this condition. To investigate this issue, 26 published or presented placebo-controlled, double-blind studies of serotonin reuptake inhibitors, imipramine or alprazolam, in DSM-III or DSM-III-R panic disorder, were subjected to meta-analysis (N = 2295). The serotonin reuptake inhibitors included paroxetine, fluvoxamine, zimeldine, and clomipramine. All three treatments were highly significantly superior to placebo in alleviating panic. The combined p values were $p = 0.00000002$ for alprazolam, $p = 0.0000003$ for imipramine and $p = 0.000000000000003$ for serotonin reuptake inhibitors. The serotonin reuptake inhibitors were also significantly superior to both imipramine ($p = 0.0004$) and alprazolam ($p = 0.004$). The superiority over imipramine was less pronounced when imipramine studies were limited to those with average doses of more than 150 mg/day ($p = 0.04$). These results underscore the importance of serotonin reuptake inhibitors in the treatment of panic disorder and indirectly suggest that serotonergic abnormalities may have a role in its etiology.

NR235 Tuesday, May 24, 12 noon-2:00 p.m.

Childhood Shyness and Psychophysiological Disorders: Personal and Family Psychiatric and Medical Histories

Iris R. Bell, M.D., Psychiatry, Univ. of Arizona, 1501 N. Campbell Ave RM 7402, Tucso AZ 85724; Gary E. Schwartz, Ph.D., Julie M. Peterson, B.S.

Summary:

Objective: The present study compared young adults with differing degrees of self-reported childhood and current inhibition (cf., shyness) for personal and family psychiatric and medical diagnoses. Previous studies of inhibited children suggest increased rates of anxiety, depression, allergies, colic, constipation, and insomnia.

Method: As part of the course requirements for an introductory psychology course, 547 students completed the Reznick et al. (1992). Restrospective Self-Report of Inhibition (re: childhood) and the Adult Self-Report of Inhibition (re: current status), as well as a checklist of physician-diagnosed psychiatric and medical conditions.

Results: The sample (age 19 ± 3 yrs; 65% women) was divided into two sets of qualities on the basis of scores on each of the inhibition measures; there were more women in the most inhibited groups on both scales. Fifty-five percent of those most inhibited in childhood remained so as young adults; 59% of those most uninhibited in childhood remained so as young adults. Those most inhibited as children reported the highest rates of personal and family diagnoses of depression (respectively, 17%, $p = 0.00007$; 25%, $p = 0.01$), anxiety (10%, $p = 0.004$; 15%, $p = 0.01$), irritable bowel (12%, $p = 0.03$; 19%, $p = 0.003$), and migraine headache (21%, $p = 0.03$; 42%, $p = 0.04$), with more family panic disorders (9%, $p = 0.01$) and premenstrual syndrome (42%, $p = 0.003$) and a trend toward more family histories of hyperactivity (9%, p =

0.06). In contrast, quartile division of the sample on the basis of current inhibition detected personal, but not family, histories of increased depression and anxiety in the most inhibited. The most currently inhibited reported the highest prevalence of personal and family irritable bowel, but no personal differences on migraine, with only a trend toward more family migraine. Neither childhood nor current inhibition quantities found group differences in personal alcohol or drug problems, but the currently most inhibited group showed a trend toward more family alcohol problems ($p = 0.08$).

Conclusions: The retrospective childhood measure of inhibition appears more capable than is the current adulthood measure of the same construct of detecting generic factors in temperament and health, especially psychiatric disorders.

NR236 Tuesday, May 24, 12 noon-2:00 p.m.

Phenomenology of OCD and Tourette's Syndrome

Euripedes C. Miguel, M.D., Psychiatry, Harvard Medical School, MGH East Bldg 149 13th St 9th, Charleston MA 02129; Barbara J. Coffey, M.D., Lee Baer, Ph.D., Cary R. Savage, Ph.D., Scott L. Rauch, M.D., Michael A. Jenike, M.D.

Summary:

Objective: The purpose of this study was to test the following hypotheses: intentional repetitive behaviors (i.e.: behaviors always performed intentionally and in a stereotyped manner) are: 1) preceded by cognitive phenomena (i.e., ideas, thoughts, or images) and autonomic anxiety, but not sensory phenomena (i.e., generalized and local uncomfortable sensations) in OCD without comorbid TS, and 2) preceded by sensory phenomena, but not cognitive phenomena nor autonomic anxiety in TS without comorbid OCD.

Method: Fifteen adult outpatients with OCD without tics and 17 adult TS patients without OCD were evaluated. A semistructured interview assessed cognitive, sensory, and affective experiences.

Results: Five out of 17 TS subjects were excluded because they had only unintentional tics. All OCD patients reported cognitions preceding their intentional repetitive behaviors, whereas only two out of 12 TS patients reported cognitions. Sensory phenomena preceding repetitive behaviors were found only in all TS subjects. Thirteen OCD subjects reported at least mild autonomic anxiety preceding repetitive behaviors, whereas no TS patients reported such symptoms.

Conclusions: Intentional repetitive behaviors in OCD differ from those in TS and are associated with cognitive and affective phenomena. Sensory phenomena preceded intentional repetitive behaviors in TS but not in OCD patients.

NR237 Tuesday, May 24, 12 noon-2:00 p.m.

Comorbidity of OCD and Personality Disorders

Albina R. Torres, M.D., Psychiatry, FMB UNESP, Rubiao Jr., Botucatu SP 18618-000, Brazil; Jose A. Del Porto, M.D.

Summary:

The aim of this study was to evaluate the presence of personality disorders in 40 patients with obsessive compulsive disorder (DSM-III-R criteria) from the Medical School of Botucatu (UNESP), Brazil. They were 24 women and 16 men, 16 to 68 years old, referred to our outpatient psychiatric service for treatment. Controls were 40 nonpsychiatric outpatients matched by sex, age, and marital status. The instrument used was the Portuguese version of the Structured Interview for DSM-III-R Personality Disorders (SIDP-R). All interviews ($n = 80$) were made simultaneously by two raters, with independent scoring so that the interrater reliability (KAPPA) of the instrument could be assessed. The consensual Axis II diagnoses in the OCD group were: avoidant (52, 5%, K = 0, 80), dependent (40%, K = 0, 83), histrionic (20%, K = 0, 83), paranoid (20%, K = 0, 74), obsessive compulsive (17, 5%, K = 0, 86), narcisistic (7, 5%, K = 1, 00) schizototypal (5%, K = 0, 65), passive-aggressive (5%, K= 0, 79) and self-defeating (5%, K = 0, 55). Only six controls had a PD diagnosis. A great deal of diagnostic overlap was found in the OCD group, especially between avoidant and dependent PDs, that seems to be secondary to the OCD. The study also suggests that there is not a close relationship between OCD and OCPD. Patients with OCPD or even three or four O C, personality traits had significantly less insight about their obsessions and compulsions.

NR238 Tuesday, May 24, 12 noon-2:00 p.m.

Relationship of Panic to Suicide in an Emergency Psychiatry Population: Demographic Data

Joseph J. Zealberg, M.D., Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425; Susan J. Hardesty, M.D.

Summary:

Emergency psychiatrists are challenged with identifying potentially suicidal patients each day. Recent studies suggest that panic may be a predictor for imminent suicidality. Although much is known about prevalence of panic in normal populations, there are no data for psychiatric emergency populations.

We present a one-year, prospective study of panic in relationship to suicidality in a psychiatric emergency population that includes all patients, aged 18 and over, seen by our psychiatric emergency service. Raters include psychiatric residents "on call" to the emergency room and mobile psychiatry emergency clinicians who see patients in the emergency room and in the field. The study instrument is a questionnaire adapted from the SCID panic module, tailored to be "user-friendly" and to require three to five minutes to administer in a clinical setting.

Preliminary data analysis ($N = 225$) reveals significant association between lifetime suicide attempts and lifetime prevalence of panic (Pearson Chi-Square significance $p = .009$). Lifetime prevalence of panic in our study population (11%) appears markedly greater than NIMH-ECA prevalence of 1.4% for general populations.

These early data suggest that screening for panic may be an important variable in the emergency assessment and care of suicidal patients. When the study ends, we will present complete data from over 1,500 questionnaires.

NR239 Tuesday, May 24, 12 noon-2:00 p.m.

Platelet Benzodiazepine Receptors in PTSD

Ronit Weizman, M.D., Mental Health Center, 9 Hatzvi St. Ramat Hatayassim, Tel Aviv 67197, Israel; Nathaniel Laor, M.D., Miri Bidder, M.D., Uri Muller, M.D., Ahuva Reiss, M.D., Moshe Gavish, Ph.D.

Summary:

Objective: Mitochondrial benzodiazepine receptors (MBR) are involved in steroidogenesis and are sensitive to stress. A decrease in platelet MBR density was previously demonstrated in patients with generalized anxiety disorder (GAD). We measured platelet MBR density in another anxiety disorder, namely, post-traumatic stress disorder (PTSD).

Method: Eighteen post-Gulf War PTSD patients and 17 age- and sex-matched controls participated in the study. The severity of symptoms was assessed using the DSM-III-R scale for PTSD, Impact of Event Scale, Beck Depression Inventory, and the State-Trait Anxiety Inventory. [^{3}H]PK 11195 was used to label platelet MBR.

Results: The psychological parameters were significantly higher in the PTSD patients compared with controls. A significant decrease ($P < 0.001$) in platelet MBR density was observed in the patients when compared with the control group.

Conclusion: The reduced platelet MBR density in PTSD patients is in accordance with the previous findings in GAD patients. It is possible that the long-term sympathetic hyperactivity is responsible for the reduction in MBR density.

NR240 Tuesday, May 24, 12 noon-2:00 p.m.

Platelet Imipramine Binding in PTSD

Ronit Weizman, M.D., Mental Health Center, 9 Hatzvi St. Ramat Hatayasim, Tel Aviv, Israel; Nathaniel Laor, M.D., Ayala Schvjovitzry, M.D., Leo Wolmer, M.D., Pnina Abramovitz-Schnaider, M.D., Moshe Rehavi, Ph.D.

Summary:

Objective: Patients with post-traumatic stress disorder (PTSD) also suffer frequently from major depression (MD). The beneficial effect of monoamine oxidase inhibitors (MAOIs) in PTSD is controversial. The present study assessed platelet imipramine binding in PTSD patients before and after phenelzine treatment.

Method: Ten PTSD patients and 10 control subjects participated in the study. All subjects were interviewed using the Structured Clinical Interview for DSM-III-R-Patient Version. Severity of symptoms was assessed before and after four weeks of phenelzine treatment, using the Impact of Event Scale (IES), Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAI). Blood for platelet [^{3}H]Imipramine binding was drawn at pre- and post-treatment time points.

Results: All the psychological measures were significantly higher in the PTSD patients as compared with controls. Comparison of pre- and post-treatment symptom severity did not reveal any significant difference. Platelet imipramine binding density was similar in untreated patients and controls, and phenelzine treatment did not induce any alteration.

Conclusions: It might be that the depression observed in PTSD is phenomenologically similar to that observed in MD, but has a distinctly different biological underpinning. The beneficial effect of phenelzine reported by several investigators seems to be unrelated to modulatory effect on the expression of the membranal serotonin transporter.

NR241 Tuesday, May 24, 12 noon-2:00 p.m.

Conditionability and Post-Traumatic Stress

Tuvia Peri, M.A., Psychiatry, Hadas Sah Univ Hospital, P.O. Box 12000, Jerusalem 91120; Gershon Bensachar, Ph.D., Arieh Y. Shalev, M.D.

Summary:

Classical conditioning is one of the mechanisms linking the PTSD syndrome to the precipitating trauma. Learned responses in PTSD, however, often do not extinguish with time and may extend to additional cues. PTSD patients' propensity to form conditioned responses to nontraumatic stimuli has not been studied. Using a differential conditioning paradigm, we exposed 13 PTSD and 10 control subjects to colored light CSs followed after 0.5 sec by binaural 105 dB white noise UCSs. Four familiarization trials (two CS+ and two CS−) preceded 18 acquisition trials (8 CS+ and 10 CS−) intermingled with 2 "CR" test trials (CS+ without UCS), followed by 12 extinction trials (6 CS+ and 6 CS−). Skin conductance responses (SCRs) in square root μSiemens were measured 1–4 seconds after each trial. PTSD subjects did not differ from controls in resting SC or SCRs to the familiarization trials. PTSD subjects showed higher responses to the 8 CS+ acquisition trials (0.63 mean ± 0.19 SD) vs. 0.35 ± 0.28, $t(21) = 2.8$, $p < .01$); the 2 CR test trials (0.34 ± 0.16 vs. 0.18 ± 0.11, $t(21) = 2.86$, $p < .01$), the 6 CS+ extinction trials (0.25 ± 0.11 vs. 0.16 ± 0.09, $t(21) = 2.14$, $p < .05$), and the first five CS- acquisition trials ($p = .06$). Hence, PTSD subjects acquired stronger conditioned responses that extinguished less well, and also generalized to early CS− cues. These results support a role for heightened conditionability in the pathogenesis and pathophysiology of PTSD.

NR242 Tuesday, May 24, 12 noon-2:00 p.m.

Trauma and PTSD in Female Psychiatric Inpatients

Jean-Michel Darves-Bornoz, CPU Psychiatry, University De Toors, CHRU De Tours 12 Rue Du Coq, St Cyr Sur Loire 37542, France; Patricia Ayache, M.D., Andree Degiovanni, M.D., Jean-Pierre Lepine, M.D.

Summary:

Clinical practice indicates that trauma in frequent in psychiatric patients. However, the occurrence and the impact of trauma in these patients are not often studied, whatever the main diagnosis.

Fifty-eight female psychiatric inpatients consecutively hospitalized in a university hospital department of psychiatry (18–84 years old, mean age 40 years) were interviewed by two psychiatrists with a clinician-rated battery of instruments (among them the S1-PTSD, Structured Interview for Posttraumatic Stress Disorder of Davidson et al.) and with a semistructured questionnaire related to social and clinical data. The DSM-III-R diagnoses leading to hospitalization were: psychoses 40% (schizophrenic, schizophreniform, schizoaffective, schizoid, and paranoid delusional disorders as well as bipolar disorder); borderline and narcissistic personalities 7%; and other disorders 53% (including mood, anxiety, eating, somatoform, dissociative, factitious, alcohol-related, and personality disorders).

Trauma appeared to be an important issue for psychiatric inpatients. Among the results, we observed that 59% of these patients had experienced at least one major stressful event (rape 26%, other sexual assault 29%, physical assault 31%, seeing somebody dying in a violent way 8%, war scene 2%, injured in an accident 2%). As a consequence, 61% of these victims of trauma have suffered from post-traumatic stress disorder during their lifetime (36% of the whole sample) and the diagnosis of post-traumatic stress disorder was still present in 21% (12% of the whole sample). In addition, we found that within the comorbidity of these inpatients, somatoform disorders and dissociative disorders were significantly present in the group who had experienced a trauma.

This clinical study encourages a deeper examination of the way of psychopathological field of trauma (including PTSD, dissociation and somatization) plays a role in many nosological categories that are not directly linked to trauma.

NR243 Tuesday, May 24, 12 noon-2:00 p.m.

A Double-Blind Placebo-Controlled Pilot Study of Fluoxetine for Panic Disorder

Duncan B. Clark, M.D., Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213; Rolf G. Jacob, M.D.

Summary:

Fluoxetine has shown promise for treating panic disorder in clinical reports (Gorman, et al., 1987; Schneier, et al., 1990). This was a double-blind, placebo-controlled study testing fluoxetine for panic disorder. After a drug-free baseline assessment, 20 panic disorder subjects without depression were randomly assigned to one of three 12-week treatment conditions: 1) fluoxetine 20 mg q.d. ($n = 7$), 2) fluoxetine 20 mg q.o.d. ($n = 6$) or 3) placebo ($n = 7$). Subjects completing at least six weeks of treatment were included in analyses ($n = 6,2,5$, respectively). Stated reasons for dropping out including scheduling difficulties ($n = 3$), fears following

news accounts linking fluoxetine and suicide (n = 2), lack of effectiveness (n = 1) and side effects (n = 1). The small number of subjects necessitated combining fluoxetine groups. Panic attack frequency and severity, determined by an independent blind evaluator, were used to calculate a Panic Index (frequency × severity). The percent change in the Panic Index was significantly different between groups (87% vs. 56%, respectively; t = 2.8, p = .02). While the study has several limitations, the results suggest that fluoxetine may be effective in reducing panic symptoms. Supported by NIMH grants MH30915 and MH19816.

NR244 Tuesday, May 24, 12 noon-2:00 p.m.

Soft Signs in OCD

Margo L. Thienemann, M.D., Psychiatry, Stanford University, 101 Quarry Road, Stanford CA 94304; Lorrin M. Koran, M.D.

Summary:

We sought to test two hypotheses: 1) the presence of numerous or particular soft signs predicts poor outcome to medication treatment, and 2) soft signs improve in medication responders. We also intended to replicate previous findings of neurological soft signs and psychometric abnormalities in subjects with obsessive compulsive disorder (OCD). We administered a battery of five neurological soft sign examinations and two neuropsychological tests to 21 adult outpatient OCD subjects before and after 10- to 12-week trials with serotonin reuptake blockers. We found that: a) soft signs were present in our subjects. (average number = 1.8, with prevalences of finger to finger: 10%, mirror movements: 33%, adventitious movements: 29%, agraphesthesia: 76%, and impaired cube drawing: 33%). The Stroop Color Word Test and Controlled Oral Word Association Test (COWAT) were abnormal in 10% and 14%. b) Neither specific soft sign, the number of signs, nor a combination of signs predicted poorer outcome to medication trial. Some findings (finger to finger, adventitious movements, Stroop and COWAT) became undetectable in medication responders, but this effect was statisically insignificant. Further study is planned to delineate the relationship between demonstrated neurological findings and the etiology, course, and treatment outcome of OCD.

NR245 Tuesday, May 24, 12 noon-2:00 p.m.

Sleep and Noradrenergic Measures in Chronic PTSD

Thomas A. Mellman, M.D., Psychiatry, Miami VA Medical Center, 1201 NW 16th Street, Miami FL 33125; Adarsh Kumar, M.D., Renee Kulick-Bell, B.A., Mahendra Kumar, Ph.D., Bruce Nolan, M.D.

Summary:

Prominent heightened arousal symptoms and findings from clinical/laboratory studies implicate the central noradrenergic systems in the pathophysiology of post-traumatic stress disorder (PTSD). Heightened arousal frequently manifests in relation to sleep in PTSD. Arousal levels during sleep are in part regulated by noradrenergic systems. In order to evaluate noradrenergic production in relation to sleep/wake activity, we obtained nocturnal/daytime urine splits with overnight sleep studies in PTSD patients and controls.

Twenty Vietnam veteran patients diagnosed with combat-related PTSD and eight non-ill, non-combat-exposed controls had overnight sleep studies. In association with sleep recording, subjects saved their urine for 24 hours in three, eight-hour collections for determining "daytime" (8AM to 4PM, 4PM to MN) and "nocturnal" (MN to 8AM) noradrenergic production.

PTSD patients had impaired sleep maintenance relative to controls and increased REM density. Twenty-four-hour norepinephrine and MHPG (the more centrally derived metabolite) did not differ between patients and controls. "Nocturnal" minus mean "daytime" MHPG was negative in the controls, slightly positive in the patients, and differed significantly between the two groups. "Nocturnal" MHPG correlated negatively with total sleep time in the PTSD patients ($R = -.43$, $p < .06$), while correlating only weakly with time in bed.

Our data support a relationship between nondiminished central noradrenergic activity at night and sleep disturbance in chronic, combat-related PTSD.

NR246 Tuesday, May 24, 12 noon-2:00 p.m.

Sertraline or Fluoxetine in the Treatment of PTSD: Early Responses Positive and Negative

Neal A. Kline, M.D., Psychiatry, Univ of Calif. San Diego, 9500 Gilman Drive Dept 0603, La Jolla CA 92093

Summary:

Objective: With post-traumatic stress disorder (PTSD) characterized by hyperarousal, prescribing a selective serotonin reuptake inhibitor (SSRI) might seem counterintuitive for clinicians who consider SSRIs "activating" antidepressants. At the first return visit, two to three weeks after being prescribed either sertraline or fluoxetine for PTSD, might hyperarousal be improved or worsened?

Method: Twelve combat veterans with PTSD, seen sequentially at our Department of Veterans Affairs outpatient PTSD clinic for psychopharmacological consultation, were randomly assigned to two tracks: six to sertraline 50 mg qd; and six to fluoxetine 20 mg qd. Exclusion criteria for this open-label pilot study were: active substance or alcohol abuse, bipolar affective disorder, psychotic disorders, organic mental disorders, and current use of SSRIs.

Results: At the first return visit, each subject was assessed with the Clinical Global Impression Scale (CGI) for improvement. Scores for the sertraline group were: 1, 2, 3, 3, 5, 7; fluoxetine: 2, 3, 5, 5, 5, 6. Four (67%) of the sertraline group were "improved"; two (33%) of the six were "worse." Two (33%) of the fluoxetine group were "improved"; four (67%) of that six were "worse." Improvement was characterized almost universally as: "I feel calm," or "less depressed." Adverse effects were usually as: "I feel revved up," or dissociated ("weird," "not myself," "numb").

Conclusion: Across both groups, PTSD hyperarousal was heterogeneously impacted by SSRIs during the first two to three weeks of treatment: six (50%) of 12 combat veterans were more symptomatic; six (50%) of 12 had symptom relief. Comparison of sertraline with fluoxetine regarding early effects in PTSD must await significant sample size and controlled study conditions.

NR247 Tuesday, May 24, 12 noon-2:00 p.m.

Panic Disorder and/or Epilepsy: Can Anticonvulsives Play a Role in the Treatment of Panic Disorder?

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Summary:

Objective: Positive relations between panic disorder (PD) and epilepsy (E) have been hypothesized to be due to many symptomatic and pathophysiological features the disorders have in common (Weilburg 1987). The ictal symptomatology, the cooccurrence of vegetative and psychological symptoms, the often chronic course, and brain dysfunctions documented in both disorders suggest their relation.

Method: We present three patients with a typical symptomatology of PD and a history of successfully treated juvenile E. Patients are three women, 23, 29, and 31 years of age. Two of them had

had partial complex and secondarily generalized, one had had absences and abortive grand mal seizures. All had focal EEG abnormalities documented for several years. In one patient morphologic brain abnormalities were found in MRI scans. All patients had been free of seizures at subtherapeutic or low-range anticonvulsive plasma levels (carbamazepine, phenytoin, phenobarbital) for more than ten years when panic attacks appeared. In two of the three cases significant agoraphobic avoidance developed secondary to the onset of panic attacks.

Results: Increasing anticonvulsive medication to therapeutic levels resulted in complete remission of panic attacks and of agoraphobic avoidance. Patients were symptom free at 12-month follow up.

Conclusions: The positive therapeutic response of panic attacks to the described anticonvulsive treatment might suggest a pathophysiologic relation between the two conditions, at least in our patients. It is discussed whether panic attacks in these patients have to be considered as an independent pathological entity or as part of the epileptic phenomenology. We hypothesize, that in a subgroup of PD patients, panic symptomatology represents a state of increased excitability of limbic system structures. Although one study in PD showed a lack of efficacy of carbamazepine (Unde 1988), there is evidence that especially in therapy-refractory cases different anticonvulsive medications might be useful (e.g. Keck 1992). We therefore suggest further research into the positive role of anticonvulsive substances in the treatment of PD.

NR248 Tuesday, May 24, 12 noon-2:00 p.m.

Psychosis with PTSD

Nita Kumar, M. D., Psychiatry, Miami VA Medical Center, 1201 NW 16th Street, Miami FL 33125; Gary S. Kutcher, Ph.D., Thomas A. Mellman, M.D.

Summary:

PTSD is categorized as an anxiety disorder and is not typically considered to feature psychotic symptoms. However, there are anecdotal reports of, and we have observed, psychotic symptoms in association with PTSD.

The goal of the study was to examine the frequency and character of psychotic symptoms in an inpatient veteran population and to address whether psychosis is accounted for comorbid diagnoses of schizophrenia, mood disorder, substance abuse, or is a primary manifestation of a PTSD subtype.

Sixty veterans participating in a specialized inpatient PTSD unit were interviewed to confirm the diagnosis of PTSD and screen for psychotic symptoms. PTSD patients with psychosis were then more formally assessed by the Structured Clinical Interview for DSM-III-R.

One patient nonspecifically endorsed symptoms and was felt to have a factitious or malingering presentation. An additional eight patients reported psychotic symptoms including auditory and visual hallucinations and persecutory delusions. The content of psychotic symptoms focused on guilt and loss. None of the patients manifested gross impairment of reality testing or formal thought disorder.

All patients with psychotic symptoms had episodes of major depression, which did not invariably temporally overlap. In one case, psychosis appeared to be contributed to by substance abuse. This patient was the only subject who met criteria for schizophrenia (paranoid subtype).

Our data suggest that psychosis with chronic PTSD is not typically accounted for by schizophrenia or substance abuse. It is possible that these psychotic symptoms are related to an affective disorder or represent a subtype of severe PTSD.

NR249 Tuesday, May 24, 12 noon-2:00 p.m.

Hypercholesterolemia in Female Inpatients with PTSD

M. Michele Murburg, M.D., 323A-MP Pava, Natl. Center for PTSD, 3801 Miranda Avenue, Palo Alto CA 94304; Judith Stewart, Ph.D., Susan A. Ballagh, M.D.

Summary:

Objective: To determine the incidence of hypercholesterolemia in female inpatients with PTSD, with and without panic symptoms.

Method: We assessed serum cholesterol 24 to 48 hours following admission in 18 fasting, nondiabetic, euthyroid female inpatients, aged 24 to 52, who met DSM-III-R criteria for PTSD, and who were admitted consecutively to the Women's Trauma Recovery Program at the National Center for PTSD.

Results: Thirteen (75%) had fasting cholesterol values above 200 mg/dl (range 144–269; $\mu \pm SEM = 216 \pm 8.4$). Eleven met DSM-III-R criteria for panic disorder (PD) by the SCID-P; three others had panic attacks (PA) without meeting criteria for PD, so that 78% of our sample had PD or PA. Among the 13 hypercholesterolemic women, 10 met criteria for PD, and two more had PA without PD, so that 93% of the hypercholesterolemic patients (vs. 20% of the eucholesterolemic patients) had either PD or PA. Patients (N = 14) with PD or PA had significantly higher cholesterol levels (mean ± SEM = 228 ± 7.0mg/dl) than patients without associated panic (184 ± 24.0mg/dl) ($t = 2.47$; $p \leq 025$). Serum cholesterol failed to correlate with age or serum glucose in our population. Serum cholesterol correlated positively with the re-experiencing subscale of the CAPS (CAPSR) ($r = 0.619$; $p \leq .01$), but not Avoidance or Arousal subscales. There was a trend ($t = 2.05$; $p \leq .06$) for a higher CAPSR score in patients with PD/PA (3.42 ± 0.26) compared to those without (2.25 ± 0.63) PD/PA.

Conclusions: Women with PTSD, particularly those who have associated panic symptoms, have a high incidence of hypercholesterolemia.

NR250 Tuesday, May 24, 12 noon-2:00 p.m.

Clinician Administered PTSD Scale Weekly: Reliability, Validity, and Sensitivity to Change

Linda M. Nagy, M.D., Psychiatry, VA Medical Center, 950 Campbell Avenue 116A, West Haven CT 06516; Dudley Blake, Ph.D., Steven M. Southwick, M.D., Frank Weathers, Ph.D., Terry Keane, Ph.D. Fred Gusman, M.S.W., Dennis S. Charney, M.D.

Summary:

This study explores psychometric properties of the Clinician Administered PTSD Scale—Weekly Version (CAPS-2), an instrument developed as a weekly rating scale of symptom severity and change for treatment efficacy studies in post-traumatic stress disorder (PTSD).

Methods: The CAPS-2 was administered to two veteran populations with PTSD: patients participating in a pharmacologic treatment trial for PTSD in CT (N = 20; Nagy et al, 1993) and inpatients participating in a neurohormone study in CA (N = 36). Patients were also administered the Impact of Event Scale (IES), and depression and anxiety ratings. An inter-rater reliability study is underway.

Results: Cronbach's alpha for the CAPS-2 total was .79 and was lowest for reexperiencing. Item-total correlations for the 17 PTSD items ranged from .15 to .57. A modest correlation was found between CAPS-2 and IES-totals ($r = .37$, $p < .01$), CAPS-2 reexperiencing and IES-intrusion subscale ($r = .36$, $p < .01$), and CAPS-2 avoidant/numbing and IES-avoidant subscale ($r = .37$, $p < .01$). Correlations with Hamilton depression ($r = .34$) and anxiety ($r = .36$) ratings were not significant. The CAPS-2 total score and each of the three subscales showed significant change

over time in the treatment trial (for total: $f = 7.2$, $p < .001$), consistent with change in the global improvement rating. Preliminary data on inter-rater reliability will be presented.

Conclusions: These data suggest that the CAPS-2 posesses adequate psychometric integrity and high treatment validity (sensitivity to change) and is a valuable tool for assessment of PTSD in clinical trials.

NR251 Tuesday, May 24, 12 noon-2:00 p.m.

Uncoupling of the Noradrenergic: HPA Axis in Panic Disorder Patients

Jeremy D. Coplan, M.D., Psychiatry, Columbia University NYSPI, 722 West 168th Street Unit 13, New York NY 10032; Daniel Pine, M.D., Laszlo A. Papp, M.D., Donald F. Klein, M.D., Jack M. Gorman, M.D.

Summary:

As both noradrenergic (NA) and HPA overactivity have been implicated in panic disorder (PD), their relationship was examined. Sixteen PD patients and 16 healthy volunteers were challenged 12 weeks apart with oral clonidine (13 from each group repeated the challenge). PD patients were treated with fluoxetine between challenges. Correlational matrices examined the relationship between the 1st and 2nd baseline serum MHPG and cortisol values and the peak (delta) MHPG and cortisol response values during both clonidine challenges. In the controls, 12 of 16 possible correlations at the trend or significant level were noted indicating that, irrespective of challenge, high baseline and delta MHPG was associated with high baseline and delta cortisol. In the PD patients, no similar correlations were observed. Fisher r to z transformations showed 6 of 16 correlations to be more strongly correlated in the controls than patients. In fact, in patients, significant "reverse" coupling was noted following fluoxetine, such that greater delta cortisol was associated with lower delta MHPG. These data raise the possibility that poor or aberrant coupling of the NA system and the HPA axis may be a persistent feature of PD, even following remission. Implications for suboptimal control of the HPA axis during stress in PD are discussed.

NR252 Tuesday, May 24, 12 noon-2:00 p.m.

Carbon Dioxide-Induced Panic and Lack of Cortisol Response

Jeremy D. Coplan, M.D., Psychiatry, Columbia University NYSPI, 722 West 168th Street Unit 13, New York NY 10032; Daniel Pine, M.D., Laszlo A. Papp, M.D., Jose Martinez, M.A., Donald F. Klein, M.D., Jack M. Gorman, M.D.

Summary:

Supporting the view that panic attacks are distinguishable from natural stressors that activate the HPA axis, cortisol levels regularly decrease during lactate-induced panic. We examined blood cortisol levels during CO_2 inhalation, which also provokes panic, but volumetric factors are not a consideration as they are during lactate infusion. The means of cortisol values from 5% and 7% CO_2 inhalation procedures were used if both were available. Cortisol levels drawn prior to CO_2 inhalation and at the point-of-panic in 10 PD subjects decreased significantly ($p < .015$). No reductions were noted after 20 minutes of CO_2 inhalation in either eight normal controls or nine non-panicking PD patients. However, in eight non-PD anxiety disorder subjects who did not panic to CO_2 inhalation, cortisol levels also dropped significantly ($p < .0025$) following the 20-minute CO_2 inhalation procedure. Voluntary hyperventilation, which did not provoke panic in any subjects, tended to increase cortisol in normal controls ($n = 4$) and decrease cortisol in anxiety-disordered subjects ($n = 8$) (interactive effect; $p < .005$). These preliminary data suggest that hemodilution cannot alone account for the absence of corticoid response during panic induced by "respiratory" panicogens. Future studies are required to replicate and characterize these findings and investigate further abnormal ventilatory/HPA interaction in anxiety disorders.

NR253 Tuesday, May 24, 12 noon-2:00 p.m.

SPECT Changes After Behavior Therapy or Clomipramine Treatment in OCD

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Summary:

Baxter et al. reported that OCD patients showed similar PET scan improvement when treated with either medication or behavior therapy. Our replication used SPECT scans instead of PET, adding frontal lobe tests (Wisconsin Card Sort, FAS, Ruff Figural Fluency) pre- and post-treatment as another method to study functional change. Subjects meeting DSM-III-R OCD criteria received pre-treatment Yale-Brown Obsessive Compulsive Score (YBOCS), and neuropsychological tests (WCST, FAS, Ruff Figural Fluency, Trails A & B), then underwent resting SPECT on TRIAD (HMPAO radiotracer). SPECT was analyzed as described by Rubin et al. Five age-matched normal volunteers underwent a SPECT scan. OCD patients were assigned clomipramine ($n = 7$; maximum recommended/tolerated clomipramine dose used), or behavior therapy ($n = 9$). Behavior therapy was modified from Foa, et al. After 12 weeks active treatment, all but one showed clinical improvement on YBOCS. Pre-treatment SPECT frontal and temporal areas of OCD patients did not differ significantly from normal controls. Right and left frontal areas did change significantly from pre to post treatment, but in opposite directions for two groups. Post-treatment frontal lobe activity decreased in the medication group but increased with behavior therapy. There was noteworthy variation in results of neuropsychological frontal lobe tests. Explanations are discussed.

NR254 Tuesday, May 24, 12 noon-2:00 p.m.

Panic Disorder During Pregnancy and the Puerperium: A Prospective Study

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Introduction: Pregnancy has frequently been referred to as a time of emotional well-being for women, providing a "protective effect" against emerging psychiatric disorder. While anecdotal and retrospective reports suggest that women may experience diminished symptoms of panic attacks during pregnancy, some investigators describe a more variable course of panic disorder during pregnancy, with persistence of anxiety symptoms, particularly in those patients with histories of severe pregravid panic disorder.

Methods: This report describes the course of panic disorder in the first 10 women with pregravid panic disorder prospectively followed in a naturalistic study of anxiety disorders during pregnancy and the puerperium. Demographic information and data regarding personal and family history of psychiatric disorder were obtained. The Structured Clinical Interview for Diagnosis (SCID) was administered at designated intervals across pregnancy and at three-month intervals during the first postpartum year. Clinical status was also assessed across pregnancy and the puerperium using the Clinical Global Impression (CGI). Pharmacotherapy (if any) across pregnancy and the puerperium was noted.

Results: Seven of 10 patients met criteria for panic disorder during all trimesters of pregnancy; one patient was noted to be in remission during pregnancy, while two had variable courses. Six of the 10 patients increased or maintained treatment with antipanic agents during pregnancy. Of those patients who were not treated with antipanic drugs (N = 3) or who decreased intensity of pharmacotherapy during pregnancy (N = 1), only one failed to meet criteria for panic disorder during pregnancy. During the postpartum period, all but one patient was noted to meet criteria for panic disorder, and most (N = 7) experienced symptoms requiring increased intensity of antipanic therapy.

Conclusion: Pregnancy may not be salutary with respect to persistence of panic attacks particularly in women with histories of pregravid panic disorder. As in patients with histories of mood disorder, patients with pregravid anxiety disorders may be at risk for postpartum worsening of their illnesses and may require intensification of treatment.

NR255 Tuesday, May 24, 12 noon-2:00 p.m.

Avoidance of the Present in the Dreams of Vietnam Veterans with PTSD and Depression

Bruce M. Dow, M.D., Psychiatry, VA Medical Ctr. and UCSD, La Jolla Village Drive, La Jolla CA 92161; J. Christian Gillin, M.D.

Summary:

Introduction: Beck and Ward (1961) reported that the dreams of patients with depression were characterized by "masochistic" themes, of being disappointed, rejected, or injured. Our study was undertaken to examine the dream content of Vietnam veterans with both post-traumatic stress disorder (PTSD) and major depression (MDD).

Methods: Three groups were studied: Vietnam veterans with PTSD and MDD (n = 11), veterans with MDD but no PTSD (n = 10), veterans with neither MDD nor PTSD (n = 10). Subjects were awakened in a sleep laboratory during each period of rapid eye movement (REM) sleep and interviewed as to dream content. Dreams were statistically analyzed (ANOVA).

Results: There were no significant ($p = .05$) differences between groups with regard to recall rate, dream length, activity, or hostility. Masochism was higher in both patient groups than in controls. Anxiety level was higher in MDD patients than in controls. Dreams of PTSD/MDD patients were less likely to be set in the present than dreams of MDD patients.

Conclusions: The results of Beck and Ward (1961) are confirmed for both MDD and PTSD/MDD patients. In addition, PTSD/MDD patients appear to avoid the present in their dreams. This may have important implications for treatment.

NR256 Tuesday, May 24, 12 noon-2:00 p.m.

Lack of Anxiogenic Effects of Flumazenil in PTSD

Penny Randall, M.D., Psychiatry, Yale University, 38 Temple Court, New Haven CT 06510; J. Douglas Bremner, M.D., Steven M. Southwick, M.D., John H. Krystal, M.D., Dennis S. Charney, M.D.

Summary:

Objective: Evidence from preclinical and clinical studies suggests a role for alterations in the benzodiazepine/GABAA receptor complex in stress and anxiety. Flumazenil is a relatively pure benzodiazepine/GABAA antagonist that has been shown to provoke panic attacks in patients with panic disorder but not in healthy subjects.

Method: Flumazenil 2 mg or placebo was administered i.v. over 90 seconds in a double-blind crossover study design to Vietnam combat veterans with PTSD. PTSD and anxiety symptoms were measured with visual analogue scales.

Results: There was no significant difference on visual analogue scales in measures of nervousness, anxiety, and fear with flumazenil compared with placebo. Panic attacks occurred at equal frequency after administration of flumazenil and placebo (1/13). Flashbacks occurred after flumazenil and placebo administration 1/13 and 0/13, respectively.

Conclusion: Administration of flumazenil at 2 mg does not produce an increase in anxiety and PTSD symptoms in patients with PTSD. This finding contrasts with previous work that shows yohimbine, an alpha2 antagonist, produces panic attacks in PTSD and panic disorder. Future studies should explore the effects of a benzodiazepine partial inverse agonist such as iomazenil in PTSD.

NR257 Tuesday, May 24, 12 noon-2:00 p.m.

Intravenous Administration of the Benzodiazepine Partial Inverse Agonist Iomazenil to Healthy Volunteers

Penny Randall, M.D., Psychiatry, Yale University, 38 Temple Court, New Haven CT 06510; Adam Darnell, M.D., J. Douglas Bremner, M.D., Keith A. Hawkins, Psy.D., Michael Serynok, M.D., Scott W. Woods, M.D., J. Seibyl, M.D., John H. Krystal, M.D., Robert B. Innis, M.D., Dennis S. Charney, M.D.

Summary:

Objective: Several lines of preclinical and clinical research suggest the benzodiazepine/GABAA receptor is involved in the pathophysiology of anxiety. Iomazenil is a benzodiazepine antagonist at the benzodiazepine receptor with partial inverse agonist properties. This compound may be a useful and safe probe to examine the benzodiazepine receptor function in human subjects.

Method: In a double-blind, placebo-controlled study design, seven healthy subjects received iomazenil (3.7×10^{-3} mg/kg) corresponding to an estimated 25% benzodiazepine receptor occupancy. Responses were measured using visual analogue scales.

Results: Mild-to-moderate anxiety, defined by a 25% or greater increase from baseline on the visual analog scale for anxiety, was exhibited by 2/7 subjects in response to iomazenil. Moreover, one of the subjects that experienced anxiety had a 26% increase in systolic blood pressure 10 minutes after the infusion. Data from the administration of iomazenil at higher dosages will be presented at the meeting.

Conclusion: Our preliminary findings demonstrate an anxiogenic effect of iomazenil in healthy subjects without evidence of epileptic activity on EEG monitoring. Iomazenil may be a safe and useful probe of benzodiazepine receptor function in anxiety disorders.

NR258 Tuesday, May 24, 12 noon-2:00 p.m.

Heart Rate Variability in Panic: Autonomic Balance

Phebe Tucker, M.D., Psychiatry, OU Health Sciences, P. O. Box 26901 5SP520, Oklahoma City OK 73190; Phil Adamson, M.D., Beverly Corbin, R.N., Dottie Williams, LPN, Jodie Groff

Summary:

Objective: Decreased heart rate variability, present in panic patients and those at risk for sudden cardiac death, results from decreased parasympathetic or increased sympathetic tone. This study uses power spectral analysis to identify sympathetic and parasympathetic components of heart rate variability in panic patients compared with controls.

Methods: Twelve panic-disordered patients by SCID-I and 11 age- and gender-matched controls without psychopathology, all

medically healthy, were recruited by advertisements. Relative high frequency power, an estimate of parasympathetic activity, and low-to-high power frequency ratio, a measure of sympathetic activity, were calculated for both groups in supine and standing positions for 15 minutes after patients were acclimated to spectral analysis EKG equipment. None panicked or reported severe anxiety. Two-way ANOVA followed by post-hoc paired T-Tests compared groups for autonomic and positional differences. Student T-Test confirmed that groups did not differ in age.

Conclusion: Panic patients had higher mean sympathetic activity while reclining than controls, though not significant. Both groups had similar reclining and standing parasympathetic input. Upon standing, controls had an expected rise in sympathetic activity ($P < .05$), as well as a decrease in parasympathetic activity ($P < .05$) in gaining cardiovascular equilibrium. Panic patients had no changes in either autonomic component. High baseline reclining sympathetic activity in panic patients may have prevented further orthostatic increase in sympathetic tone. Spectral analysis may prove a useful measure of increased risk in panic patients with cardiac disease; normalization of heart rate variability with panic treatment may improve this risk as well as quality of life.

NR259 Tuesday, May 24, 12 noon-2:00 p.m.

Trauma History in Social Phobia and Panic Disorder

Diane Majcher, M.D., Psychiatry, Mass General Hospital, ACC 815 15 Parkman Street, Boston MA 02114; Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Susan A. Sabatino, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

The present study examines the prevalence and correlates of trauma history of PTSD in patients with social phobia compared to a group with panic disorder.

Method: Sixty-five consecutive patients with social phobia and 65 with panic disorder presenting to a psychopharmacology research clinic received SCID interviews and were examined with KSADS-E and DICA-P to assess the presence of childhood anxiety disorders. Information was obtained regarding demographics, ages of onset of disorders, presence and type of trauma, and severity of overall social phobia or panic disorder.

Results: A history of trauma was observed in 41.9% of the social phobia patients; 22.4% had a history of trauma before the onset of social phobia and 3.4% met criteria for PTSD. Social phobics with histories of trauma before or after the onset of social phobia had significantly greater rates of comorbid dysthymia and of major depression histories than social phobics without a trauma history. A similar analysis will be conducted with the panic disorder patients and will be compared with the social phobia data.

Conclusions: These findings suggest that a history of trauma may place social phobic patients at greater risk of depressive disorders, and that this history may bear on treatment choice.

NR260 Tuesday, May 24, 12 noon-2:00 p.m.

Anxiety Disorders in General Practice in France

Corinne Martin, M.D., Psychiatrie, University Bordeaux, 121 Rue De La Bechade, Bordeaux 33076, France; Sylvie Maurice-Tison, M.D., Jean Tignol, M.D.

Summary:

Objective: This epidemiological study, conducted in Aquitaine, France, was designed to assess frequency and treatment of anxiety disorders in general practice patients.

Method: The assessment was cross-sectional; a random sample of 312 patients was chosen and evaluated during the last week of May 1993, by 55 general practitioners. Anxiety disorders were assessed by the Composite International Diagnostic Interview; degrees of depression were self evaluated by the Beck Depression Inventory. The physicians reported current psychological and psychopharmacological treatments, and which treatment each patient requested.

Results: Frequency of anxiety disorders (25%) is concordant with epidemiological data available from the French general population. An exception exists for social phobia, which is more frequent in our sample (11% vs 3%). No sex differences for anxiety disorders were found in this study. This is in opposition to what is known in the general population ($\chi 2 = 1.47$, $p > .05$). More women are treated than men (drugs: $\chi 2 = 7.31$, $p < .01$; psychotherapies: $\chi 2 = 7.58$, $p < .01$). However, women do not request more treatment than men ($\chi 2 = .59$, $p < .05$). Benzodiazepines and psychodynamic-oriented therapies are the most frequently utilized treatments for any anxiety disorder. Specific treatments such as antidepressant drugs and behavioral therapy for anxiety are very rarely prescribed.

Conclusion: This study shows the discrepancy between the current theoretical knowledge of anxiety disorders and the treatment of these disorders in general practice. Contrary to what is often found in the literature, it is suggested that the patient's request for treatment is not a determining factor in what therapy is actually prescribed. Different hypotheses will be discussed.

NR261 Tuesday, May 24, 12 noon-2:00 p.m.

Increased Platelet MAO Activity in Patients with Panic Disorder

Sergio Gloger, M.D., Psychiatry, Catholic University, Marcoleta 352, Santiago, Chile; Mario Seguel, M.D., Patricio G. Fischman, M.D., Francisco O'Ryan, M.D., Rafael Torres, M.D., Vilma Vidal, B.S.

Summary:

Few studies have examined and conflicting results have been reported on platelet monoamine oxidase (MAO) activity as a possible peripheral biological marker in anxiety disorders. This study assessed platelet MAO activity in a carefully selected and thoroughly evaluated group of 13 (nine women, four men) DSM-III-R/SCID-P panic disorder (PD) outpatients compared with 26 healthy age- and sex-matched controls. MAO activity was determined with ^{14}C phenylethylamine as a substrate.

MAO activity values for the panic disorder group were significantly higher than those found in the control group (PD mean ± S.D. = 183.7 ± 40.86; controls mean ± S.D. = 93 ± 44.63, $p < .001$). The striking difference found between both groups in this study suggests that the assessment of platelet MAO activity could become a valuable tool as a possible marker for this particular anxiety disorder. Given the previous conflicting results and the fact that many other psychiatric disorders have also been associated with changes in MAO activity, future research in this area should consider larger samples and comparison groups with other psychiatric pathologies.

NR262 Tuesday, May 24, 12 noon-2:00 p.m.

Panic Associated Suicide and Violence

Martin L. Korn, M.D., Psychiatry, Albert Einstein Col Med, 88 W. Garden Road, Larchmont NY 10538; Robert Plutchik, Ph.D., Herman van Praag, M.D.

Summary:

Previous research has examined the relationship between panic attacks and a history of suicidal behavior. Many studies have shown a positive relationship between these two variables. Several case reports have noted a direct temporal relationship with suicidal as well as violent behaviors occurring during the panic attack itself. The present study was designed to identify the extent

to which these behaviors are reported as directly associated by patients diagnosed with panic disorder.

Patients in this study consisted of 19 with pure panic disorder, 28 with comorbid panic and major depression, and a comparison group of 22 patients with pure major depression. The study demonstrated that patients reported the occurrence of suicidal and violent acts during the panic state. Comorbidity increased the rate of suicidal ideation but not attempts, and increased the rate of violent behavior. Inwardly and outwardly directed aggression during panic correlated significantly with each other as well as with measures of impulsivity, suicide risk, and violence risk. Other comparisons with the group of depressed patients are discussed.

NR263 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Gender Differences in Schizophrenia: Phenomenology and Neuroleptic Response

Debra A. Pinsky, M.D., EXP Therapeutics, Mental Health RM 4N212, 9000 Rockville Pike Bldg 10, Bethesda MD 20892; Anil K. Malhotra, M.D., Alan F. Breier, M.D., David Pickar, M.D.

Summary:

Objective: This study was conducted to 1) define phenomenological differences between drug-free male and female schizophrenic patients on a research ward and 2) examine neuroleptic response of the two groups.

Methods: 80 males (m) and 46 females (f) who met RDC criteria for schizophrenia or schizoaffective disorder entered a double-blind, placebo-controlled study. Age of illness onset, premorbid social function, and illness severity were evaluated at baseline using structured interview and Phillips scale. BPRS ratings were administered after one month drug-free. 24 male and 20 female patients were then treated with typical neuroleptic medications for one month followed by BPRS ratings. Treatment response was defined as a 20% reduction in BPRS total score from the drug-free to the neuroleptic-treated period.

Results: Schizophrenic males had lower premorbid social function than females (Phillips score $x_m = 19.52$, $x_f = 16.96$, $p < .05$). Male schizophrenic patients did not significantly differ from females in age of onset or number of prior hospitalizations. No significant differences were found between the drug-free groups in total, positive, or negative symptom BPRS scores. 50% of male patients and 55.6% of female patients (X^2 = ns) met criteria for neuroleptic response.

Conclusions: This study suggests that premorbid social function is significantly different between male and female schizophrenics, despite no differences in age of onset or number of prior hospitalizations. Moreover, through a careful double-blind, placebo-controlled study, no significant gender differences were found in drug-free symptomatology nor in neuroleptic response.

NR264 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Neurodevelopmental Brain Anomalies in Schizophrenia

Peggy C. Nopoulos, M.D., Psychiatry, University of Iowa, UIHC 2911 JPP, Iowa City IA 52242; Victor Swayze, M.D., Michael A. Flaum, M.D., Nancy C. Andreasen, M.D.

Summary:

A variety of developmental brain anomalies have been reported in patients with schizophrenia. We examined the incidence of two types of developmental anomalies, cavum septum pellucidum (CSP) and gray matter heterotopias (GMH), in a sample of patients with schizophrenia and normal controls.

The sample consisted of 48 patients with *DSM-II-R* schizophrenia (34M/14F). The control group was comprised of 56 normals (32M/24F). The groups were equivalent in terms of age and parental education. All subjects underwent MRI scanning which yielded contiguous 1.5 mm slices. All scans were visually inspected by two independent raters who were blind to diagnosis.

The incidence of small (1–4 mm) CSP was found to be high and did not differ across groups (61% in patients and 62% in controls). Of those with a CSP, the incidence of large (>4 mm) CSP was significantly higher in patients than in controls (20% vs. 6%), and all of the large CSP were found among the male patients. Two cases of GMH were found among the patient group, while none were observed among the controls.

This study suggests that subtle midline and neuronal migration abnormalities may be more common in schizophrenia and that abnormal brain development may play an important role in the pathophysiology of the illness.

NR265 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Racial Comparisons in Schizophrenic Veterans

William B. Lawson, M.D., Psychiatry, NLR VA Medical Center, 2200 Ft. Roots Drive 116A NLR, North Little Rock AR 72114; Brian J. Cuffel, Ph.D.

Summary:

Racial differences have been reported in the treatment of African Americans in the mental health system but such studies are often confounded by such factors as social class. We assessed the treatment of African Americans with schizophrenia in the VA system. Racial comparisons in the VA system can be more accurately made because access to care is not related to income and the population is otherwise homogeneous. Fifty white and 50 African American schizophrenics were randomly selected from all nonduplicated admissions over a one-year period to a 200-bed neuropsychiatric Veterans Administration Medical Center. We previously reported that unlike other studies involving the public sector, no racial differences were seen in misdiagnosis, involuntary admissions, seclusion and restraints, length of stay, or number of admissions. African Americans were more likely to show a greater number of disruptive behaviors, and lifetime symptoms. Increased likelihood of substance abuse was seen, accounted for entirely by increased likelihood of stimulant, usually cocaine, use. Controlling stimulant abuse eliminated these racial differences. Stimulant abuse may be especially detrimental to African Americans who are severely mentally ill.

NR266 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Dystonia in Schizophrenic Drug Abusers

William B. Lawson, M.D., Psychiatry, NLR VA Medical Center, 2200 Ft. Roots Drive 116A NLR, North Little Rock AR 72214

Summary:

Twenty percent of schizophrenic patients hospitalized in public facilities abuse cocaine. Thus, cocaine abuse is far more common in this population than in most other samples. Cocaine and other stimulants are dopamine agonists which could affect dopamine-based responses such as the movement disordered side effects associated with antipsychotic medications. To test this hypothesis, we evaluated neuroleptic related abnormal involuntary movements in 93 DSM-III-R (+) substance abusing schizophrenic veterans. Twenty-seven of 30 stimulant abusers (90%) vs. 45 of 64 abusers of other drugs (70%) gave a past history of dystonic reactions ($p < .05$). The groups did not differ significantly in chronicity of schizophrenia or substance abuse, neuroleptic dose at admission, exposure to high potency neuroleptics, age, history of head injury, or birth complications. After at least two weeks of withdrawal, Simpson-Angus ($p < .20$) and AIMS ($p = .09$) tended to be higher in patients with a history of stimulus abuse and a

significant positive relationship was seen between years of stimulant exposure and both the Simpson-Angus ($r = 0.35$, $p < .02$) and AIMS ($r = 0.29$, $p < .05$). These results give some credence to the notion that stimulant abuse may predispose patients with schizophrenia to the extrapyramidal symptoms associated with treatment by antipsychotic agents.

NR267 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Randomly Assigned Haldol Plasma Levels for Acute Psychosis

Philip G. Janicak, M.D., Research, Ill. State Psych Inst., 1153 N. Lavergne Avenue, Chicago IL 60651; Javaid I. Javaid, Ph.D., Rajiv P. Sharma, M.D., Anne Leach, M.D., Sheila Dowd, B.S., John M. Davis, M.D.

Summary:

Six fixed-dose studies found a therapeutic haloperidol (HPDL) range (averaging 5–18 ng/ml); however, one prospective, targeted plasma level study found no difference in response based on assignment to low, middle, or high plasma levels.

Objective: To determine if there is an optimal HPDL level to control symptoms of an acute psychotic exacerbation.

Method: We assign inpatients to a low (<5 ng/ml), middle (5–18 ng/ml), or high (>25 ng/ml) HPDL plasma level under double-blind conditions. After two weeks, nonresponders are randomly reassigned to either (1) continue in the same group or (2) as follows: a) low group—raised to middle group; b) middle—raised to high c) high—lowered into middle.

Results: 87 acutely psychotic (primarily schizophrenic) patients have participated (average wash-out two weeks). During the first phase, an ANCOVA with baseline scores as covariate revealed no differences in total BPRS change scores based on plasma level assignment ($F = .32$; $df = 2$; $p = .7$). In the second treatment phase, there was a trend for greater improvement in the high level nonresponding patients reassigned to the middle level ($t = -2.23$; $p = .08$) when compared to those nonresponders who remained in the high level. No differences were found, however, between those in the low group reassigned to the middle group versus those who remained in the low level.

Conclusions: Thus far, the low HPDL plasma level has been as effective as middle and high levels ($x = 1.87$, 13.4, and 39.6 ng/ml, respectively) for acute psychosis. (Supported in part by USPHS Grant MH-45465)

NR268 Tuesday, May 24, 3:00 p.m.-5:0 p.m.

Clinical Neuropsychiatric and Treatment Findings in Obsessive Compulsive Schizophrenics: Preliminary Report

Michael Y. Hwang, M.D., Psychiatry, Columbia University, 722 West 168th Street Unit 66, New York NY 10032; Lewis A. Opler, M.D., Marc Vital-Herne, M.D., David M. Klahr, M.D., Daphne Simeon, M.D.

Summary:

While obsessive-compulsive (OC) phenomena in schizophrenia have long been recognized, its clinical and pathophysiological implications remain obscure. Prior to *DSM-III-R,* diagnostic convention precluded simultaneously diagnosing schizophrenia and obsessive-compulsive disorder (OCD), and as a result OC schizophrenia was believed to occur only rarely. Recent epidemiological studies (e.g., ECA study) and clinical reports, however, indicate significantly higher comorbidity and worse prognosis in OC schizophrenics. We have investigated clinical and neuropsychiatric profiles of ten OC schizophrenics in comparison to ten non-OC schizophrenics. Preliminary data suggest poorer clinical course and lower functioning levels among OC patients. In addition, these patients demonstrated greater negative symptoms with more pervasive frontal lobe impairments. Treatment with the specific serotonin reuptake inhibitors (SSRIs) in addition to ongoing neuroleptics in seven subjects have brought about marked symptom reduction and functional improvements. Our observations also suggest differential symptom response to the SSRIs. While OC symptoms and WCST performance have shown improvements with SSRI, no significant improvements were noted in their positive and negative symptomatology. These findings suggest that the OC schizophrenics may possess distinct clinical and neurobiological profiles and may require specific symptom assessment and treatment strategies for optimal outcome.

NR269 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Cognitive Status of Axis I Disorders

Keith A. Hawkins, Psy.D., Psychiatry, Yale Medical School, 34 Park Street, New Haven CT 06517; William H. Sledge, M.D., Ralph E. Hoffman, M.D., Donald M. Quinlan, Ph.D., Jaak Rakefeldt, Ph.D., Nancy M. Docherty, Ph.D.

Summary:

Objective: Few neuropsychological studies comparing schizophrenic and bipolar patients have been undertaken. The goal of this study was to compare these diagnostic groups on key cognitive variables, and to relate cognitive status to clinical presentation.

Method: 48 schizophrenic, 25 bipolar (per SADS), and 26 normal controls were administered the SANS and SAPS, and attention (Digit Span, Digit Symbol, Auditory CPT, Trails A & B, mental arithmetic), reasoning (WAIS-R Similarities), reading, writing, and language tests (including the Boston Naming Test, Verbal Fluency, and an abbreviated aphasia screen). Test results were related to diagnosis, symptoms, and treatment.

Results: Although the schizophrenics, as a group, performed more poorly than the bipolars, cognitive impairment was more closely related to clinical presentation than to diagnosis. Negative rather than positive symptoms correlated with poor cognition, irrespective of diagnosis. Moreover, schizophrenics treated with adjunctive lithium or related medications (presumably in response to affective features) were cognitively indistinguishable from the bipolars.

Conclusions: Cognitive deficiency is related to negative symptom status rather than diagnosis per se. Schizophrenics displaying affective symptoms, and/or few negative symptoms, appear to be relatively cognitively intact. In many circumstances research interests (e.g. in brain structure, pathophysiology, or genetics) may be best served by grouping patients on the basis of specifics of clinical presentation rather than diagnosis, since conventional diagnostic boundaries may obscure important commonalties and differences among psychiatric patients.

NR270 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Plasma 5-hydroxyindoleacetic Acid Reflects Central Serotonin Activity in Medicated and Unmedicated Schizophrenic Patients

William A. Wolf, Ph.D., Research, VA Medical Center, Southfield and Outer Drive, Allen Park MI 48101; Lynda L. Hulst, M.A., Larry D. Alphs, M.D.

Summary:

Psychobiological studies have implicated serotonin (5-HT0, as well as dopamine (DA), in the pathophysiology of schizophrenia. Most of these studies have measured cerebrospinal fluid (CSF) levels of 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) as indirect indices of 5-HT and DA release and functional activity. CSF is difficult to obtain routinely in psychiatric patients, however, and is not practical for exploring relationships

between neurochemistry and behavior. Although plasma HVA is used as a marker for central DA function, few studies have investigated whether plasma 5-HIAA is a reliable measure of central 5-HT function and, if so, how medication state affects its expression. In the present study, 11 *DSM-III-R* diagnosed schizophrenic inpatients were challenged with buspirone, a 5-HT_{1A} agonist which reduces central 5-H activity, when unmedicated and after standardized neuroleptic treatment. Buspirone significantly lowered plasma 5-HIAA in both medicated ($F = 6.39$, $p < .002$) and unmedicated ($F = 3.13$, $p < .05$) schizophrenic patients. As previously observed in CSF, neuroleptic-medicated patients also had a significantly higher plasma HVA/5-HIAA ratio at baseline than did unmedicated patients ($t = 2.74$, $p < .05$). Our results suggest that plasma 5-HIAA is a reliable index of central serotonergic function in schizophrenic patients and that baseline variance increases under unmedicated conditions.

NR271 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Neuronal Morphometric Studies of the Hippocampal Formation in Schizophrenia

Steven E. Arnold, M.D., Psychiatry, Univ of Pennsylvania, 10 Gates 3400 Spruce Street, Philadelphia PA 19104; Bryan Franz, B.A., Ruben C. Gur, Ph.D., Raquel E. Gur, M.D., John Q. Trojanowski, M.D.

Summary:

In this study, we characterize the hippocampal formation in patients with schizophrenia with measurements of neuron density, neuron size, and variability of neuronal axis orientation. Brain tissue was obtained from 15 elderly patients with chronic schizophrenia and 10 age- and post-mortem interval compatible, non-psychiatric controls. Ten regions of interest were identified on Nissl stained sections (CA4, CA3, CA2, CA1, subiculum, layers II, III, and V-VI of entorhinal cortex, primary motor cortex, and primary visual cortex) and used in blind, automated, computer-based neuronal morphometric analyses. Neuronal size was decreased in all hippocampal and entorhinal subfields; however, this reached statistical significance only in subiculum (ANOVA, $p < .01$) and CA1 ($p < .03$). In contrast, neuron size in primary motor and visual cortices were nearly identical. No differences in neuron density or in variability of neuronal axis orientation were identified in any region. Analysis of covariance revealed no significant effects of potential confounding variables (age, post-motem interval, and drug exposure) on the measures obtained. The subiculum and CA1 are the major sources of output from the hippocampal formation to widespread cortical and subcortical targets. Smaller neurons in these subfields may indicate a weakening in these connections and have important cognitive sequelae.

NR272 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Is the Neuropsychological Deficit in Schizophrenia Progressive?

Nancy C. Andreasen, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive RM 2911 JPP, Iowa City IA 52242; Sanjay Gupta, M.D., Laura A. Flashman, Ph.D., Michael A. Flaum, M.D., Peggy C. Nopoulos, M.D., Daniel S. O'Leary, Ph.D.

Summary:

In a previous study we found neuropsychological functioning to be stable in a group of new onset (n = 35) schizophrenics over a period of two years, arguing against an ongoing cognitive decline in schizophrenia. In order to further examine the course of neuropsychological functioning in schizophrenia, we compared performance among new onset cases with that of subchronic and chronic schizophrenics.

The "new onset" cases included 42 subjects who met *DSM-III-R* criteria for schizophrenia or schizophreniform disorder, and who had no prior treatment with neuroleptics. The "subchronic" group included 46 subjects who all been previously treated, but had been ill for less than five years (mean duration of illness = three years). The "chronic" group included 109 subjects who had all been treated for schizophrenia for greater than five years (mean duration of illness = 13 years). All subjects completed the same comprehensive neuropsychological battery, which included tests of attention, memory, motor coordination, and general intellectual functioning.

Overall, there were very few differences across the groups. The few significant differences that were observed were all in the direction of poorer performance among the new onset group compared to the chronic group. No differences were observed between the subchronic and chronic groups.

These data support and extend our previous study and suggest that the neuropsychological dysfunction which characterizes schizophrenia may be stable throughout the course of the disorder, rather than one of progressive deterioration.

NR273 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Schizophrenia: Neuropsychological and MRI Findings

Paul G. Nestor, Ph.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Martha E. Shenton, Ph.D., Cynthia G. Wible, Ph.D., Matthew O. Kimble, B.A., Lloyd Smith, M.S., Robert W. McCarley, M.D.

Summary:

Objective: Do neuropsychological deficits in schizophrenia show distinct MRI prefrontal and temporal lobe correlation patterns?

Method: A sample of mixed but predominantly positive-symptom schizophrenic patients (n = 15) had quantitative volumetric MRI evaluation (SPGR 1.5 x 1 x 1 mm voxels) of temporal lobe and prefrontal structures. Patients were also evaluated on neuropsychological measures of memory (Wechsler Memory Scale-Revised; WMS-R), abstraction (Similarities subtest of WAIS-R), and attention, such as switching attention (Trails B, Alternating Semantic Categories) and temporary storage (Hebb's Recurring Digits). The Wisconsin Card Sorting Test (WCST) was used as a measure of "executive functions" presumably including both attention and abstraction. The Thought Disorder Index (TDI) assessed formal thought disorder.

Results: There was a rather striking segregation of poor test performances into two groups of correlations with MRI volumes (all listed Pearson's r's have 2-tailed p's < 0.05): *Temporal Lobe.* (1) left posterior superior temporal gyrus (PSTG) & both the Verbal Paired Associates Learning test of the WMS-R ($r = .64$) and the TDI ($r = .71$); (2) bilateral parahippocampal gyrus/PSTG & both the WCST (r's > 0.68) and the Similarities subtest (r's > 0.69). *None* of these measures showed significant or even trend (p's < .1), r values for prefrontal correlates. *Prefrontal* (1) left prefrontal white matter & Hebb's Recurring Digits ($r = .62$). (2) right prefrontal gray matter & Trails B ($r = .61$)—Trails B also had 1 significant temporal lobe correlate, right hippocampus/amygdala. (3) bilateral prefrontal & Alternative Semantic Categories (trends).

Conclusions: Neuropsychological impairments in attention, sometimes described in terms of "working memory", are related to prefrontal structures. By contrast, deficits in categorization, abstraction, and verbal memory, all of which may underlie thought disturbance and may reflect a fundamental disturbance in semantic processing, are related to temporal lobe structures in these schizophrenic patients.

NR274 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Qualitative and Quantitative Behavioral Response to Methylphenidate in First-Episode Schizophrenia

Amy R. Koreen, M.D., Research, Hillside Hospital, Long Island Jewish Medical Ctr, Glen Oaks NY 11004; Jeffrey A. Lieberman, M.D., Darlene Jody, M.D., Jose Ma. J. Alvir, Dr.P.H., Miranda Chakos, M.D., David Meyerhoff, M.D.

Summary:

Traditionally, schizophrenic patients have been categorized qualitatively by differences in their psychopathology, and longitudinal studies have described changes in symptoms over time that reflect progression of the illness. In order to understand the pathophysiologic basis of illness progress and change in psychopathology over time, methylphenidate (0.5 mg/kg), was given intravenously to 51 acutely ill first-episode schizophrenic patients and behavioral response was assessed. Quantitative (an increase in psychosis) and qualitative (an emergence of new psychotic symptoms) behavioral activation was determined. Patients were then followed prospectively.

Fifty-nine percent of patients were quantitative activators whereas only 22% were qualitative activators. At baseline quantitative activators were less ill, and had less thought disorganization and negative symptoms than quantitative nonactivators. Qualitative activators, however, had more thought disorganization at baseline. Methylphenidate resulted in an overall increase in thought disorganization, negative symptoms, affective symptoms, and global scores, but only as increase in positive symptoms in activators. Baseline diagnosis was more heterogeneous for the qualitative activators than nonactivators and over the course of follow-up (5 (46%) of the qualitative activators as compared to only seven (18%) of the nonactivators met criteria for the deficit state. These and other analyses will be described and a hypothesis relating activation status to progression of the illness and a change in psychopathology over time will be proposed.

NR275 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Behavioral Effects of m-Chlorophenylpiperazine and Methylphenidate in First-Episode Schizophrenia and Normal Controls

Amy R. Koreen, M.D., Research, Hillside Hospital, Long Island Jewish Medical Ctr, Glen Oaks NY 11004; Jeffrey A. Lieberman, M.D., Sally R. Szymanski, D.O., Miranda Chakos, M.D., Jose Ma. J. Alvir, Dr.P.H., Rafael Munne, M.D.

Summary:

Next to dopamine (DA), serotonin (5HT) has historically been one of the neurotransmitters most often implicated in schizophrenia. Renewed interest in the 5HT system has been stimulated by the development of specific atypical antipsychotic drugs that have potent 5HT activity. However, evidence for 5HT system dysfunction is lacking. Several studies of behavioral response to MCPP in schizophrenia have produced conflicting results.

In order to determine if MCPP is psychotogenic, the behavioral response of acutely ill neuroleptic naive first-episode schizophrenic patients and normal control subjects to intravenous MCPP (0.1 mg/kg) and methylphenidate (0.5 mg/kg) were assessed. Repeated measures of variables and cross tabulation of infusion changes in symptoms compared the schizophrenic group's response to MCPP to that of controls, and the schizophrenic group's response to MCPP to their response to methylphenidate. Positive symptoms increased significantly with methylphenidate but not with MCPP; Otherwise there were no significant differences between the schizophrenic group's behavioral response to MCPP vs methylphenidate. The schizophrenic's response to MCPP did not differ from the normal controls' response. Further analyses of specific items for individuals by infusion type were also analyzed. Since the behavioral effects of MCPP stimulation appear to be nonspecific and not psychotogenic, 5HTs role in the pathophysiology of schizophrenia and symptom production remains unclear. Hypotheses about 5HTs role will be discussed.

NR276 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Effect of Clozapine on the Rate of Hospitalizations and Status of Schizophrenics

Lynne Jones, R.N., Crisis Stabilization, University Hospital, 1116 North Kedzie, Chicago IL 60651; Michael Reinstein, M.D., Chris Mullally, B.S.

Summary:

We conducted a two-year study comparing the rate of hospitalizations and length of stay of 48 schizophrenic patients on standard neuroleptics for one year and clozapine for the next year. In each case the hospitalizations were precipitated by an increase in psychosis and/or aggressive behaviors. We found that after starting the clozapine: 12% exhibited remarkable improvement; 54% moderate improvement; 30% no change in psychosis, but decrease in side effects; 4% decompensated. Effect on hospitalizations after starting clozapine: 44% decrease in hospitalizations; 40% decrease in average length of stay; 62% decrease in utilization of hospital days. Overall there was a marked reduction in each area. The data supports the theory that clozapine has a different method of operation and a different mode of action than the standard neuroleptics.

NR277 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Neuropsychological Functions and Clinical Outcome

Marshall L. Silverstein, Ph.D., Psychology, Long Island University, Brookville NY 11548; Michael Silver, M.D., Martin Harrow, M.D.

Summary:

Objective: It is now well-established that a number of major psychiatric syndromes have prominent neuropathological antecedents; however, neurobehavioral correlates have not been investigated longitudinally. This report examines the stability of neuropsychological performance between an acute episode and a two-year follow-up. Cognitive functioning on neuropsychological measures is investigated in relation to clinical outcome.

Method: The sample consisted of 40 schizophrenic and severe mood disorder patients hospitalized for an acute episode, who were subsequently followed up two years after discharge. The sample was divided into good and poor outcome subgroups, based on three outcome areas: social functioning, work functioning, and rehospitalization. The neuropsychological measures were the WAIS and Halstead-Reitan Battery.

Results: There was a significant difference between the good and poor outcome subgroups on the composite of the neuropsychological variables ($p < .03$), with a greater degree of improved performance at follow-up in the good outcome subgroup, notably for work functioning ($p < .03$) and rehospitalization ($p < .004$).

Conclusions: Patients with a poor clinical outcome failed to demonstrate neuropsychological improvement or recovery. Unfavorable clinical outcome is associated with only marginal changes in neuropsychological performance, whereas good outcome status is associated with cognitive improvement.

NR278 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Insight and Cognitive Impairment in Schizophrenia

Paul Lysaker, Ph.D., West Haven VAMC 116B, 950 Campbell Avenue, West Haven CT 06516; Morris D. Bell, Ph.D.

Summary:

Research has suggested that poor insight in patients with schizophrenia is associated with poorer treatment compliance and outcome. Little is known about the etiology of poor insight. Poor insight has been attributed to a willful preference for illness, a psychological defense, or cognitive impairments. To test the hypothesis that poor insight is related to enduring cognitive deficits, the performance of 29 patients with schizophrenia and impaired insight and 63 patients with schizophrenia and unimpaired insight, were compared on repeated administrations of Wisconsin Card Sorting Test. Results indicate that subjects with impaired insight demonstrate consistently poorer performance over a period of one year than subjects with unimpaired insight. Subjects with impaired insight made significantly more perseverative errors and achieved fewer categories correct, a pattern of performance deficits identified with neuropsychological dysfunction in schizophrenia. These results support the hypothesis that cognitive impairment may underlie poor insight in schizophrenia.

NR279 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Negative Symptoms and Work Capacity in Schizophrenia

Paul Lysaker, Ph.D., West Haven VAMC 116B, 950 Campbell Avenue, West Haven CT 06516; Morris D. Bell, Ph.D.

Summary:

Interest in negative symptoms as a marker of a schizophrenia subtype has grown dramatically in the last decade. One hypothesized correlate of negative schizophrenia which has received somewhat less attention is deteriorated work function. To address this issue the present study compared biweekly measurements of work performance for 21 patients with prominent negative symptoms and 29 patients without prominent negative symptoms, enrolled in a 26-week supported work program. Results indicate that subjects with prominent negative symptoms demonstrate poorer performance than other subjects with schizophrenia on Task Orientation (understanding and persisting at assignments), Social Skills, (socializing with co-workers) and Personal Presentation (alertness, friendliness, and good hygiene). Social Skills improved across the 26 weeks for both negative and non-negative groups whereas Task Orientation improved for negative subjects only. These results support the validity of the negative syndrome subtype and suggest patients with prominent negative symptoms may need special forms of vocational assistance.

NR280 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Polydipsia-Hyponatremia: Prevalence and Outcome

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Summary:

Objective: We provide naturalistic prevalence and outcome information on polydipsia-hyponatremia (PH), a disorder thought to represent a major health hazard for institutionalized psychiatric patients.

Method: Study 1 examines sodium levels on all Creedmoor Psychiatric Center inpatients undergoing routine chemistries during a four-week period (n = 401), considering only the lowest values for repeated blood-tests. Study 2 examines outcome in 25 inpatients with PH at Pilgrim Psychiatric Center followed an average of 15 months.

Results: Study 1 12.5% of the patients had sodium concentrations of 133 mmols/1 or less with 6.0%, and 2.2% of the patients, respectively, having sodium concentrations of 130 mmols/1 or less and 125 mmols/1 or less. There was a similar proportion of schizophrenia patients in the normo- and hyponatremic groups but the latter was older and hospitalized significantly longer ($p < .05$). *Study 2* At follow-up, continued evidence of PH was observed in 76% of the sample. All three patients with episodes of water intoxication at follow-up were noted to have had seizures on initial evaluation.

Conclusions: Hyponatremia is not uncommon in psychiatric inpatients and, once established, PH follows a chronic course with substantial temporal stability.

NR281 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Adolescent Schizophrenia: Reduced Memory and Brain

Lee Friedman, Ph.D., Psychiatry, University Hospital, 2074 Anbington Road, Cleveland OH 44210; John T. Kenny, Ph.D., Diane Cola, M.A., Jason Buck, Robert L. Findling, M.D., S. Charles Schulz, M.D.

Summary:

Objective: The objective of this study was to determine if adolescent schizophrenic patients have similar cognitive and brain structure abnormalities as adult patients with this disease.

Methods: To date we have studied seven schizophrenic patients and 11 controls. Normal controls were recruited from the community by advertisement, and were matched to the patients in age, gender, race, and socio-economic status. The mean age ± standard deviation was 15.6 ± 1.4 years for the patients and 15.0 ± 1.0 years for the controls. The neuropsychological battery included measures of attention (Paced Auditory Serial Additional Test; Stroop Color Naming Test; Digit Span Distraction Test), short-term memory (Consonant Trigram Recall Test), executive function (Wisconsin Card Sorting Test; Maze Test-Wechsler Intelligence Scale for Children-Revised), long-term memory (Logical Memory Test-Wechsler Memory Scale-Revised; Selective Reminding List Learning Test; Warrington Recognition Memory Test), and remote memory (Controlled Oral Word Retrieval; Category Instance Retrieval Test). To reduce the number of variables, the measures were grouped into five composites according to the major cognitive component listed above. The IQ measure was analyzed separately. For MRI analysis, we have implemented the methods of Lim and Pffeferbaum (1989), in collaboration with those authors. The image data for this analysis are standard clinical double-echo spin-echo axial scans (TE = 15/90, TR = 2500, FOV = 230, Matrix = 256*256, Thickness = 5 mm, 2 mm gap). The MRI measures included brain volume, ventricular volume and sulcal fluid volume.

Results: There was no significant difference between schizophrenic patients and normal control subjects in terms of WISC-R estimate of IQ ($p = 0.30$). In addition, the adolescent schizophrenic patients were not impaired compared to controls in terms of the attention ($p = 0.17$), executive function ($p = 0.11$), or remote memory ($p = 0.50$) composites. There were, however, significant differences between the two groups of subjects on the composite domains of both short-term ($p = 0.003$) and recent long-term memory ($p = 0.01$) recall. Of the MRI measures, there was only one statistically significant results: patients had reduced brain volume compared to controls ($p = 0.02$). There was no evidence of ventricular enlargement or sulcal widening in the adolescent subjects. Visual inspection of the MRI scans indicated that, although some patients had large ventricles, some of the controls also had large ventricles. Thus, the absence of a finding may be related to either the sample size of the control group or the fact that they were community, not medical controls.

Conclusions: These findings suggest that deficits in attention and executive functions emerge later in the course of the illness (during early adulthood), whereas memory deficits emerge at an earlier stage (during adolescence). These findings also show that

the cognitive impairment in adolescent schizophrenics cannot be due to global intellectual impairments or attentional dysfunction. Reduced brain volume has been reported previously in adult schizophrenics, and could be caused by a neurodevelopmental abnormality. Additional subjects and measures, including measures of hippocampal volume and laterality-related measures will be available and presented also.

NR282 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Social Unrelatedness and Schizophrenic Phenomenology

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Summary:

In order to examine the effect of chronicity on affect, a cohort of schizophrenic patients (N = 51; Chronic = 30, Acute = 21) were interviewed and rated on the Manifest Affect Rating Scale (MARS). Subjects were additionally rated on the Positive and Negative Syndrome Scale (PANSS) in order to determine whether degree of general psychopathology or phenomenlogical positivity and negativity would covary with ratings of affect. As a means of consolidating data, chronic vs. acute patient ratings on three MARS factors, derived from a principal components analysis, were compared. Results revealed that, while no group differences were noted on medication dose, extrapyramidal ratings, degree of general psychopathology, or degree of positive or negative symptoms, the chronic group displayed a significantly greater degree of emotional unrelatedness ($p < .0001$, 2-tailed) [MARS factor 1], expressive immobility ($p < .0001$, 2-tailed) [MARS factor 2), and inappropriateness of affect ($p < .0001$, 2-tailed) [MARS factor 3]. These results are consistent with the hypothesis that, in addition to positive and negative syndromes, a third dimension covarying with chronicity may represent a disorder marked by a decrement in skills specific to social relatedness.

NR283 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Clozapine Levels and Treatment Response

Michael H. Kronig, M.D., Psychiatry, Hillside Hospital, 75-59 263 Street, Glen Oaks NY 11004; Rafael Munne, M.D., Simcha Pollack, Ph.D., Thomas Cooper, M.A., John M. Kane, M.D., Jeffrey A. Lieberman, M.D.

Summary:

Objective: The purpose of this study was to determine if plasma clozapine levels were associated with treatment response.

Method: To examine this question, neuroleptic nonresponsive patients with schizophrenia or schizoaffective disorder were titrated to clozapine 500 mg/day by day 14 of treatment, and then the dose held fixed at least through day 21. Subsequently, clozapine doses were adjusted as clinically indicated, up to a maximum of 900 mg/day. Plasma clozapine levels were obtained at weeks 3 and 6, and standard clinical ratings (BPRS-A and CGI) were done at baseline and at the above time points.

Results: Data from 45 subjects were analyzed. There were no correlations between plasma clozapine levels and change in BPRS scores at treatment weeks 3 and 6. However, when the sample was classified into responders and nonresponders, therapeutic response was associated with clozapine blood levels >350 ng.

Conclusion: This study suggests that clozapine blood levels are correlated with clinical response.

NR284 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Prevalence of Tardive Dystonia in a Chronically Mentally Ill Population

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Summary:

Tardive dystonia (TDys) has been reported as a relatively rare complication of neuroleptic treatment. In order to determine the cross-sectional prevalence of the disorder, we examined videotapes of 119 schizophrenic patients undergoing structured neurological examinations. Severity of dystonia was recorded on a 0 to 4 scale in 12 body parts (tongue, jaw, periorbital, neck, fingers, elbow, wrist, shoulder, toes, ankles, knees, and trunk). Strict criteria for the presence of TDys were defined as scores of at least 2 in two body parts or one score of at least 3 in any body part. The patients were also rated for evidence of drug-induced Parkinsonism and tardive dyskinesia using standardized rating scales.

Thirteen patients (11%) met strict criteria for presence of TDys and another 14 (12%) had mild symptoms. All strict criteria patients had dystonic postures in the upper extremity. Overall severity (sum of scale items) of TDys was significantly correlated ($p < .005$) with age ($r = .34$), total parkinsonism ($r = .32$), and total dyskinesia ($r = .31$). Hierarchical linear regression indicated that the three variables together accounted for 20% of the variance in total dystonia $F(3, 112) = 9.8$, $p < .001$). Age accounted for 12% ($p < .001$), parkinsonism for 3% ($p < .05$), and dyskinesia for 6% ($p < .05$).

NR285 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

An Investigation of Drug Abuse in Schizophrenic Patients

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Summary:

Objective: The aim of the current study was to compare schizophrenic patients with and without comorbid drug abuse (other than alcohol abuse).

Method: Five hundred thirty-four schizophrenic patients (298 with comorbid drug abuse and 236 without) were drawn from a sample of hospitalized patients obtained by systematically screening all psychiatric admissions to facilities in the Baltimore area between 1983 and 1989. Best-estimate research diagnoses, based on hospital records, patient hospital interview, and six-month outcome functioning, were formulated by psychiatrists.

Results: The schizophrenic patients with comorbid drug abuse were younger, and a greater proportion were male. They had a more florid presentation of psychotic symptoms, as well as earlier age of onset of psychosis, earlier age at first hospitalization, and greater number of hospitalizations. The first-degree relatives of the schizophrenic probands with drug abuse had a significantly greater lifetime prevalence of major depression. In contrast, the rates of schizophrenia were similar for the relatives of the two groups of schizophrenic patients.

Conclusion: Given the potential impact of drug abuse on the course and clinical presentation of schizophrenia, the basis of the high rate of comorbidity between these disorders warrants further investigation.

NR286 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Disorientation: A Primary Feature in Schizophrenia

Janel Lombardi, M.A., CNC Bld 11, Pilgrim Psychiatric Ctr, Box A, West Brentwood NY 11717; Philip D. Harvey, Ph.D.,

Leonard White, Ph.D., Michael J. Parrella, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

Age disorientation of five years or more has been reported in about 25% of chronic schizophrenic patients, with this phenomenon found to be correlated with both the severity of global cognitive impairments and structural brain abnormalities. Temporal (e.g., age and year) and spatial orientation were found to be independent factors in previous studies. Since the earlier studies examined only younger patients, who are less likely to manifest global cognitive impairments than geriatric inpatients, we were interested in whether deficits in personal and temporal orientation were associated with the severity of cognitive impairment in samples with a high prevalence of cognitive impairment. Measures of orientation, including temporal (age, year of birth, admission year), and spatial orientation (year, date, etc.) collected on 162 geriatric and nongeriatric schizophrenic inpatients ranging in age from 25 to 95 years of age and were related to global cognitive impairments measured with the Clinical Dementia Rating Scale (CDR). Consistent with earlier results, temporal and spatial orientation loaded on separate factors in a factor analysis and patients who manifested age disorientation had significantly greater cognitive impairment with each of the seven decades of age of the subjects. The temporal disorientation factor alone correctly classified over 80% of the patients in a discriminant function analysis predicting their global CDR scores (0, 1, 2, or 3). Classification accuracy was consistent across all of the adjacent CDR categories. In fact, scores on two items, age disorientation and knowledge of the current year, alone correctly classified 80% of the schizophrenic patients according to global CDR. These data suggest that personal and temporal disorientation are central features of global cognitive impairment in schizophrenia, classifying the severity of global cognitive impairment as well as a full neuropsychological assessment previously performed on these same subjects. The neurological structures responsible for these functions, probably the temporal lobe and hippocampus, may be important determinants of the global cognitive impairment seen in chronic schizophrenics.

NR287 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Secondary and Drug-Induced Catatonic Syndromes: Application of Criteria and a Review of the Literature

John C. Kennedy, M.D., Psychiatry, The Ohio State University, 473 W. 12th Avenue, Columbus OH 43210; Brendan T. Carroll, M.D., Theodore J. Anfinson, M.D.

Summary:

Catatonic disorder due to a general medical condition has been added to the *DSM-IV* nosology. Diagnostic criteria for catatonic disorders have been proposed but there has not been any comparison of sets of criteria for catatonia in the literature.

An exhaustive review of the literature of catatonia associated with neurological, medical, drug-induced, and toxin-induced conditions was performed using a MEDLINE search and references from cited references. Patients were included if they were the subject of a case study or case series in which the presence of catatonic signs was reported. Factor analysis was used to identify clustering of signs in these catatonic disorders.

A total of 257 patients had specific catatonic signs reported. Neurologic conditions accounted for 82.5% of these case reports. Most (90.6%) met *DSM-IV* criteria. A smaller number (40.5% and 47.9%) of reports met the research criteria. We used 70 reports (27.2%) which met all sets of criteria to delineate catatonic signs. Seven factors were identified. Catatonic stupor did not emerge as a separate syndrome.

These findings suggest that secondary catatonic disorder may exhibit a different pattern of signs than has been described for primary (psychiatric) catatonic disorders. These criteria differed in restrictiveness which holds implications for the use of criteria in research settings. Further study of these and other criteria for catatonic disorder due to general medical conditions and drug-induced states is necessary.

NR288 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Dopamine Metabolism in Relatives of Schizophrenic Probands

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Summary:

Many first-degree relatives of schizophrenic patients are known to display attenuated symptoms of schizophrenia, particularly the social deficit symptoms. The deficit dimension of schizophrenic symptoms has been hypothesized to be associated with decreased brain dopamine (DA) activity. This raises the possibility that dopamine abnormalities may be present in at least some relatives of schizophrenic probands. The major DA metabolite, homonvanillic acid (HVA), in plasma was measured in a group ($n = 62$) of physically healthy, non-psychotic, first-degree relatives of schizophrenic probands and in a comparison group ($n = 20$) of normal controls. *DSM-III-R* Axis-II diagnoses of the relatives were determined by using face-to-face interviews of the relatives and their informants. Plasma HVA was measured at 10:00 AM after an overnight fast. The relatives were divided into four groups according to their *DSM-III-R* Axis-II diagnoses: schizotypal personality disorder (SPD) ($n = 11$); other odd-cluster personality disorders ($n = 7$); non-odd cluster personality disorders ($n = 6$); and "normal" relatives who did not meet any Axis-II diagnoses ($n = 38$). The SPD relatives were found to have significantly decreased plasma HVA compared to the normal controls as well as the "normal" relatives (ANOVA $p < 0.002$, Tukey $p < 0.05$), though the difference with other groups did not reach statistical significance. In the relatives, plasma HVA correlated negatively with a combined measure of the deficit-related characteristics ($r = 0.36$, $df = 60$, $p < 0.005$) derived by averaging the Chapman Physical Anhedonia scores, the Chapman Social Anhedonia scores, the sum of *DSM-III-R* deficit-related SPD symptoms, and the sum of negative syndrome scores on the Positive and Negative Syndrome Scale. Our results support the possibility that a decreased DA activity, associated with the deficit-related characteristics, exists in the non-psychotic first-degree relatives of schizophrenic probands.

NR289 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Selective Attention and Intention in Schizophrenia

Ede Frecska, M.D., Psychiatry, Veterans Admins. Med Ctr, 79 Middleville Road, Northport NY 11768; Lawrence Greenberg, M.D., Jeffrey Sparks, R.N., Kathy Piscani, R.N.

Summary:

Background: Behavioral studies in humans have suggested that each hemisphere is important for mediating selective attention and response preparation (intention) in contralateral hemispace. In addition, there is evidence that the medial frontal lobe has a major role in response preparation (Verfaellie et al. 1987).

Objective: The aims of this study were to provide an experimental neuropsychological assessment of response preparation and selective attention in schizophrenia and to evaluate the hypotheses of medial frontal lobe dysfunction and/or hemispheric asymmetry in this disorder.

Method: Age- and sex-matched group of 21 chronic schizophrenic patients and 21 normal subjects were tested on a choice reaction time task in which they were given preliminary information about where a target stimulus would occur (selective attention) and which hand to use for responding (response preparation). Data were analyzed using repeated measures ANOVA.

Results: Schizophrenic patients provided longer reaction times than normal controls ($F = 64.3$; $df = 1,40$; $p < 0.0001$), which effect was more prominent when the target stimuli was presented in the right hemispace ($F = 4.1$; $df = 1,40$; $p < 0.05$). All subjects, controls and patients, benefited from preparatory information regarding subsequent responses.

Conclusions: The results of the attentional paradigm indicate, that the deficit of information processing in schizophrenia may affect left hemispheric mechanisms to a larger extent. According to the response preparation model, there was no evidence of medial frontal lobe impairment.

NR290 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Fluctuating Dermatoglyphic Asymmetry, HLA Homozygosity and Schizophrenia

Diana O. Perkins, M.D., Psychiatry, University of N. Carolina, CB# 7160, Chapel Hill NC 27599; John H. Gilmore, M.D., Christine Sears, B.A.

Summary:

Objectives: The neurodevelopmental hypothesis of schizophrenia proposes that schizophrenia is related to altered fetal central nervous system development. Fluctuating dermatoglyphic asymmetry (FDA) has been proposed as a marker for altered second trimester cell migration, and has been associated with schizophrenia. Homozygosity at HLA Class II antigens (HLA DR and HLA DQ antigens) and the resultant maternal-fetal HLA compatibility has been associated with poor fetal outcome, and theoretically may be a genetic vulnerability factor for schizophrenia. In this study we examine the relationship of FDA with schizophrenia and homozygosity with HLA class II antigens.

Method: Subject included 23 with schizophrenia and 28 controls. Finger print patterns between corresponding digits of left and right hands were compared. Finger prints were considered symmetrical if all corresponding digits had matching patterns, and asymmetrical if one or more corresponding digits had non-matching patterns. HIA typing was done using standard tissue typing techniques.

Results: Patients with schizophrenia were more likely to have dermatoglyphic asymmetry than controls ($OR = 2.9$, $p = .10$). In the patients with schizophrenia, dermatoglyphic asymmetry was present in 90% (10/11) who were homozygous for HLA class II antigens compared with 67% (4/6) who were heterozygous for HLA class II antigens ($p = .21$).

Conclusion: FDA is associated with schizophrenia. Homozygosity for HLA Class II antigens may contribute to the altered cell migration associated with FDA and schizophrenia, either directly, or through resultant maternal-fetal HLA compatibility. These findings need to be confirmed in larger samples.

NR291 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Impaired Memory and Attention Associated with Abnormal Brain Morphology in Schizophrenia Multiplex Families

Karen J. Shedlack, M.D., Psychiatry, SUNY Stony Brook, HSC T-10-020, Stony Brook NY 11794; Gregory R. Lee, M.A., Michael Sakuma, M.A., John R. Pepple, Ph.D., Anne L. Hoff, Ph.D., Lynn E. DeLisi, M.D.

Summary:

Objective: This study postulates that memory and attentional deficits are inherited markers for schizophrenia and that brain morphology is correlated with cognitive ability in schizophrenic pedigrees.

Method: 16 schizophrenia multiplex families (12 non-schizophrenic siblings (NSS) and 31 schizophrenia-spectrum diagnosis siblings (SS)) and 20 unrelated, matched controls (NC) received neuropsychological testing while 20 members of the schizophrenia families and the 20 NC received MRI scans. Results: SS had significantly larger left lateral ventricles and smaller bilateral hippocampi than NC. Family and socioeconomic status but not diagnosis, were strong predictors of verbal IQ, but were unrelated to morphology. SS were significantly impaired on the Logical Memory subtest (LogMem) and on the quiet condition (AudQ) of the Auditory Discrimination Test as compared to NSS and NC. Significant correlations emerged between hippocampal volumes and LogMem, Visual Memory, Digits Backward, and AudQ for SS but not for NC. On all memory and attention tests NSS scores were intermediate between SS and NC but these differences tended toward significance only for AudQ.

Conclusion: This study replicates the reports of impaired memory and attention and altered hippocampal and ventricular volumes in schizophrenia. We report significant relationships between hippocampal volumes and cognition that occur in SS. We postulate that the mild cognitive impairment demonstrated by NSS may be a marker for the transmission of schizophrenia.

Support: VA/Stony Brook Collaborative Study #366 and NIMH RO1 MH4424503

NR292 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

HLA Homozygosity: Genetic Risk for Schizophrenia

John H. Gilmore, M.D., Psychiatry, University of N. Carolina, CB# 7160, Chapel Hill NC 27599; Diana O.Perkins, M.D., James D. Folds, Ph.D., Emily G. Reisner, Ph.D.

Summary:

Objectives: Maternal-fetal compatibility for HLA class II antigens is associated with spontaneous abortions, male gender, low birth weight, and minor physical abnormalities, which in turn have been associated with schizophrenia. Maternal-fetal HLA compatibility may make a fetus more vulnerable to an *in utero* environmental insult to brain development, thereby increasing the risk of schizophrenia. To test this hypothesis, we determined rates of HLA homozygosity (necessarily resulting in maternal-fetal HLA compatibility) in patients with schizophrenia.

Methods: 23 subjects with schizophrenia and 106 controls were HLA typed.

Results: A logistic regression model controlling on gender and ethnicity revealed subjects with schizophrenia were more likely to be homozygotic for either HLA-DR or DQ antigens ($p = 0.04$). All females ($n = 6$) were homozygotic for either HLA-DR or DQ, suggesting a stronger association with schizophrenia and HLA homozygosity in females. No increased rates of homozygosity were found in the HLA-A, B, or C loci.

Conclusions: Homozygosity for HLA Class II loci appears to be associated with increased risk for schizophrenia. This may reflect increased vulnerability to altered brain development due to maternal-fetal HLA compatibility, HLA homozygosity itself, or homozygosity at genes linked to HLA genes.

NR293 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Soft Neurological Signs: Reliability and Validity

Nigel M. Bark, M.D., Aecom Schiz. Res., Bronx Psychiatric Center, 1500 Waters Place, Bronx NY 10461; Sandra Grochowski, B.A.

Summary:

Objective: To create a battery of soft neurological signs that includes all those soft signs found useful or interesting in the study of schizophrenia and to demonstrate the reliability and normality of the scale and its subscales.

Method: The basis of the scale was the neurological evaluation scale of Buchanan and Heinrichs (without 'reflexes' or memory) and with the putative 'frontal' signs from Merriam et al and two from Hollender et al added. It was tested on 30 patients with schizophrenia and correlated with dimensions of schizophrenia and psychological test results. Internal reliability of the total scale and subscales was examined and refined with Cronbach's alpha. Skewness and kurtosis were examined for normality of the scale.

Results: Cronbach's alpha for the total scale was .83, for the Sensory subscale .66, for Sequencing .85, and for Coordination .64. The remaining items, including adventitious and eye movements, did not contribute to reliability. The scores on the scale and subscales showed normal variation. The validity was supported by significant correlations with IQ and other dimensions of psychology and psychopathology.

Conclusion: This soft neurological sign scale and its subscales are reliable and valid, could be shortened by eliminating the remaining items, and may contribute to the understanding of schizophrenia.

NR294 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Soft Neurological Signs and Dimensions of Schizophrenia

Nigel M. Bark, M.D., Aecom Schiz. Res., Bronx Psychiatric Center, 1500 Waters Place, Bronx NY 10461; Sandra Grochowski, B.A., Denize Da Silva, M.D., Jorge Barros-Beck, M.D., Jean-Pierre Lindenmayer, M.D.

Summary:

Objective: To use soft neurological signs (SNS)—particularly those that are lateralized—to better understand the nature of schizophrenia by correlating them with dimensions of psychopathology and psychological test results.

Method: 30 patients with chronic schizophrenia have so far been examine for SNS and also with the Positive and Negative Syndrome Scale (PANSS) and a battery of psychological tests.

Results: Sensory SNS and total Right SNS correlate with total PANSS score. Examining the PANSS five factors there are no correlations with the positive factor, only sensory SNS correlate with the negative factor but total SNS sensory SNS, and sequencing SNS correlate with the cognitive factor and right sensory SNS correlates strongly (.004) with the cognitive factor. Right sensory SNS (as well as total SNS, sensory SNS, and right and left coordination SNS) correlate strongly with perseverative errors on the Wisconsin Card Sort Test. Only sensory SNS correlate with the Stroop test. Right sensory SNS do not correlate with IQ.

Conclusion: The findings support a cognitive (or disorganisation) dimension (or even subsyndrome) of schizophrenia associated with SNS and suggest a particular association with the left parietal-temporal area of the brain. They do not support associations of the negative factor with putative frontal SNS and psychological tests.

NR295 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Temporal Lobe Asymmetries in Functional Psychoses

James M. Russell, M.D., Psychiatry, Univ of Texas Med Branch, Route D28, Galveston TX 77550; Javier Villanueva-Mey, M.D., Terrence S. Early, M.D., Justin L. Martin, B.A.

Summary:

Both structural and functional neuroimaging studies point to the temporo-limbic system in the pathogenesis of schizophrenic and affective psychoses. Whether there is a characteristic pattern of temporal lobe regional cerebral blood flow indicative of the emergency of hallucinations and delusions remains to be seen.

Eighteen unmedicated individuals with a *DSM-III-R* diagnosis of schizophrenia and six individuals with a diagnosis of bipolar disorder had an HMPAO-SPECT scan at rest. There were 11 female and 13 male subjects with a mean age of 33.46 ± 9.50 years, and a mean duration of illness of 7.12 ± 9.27 years. A total of 92% (22) of the individuals reported hallucinations or delusions at the time of assessment.

A total of 78% (14) of individuals with schizophrenia had left temporal hypoperfusion. In individuals with bipolar disorder 33% (2) had left temporal hypoperfusion, and 50% (3) had right temporal hypoperfusion. Although both individuals with schizophrenia and bipolar disorder in our sample display temporal lobe perfusion asymmetries,psychosis in individuals with schizophrenia and not bipolar disorder appears to be associated with relative left temporal hypoperfusion. A further understanding of the nature of lateralized temporal lobe dysfunction in psychoses is needed to improve our ability to treat the underlying symptoms of these disorders.

NR296 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

A Controlled Study of Early Intervention in Schizophrenia

Marvin I. Herz, M.D., Psychiatry, University of Rochester, 1650 Elmwood Avenue, Rochester NY 14620; J. Steven Lamberti, M.D., Suzanne W. Brown, M.P.A., Ruth A. Scott, M.S.N., Susan P. O'Dell, M.S.N., Syed I. Mustafa, M.D.

Summary:

Despite antipsychotic drug treatment, up to 40% of all schizophrenic patients with relapse within two years of experiencing an acute episode. "Early Intervention in Schizophrenia" is a federally funded demonstration project which seeks to determine whether an early intervention strategy is effective in reducing relapse and rehospitalization rates in schizophrenic patients at high risk for relapse. The investigators will present initial findings from this eighteen month prospective treatment study.

Eighty-eight medicated outpatients with SCID confirmed diagnoses of schizophrenia or schizoaffective disorder were randomly assigned to receive either standard treatment, consisting of biweekly supportive therapy visits, or early intervention treatment. Early intervention treatment consisted of a combination of weekly group therapy emphasizing coping skills, multifamily group psychoeducation, and active monitoring for prodromal symptoms. Intervention occurred whenever prodromal symptoms were observed. Measures obtained at regular intervals throughout the study included clinical measures, family assessments, service utilization measures and cost measures.

Analysis of data at six months shows a trend toward less use of emergency room and inpatient services in the early intervention group compared to the standard treatment group. Further data and results will be presented and discussed.

NR297 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Written Sentence Production in Schizophrenia

Brian F. O'Donnell, Ph.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Maria C. Van Der Pahlen, B.A., Margaret A. Niznikiewicz, Ph.D., Matthew O. Kimble, B.A., S. N. Sridhar, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: Schizophrenic patients often show disturbed language production. We studied the linguistic and pragmatic aspects of written sentence production in 17 male, right-handed schizophrenic and 14 age, gender, and handedness matched control subjects.

Methods: Subjects were asked to write sentences that described simple scenes presented on a video monitor which depicted static objects or changes in state (Sridhar, 1988). Sentences were scored by raters blind to diagnosis for errors of content, temporal and spatial relationships, and linguistic form. Linguistic form was scored for errors of syntax (e.g., word and phrase relationship within a sentence), grammar (e.g, verb-noun agreement), and orthography (e.g., spelling and punctuation). Scores were compared with two-tailed t-tests using a $p < .05$ criterion for significance.

Results: In terms of semantic content, schizophrenic patients were more likely to omit nouns or verbs describing the elements of a scene than control subjects. Patients described objects in a scene effectively, but had difficulty describing changes in spatial relationships within a scene. More orthographic and syntactic errors were made by the patients.

Conclusions: The reduced intelligibility of sentences produced by schizophrenic patients, therefore, cannot be attributed to a single type of linguistic failure, but rather to pervasive abnormalities affecting semantic, syntactic, and pragmatic aspects of the sentence production.

NR298 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Event Related Potential and MRI Evidence of Deterioration in Schizophrenia

Brian F. O'Donnell, Ph.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Steven F. Faux, Ph.D., Robert W. McCarley, M.D., Martha E. Shenton, Ph.D., Matthew O. Kimble, B.A., Paul G. Nestor, Ph.D.

Summary:

Objective: Event-related potential (ERP) and MRI measures were used to test whether schizophrenic patients showed evidence of neurodegenerative change after onset of the illness.

Method: We evaluated 47 chronic, male, right-handed schizophrenic patients and 47 age, gender, and handedness matched controls between the ages of 20 and 60. An auditory "oddball" paradigm was used to elicit the P300 component of the event-related potential at the Fz, Cz, and Pz electrode sites. P300 latency is a sensitive index of neurodegenerative changes in dementia, and to neural changes with age.

Results: The slope of P300 latency on age was steeper in schizophrenic compared to controls at Fz ($b = 3.0$ ms/year vs. 0.7 ms/year; $p < .05$) and Cz ($b = 3.2$ ms/year vs. 1.2 ms/year; $p < 0.05$). The slope of P300 latency on age was not affected by current inpatient or outpatient status, or percent time hospitalized since first episode. A subset of 15 patients and 15 control subjects also received quantitative MRI evaluation of the grey matter volume of the posterior superior temporal gyrus (STG), a probable generator site of the P300 component. The volume of the left posterior STG diminished with age in schizophrenic ($r = .61$), but not in controls ($r = .20$, N.S.).

Conclusions: More rapid P300 latency prolongation and left posterior STG grey matter tissue reduction with age provide pathophysiological support for a neurodegenerative process in chronic male schizophrenic patients.

NR299 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Event Related Potential Indices of Language Problems in Schizophrenia

Margaret A. Niznikiewicz, Ph.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: Language problems are a prominent feature of schizophrenia. We used a semantic incongruity event related potential (ERP) paradigm to explore electrophysiological correlates of schizophrenic language. The waveform components sensitive to language processes are the N400, peaking around 400 msec, which is sensitive to the activation of the lexical memory network, and the P600, peaking about 600 msec, after stimulus presentation, which is thought to be sensitive to meaning integration.

Methods: In this study sentences were presented one word at a time to ten male, right handed, chronic medicated schizophrenics (Sz) and 12 normal, age matched males, in both visual and auditory modalities. One hundred sentences were semantically correct, e.g., *Jane has never been to Boston* (congruent completion) and one hundred were not, e.g., *John wanted to eat one more sleeve.* (incongruent completion).

Results: The subjects judged if sentences made sense. In Sz, N400 amplitude in both modalities was more negative to both congruent and incongruent completions suggesting excessive activation of lexical network. This result corroborates earlier findings where smaller N400 amplitude was reported for the difference waveform (incongruent minus congruent condition). N400 amplitude was larger in the auditory than in the visual modality (group × modality × electrode $p < .06$) in the Sz group corroborating earlier EP and clinical findings of larger impairment in this modality. Smaller P600 amplitudes were recorded in the Sz group in both modalities (group × condition × electrode $p < 003$) suggesting impaired processes of semantic integration. Prolonged peak latencies of both the N400 ($p < .0001$) and the P600 (group × modality $p \times .07$) in Sz suggest the slowing of language processing in schizophrenia.

Conclusion: These data are compatible with a model of excessive activation of semantic network in schizophrenia due to loss/damage of neuronal structure subserving language as suggested by MRI data from our lab and others.

NR300 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Relationship of Brain Dopamine Functioning to Intellectual Performance in First-Episode Schizophrenia

Brian Sheitman, M.D., Research, Hillside Hospital, P.O. Box 38, Glen Oaks NY 11004; Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Gail Reiter, M.A., Jose Ma. J. Alvir, Dr. P.H., Miranda Chakos, M.D.

Summary:

The prevalence of schizophrenia has repeatedly been shown to be greater in the intellectually impaired than in the general population. Nevertheless, the nature of this complex interaction remains poorly understood. This study investigated the relationship between full-scale IQ and a variety of biological and clinical variables which have been shown to be related to brain dopamine function. The data were derived from an ongoing prospective investigation of neuroleptic naive first-episode schizophrenics. Patients were assessed at baseline, and followed for a period up to five years. Full scale IQ scores were measured at six months.

Plasma homovanillic acid (n = 33), growth hormone (n = 41), and prolactin (n = 41), showed very weak correlations with full scale IQ scores (range 65–128). However, FSIQ was found to be

a significant predictor of tardive dyskinesia (TD) ($x^2 = 5.939$, df = 1, p = 0.01).

These results indicate that a low FSIQ score is associated with the emergency of TD and is consistent with previous reports of cognitive impairment being a risk factor for TD. It further suggests that TD vulnerability is part of the diathesis of a subtype of schizophrenia.

NR301 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Increased Inter-Putamen Distance-Brain Width Ratio in First-Episode and Chronic Schizophrenic Patients

Houwei Wu, M.D., Research, Hillside Hospital, P.O. Box 38, Glen Oaks NY 11004; Rafael Munne, M.D., Robert Bilder, Ph.D., Bernhard Bogerts, M.D., Jeffrey A. Lieberman, M.D.

Summary:

Basal ganglia enlargement has been reported as one of the brain abnormalities in schizophrenic patients. In this study, we used a simple measurement to assess the differences in basal ganglia size between schizophrenic patients and normal controls. Two groups of patients were studied: a first-episode schizophrenia sample (N = 80) and a chronic schizophrenia sample (N = 40). Each group had separate controls (Ns = 50 and 21, respectively). We measured the distance between the two lateral boundaries of the putamen (inter-putamen distance, IPD), as an index of the basal ganglia size. These measures were made on coronal magnetic resonance images at the level of the anterior commissure. Brain width (BW) was measured on the same slice. There was a significant increase in the ratio of IPD/BW in both groups of patients relative to controls (first episode: $F(1,129) = 18.23$, $P < .0001$; chronic: $F(1,59) = 13.81$, $P < .0005$). The findings are consistent with the recent literature, and provide a simple method for investigating the size of the basal ganglia.

NR302 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Sexual Dysfunctions in Male Schizophrenic Patients

Dov Aizenberg, M.D., Geha Hospital, P.O. Box 102, Petah-Tikva 49100, Israel; Zvi Zemishlany, M.D., Pnina Dorfman-Etrog, M.D., Abraham Weizman, M.D.

Summary:

Objective: Neuroleptic treatment in schizophrenic patients is associated with sexual dysfunction. However, it is not clear to what extent the disorder and/or the pharmacological treatment are responsible for the impairment. The aim of the present study was to evaluate the sexual function of untreated and treated male schizophrenic patients in comparison to healthy subjects.

Methods: Sexual functions and behavior were evaluated in 122 male subjects: 20 drug-free schizophrenic patients, 51 neuroleptic-treated schizophrenic patients, and 51 normal controls. The participants underwent a detailed structured interview assessing male sexual function quantitatively and qualitatively (Schiavi et al, 1990).

Results: High frequency of sexual dysfunction was reported by both groups of patients. Impairment in arousal items (erection) and orgasm during sex were mainly reported by the treated patients. Desire was reduced in both schizophrenic groups, but reduction in the frequency of sexual thoughts was confined to the untreated ones ($p = 0.01$). The schizophrenic patients were more involved in masturbatory activity. Treated patients disclosed dissatisfaction with their sexual function ($p < 0.0001$).

Conclusion: Sexual desire seems to be more impaired in untreated schizophrenic patients. Neuroleptic treatment is associated with impairment in erection, orgasm, and satisfaction.

NR303 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Multi-Assessment of Risperidone Effects: A Retrospective Study

Roch Hugo Bouchard, M.D., Psychiatry, CH Robert Giffard, 2601 de la Canardiere, Beauport Quebec G1J2G3, Canada; Emmanuelle Pourcher, M.D., F. Chasse, Ph.D., Marie-Josee Filteau, M.D., Philippe Baruch, M.D., W. Pilon, Ph.D.

Summary:

Introduction: Risperidone (Ris), a novel D_2 and S_2 antagonist has been shown to improve negative symptoms. Data on the actual relevance of this improvement on long-term clinical outcomes of schizophrenia patients, in terms of functional autonomy and social cost, are sparse.

Methods: Two-way analysis of variance with repeated measures was performed. Two groups of 16 chronic schizophrenic residents were matched for age, global/psychiatric/physical levels of care, and degree of functional autonomy. One group received Ris for six conventional neuroleptics. Patients were evaluated with Functional Autonomy Scale (Fas) and new York level of care survey (NYS) and groups and periods were compared after six months of treatment.

Results: The only significant differences observed were in the risperidone group and were noted between the two periods of evaluation for the following scales: global level of care ($F = 9.30$, $p < .004$), physical level of care ($F = 22.09$, $p < .0001$), psychiatric level of care ($F = 6.39$, $p < .017$), personal autonomy ($F = 5.66$, $p < .02$), social autonomy ($F = 6.12$, $p < .01$). In addition community autonomy ($F = 4.73$, $p < .037$) but analysis of contrasts didn't find a difference in the risperidone group or control group. Another result obtained was a significant difference between the two periods of evaluation for the global score of the functional autonomy scale ($F = 10.44$, $p < .003$) and that was observed for both the risperidone group ($F = 6.66$, $p < .01$) and control group ($F = 3.95$, $p < .05$).

Conclusion: Results underline the necessity of integrating multidimensional evaluations in the overall assessment of a new pharmalogical intervention and suggest that risperidone may reduce healthcare costs. This should be confirmed in a larger study.

NR304 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Quantitative Autoradiography of 5-HT1a Receptors in Schizophrenia and Nonpsychotic Suicide Patients

Donald C. Ohuoha, M.D., Neuropathology, NIMH CBDB 1RP, 2700 Martin L. King Avenue, Washington DC 20032; Thomas M. Hyde, M.D., Mary M. Herman, M.D., Joel E. Kleinman, M.D.

Summary:

Prefrontal hypofunction has been implicated in the cognitive deficits in schizophrenia, which tend to be unaffected by antidopaminergic drugs. Recent animal studies suggest that limbic dopaminergic projections from the ventral tegmental area to the nucleus accumbens, which have long been linked to the production and pharmacological treatment of psychosis, are closely regulated by the prefrontal cortex. The role of serotonin receptors in the mechanism of this regulation, is unclear. Measurements of 5-HT1 and 5-HT1a receptor densities (Bennet et al 1979, Whitaker et al 1981; Hashimoto et al 1990) found opposing results in the prefrontal cortex.

In this study, we examined 5-HT1a receptor density in postmortem prefrontal cortex (Broadman Area 9) using quantitative autoradiography, comparing patients with schizophrenia to normal controls, nonpsychotic suicides, and nonschizophrenic neuroleptic-treated psychiatric patients. Quantitative autoradiography of 5-HT1a receptors was~ performed using 2nM [3H]8-OH-DPAT. Nonspecific binding was determined by incubating consecutive brain sections in the presence of 1uM 8-OH-DPAT. Preliminary

analysis of autoradiograms using computerized image analysis did not reveal any significant differences between patients with schizophrenia and those that committed suicide and other groups. These findings suggest that alteration of 5-HT1a receptor density in the prefrontal cortex is not a primary feature of schizophrenia.

NR305 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Geriatric Schizophrenic Inpatients Versus Outpatients

Katherine M. Putnam, M.A., Bldg 11, Pilgrim Psych Center, Box A, W. Brentwood NY 11717; John M. Herrera, Ph.D., Philip D. Harvey, Ph.D., Donald M. Quinlan, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

There are very few studies of geriatric schizophrenics who are receiving treatment as outpatients. In this study, 25 geriatric schizophrenic outpatients were compared on cognitive functioning (MMSE scores), and positive and negative schizophrenic symptoms (PANSS scores) to the normative standards developed on a sample of 308 geriatric schizophrenics still receiving inpatient care. The outpatient subjects were very different from the inpatient sample on MMSE scores (23.6 vs. 15.0; $t = 4.3$, $p < .001$) and negative symptoms (12.9 vs. 27.3; $t = 7.3$, $p < .0001$), while manifesting a relatively minimal difference in the severity of positive symptoms (14.4 vs. 18.1; $t = 2.4$, $p < .025$). In an effort to minimize demographic differences, a sample of geriatric inpatients were matched to the outpatients on the basis of gender, education, age, and MMSE total scores. After matching, the difference between the samples in positive symptoms was increased ($t = 2.9$, $p < .005$) while the effect size of the difference between the samples in negative symptoms was decreased by about 50% ($t = 3.8$, $p < .001$, inpatient-matched sample mean = 18.6). These data suggest that although outpatient schizophrenic patients manifest considerable cognitive impairment, the differences between them and inpatients are substantial. It appears that geriatric inpatients are hospitalized for two separate reasons: severe cognitive impairment in most cases and severe positive symptoms in cases where cognitive impairment is relatively minimal.

NR306 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

1H-Magnetic Resonance Spectroscopy in Schizophrenia: Putative Neurodevelopmental and Cognitive Correlates

Peter Buckley, M.D., Psychiatry, Case Western Reserve, 2040 Abington Road, Cleveland OH 44106; Constance Moore, Ph.D., Helen Long, B.A., Conall Larkin, M.B., Fiona Mulvany, B.A., John L. Waddington, D.Sc.

Summary:

Objective: To examine the relationship of putative neurodevelopmental indices [obstetric complications (OC's), family history of schizophrenia (FH), and minor physical anomalies (MPA's)] to cerebral function as measured by ^{1}H-magnetic resonance spectroscopy.

Method: ^{1}H MRS of the left temporal and frontal lobes was performed in 28 patients with *DSM-III-R* schizophrenia and 20 healthy, matched volunteers; putative neurodevelopmental and clinical data were also obtained.

Results: Male patients showed a significant reduction in frontal n-acetylaspartate (NAA) values in comparison with male controls (35.1 ± 8.0 vs 45.3 ± 8.9, $p < .01$) and female patients (45.9 ± 7.2, $p < .005$); frontal choline values were raised ($p < .01$) in male patients relative to these groups. Neither OC's, FH, nor MPA's were associated with distinct patterns on ^{1}H-MRS. However memory function in patients, as assessed by the Weschler Memory Scale-Revised, was related to temporal, but not frontal MRS measures; this pattern was less apparent in controls.

Conclusions: Though gender specific patient-control differences were evident, MRS measures proved unrelated to putative neurodevelopmental indices; also they were differentially associated with memory function in patients versus controls. The relative decrement in NAA (which is distributed intraneuronally) may reflect frontal hypoplasia/dysplasia that predominantly affects male patients.

Supported by the Health Research Board of Ireland and the St. John of God Order.

NR307 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Affective Reactivity of Language in Schizophrenic Patients and Their Parents

Nancy M. Docherty, Ph.D., Psychiatry, yale University Sch Med, 34 Park Street Room 247, New Haven CT 06519

Summary:

Objective: We hypothesized that poor linguistic reference performance, a measure of communication disturbance, represents a vulnerability marker for schizophrenia and as such is present in some healthy parents of schizophrenic patients. We also hypothesized that this kind of language disturbance is immediately exacerbated by negative affect in the patients, but not in the parents.

Method: We assessed linguistic reference performance in the speech of ten stable schizophrenic out-patients, 18 of their "unaffected" parents, and ten nonpsychiatric controls, in affectively negative vs. affectively positive conditions.

Results: As in our earlier study, patient and parent groups scored approximately equally on the reference performance measure in the positive condition, and significantly in the negative condition while parents' and controls' speech did not. The degree to which patients' speech was reactive to negative affect corresponded to the severity of their core positive symptoms of delusions and hallucinations.

Conclusions: These data support the hypothesis that poor reference performance represents a vulnerability marker for schizophrenia, and that affective reactivity of language symptoms is associated with an underlying positive schizophrenic process.

NR308 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Working Memory, Attention and Language in Schizophrenia

Nancy M. Docherty, Ph.D., Psychiatry, Yale University Medical, 34 Park Street Room 247, New Haven CT 06519; Keith A. Hawkins, Psy.D., William H. Sledge, M.D., Ralph E. Hoffman, M.D., Donald M. Quinlan, Ph.D., Jaak Rakfeldt, Ph.D.

Summary:

Objective: We hypothesized that communication disturbances are different in nature and therefore have different cognitive underpinnings in schizophrenic vs. manic and nonpsychiatric speakers. In particular, we wanted to demonstrate that schizophrenic communication disturbances reflect specific deficits in the areas of working memory and attention.

Method: We administered cognitive tests assessing working memory, attention, concept formation, and verbal fluency to schizophrenic, manic, and non-psychiatric control subjects. We also rated free speech samples of the same subjects for levels of communication disturbance by assessing their linguistic reference performance. We then examined the cognitive correlates of poor linguistic reference performance in each of the diagnostic groups.

Results: Reference performance ratings in the schizophrenic patients were associated with scores on tests of working memory

and attention, but were not related to scores on concept formation or verbal fluency tests. In contrast, in the manic and nonpsychiatric subjects, reference performance was significantly associated with concept formation and verbal fluency scores, but was not related to scores on tests of working memory. Differences between diagnoses in the cognitive correlates of communication disturbance were marked.

Conclusions: These findings support the idea that communication disturbances have different cognitive substrata in schizophrenic vs. manic and nonpsychiatric speakers.

NR309 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Work and Symptom Change in Schizophrenia

Morris D. Bell, Ph.D., West Haven VAMC 116B, 950 Campbell Avenue, West Haven CT 06516; Paul Lysaker, Ph.D.

Summary:

Sixty-three subjects with schizophrenia participated in 22 weeks of work activity (e.g. in maintenance, medical records, mailroom, and laundry). In a quasi-experimental, repeated measures design, weekly symptom assessments using the Positive and Negative Syndrome Scale were performed yielding five component scores (Positive, Negative, Excitement, Hostility, and Emotional Discomfort) and a Total symptom score for each observation. Results of the repeated measures ANOVA revealed significant time effects for total score ($p < .0001$) and all components. Correlation of Total Score means by week produced an $r = -.96$ ($p < .0001$) and similar results were found for the components as well (r's ranged from .96 to .80). On total score, 38% were much improved (defined as 20% symptom reduction) at the conclusion of 22 weeks of work while only 5% were much worse (defined as 20% symptom increase). The highest percentage of subjects improved on the Positive component (54%), followed by Negative (49%), Hostility (4%), Emotional Discomfort (46%), and Cognitive (32%) components. Subjects who worked were compared with 35 similar subjects, who declined participation because they did not receive a pay incentive, on intake and 22-week PANSS. ANCOVA revealed significant group differences on Total Score ($p < .0001$) and on Positive ($p < .01$), Hostility ($p < .05$) and Emotional Discomfort ($p < .0001$) components. Percentages of subjects were improved (20% improvement) differed between groups on PANSS Total Score ($p < .05$) and on Positive ($p < .0001$), Negative ($p < .05$), and Emotional Discomfort ($p < .01$) components. Discussion focuses on the clinical benefits of work activity, limitations of this design, and recommendations for more controlled studies.

NR310 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Symptoms and Work Performance in Schizophrenia

Morris D. Bell, Ph.D., West Haven VAMC 116B, 950 Campbell Avenue, West Haven CT 6516; Paul Lysaker, Ph.D.

Summary:

The present study examined the relationship between psychiatric symptoms and work performance for 65 subjects with *DSM-III-R* diagnoses of schizophrenia or schizoaffective disorder who participated in a work rehabilitation program. Symptoms were assessed using the Positive and Negative Syndrome Scale to predict performance ratings on the Work Personality Profile, a measure of five dimensions of work function. The predictive power of concurrent ratings and ratings taken at three weeks and three months apart were compared in order to determine how sensitive these relationships were to the passage of time. Results indicated that up to 27% of the variance in work performance measures could be explained by symptom domains. PANSS cognitive and negative components were most often related to work function. The positive component did not predict work performance. Concurrent ratings were the most powerful predictors, ratings three weeks apart were less powerful, and ratings 13 weeks apart were least powerful. Concurrent ratings at 13 weeks revealed significant relationships for all five work performance factors with R squares ranging from .27 for Task Orientation to .17 for Work Conformance ($p < .001$). We conclude that symptoms have a significant relationship to work performance. Previous research may have failed to detect these relationships at least in part because of global symptom measurement which overemphasize positive symptoms and because assessments were not done concurrently.

NR311 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Is Schizophrenia Primarily a Right Sided, Rhinencephalic Defect?

Murray A. Cowen, M.D., Brain Research, Nathan Kline Inst., Orangeburg NY 10962; David N. Bertollo, B.A., Maurice R. Green, M.D.

Summary:

A recently proposed model of the non-paranoid schizophrenias suggests that the primary defect lies in the embryogenesis of the olfactory and associated structures, which leads to secondary, symptom producing, defects in lidline and limbic areas of the brain (1). Consideration of the putative role of fetal blood flow asymmetry in brain development, and lateral asymmetries in blood flow patterns associated with schizophrenic symptom cluster analyses (2), further suggest that the primary olfactory defects might be more right-sided and uncrossed, while the secondary defects might be crossed and bilaterally symmetrical. PET brain deoxyglucose images, which had been collected on eight male schizophrenics and eight male controls, were analyzed. The schizophrenics showed major right-sided defects in the primary olfactory discrimination cortex of the posterior lateral orbital cortex, and bilateral defects in the limbic projection area of the rostral medial orbital cortex. While highly compatible with the model (1), more extensive studies including female subjects would be necessary for its confirmation.

NR312 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Effects of Medication History on Resting EEG Measures in Schizophrenia

Roland J. Erwin, Ph.D., Psychiatry, Univ of Penn. 10th Flr., 3400 Spruce St. Gates Bldg, Philadelphia PA 19104; Ruben C. Gur, Ph.D., Raquel E. Gur, M.D.

Summary:

Objective: Some studies have reported increases in EEG theta activity in patients exposed to neuroleptic medications although few have examined the regional distribution of theta increases and the findings are mixed. Since the left hemisphere has been implicated as abnormal in schizophrenia, it was hypothesized that theta increases may be lateralized to the left hemisphere.

Methods: Resting eyes-open EEG was recorded from 18 electrode sites (linked madible reference) of 12 normal controls, 12 neuroleptic naive patients with schizophrenia, and 12 previously medicated patients (off medication for two weeks prior to study) for a minimum of four minutes. Artifact-free EEG was submitted to spectral analyses and the spectra obtained were then collapsed into frequency bands: delta (1–3 Hz), theta (4–7 Hz), alpha1 (8–13 Hz), and beta (13–32 Hz).

Results: Mixed model analyses of variance were then conducted separately for each frequency band. The major finding was a significant hemisphere × group interaction ($F(2,29) = 5.48$, $p < .01$) for the theta band. This interaction was due to increased theta activity over the left hemisphere in previously medicated

patients relative to both neuroleptic naive patients and controls. This effect was not obtained for any other frequency band.

Conclusion: The findings suggest that neuroleptic exposure may have greater physiological consequences for the left hemisphere in schizophrenia.

NR313 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Diagnoses in Child Schizophrenic Relatives

Marge C. Lenane, M.S.W., NIMH Bldg 10 RM 6N240, 9000 Rockville Pike, Bethesda MD 20892; Kathleen McKenna, M.D., Jean Frazier, M.D., Judith L. Rapoport, M.D.

Summary:

Very little is known about rates of psychiatric illness in the first-degree relatives of children and adolescents with childhood onset schizophrenia (COS). We now report the results of a systematic prospective investigation utilizing personal interviews with 49 of 58 biologic first-degree relatives (84%) of 19 consecutively admitted children, aged 10 to 18, with COS seen by the NIMH Child Psychiatry Branch in our ongoing study examining the phenomenology, neurobiology, and drug treatment of COS. Eighteen mothers, 15 fathers, seven brothers, and nine sisters were evaluated, utilizing the Schedule for Affective Disorders and Schizophrenia-Lifetime (SADS-L), Diagnostic Interview for Children and Adolescents (DICA-P), family history, and genogram. One child has been adopted and there was no information available about her biologic parents. In addition, one mentally retarded sister and one autistic sister were not evaluated. Two (4%) first-degree relatives met criteria for schizophrenia, one individual was given a "possible" diagnosis (6%); 12 (24%) met criteria for affective disorders; 20 (41%) for anxiety disorders and seven (14%) for alcoholism. Fifteen relatives were free of psychiatric disorders. Axis II disorders (including schizoid and schizoptypal) were evaluated using the Structured Interview for *DSM-III* Personality (SIDP) and will be reported.

NR314 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Effects of Clozapine on Cognition in Schizophrenia

Theo C. Manschreck, M.D., Dartmouth Medical School, 105 Pleasant Street, Concord NH 03301; Crystal R. Blyler, M.A., Brendan A. Maher, Ph.D., Deborah A. Redmond, M.A., Scott M. Beaudette, B.A.

Summary:

Objectives: We examined the relationship between cognitive changes and clinical outcome with clozapine treatment.

Methods: Fifty-five DSM-III-R schizophrenic and schizoaffective inpatients of New Hampshire Hospital were accepted for clozapine treatment. Symptomatology, measured by the Brief Psychiatric Rating Scale and the Scales for the Assessment of Positive and Negative Symptoms, and performance on numerous cognitive tasks were assessed every three months.

Results: Symptoms at baseline did not differentiate patients who were discharged from those who remained hospitalized. Baseline performances for discharged patients, however, were superior to those of nondischarged patients on Trails, Wechsler memory Designs, Controlled Oral Word Association (FAS), the Mini Mental Status Examination, and the block design subtest of the Wechsler Adult Intelligence Scale. Overall, patients improved on Trails, FAS, graphesthesia, and motor tapping accuracy. After treatment, however, there was some decrement of performance on alternating responses and motor tapping speed. Although symptoms improved significantly with treatment, multiple regression analyses revealed that these changes were independent of changes in cognition.

Conclusions: Certain trait-like cognitive tasks may be used to develop criteria for predicting outcome of clozapine therapy. The independence of cognitive and symptom changes may reflect drug effects on different pathophysiologic mechanisms relevant to psychosis.

NR315 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Schizophrenia, Lung Cancer and Vitamin C

J. Daniel Kanofsky, M.D., Psychiatry, Albert Ein. Coll. of Med, 1500 Waters Place, Bronx NY 10461; Edward P. Norkus, Ph.D., Barry Geller, B.A., Robert Lowinger, M.D., Paul B. Kanofsky, Ph.D., Gary J. Kennedy, M.D.

Summary:

Objective: Over 60% of patients with schizophrenia smoke. This is a smoking rate roughly double that of the general population. Schizophrenics should then have a higher rate of lung cancer. However, existing research indicates a rate equivalent to or less than the general population. Epidemiological studies suggest beta carotene and vitamin C offer protection against lung cancer. Smoking consistently reduces serum vitamin C levels by 25% to 40% in normals. We speculate that schizophrenics are partially protected from developing lung cancer by maintaining relatively high serum vitamin C levels even if they smoke. The effect of smoking on serum vitamin C level was investigated in a group of elderly schizophrenics.

Method: We previously reported high vitamin C and low beta carotene levels in 22 elderly state hospitalized schizophrenics. A further analysis reveals that in our patients the mean serum vitamin C level for smokers was 1.33 mg/dl (n = 15) versus 1.44 mg/dl (n = 7) in non-smokers. In our community controls the respective means were 0.60 mg/dl (n = 14) versus 0.95 mg/dl (n = 20).

Results: Using a t-test the p-values for the differences between the smoking and non-smoking means were, respectively, $p = .40$ and $p = .0001$.

Conclusions: Smoking may not substantially lower serum vitamin C levels in schizophrenics. This may place them at lower risk for developing lung cancer.

NR316 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

MRI Predictors of Clozapine Response: A Preliminary Study

John Lauriello, M.D., Psychiatry 116A, Veterans Affairs, 3801 Miranda Avenue, Palo Alto CA 94304; Daniel H. Mathalon, Ph.D., David L. Ringo, M.D., Edith V. Sullivan, Ph.D., Kelvin O. Lim, M.D., Adolf Pfefferbaum, M.D.

Summary:

Treatment refractory schizophrenics (SZ) show a 30% to 60% decrease in symptoms with clozapine, usually within three months. Friedman et al. (1991) reported an inverse relationship between prefrontal sulcal prominence and clozapine response after six weeks. We used MRI to test whether brain morphology predicts improvement on BPRS with longer-term clozapine treatment (3 to 17 months, median = 4 months). 19 SZ men (age = 40.3 ± 6.8 years, symptom onset age = 23.4 ± 5.0 years, illness duration = 16.8 ± 7.6 years) were medicated with typical neuroleptics at baseline and with 300–900 mg/day clozapine at follow-up (median = 500 mg). SZ had prefrontal gray matter deficits ($p = .0001$) and enlargement of prefrontal sulci ($p < .015$) and lateral and third ventricles ($p = .0001$). A total of 47% had at least a 20% improvement on total BPRS and also showed significant improvement on conceptual disorganization, thought disorder, and positive symptoms ($p \leq .05$). Although improvement did not correlate significantly with prefrontal measures, improvement on conceptual disorganization correlated with smaller lateral and third ventricles.

These preliminary results suggest that there are some brain morphological predictors of clozapine response, but even SZ with significant brain dysmorphology can have a positive clinical response to clozapine. *[Supported by MH30854, DVA, Norris Foundation, and Sandoz Pharmaceutical Corporation]*

NR317 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Does Diminished Affective Expression in Schizophrenia Reflect Affective Deficit or Neuromotor Dysfunction?

Scott C. Clark, M.D., Clin. Psychbio, NY Psych Inst., 722 W. 168th Street Unit 2, New York NY 10032; Robert H. Dworkin, Ph.D., Xavier F. Amador, Ph.D., Lewis A. Opler, M.D., Stephanie R. White, B.A., Jack M. Gorman, M.D.

Summary:

A dissociation between affective expression and affective experience has been documented in the neurological literature, and the existing approaches to affective deficits in schizophrenia typically examine only one of these two different components of affective responsivity. We have developed a cartoon-based measure in which self-reported affective experience and observer-rated affective expression are assessed concurrently (Self and Observer Affect Rating Scale; SOARS). Using this measure we replicated the finding that patients with schizophrenia manifest diminished affective expression in the presence of normal affective experience. Based on this apparent dissociation between affective expression and affective experience, we hypothesized that diminished affective expression, rather than reflecting an affective deficit, may reflect the neuromotor dysfunction that is prevalent in schizophrenia. We used the Scale to Assess Neurological Abnormality (SANA), a measure of sensory and motor deficit, to test this hypothesis. We examined the relationships among the SOARS affective expression and experience measures, the SANA, thermal pain insensitivity, and clinical ratings of positive and negative symptoms in a sample of patients with schizophrenia. Preliminary analyses of the data are consistent with the hypothesis that in patients with schizophrenia diminished affective expression reflects neuromotor dysfunction and that affective experience, when diminished (i.e., anhedonia), reflects an affective deficit.

NR318 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Lateralized P300 Voltage Asymmetries in Left-Handed and Right-Handed Schizophrenic Subjects: An Update

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Summary:

We have differentiated left-handed (LH) and right-handed (RH) schizophrenic males on the basis of different left-right voltage asymmetries in P300; this phenomenon suggests that the pathophysiology of P300 generators is lateralized according to handedness in schizophrenia (Holinger et al., *Electroenceph. Clin. Neurophysiol.,* 1992). We have now sought to determine the replicability of this effect in a new subject group of: LH schizophrenic males (8), RH schizophrenic males (9), LH control males (8), and RH control males (7). Schizophrenics met *DSM-III-R* criteria; controls were assessed with the MMPI-2. Subjects were matched for age and IQ; handedness was assessed with Oldfield's Edinburgh Inventory. MANOVA analyses on T3, C3, Cz, C4, and T4 electrodes showed an overall group effect ($p < .01$), indicating that LH and RH schizophrenics had lower overall P300 voltage than normals. Even with this modest N, the hand × diagnosis × electrode interaction showed a trend toward statistical significance ($p = .1$), and there was a significant handedness × electrode interaction for LH and RH schizophrenics ($p < .05$). At this subject N, there is thus suggestive but not statistically conclusive evidence for a complete replication, while the left vs. right differences in schizophrenics are replicated.

NR319 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Syndrome Typology Effects Upon Engagement and Outcome in Schizophrenic Substance Abusers

Richard N. Rosenthal, M.D., Psychiatry, Beth Israel Medical Ctr., First Avenue at 16th Street, New York NY 10003; David J. Hellerstein, M.D., Christian Miner, Ph.D.

Summary:

Objective: To assess the contribution of schizophrenia syndromes to the development of appropriate treatments for patients with RDC/*DSM-III-R* schizophrenia and substance abuse (PSUD/S).

Method: We used regression procedures to model and predict post-hospital treatment engagement in 63 patients screened at index hospitalization with SANS and SAPS as part of a randomized study comparing integrated and non-integrated psychiatric and addiction outpatient treatment of PSUD/S patients. We also used the Addiction Severity Index to compare differential response to treatment across groups by syndrome type at four months post-hospitalization ($N = 31$).

Results: A significant model was based upon two negative predictors alone, male gender and mixed syndrome with $R^2 = .213$ [$F = 8.13$; $df = (2,60)$; $p = .001$]. Predicted scores from this model correctly identified 71.4% for engagement status [Fisher exact $p = .001$]. Comparing differential response to treatment by syndrome type, we found a significant syndrome effect four months post-hospitalization for addiction severity [$F = 3.36$; $df = (2,1,27)$; $p .05$] and for psychiatric severity [$F = 4.96$; $df = (2,28)$; $p .05$]. Negative syndrome patients reported significantly worse addiction severity than positive syndrome patients [Tukey HSD test, $p = .048$]. Mixed syndrome patients had more severe psychiatric problems than the negative syndrome patients [Tukey HSD test, $p = .012$].

Conclusions: PSUD/S patients with different syndrome types fare differently in engagement and over the early phases of treatment, with each syndrome posing somewhat distinct challenges for outpatient service providers.

NR320 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The P50 and Mismatch Detection in Normal Volunteers: Implications for the Study of Sensory Gating in Schizophrenia

Nashaat N. Boutros, M.D., Psychiatry, The Ohio State University, 473 West 12th Avenue, Columbus OH 43219; Brandy Barker, Michael Torello, Ph.D.

Summary:

Objective: To further study the different aspects of sensory gating in normal volunteers. Sensory gating is a complex multistage, multifaceted psychological function believed to be protecting higher cortical centers from being flooded with incoming irrelevant sensory stimuli. Failure of such mechanisms is hypothesized as one of the mechanisms underlying the development of psychotic states.

Method: In the current study, we investigated the responsiveness of the P50 evoked response to changing the physical characteristics of ongoing trains of auditory stimuli. Forty normal volunteers were studied in a modified odd-ball paradigm. Auditory clicks of four msec duration and 85 dbs loudness were presented every two seconds. A rare click of 1500 Hz frequency was interspersed with more frequent 500 Hz clicks (10% to 90% respec-

tively). Data were collected from the left and right frontal, central, and temporal regions, as well as the central scalp region (C_Z). The amplitude of the response to frequent (F), and to the infrequent (IF) stimuli, as well as an IF/F ratio were calculated for each scalp region studied.

Results: Utilizing a one-way analysis of variance (ANOVA), the amplitudes of the P50 was higher in response to the infrequent stimuli, at all cerebral locations studied ($p < .001$). For the IF/F ratio electrode location was a significant factor ($p < .03$). Higher ratios were seen at the right central and temporal regions.

Conclusions: We postulate that the increase in amplitude of the P50 reflects the system's recognition of novel stimuli or "gating in" of sensory input. Our findings suggest that such "gating in" mechanisms may begin at an early pre-attentive stage as reflected by the P50 wave. Although this study only included normal subjects, the data generated contribute to the understanding of sensory gating mechanisms.

NR321 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

How Do Schizophrenics Discriminate the Origin of Information?

Sophia Vinogradov, M.D., 116C, V.a. Medical Center, 4150 Clement Street, San Francisco CA 94121; Emily Marton, B.A., John H. Poole, Ph.D., Beth A. Ober, Ph.D., Gregory K. Shenaut, Ph.D., Leora Benioff, Ph.D.

Summary:

A hallmark of the hallucinations and delusions in schizophrenia is the impaired ability to discriminate between externally and internally generated information, which Johnson et al. (1981) have proposed is related to cognitive processes attending memory formation, and retrieval. In this study, we developed a word-generation and recognition task which tested subjects on both recognition-recall and "reality monitoring" (i.e., the ability to discriminate among words previously presented by the examiner, words previously generated by the research subject, and those newly presented at the time of testing). We administered this task to 21 *DSM-III-R* schizophrenics (medication-free for one week and to 21 demographically and IQ-matched normal controls. All subjects were also given an operationalized examination for neurologic soft signs related to frontal lobe functioning, were administered the Wisconsin Card Sort Test (WCST), and were rated on the Brief Psychiatric Rating Scale.

We found that schizophrenic subjects did not differ from controls in the number of simple recognition-recall errors. However, they showed significantly more errors in discriminating previously self-generated words from both experimenter-generated words (one-way ANOVA: $F = 7.31$; $p < 0.01$) and newly presented words ($F = 10.579$, $p < 0.002$). Thus, schizophrenic subjects had more difficulty than controls in correctly discriminating between externally presented stimuli and internally generated information. This finding did not correlate with impaired performance on the WCST or with the presence of neurologic soft signs. The relation of these findings to clinical profiles will also be presented for the schizophrenic sample.

NR322 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

A Poisson-Erlang Model Analysis of Choice Reaction Time in Negative Schizophrenia

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Summary:

Slowing of choice reaction time (CRT) in schizophrenics is a well-known observation. In addition, an extreme intrasubject variability is reported (Schwartz, 1988). Besides mean RT, analysis of RT distribution provides more information. Poisson-Erlang model proposes that RT distribution is generated by two states: processing and distraction. In any trial, processing time (PT) corresponds to the cognitive operations necessary to give a correct answer. PT is constant for a given task condition. PT and total distraction time (TDT) are estimated by an algorithm for each subject at each task.

Methods: Study included 24 *DSM-III-R* schizophrenic patients (5 F + 19 M; age: 42.2 ± 9.4 yrs) with predominant negative symptoms (>20 on negative subscale of the Positive and Negative Scale for Schizophrenia (PANSS)) and 24 controls without psychiatric disorder (6 F + 18 M; age: 38.5 ± 6.9). Patients were all treated with a stable regimen of depot neuroleptic ± antiparkinsonian medication without other psychotropics allowed. Their clinical state was stable (<20% variation on total PANSS score at a one-month interval). All subjects were assessed twice (first session for training) using a computerized CRT corresponding to word and color series of Stroop test. The results of the second evaluation are presented.

Results: On both word and color series, when compared to controls, schizophrenics presented an increased mean RT ($p < .02$), PT ($p < .02$) and TDT ($p < .002$).. Interestingly, using mean RT, the only correlation observed in patients is between Word RT and the PANSS General sub-score ($r = .43$, $p < .05$). However, using the Poisson-Erlang model, we observed no correlation between word and color PT and PANSS subscores, but significant correlations between both word and color TDT and both PANSS Negative and General sub-scores (r ranging from .4 to .57, $p < .05$).

Conclusions: These results suggest that distractibility is an important component of slowing of CRT in schizophrenics even in those with predominant negative symptoms and that the distractibility may be more state-dependent than PT slowing. Moreover, compared to mean analysis, analysis of distribution using Poisson-Erlang model is a useful approach for the assessment of distractibility in schizophrenia.

NR323 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Premorbid Function in Schizophrenia and Mania

Scott Smith, M.A., Psychiatry, Elmhurst Hospital, 79-01 Broadway, Elmhurst NY 11373; David B. Schnur, M.D., Shaoshan Li, M.S.W., Elizabeth Horwitz, M.D., Adam Smith, Ph.D.

Summary:

Objective: Impairments in premorbid function are said to have implications for subtyping and prognosis in schizophrenia. The present study sought to provide pilot data on the diagnostic specificity of such impairments by comparing standardized ratings of premorbid functioning in schizophrenic and bipolar manic patients.

Method: After obtaining acceptable interrater reliability, we examined 15 schizophrenic and 11 bipolar manic patients using the premorbid adjustment scale (PAS). The sample comprised inpatients in a research unit of an acute care psychiatry department. In all cases information was obtained from interviews with patients and relatives as well as from the clinical chart.

Results: There were trends for manics and women to have better overall premorbid adjustment ($p < .1$). Males ($n = 18$) had poorer academic performance ($p = .02$) and schizophrenic patients showed worse social-sexual adjustment during late adolescence ($p = .05$). None of these items were significantly correlated with age of onset nor were there diagnostic or gender differences in age of onset in this sample.

Conclusions: Both gender and diagnosis may determine levels premorbid functioning in manic and schizophrenic patients. Our findings do not appear to result from differences in age of onset.

NR324 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Cognitive Deficits and Psychopathology in Elderly Schizophrenics: Does Old Age Affect the Phenomenology of Schizophrenia

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Summary:

Objective: The psychopathological profile and its relationship to cognitive functioning in elderly schizophrenics is not well understood. Aims of our study were to examine (1) psychopathological and cognitive profiles of elderly institutionalized schizophrenics compared to a sample of younger schizophrenics, (2) the correlation of psychopathology with deficits in attention, memory, and information processing.

Method: 20 *DSM-III-R* schizophrenic inpatients aged 66.7, on stable medication, were assessed on a multidimensional rating battery (PANSS, Hamilton-D, EPS Scales, and Cognitive tests, including IQ). They were compared to 30 younger schizophrenic inpatients aged 39.7, matched on gender and medication status.

Results: There was no difference in positive, negative, excitement, depression, and cognitive symptoms, including IQ between the two samples. Clinical Dementia Rating of the older group indicated overall questionable dementia (range 0.25–0.27) together with better recall in California Verbal Learning Test's subitems of five-trials recall ($t = -2.2$, $p < .03$) and number of correct hits ($t = -3.7$, $p < 0.0007$) than the younger schizophrenics. No differences were seen on short-/long-term memory. In elderly schizophrenics, negative and cognitive symptoms correlated with IQ and cognitive integrity.

Conclusions: Older age did not affect the symptom profile of this schizophrenic sample. Patients showed overall low dementia measures, also supported by better recall measures and comparable short-/long-term memory functions. This older schizophrenic sample did not show a significant dementing process.

NR325 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Memory Activation in Late Onset Schizophrenia

John M. Herrera, Ph.D., Psychiatry, Elmhurst Hospital, 79-01 Broadway, Elmhurst NY 11373; Hung Lee, M.D., Donald M. Quinlan, Ph.D., Victoria Ongsiako, M.D., Dinshaw Bamji, M.D., Richard Mohs, Ph.D.

Summary:

Increasing attention (see *Schizophrenia Bulletin,* 19, 1993) is being devoted to patients who develop schizophrenia late in adulthood (LS, after age 45). This clinical distinction dates to the turn of the century and the Kraepelinian diagnoses of paraphrenia vs. dementia precox. The authors have reported that delayed word recall tasks activate the frontoparietal cortex in aged normal controls (NA) and that Alzheimer's disease (AD) and aged schizophrenics (AS) patients fail to activate rCBF (Herrera, Lee, Quinlan, et al., 1993). It is hypothesized that LS patients with demonstrate *similar* hypofrontal rCBF activation patterns, the methodology includes two Tc-99m-HMPAO SPECT brain scans in a 3 (LS vs. ES vs. NA) × 2 (word recall vs. no recall) repeated measures design. This study was conducted at Elmhurst Hospital Center (EHC), an academic affiliate of Mount Sinai School of Medicine (MSMS). 5 LS (1 man, 4 women; mean age = 68.5 years; mean MMSE = 27.2) were recruited for clinical and neuropsychological ratings and asked to consent to SPECT scans. *DSM-III-R* criteria was determined on the basis of Comprehensive Assessment of Symptoms and History (CASH, Andreasen, Flaum, & Arndt, 1992) interviews and symptom ratings were determined with the Positive and Negative Symptom Rating Scale (PANSS, Kay, Opler, & Fiszbein, 1986) interviews. The use of the CASH, in conjunction with the PANSS is an established procedure at all affiliate MSMS research sites and mandatory training and interrater reliability sessions are conducted monthly throughout the year on a revolving site basis (VA, ELM, MSMS, Pilgrim). 10 NA (5 men, 5 women; mean age = 70.4; MMSE score = 29.0) and 10 ES (5 men, 5 women; mean age = 67.8 years≥an MMSE = 28.2) from previously reported samples served as comparison groups. The delayed recall task is adapted from the neuropsychological battery of the multicenter CERAD (Morris, Heyman, Mohs, et al., 1989) study, the activation paradigm includes four five-minute blocks: (1) word list learning task; (2) intervening constructional task; (3) injection of radionuclide followed by delayed word recall task; and (4) delayed word list recognition task. Data acquisition is initiated after injection (10 mCi of 99mTc-HM-PAO) and the subject is directed to actively complete the delayed recall task procedure during the 2 minute period required for the radionuclide to cross the blood-brain barrier and bind to blood flow, rCBF activity during this 2 minute period is thus depicted on the subsequent SPECT brain image. Functional brain images are acquired using the Trionix Triad three-detector head digital SPECT camera and 12 transverse slices (4.5 mm/slice) were selected at three brain levels for data analysis. The statistical model employed was a repeated measures multivariate analysis of variance (MANOVA) with three between (LS, ES, NA) group by two within subject (No Recall and Recall) task conditions; the principal F ratio for assessment of the effects of memory task activation was the group by condition interaction. The repeated measures MANOVA yielded a significant group by condition interaction effect ($F = 4.48$, $p = .01$) at the upper brain level and a priori comparisons revealed significant differences ($p = .02$) between both patient (LS, AS) groups and the NA group. Late onset schizophrenic patients fail to activate rCBF in the frontal association cortex.

NR326 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Schizophrenic Premorbid Adjustment: Event-Related Potential and Memory

James J. Levitt, M.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D., Paul G. Nestor, Ph.D., Martha E. Shenton, Ph.D., Jennifer E. Haimson, B.A.

Summary:

Objective: Premorbid adjustment in schizophrenia (SZ) is a significant predictor of subsequent psychosocial and biological pathology (Levitt et al., in press). Here we examined premorbid adjustment in schizophrenia and its relationship to event-related potential (ERP) and neuropsychological data after onset of the illness.

Method: We interviewed 13 chronic male SZ veterans, who received ERP and neuropsychological testing, and their first-degree relatives, using the Cannon-Spoor et al. Premorbid Adjustment Scale (PAS), and also obtained objective data from school records. The N2 component of the event-related potential was elicited using an auditory oddball paradigm, and measured at a band of coronal electrode sites (T3, Cz, T4). We have previously found the N2 component to be reduced in SZ, and associated with temporal lobe grey matter reduction.

Results: Worse premorbid adjustment in SZs was associated with marked reduction of the N2 component of the auditory event-related potential. Overall PAS scores were correlated with left temporal and central N2 amplitude (T3, $r = .54$, $p = .056$; CZ, $r =$

.62, p = .02; T4, r = .26, p = .38). As N2 amplitude decreased age specific SZ PAS period scores from childhood, early and late adolescence, and an average score of these three age periods, revealed the same pattern of associations. Neuropsychologically, worse overall SZ PAS scores were associated with more perseverative errors on the Wisconsin Card Sort (WCS) task (r = .50, p = .057) and worse performance on the WMS-R visual memory span task (r = −.64, p = .03). Age specific PAS scores from childhood, early and late adolescence, as well as an average score of these three age periods, yielded a similar pattern of correlations.

Conclusions: Premorbid adjustment may predict the severity of subsequent neurophysiological and neuropsychological abnormalities in schizophrenia.

NR327 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Amygdala-Anterior Hippocampus Shrinkage in Male Schizophrenia: A Magnetic Resonance Controlled Study

Alessandro Rossi, M.D., Psychiatry, University of L'Aquila, SM Collemaggio Hospital, L'Aquila I 67100, Italy; Paolo Stratta, M.D., Fabrizio Mancini, M.D., Paolo Mattei, M.D., Massimo Casacchia, M.D.

Summary:

Recent magnetic resonance (MR) studies reported abnormalities of medial temporal lobe and basal ganglia structures. We used an inversion recovery (IR) MR protocol with the assistance of the Talairach atlas to identify neuroanatomical regions of interest in 30 male schizophrenic patients and 20 matched controls. The patient group showed smaller amygdala-hippocampus volume as compared with normal controls. This finding was more pronounced for the left side, although no diagnosis by side interaction was present. Third ventricle volume was also enlarged in schizophrenics. A trend toward an overall reduction of basal ganglia (accumbens, striatum, and lenticular nucleus) and limbic structures and toward a VBR increase was also seen. Neuropsychological testing of the schizophrenic patient showed deficit of frontal lobe performances that correlated with amygdala-hippocampus shrinkage.

The study confirms previous evidence of mesial temporal lobe shrinkage, more evident on the left side in a group of relapsing non-institutionalized male schizophrenics.

NR328 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Neuroleptic Discontinuation in Schizophrenics

Andre Tapp, M.D., Psychiatry, VA Medical Center, 5500 Armstron Road, Battle Creek MI 49016; Rajiv Tandon, M.D., Alan B. Douglass, M.D., Evelyn Dudley, R.N., Robert Scholton, R.N., Michael J. Underwood, M.A.

Summary:

As many as one third of patients suffering from schizophrenia have persistent severe psychotic symptoms despite high dose neuroleptic treatment. The induction of psychotic episodes "a supersensitivity psychosis" has been proposed as possible side effects of neuroleptic exposure. As part of a protocol to medicate chronic hospitalized treatment resistant schizophrenic patients with clozapine, we attempt to evaluate the benefit of high dose chronic neuroleptization, the safety of their brief discontinuation, and the evidence for the occurrence of a supersensitivity psychosis. Seventeen patients meeting RDC criteria for chronic schizophrenia, hospitalized for at least 24 months, were tapered of all their neuroleptic medication over an average of 42 days. All patients were on large dose of medication (mean ± sd = 2058 ± 1243 chlorpromazine equivalent). No significant differences were found in comparisonwise t-tests to evaluate BPRS scores between baseline, end of taper, one and three weeks medication free periods. Multivariate analysis for testing differences between BPRS subscales also shows no significant difference.

In treatment resistant chronic schizophrenic patients, there is no evidence for the benefit of high doses of neuroleptics, during a period of neuroleptic taper and withdrawal. There is also no evidence for the induction of a relapse or supersensitivity psychosis.

NR329 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Depression in Severe Chronic Schizophrenia

Andre Tapp, M.D., Psychiatry, VA Medical Center, 5500 Armstron Road, Battle Creek MI 49016; Rajiv Tandon, M.D., Alan B. Douglass, M.D., Evelyn Dudley, R.N., Robert Scholton, R.N., Michael J. Underwood, M.D.

Summary:

The most deteriorated schizophrenic patients, requiring continuous care, may represent a subgroup of schizophrenia. The frequency of depression in this subgroup is unknown. We compared the prevalence of depression in long-term treatment-resistant hospitalized (Kraepelinian, "K") and recurrent non-hospitalized (Non-Kraepelinian "NK") schizophrenic patients, and analyzed the association of depression with psychotic symptoms and neuroleptic side effects. Sixty-four K and 27 NK patients meeting *DSM-III-R* and SADS-RDC criteria for schizophrenia, receiving stable doses of neuroleptics, were rated with the Hamilton Rating Depression scale (HAM-D), the Brief Psychiatric Rating Scale (BPRS), and the Simpson-Angus scale (SA) for extrapyramidal side effects (EPS).

Patients with a HAM-D ≥ 16 had less positive symptoms (t = 3.099, df = 55, p = 0.00153) but did not present with more EPS (t = 1.196, df = 55, p = 0.1184).

Depression was more frequent in the NK compared to the K patients (*36.8% versus 6%*). These findings suggest that while the depression observed in schizophrenia is not part of the psychotic syndrome, and is unlikely to be a side effect of the medications, it occurs rarely in a subgroup of treatment resistant schizophrenic in need of continuous hospital care.

NR330 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Brain Impairment and Adaptation in Schizophrenia

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Summary:

This study looked at psychosocial adaptation of schizophrenia. Two subgroups of persons with schizophrenia were identified by measuring ventricular-brain ratio and cortical atrophy. One group demonstrated neuropsychiatric impairment (n = 26); the other group showed schizophrenic symptomatology without brain impairment (n = 16). To measure psychosocial adaptation each subject was interviewed by a researcher who was blind to the subgroups using the Quality of Life Scale, Premorbid Adjustment Scale, Scale for the Assessment of Negative symptoms, Scale for the Assessment of Positive Symptoms, Index of Self-Esteem, Everyday Worries Scale, and Mini-Mental Status Exam. Statistical analyses that tested differences among social adaptation measures between the groups were cross-tabulations, chi-square, student t-test, correlation analysis, discriminant analysis, and multiple analysis of variance. The results showed that there were few differences between the groups on the social adaptation measures. However, there were significant differences when subjects of both groups were compared by race and gender. Females and

African-Americans showed a more benign course of illness as demonstrated by later age of onset, later age at first use of psychiatric medication, and later age at first psychiatric hospitalization. Females had significantly higher self-esteem and better psychosocial adaptation than males.

NR331 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Medication Adherence and Outcomes in Schizophrenia

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Summary:

Objective: To study medication adherence and its effects on symptomatic outcomes in patients with schizophrenia.

Method: Data were collected during an ongoing longitudinal study of outcomes of care for schizophrenia. 100 inpatients with a research diagnosis of schizophrenia were enrolled, and continued in standard care. At baseline and six-month follow-up, the following data were collected: the Brief Psychiatric Rating Scale (BPRS), subjects' reported medication adherence (30 days before hospitalization or follow-up; 1–5 scale), reported side effects (0–100), and observed extrapyramidal side effects (0–10).

Results: Prior to admission, 54% of subjects, and 79% at follow-up reported essentially complete medication adherence. The regression of follow-up BPRS total score on medication adherence, reported side effects, observed side effects, and baseline BPRS total was significant ($F = 10.3$, $p = 0.0001$, $n = 49$), and explained 44% of the variance. Medication adherence, reported side effects and baseline BPRS are significant predictors of follow-up severity (3.32 ± 0.91, $p < 0.001$; 0.12 ± 0.044, $p < 0.01$; 0.45 ± 0.13, $p < 0.005$, respectively).

Conclusions: These data suggest that medication adherence is an important predictor of symptom severity in schizophrenia. Adherence rates are similar to those reported in other studies in schizophrenia. Patients had lower adherence rates prior to admission than at follow-up, suggesting that improving adherence rates will lead to clinical improvement.

NR332 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Facial Affect Recognition and Visual Attention in Schizophrenia

Jean M. Addington, Ph.D., Psychiatry, Calgary University, Foothills Hosp. 1403-29 St NW, Calgary AB T2N 2T9, Canada; Donald E.N. Addington, M.D.

Summary:

This study examined longitudinally the relationship between the ability of schizophrenic patients to recognize facial effect and their performance on measures of visual attention. Subjects included 40 inpatient admissions to two psychiatric units in a general hospital, who met *DSM-III-R* criteria for schizophrenia. Two control groups were included—a normal control group ($n = 40$) and a psychiatric comparison group of 40 outpatients with bipolar disorder. The performance of the schizophrenics on measures of facial recognition, facial affect recognition, and visual attention were measured at hospitalization and again three months later during a period of remission. Results are that despite a significant improvement in symptoms, schizophrenics' performance on the affect recognition tasks did not change from the inpatient phase of the illness to a period of relative remission. Schizophrenic subjects performed more poorly on all tasks than either control group, with the bipolar subjects performing more poorly than the normal group. Relationships between visual attention and facial affect recognition varied within the different groups. No clear pattern of relationships emerged. Results are considered in the context of vulnerability factors and implications for skills training.

NR333 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Positive and Negative Syndrome Scale in a French Population of Schizophrenics

Christophe Lancon, Psychiatry, Chu Ste Marguerite, BD Ste Marguerite, Marseille F 13274, France; Jean Luc Martinez, Pascal Auquier, P. Michel Llorca, Thierry Bougerol

Summary:

There are few data on the validation and factorial analysis of the French translation of the Positive and Negative Syndrome Scale (PANSS). 80 chronic schizophrenic (52 males, 28 females) patients, according to the *DSM-III-R*, aged 33 ± 10.8 years, were included. The duration of the illness was 12 ± 9 years. For the interrater reliability, mean Pearson's r were 0.82 for the general psychopathology (item range 0.40 to 0.98); 0.92 for the positive syndrome (item range 0.77 to 0.92) and 0.77 for the negative syndrome (item range 0.46 to 0.89).

For the internal reliability, the alpha cronbach's coefficient for the total subscales scores were 0.78 for the negative scale; 0.77 for the positive scale and 0.62 for the general psychopathology.

We computed a factorial analysis. We found four factors solution explaining 64% of the total variance. These factors can be labeled as: negative, positive, depressive, and cognitive.

NR334 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

New Onset Echolalia in a Chronic Institutionalized Schizophrenic: Focal Neurological Deficit or Chronic Regression

Emmanuel Hriso, M.D., Psychiatry, Essex County Hospital, P.O. Box 500, Cedar Grove NJ 07009; Teresa A. Bielawski, M.D., Paul A. Hriso, M.D.

Summary:

The authors present the case of an institutionalized 52-year-old woman diagnosed as having chronic undifferentiated schizophrenia who, late in the course of her long hospitalization, developed echolalia. Neurological examination was essentially normal except for this language dysfunction. A magnetic resonance imaging study (MRI) of the head revealed a large cystic tumor in the left inferior frontal gyrus.

Although echolalia has been described in chronic schizophrenia and other psychiatric illnesses, such as Tourette's syndrome and autism, it can be the focal sign of a language disorder secondary to demonstrable pathology in the left perisylvian area, frontal operculum, or supplementary motor area. The fact that this was a slowly growing tumor and not a destructive type of lesion, such as an infarction, explains why this was an incomplete aphasic syndrome, i.e. echolalia.

This case illustrates the importance of neurological, neuropsychiatric, and radioimaging evaluation in a patient whose signs and symptoms could have just been explained as a function of a deteriorating schizophrenic state.

NR335 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Electroencephalograms in Patients with Catatonic Disorders

Brendan T. Carroll, M.D., Psychiatry, The Ohio State University, 473 W. 12th Avenue, Columbus OH 43210; Nashaat N. Boutros, M.D.

Summary:

Catatonia is a neuropsychiatric syndrome of motor signs most frequently found in affective disorders and schizophrenia. Catatonic disorder due to a general medical condition has been added to the *DSM-IV* nosology. Laboratory studies, such as electroencephalography (EEG) may assist in the differential diagnosis of catatonic states.

Twenty-six patients hospitalized on a general psychiatric unit or medical psychiatric unit received electroencephalograms (EEGs) as part of their routine care. EEG abnormalities were reported in 17 of these patients. The presence of abnormalities was associated with age greater than 40, diagnosis of neuroleptic malignant syndrome, and the presence of general medical conditions frequently associated with the development of catatonia. Three episodes of non-convulsive status epilepticus were detected by EEG monitoring.

Although no specific EEG patterns were associated with catatonic disorder due to general medical conditions, these findings suggest that the EEG is an important tool in the evaluation of patients presenting with catatonia.

NR336 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Treatment of Clozapine-Induced Agranulocytosis

J. Steven Lamberti, M.D., Psychiatry, University of Rochester, 1650 Elmwood Avenue, Rochester NY 14620; Terrence J. Bellnier, M.P.A., Eugene Schneider, M.D., John P. Veneron, R.Ph., Steven B. Schwarzkopf, M.D.

Summary:

Despite careful blood monitoring, 256 cases of clozapine-induced agranulocytosis with nine fatalities have occurred in the United States since 1990. Recombinant granulocyte colony-stimulating factor (rG-CSF) has recently been reported effective in treating clozapine-induced agranulocytosis (Gershon et al. 1992; Weide et al. 1992). We present three patients with clozapine-induced agranulocytosis successfully treated with rG-CSF.

A.C. is a 42 y/o man with chronic paranoid schizophrenia who developed biopsy-confirmed agranulocytosis after 11 weeks of clozapine therapy. WBC and absolute neutrophil count (ANC) at the time of rG-CSF initiation were 1100 and 0, respectively. Following eight days of treatment with rG-CSF 300 ug sq daily, WBC/ANC rebounded to 6600 and 4300, respectively. A.M. is a 45 y/o man with chronic paranoid schizophrenia who developed biopsy-confirmed agranulocytosis following seven weeks of clozapine. WBC/ANC at the time of rG-CSF initiation were 2000 and 60, respectively. rG-CSF was begun at 300 ug sq daily, and WBC/ANC rebounded 5400/1500 after six days of treatment. M.W. is a 47 y/o man with chronic paranoid schizophrenia who developed agranulocytosis with a WBC/ANC of 1100/0 following 10 weeks of clozapine. WBC rebounded to 8100 following eight days of rG-CSF 300 ug sq. Treatment with rG-CSF appears to reduce the duration of clozapine-induced agranulocytosis, and may decrease the incidence of serious infection in this disorder.

NR337 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Clinical Characteristics of Psychotic Adolescents

John D. O'Brien, M.D., Psychiatry, Elmhurst Hospital, 79-01 Broadway, Elmhurst NY 11373; Manuel D. Reich, D.O., Barbara Cornblatt, Ph.D., Michael Obuchowski, M.A.

Summary:

Objective: The Elmhurst Adolescent Project is concerned with clinically characterizing first break psychotic adolescents.

Method: Eleven adolescent patients (mean age 15) were rated on an adolescent version (A-PANSS) of the adult PANSS, a state measure divided into three scales: Positive Scale, Negative Scale, and General Psychopathology Scale. Adolescent were compared with 16 multi-episode adult psychotics (mean age 30). Both were rated before medication and four weeks after medication was begun.

Results: On the positive symptom scales there were no differences either between age groups or between sexes. All positive symptoms were responsive to treatment. On the negative symptom scales women tended to be worse on emotional withdrawal, poor rapport, and passive/apathetic social withdrawal. With medication, negative symptoms are not appreciably alleviated.

On the general psychopathology scales the adolescents are significantly higher than the older schizophrenics on depression ($P = 0.040$) and there was a tendency for females to be worse on the depression scales. However, these symptoms improved with medication.

Conclusions: By looking at the individual items, it is clear that adolescents were hospitalized for their positive symptoms and discharged when positive symptoms responded; the negative symptoms were not very much influenced by the medication.

NR338 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

P300's Latency and Response to Neuroleptics

Thierry Bougerol, Psychiatry, Chu Ste Marguerite, BD Ste Marguerite, Marseille F 13274; France; Abdel Benraiss, P. Michel Llorca, Christophe Lancon

Summary:

Auditory event related potentials were recorded during an oddball paradigm in 12 schizophrenic patients (according to *DSM-III-R* criteria. The mean age was 35,5 years (range = 22–54). The patients were tested twice and the mean interval between test sessions was 15,5 months (range = 6–28). All patients were treated with neuroleptics. At each time the clinical status of the patients was assessed by the BPRS. An auditory attention task (counting of infrequent stimuli) was used to elicitate P 300 component. Auditory stimuli were tone, either low (frequent stimuli of 750 Hz = 80% of all stimulations) or high (infrequent stimuli of 200 Hz = 20% of all stimulations). The AEP were recorded with electrodes from frontal (Fz), central (Cz), and parietal (Pz) scalp sites according to the 10–20 system and referred to mastoids. The comparison of ERP waveforms recorded during the first session (T1) and the second one (T2) shows that the measures of the different components are not statistically different between T1 and T2 for all the patients, independently of clinical modifications assessed by changes in BPRS scores between T1 and T2). Five patients had worsened, six were improved and one did not change during this time. The comparison of AEP recorded at T2 in the good responders and the bad responders shows a statistically significant difference of P 300's lantency ($p < 01$). The same comparison at T1 shows the same discrepancy, the good responders to treatment having significantly shorter P 300's latencies than the bad responders.

NR339 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Unifying Aspects of OCD and Schizophrenia

Jose A. Yaryura-Tobias, M.D., Research, Biobehavioral Therapy, 935 Northern Blvd, Great Neck NY 11021; Theresa Campisi, M.A., Dean McKay, Ph.D.

Summary:

Considering the upcoming changes in classifying obsessive compulsive disorder (OCD) in *SM-IV,* it becomes evident that overlapping aspects exist with schizophrenia. Historically, it has been clinically determined that there are shared aspects to both pathologies. Further, with the advent of research into a spectrum

of obsessive compulsive pathologies, assessment of thought processes is necessary to establish the existence of obsessive compulsive psychosis. In order to understand similarities between these disorders, a battery of assessment instruments was administered to a diagnosed group of OCD and schizophrenic patients. This included a test of perceptual processes, two OCD assessment instruments, and a clinical interview to establish other comorbid disorders. Exclusions rules for schizophrenia were ignored to better understand comorbidities. It was anticipated that there would not be significant differences between diagnostic groups on measures. Tests of distortions in auditory, visual, tactile, taste, olfactory, and time perception were not significant (all ts < 1), although the majority of scores were clinically relevant. Further, substantial rates of obsessive and compulsive behavior were reported on the self-rated symptom scale and on the Yale Brown Obsessive Compulsive Scale (Y-BOCS) for both groups. These data lend credence to the overlapping nature of OCD and schizophrenia.

NR340 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Correlates of Suicidality in Schizophrenia

Naveed Iqbal, M.D., Psychiatry, Montifore Med. Center, 111 East 210 Street, New York NY 10467; Lloyd Goldsamt, Ph.D., Bruce J. Schwartz, M.D., Gregory M. Asnis, M.D., Robert Plutchick, M.D., Alec Cecil, Ph.D.

Summary:

The risk of suicide in schizophrenic patients is 10 times that of the general population. It has been estimated that 10% of all schizophrenics kill themselves and that 55% of all schizophrenics make at least one suicide attempt during their lifetime. Research regarding risk factors for suicide has yielded less than satisfactory results, and further studies in this area are essential to our understanding of both suicide and schizophrenia.

The present study used two separate samples of patients treated in an outpatient mental health clinic. The first sample consisted of 69 schizophrenic patients, and was used to determine the historical prevalence suicidal ideation, plans, or attempts, using the Harkavy-Asnis Suicide Survey (HASS) in our outpatient clinic. These data showed that 48% of patients had a history of either suicidal ideation or plan. The second sample consisted of 32 schizophrenic patients who were assessed using the Positive and Negative Syndrome Scale (PANSS), the Suicide Risk Scale (SR), the Impulse Control Scale (ICS), the Past Feelings and Acts of Violence Scale (PFAV), and a scale measuring depression (PVP-II), in addition to the HASS. Significant differences between patients with (n = 14) and without (n = 18) a history of suicidal ideation or plan were found on the depression subscale of the PANSS ($f = 7.8$, $p \leq .05$), on the SR ($f = 21.0$, $p \leq .01$) and on the PVP-II ($f = 9.5$, $p < .05$). The second sample will be increased to 100 schizophrenic patients.

NR341 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Pallidothalamic Circuits in Post-Stroke Mania

Edward C. Lauterbach, M.D., Psychiatry, Mercer Univ. Med. Center, 1550 College Street, Macon GA 31207; Ami N. Wilson, B.A., Spencer T. Price, B.S., Joseph G. Jackson, M.D.

Summary:

Objective: To understand bipolar disorder pathophysiology.

Method: 45 post-stroke subjects selected for MRI-identified strokes limited to basal ganglia and cerebellum entered and completed a five-hour outpatient neuropsychiatric examination. Measures included age, sex, lesion location and duration, modified Folstein et al., MMSE, Hamilton and Beck depression scales, family history, dystonia and Parkinson rating scales, psychiatric interview, neurologic, and movement disorder examinations. We compared subjects with post-stroke secondary *DSM-III-R* bipolar mood disorders (n = 3) to similar controls lacking any history of life mood disorder (n = 22). We hypothesized pallidal integrity in these post-stroke bipolar disorders.

Results: Pallidal lesions were absent in all bipolar subjects (Fisher's Exact $p < .048$). Bipolar subjects did not differ from controls on demographic, social, or other factors except for age. Bipolar subjects were younger (35.3 ± 10.1 vs. 61.6 ± 15.4 years, Mann-Whitney $U = 5.00$, $p < .019$) and all lacked family psychiatric histories, including depression, mania, suicide, or alcohol abuse. Al denied histories of substance abuse.

Conclusions: Pallidal integrity may mediate bipolar disorders, perhaps through pallidothalamic inhibition of the magnocellular mediodorsal (MDmc) thalamus This system may be pruned later in life. Diminished MDmc thalamocortical stimulation of orbitofrontal cortex could eventuate dorsal prefrontal cortex disinhibition, consistent with PET scan findings in mania.

NR342 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Post-Stroke Depression: Pallidothalamic Circuits

Edward C. Lauterbach, M.D., Psychiatry, Mercer Univ. Med. Center, 1550 College Street, Macon GA 31207; Spencer T. Price, B.S., Ami N. Wilson, B.A., Joseph G. Jackson, M.D.

Summary:

Objective: To understand unipolar depression pathophysiology.

Method: 45 post-stroke subjects selected for MRI-identified strokes limited to basal ganglia and cerebellum entered and completed a five-hour outpatient neuropsychiatric examination. Measures included age, sex, lesion location and duration, modified Folstein et al., MMSE, Hamilton and Beck depression scales, family history, dystonia and Parkinson rating scales, psychiatric interview, neurologic, and movement disorder examinations. We compared subjects with post-stroke secondary unipolar *DSM-III-R* major depression (n = 9) to similar controls lacking any history of life mood disorder (n = 22). We hypothesized pallidal lesions in post-stroke depression.

Results: Pallidal lesions were present in eight of nine depressed subjects and left posterior pallidal lesions were more common in major depression (four subjects) than in controls (two subjects, $p < .022$). Depressed subjects did not differ from controls on demographic, social, or other factors except depression scores (as expected; Beck $U = 158.5$, $p < .0018$; Hamilton $U = 174.0$, $p < .00012$) and family history (in seven depressed subjects, $p < .026$).

Conclusions: Magnocellular mediodorsal thalamus disinhibition presents a possible mechanism for post-stroke depression. The data support left-lateralization theories of depression and suggest posterior pallidal limbic circuits. Prevalent family psychiatric histories raise depression attribution considerations. Consequently, further research is needed to establish these findings.

NR343 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Clozapine in Psychotic Demented Patients

Jacobo E. Mintzer, M.D., Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425-0742; Janet Pitner, Ph.D., Sharon R. Burnside, M.D.

Summary:

The *objective* of this study was to evaluate the efficacy of clozapine (Clozaril, Sandoz) in the treatment of drug resistant organic psychosis in demented patients using a single case open label design.

The *methodology* called for male or female patients 65 years or older consecutively admitted to a specialized dementia unit.

The inclusion criteria required a diagnosis of dementia and organic delusional syndrome with paranoid symptoms according to the criteria established by the *DSM-III-R*. Severity of paranoid symptoms were measured using the University of Washington paranoia scale. All patients had a history of psychotic symptoms with paranoid content which did not respond to at least two consecutive trials of neuroleptic medications. Patients were required to be medically stable with no changes in medical treatment for at least two weeks and laboratory work-up within normal limits. Following a careful evaluation patients were started on a single 12.5 mg a day dose with the expectation of increasing the dose by 6.5 mg every other day as clinically indicated. Standard evaluation protocol for use of clozapine was also included in pretreatment evaluations and follow ups.

Results here reported included four patients only since all patients showed severe focal neurological symptoms developed. The symptoms included acute and severe deterioration in level of consciousness in all of the patients with additional neurological symptomatology, i.e., extrapyramidal symptoms and worsening in mental status. All patient required transference to an acute medical unit. In all cases symptoms onset within the first 24hs of treatment and resolved within 24hs of treatment discontinuation. Only in the first case treatment was reinstated; however, symptoms were observed again, and again symptoms resolved within 24hs of treatment interruption. The study was discontinued following these events.

Conclusion: Although clozepine may be a useful tool in elderly demented patients suffering from drug resistant psychosis extreme caution should be exercise in the first few days following initial administration.

NR344 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Psychotic Symptoms and Neuropsychological Deficits

Blaine S. Cloud, M.D., Psychiatry, Crozer Medical Center, Medical Center Blvd., Upland PA 19013; Wendy E. Shumway, M.D., Steven D. Targum, M.D., David J. Libon, Ph.D., Robyn Resh, M.A., H.L. Gitlin, M.A.

Summary:

Objective: Delusions and other psychotic symptoms (DPS) are frequently present in demented patients. Some theories posit that an interaction of cognitive deficits involving impairment in visuoperceptual functioning, executive functions, and memory are responsible for DPS in dementia. This research examined the relationship between the severity of DPS in demented subjects and these three domains of neuropsychological functioning.

Method: Thirteen subjects with Alzheimer's disease (AD) or cerebrovascular dementia (CVD) were studied (M age = 78.5; M MMSE = 18.9). No patient was taking psychotropic medication. Based on a structured interview of the subject's spouse, all DPS were rated on five separate subscales. The total severity score (TSS) of DPS ranged from 9 (mild) to 68 (severe).

Results: Correlational analyses indicated that, as the TSS increased subjects performed worse on tests of executive functions (Trail Making Test-Part B, $r = .72$, $p < .01$); made more perseverations and graphomotor errors on clock drawings ($r = .85$, $p < .001$); and demonstrated better performance on a recognition test from the California Verbal Learning Test ($r = .66$, $p < .01$). Correlations between the TSS and visuoperceptual tests were not significant.

Conclusions: These results suggest that an interaction between specific neuropsychological deficits may contribute to the development of DPS in dementia.

NR345 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Cerebral Blood Flow During Memory and Executive Task Performance: A PET 150 Study of Normal Control Subjects

J. Daniel Ragland, Ph.D., Psychiatry, Univ of Penn. 10th Flr., 3400 Spruce St. Gates Bldg, Philadelphia PA 19104; Ruben C. Gur, Ph.D., David Censits, B.A., Robin Smith, Ph.D., Abass Alavi, M.D., Raquel E. Gur, M.D.

Summary:

The Paired Associate Recognition Test (PART) was developed as a test of declarative memory using Wisconsin Card Sorting Test (WCST) stimuli, for use in physiologic brain imaging studies of memory and executive function in schizophrenia. The WCST is a test of cognitive flexibility sensitive to frontal lobe lesions that has been associated with performance deficits and hypofrontality in CBF studies of schizophrenia. Given recent evidence of memory deficits in schizophrenia, the PART was developed using WCST stimuli so both tasks could be applied during neuroimaging. The PART, WCST, and baselines were administered during four subsequent 10 min. ^{15}Oxygen PET scans using the equilibrium method to a group of 12 healthy young adult volunteers (8 men 4 women). Regional CBF data employing MRI co-registration of regions of interest (ROI) reveals that whole brain flow was equivalent across conditions, as was the pattern of regional activity (region/whole brain) within a condition. When activation (task-baseline) was examined, however, regionally distinctive increase in CBF were observed. Replicating previous findings, selective activation of frontal ROIs occurred during performance of the WCST. During the PART there were prominant increases in parahippocampal (uncus ROI) and frontal brain regions. These preliminary data support the reliability of the equilibrium method, and application of the PART as a memory probe during neuroimaging studies of schizophrenia.

NR346 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Brief Neuropsychiatric Cognitive Examination and MRI, CT Scan Data

Joseph M. Tonkonogy, M.D., Psychiatry, Univ of Mass Med. Center, 55 Lake Avenue North, Worcester MA 01655; James R. Armstrong, Ph.D.

Summary:

The Brief Neuropsychiatric Cognitive Examination (BNCE) is devised as a next step in the move from general cognitive assessment to standardized cognitive tests reflecting the underlying severity and localization of abnormalities in the cortical and subcortical brain structures. The BNCE consists of ten subtests which are simple and do not present any difficulties for person with minimal educational background. Five of ten subtests reflect the processing of new information primarily by the frontal lobe and subcortical structures while the remaining five subtests are directed to the more conventional types of information processing mainly by the temporo-parietal structures. The results of the BNCE are presented as a summary score and a profile which facilitate the comparison of cognitive assessment with brain imaging data as well as with the data of subsequent cognitive examinations in the course of the disease progression. The BNCE was tested in 55 psychiatric inpatients, 26 patients with psychiatric manifestation of neurological diseases (PMND group) and 29 patients with schizophrenia (SCH group). MRI or CT scan was done in 23 out of 26 patients of PMND group and in 17 out of 29 patients of SCH group. The BNCE was also administered to 51 normal subjects. Statistical analysis found the BNCE to be valid and reliable. The test scores showed statistically significant correlations with the severity and in some cases localization of abnormalities in PMND group as well as with functional status of patients in PMND and SCH groups.

NR347 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Superior Effect of Clozapine in Comparison with Typical Neuroleptics on Cognitive Function in Schizophrenia

Myung A. Lee, M.D., Psychiatry, Univ Hosp of Cleveland, 2040 Abington Road Room B68, Cleveland OH 44106; Corinne Hagger, Ph.D., Paul Thomas, Ph.D., Herbert Y. Meltzer, M.D.

Summary:

Typical neuroleptics have been reported to have little beneficial effect on the cognitive impairment of schizophrenia. Goldberg et al (1993) reported that clozapine, which is superior to typical neuroleptics in regard to improvement in psychopathology, had no significant effect on cognitive function in treatment-resistant schizophrenia (TR-SCH). By contrast, we found improvement in cognitive function with CLOZ treatment in TR-SCH (Hagger et al, 1993). We have now examined the effect of CLOZ on cognitive function in non-treatment resistant (NTR) SCH (N = 46) as well as in TR-SCH (N = 44). All the TR-SCH (TR-CLOZ) and 24/46 NTR-SCH were treated with CLOZ (NTR-CLOZ), and 22/46 NTR-SCH were treated with typical neuroleptics (NTR-TNL). Neuropsychological tests which assess attention, semantic memory, recall memory, and executive function were administered while drug-free (baseline) and after six weeks, six and 12 months of drug treatment. Improvement in all four domains of cognition, but not all tests, was found at six weeks, six months and 12 months in the NTR-CLOZ and TR-CLOZ. The NTR-TNL showed improvement only in recall memory at six weeks or six months. The comparative effect of CLOZ on cognition between the NTR-CLOZ and TR-CLOZ and the comparison between CLOZ and TNL will be presented. These data suggest that CLOZ is superior to TNL in improving some domains of cognitive function in both TR- and NTR-SCH.

NR348 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

SPECT Imaging Studies in Cortical Lobar Atrophies

Sophie Auriacombe, Psychiatrie, University Bordeaux, 121 Rue De La Bechade, Bordeaux 33076, France; Marc Auriacombe, M.D., Martine Guyot, M.D., Jean Tignol, M.D.

Summary:

Introduction: Cortical lobar atrophies (CLA) are increasingly recognized syndromes characterized by an isolated neuropsychological deficit (e.g. aphasia, apraxia) progressing slowly to dementia, with various underlying pathologies. Four syndromes have been described: dementia of frontal type (DFT), primary progressive aphasia (PPA), progressive apraxia (PA), and posterior cortical atrophy (PCA). We present five clinical cases investigated with SPECT imaging.

Methods: All five cases underwent complete psychiatric, neurological, and neuropsychological examinations, classical neuroimaging studies by CAT-scan or MRI, and Tc 99m HM-PAO SPECT studies of cerebral blood flow.

Results: Two cases presented with symptoms of DFT. One had a normal CAT-scan and the second a bifrontal atrophy. By contrast, SPECT showed large fronto-temporal metabolic defects in both patients. Two cases presented with PPA. One had a normal CAT scan but a SPECT showing a large left hemispheric hypometabolism. The second had bitemporal atrophy with predominance in the left hemisphere on CAT scan and the SPECT showed bilateral temporal hypometabolism, but more markedly pronounced on the left. One case presented as a PA. MRI showed global cortical atrophy, while SPECT demonstrated bilateral parietal hypometabolism predominantly on the right.

Conclusion: Diagnosis of CLA is primarily clinical. SPECT imaging studies significantly support the diagnosis by showing clear hypometabolism in clinically suspected brain regions, where classical neuroimaging studies show, at best, focal atrophy. This allows increased recognition and understanding of these newly described syndromes.

NR349 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

The Accuracy of Standardized Substance Abuse Instruments in Patients with Traumatic Brain Injury

Eric Fishman, Ph.D., Psychiatry, Medical College PA, 320 East North Avenue, Pittsburgh PA 15212; Mark Fuller, M.D., Nicholas Carosella, M.D., Ravi Kant, M.D.

Summary:

Objective: There is a need for accurate methods of identifying substance abuse in traumatic brain injury (TBI) patients.

Method: Fifty consecutive admissions to a TBI program with a history of TBI and no more than moderate cognitive impairment were screened for substance abuse using a comprehensive *DSM-III-R* psychoactive substance dependence checklist completed by the patient's psychiatrist. Subjects were divided by this *DSM-III-R* diagnosis into a substance dependent group (N = 24) and a non-substance dependent group (N = 26). Performances on four widely used substance abuse evaluation instruments (the CAGE, Brief MAST, SASSI, and ASI) were compared.

Results: While specificity of the CAGE and BMAST remains similar in a TBI sample (85%) to other groups of medical patients, sensitivity declines (TBI sample 63%, other medical groups 85%). This decline in sensitivity without affecting specificity appears to represent the effects of TBI. Reducing the BMAST cut-off score increases sensitivity for patients with TBI.

Conclusions: Due to the high incidence of substance abuse in TBI patients and the importance of detecting substance abuse in this population, use of the BMAST with TBI patients is recommended as the best available instrument for this purpose. However, there is need for development of a new substance abuse instrument designed specifically for TBI patients.

NR350 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Functional Differences in Dopamine Receptor Phenotypes

Fabrice Duval, M.D., Psychiatry, Centre Hospitalier, 27 Rue Du 4 RSM, Rouffach 68250, France; Marc-Antoine Crocq, M.D., Antonia Mayerova, M.D., Pierre Sokoloff, M.D., Ernst Natt, M.D., Lars Lannfelt, M.D., M-Claude Mokrani, Ph.D., Paul Bailey, M.D., Jean-Charles Schwartz, M.D., Jean-Paul Macher, M.D.

Summary:

Objective: The human dopamine D3 receptor (DRD3) is expressed in the hypothalamic cells releasing CFR. Therefore we studied the association between: (1) a two-allele polymorphism leading to a Serine (allele 1) to Glycine (allele 2) amino acid substitution in the N-terminal part of the D3 receptor protein; and (2) cortisol and ACTH responses to the dopamine agonist apomorphine (0.75 mg s.c.).

Method: We investigated 48 drug-free inpatients who satisfied *DSM-III-R* criteria for schizophrenia (N = 29) or major depression (N = 19). The genotypes were determined by PCR amplification of the first exon of the DRD3 gene and Bal I enzymatic digestion.

Results: The distribution of the 1-1, 1-2, and 2-2 genotypes did not differ significantly in schizophrenics (11 : 13 : 5) and depressives (7 : 11 : 1). Compared with 1-2 heterozygotes and 1-1 homozygotes, 2-2 homozygotes had significantly reduced stimulations of ACTH (Kruskal-Wallis p = 0.048) and cortisol (p = 0.018). DRD3 genotypes were not associated with differences in baseline 8 AM levels of prolactin, TSH, cortisol, or ACTH, or with GH

stimulation or prolactin suppression after apomorphine. Sex and diagnostic status did not influence the results.

Conclusion: These results suggest that the DRD3 may be involved in the production of CRF, which mediates the release of ACTH and cortisol induced by apomorphine. Furthermore, various DRD3 phenotypes may show functional differences and that associated with allele 2 may be less responsive to the acute administration of apomorphine.

NR351 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

An Association Between Bipolar Disorder and a Highly Polymorphic DNA Marker From Tyrosine Hydroxylase

Jeronimo Saiz-Ruiz, M.D., Psychiatry, Hospital R. Y Cajal, Carretera de Colmenar, KM9100, Madrid 28034, Spain; Jose F. Piqueras, Ph.D., Consuelo Llinares, M.D., Javier Santos, Ph.D., Ignacio P. de Castro, Ph.D., Guillermo Visedo, Ph.D.

Summary:

Objective: We have looked for a possible association between bipolar affective illness and a tetranucleotide repeat polymorphism (CATT)n at the Tyrosine hydroxylase (THE) locus on chromosome 11.

Method: We studied 46 unrelated bipolar patients (20 males and 26 females) diagnosed on *DSM-III-R* criteria and 47 unrelated normal controls (23 males and 24 females), All them were Caucasians, older than 40 years, and living in Central Spain.

PCR amplified products were resolved by gel electrophoresis and detected by silver staining. Fragment sizes were measured and a total of five alleles differing in tetranucleotide repeats's number were found.

In population-based association analysis, we compared the allele frequencies in patients vs. controls, separately for each sex and for all together. All possible pairwise associations were examined.

The statistical significance was tested by the chi-square and the magnitude of the association measured by D' coefficient.

Results: We found significant association between the allele with the greater number of repeats (th10) and the illness in males. The association's intensity is moderate; D' = 0.353 for th10 allele vs. the other alleles, and D' = 0.362 for allele th10 vs. th9 one.

Conclusions: The THE gene could be involved in conferring vulnerability to bipolar illness but the moderate intensity of this association together with the differences observed between sex suggest that other gene(s) could be also involved, some of them carried on a sex chromosome.

NR352 Tuesday, May 24, 3:00 p.m.-5:00 p.m.

Tourette's Syndrome and ADHD: Evidence Against a Genetic Relationship

Valsamma Eapen, M.B., Psychiatry, UCL Medical School, Middlesex Hospital Mortimer St, London W1N 8AA, England; Mary Robertson, M.D.

Summary:

Previous studies have suggested a relationship between Gilles de la Tourette Syndrome (GTS) and attention deficit hyperactivity disorder (ADHD). However, the findings are inconsistent as to the exact nature of the relationship; some suggesting a genetic link and others not. There is debate as to whether the disparate findings are due to ascertainment and referral bias, the use of high density multiply affected kindreds, and family history data. We studied 40 consecutive GTS probands and their 168 first-degree relatives to test whether or not the two disorders share a common genetic mechanism. All subjects included in the study were directly interviewed. Although the rate of ADHD was increased (40%) in the GTS probands, the rate among first degree relatives (6.5%) was not significantly higher than in general population. However, the rate of ADHD among relatives of probands with both GTS and ADHD, was more than double that observed in relatives of probands with GTS only. In these families of probands with GTS and ADHD, there was no evidence to suggest co-segregation of the two disorders. Thus, our data do not support the view that ADHD may be an alternative expression of the putative GTS gene.

NR353 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Thyroid Function in Lithium-Free Bipolar Patients

Jose L. Ayuso-Gutierrez, M.D., Psychiatry, Hospital San Carlos, Martin Lagos SN, Madrid 28040, Spain; Jesus Valle, M.D., Jose L. Ayuso-Mateos, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the thyroid function in rapid cycling and non-rapid cycling bipolar patients who had not been treated with lithium.

Summary:

Objective: The evidence linking hypothyroidism and rapid cycling is limited and contradictory. All the studies published in the literature have been carried out with samples that included lithium-treated patients. The present study was designed to assess thyroid function in rapid-cycling (RC) and non-rapid-cycling (NRC) bipolar patients who had not been treated with lithium previously.

Method: Thyroid function was studied in a sample of 51 patients with type I and type II bipolar affective disorder (Research Diagnostic Criteria) that included 42 NRC and nine RC. None of the patients had previously received lithium. Thyroid function was evaluated through the determination of T3, T4, and TSH, both basally and in response to 500 mg of proliterin.

Results: Mean serum T3, T4, TSH, and TRH-stimulated TSH did not differ in the two groups of patients. Four patients (three NRC and one RC) had subclinical hypothyroidism. Four patients (three NRC and one RC) showed tyroid hyperfunction.

Conclusions: This study shows a low rate of thyroid abnormalities in lithium-free bipolar patients (7.8%). No differences were found in the prevalence of thyroid disfunction between RC and NRC bipolar patients. Our data do not support the hypothesis that a dysfunction in the thyroid axis predisposes bipolar patients to suffer a rapid cycling course.

References:

1. Baur MS, et al. Rapid cycline bipolar affective disorder. I Association with frade 1 Hypothroidism. *Arch. Gen Psychiatry* 47, 429–32, 1990.

2. Joffe RT, et al. Thyroid Function and bipolar affective disorder. *Psychiatr. Res.*, 25, 117–21, 1988.

NR354 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Predictors of Tardive Dyskinesia

Miranda Chakos, M.D., Psychiatry, Hillside Hospital, 75-59 263 Street, Glen Oaks NY 11004; Jose Ma. J. Alvir, Dr. P.H., Robert Bilder, Ph.D., Margaret Woerner, Ph.D., John M. Kane, M.D., Jeffrey A. Lieberman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand taht certain clinical and biological factors may predict vulnerability to tardive dyskinesia in patients chronically treated with neuroleptics.

Summary:

In order to determine predictors of tardive dyskinesia in schizophrenic patients we analyzed data on 70 patients who have been followed longitudinally in an ongoing prospective cohort study of first-episode schizophrenics at Hillside Hospital. Patients received standardized antipsychotic treatment and had MR brain scans, neuropsychological testing, and regular assessments of psychopathology and side effects. TD development was predicted by poorer level of remission from first psychotic episode, longer duration of psychotic symptoms prior to study entry, poorer levels of early adolescent social adjustment, enlargement of the frontal horns of the lateral ventricles, and global impairment on neuropsychological testing. Neuroleptic dose was a trend level predictor of TD development. When level of remission and dose as a time dependent covariate were entered simultaneously, level of remission remained a significant predictor of time to TD development (risk ratio-7.34, 95% CI = 1.75, 30.87, x^2 = 7.40, df = 1, p = .007), while the effects of dose were eliminated (risk ratio per 2 fluphenazine units = 1.02, 95% CI = 0.95, 1.09, x^2 = 0.29, df = 1, p = .59). Our findings indicate that TD development is primarily a consequence of disease related vulnerability to the disorder which is manifest with drug exposure, rather than a consequence of increased drug exposure.

References:

1. Kane, Woerner, Lieberman and Kinon. Tardive dyskinesias and drugs. *Drug Development Research,* 9: 41–51, 1986.

2. Morgenstern, Glazer. Identifying risk factors for tardive dyskinesia among long-term outpatients maintained with neuroleptic medications. *Arch Gen Psychiatry* 50: 723–733, 1993.

NR355 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Risperidone for Treatment Refractory Schizophrenia

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate knowledge of the response of a group of treatment refractory patients with schizophrenia and schizoaffective disorder to risperidone.

Summary:

In a randomized double-blind study, 523 *DSM-III-R* schizophrenic patients received one of four doses of risperidone (2, 6, 10, or 16 mg/day), 20 mg/day of haloperidol, or placebo for eight weeks. EPS were evaluated with the Extrapyramidal Symptom Rating Scale and a patient subjective questionnaire. Mean change scores over time, worst scores, and use of anticholinergic medication were analyzed. Increases from baseline in mean rigidity scores were not seen in patients receiving placebo or 2 and 6 mg/day of risperidone; scores increased significantly in patients receiving 10 and 16 mg/day of risperidone and 20 mg/day of haloperidol, the greatest increases being seen in haloperidol patients. Changes in tremor showed the same pattern. Buccolingual masticatory movements decreased significantly in patients receiving 2, 10, and 16 mg/day of risperidone. The use of anticholinergics was highest among haloperidol patients. The incidence of EPS was similar in patients receiving placebo and the therapeutically effective dose of 6 mg/day of risperidone. Data on the patients' subjective reports on EPS will be presented. it is concluded that the incidence of rigidity and tremor is dose dependent and generally low in patients receiving risperidone.

References:

1. Chouinard G, Jones B, Remington, G, et al: A Canadian multicenter placebo-controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenic patients. *J Clin Psychopharm* 13:25–40, 1993.

2. Kane J, Honigfeld G, Singer J, et al: Clozapine for the treatment-resistant schizophrenic: a double-blind comparison with chlorpromazine. *Arch Gen Psychiatry* 45:489–496, 1988.

NR356 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Risperidone Versus Clozapine in Psychosis

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand differential indications for and clinical, cognitive effetcs, and side effects of risperidone and clozapine in treatment resistant psychotic disorders.

Summary:

Risperidone and clozapine are novel neuroleptics that share serotonin-2 and dopamine-2 receptor blocking activity, but differ in their antagonism of muscarinic, adrenergic, and dopamine type I receptors. Previous evidence suggested that clozapine may be effective in reducing psychiatric symptoms in treatment resistant schizophrenic patients, but may not improve cognitive function. This issue has not been examined in a comparison with risperidone.

In this study, we present the initial results of a randomized crossover, dose optimized study in which risperidone and clozapine are directly compared. Eighteen treatment resistant psychotic patients have participated thus far. All raters were blind to medication status.

Matched pair T-tests suggested that clozapine and risperidone were equally effective antipsychotics in terms of both the positive and negative symptom subscales of the PANNS and on the CGI (severity of illness subscale). Risperidone appeared to produce less weight gain and daytime sedation than clozapine. Patients were more likely to require benztropine for extrapyramidal symptoms with risperidone than with clozapine. Neurocognitively, differences between the two were also apparent. Clozapine was beneficial for tests of vigilance and reaction time, while risperidone was beneficial for tests of set shifting and visual memory. These results suggest differential cortical and subcortical effects of these two medications.

References:

1. Gelders YG, Heylen SLF, Vanden Bussche G, Reyntiens AJM, and Janssen PAJ: Pilot clinical investigation of risperidone in the treatment of psychotic patients: *Pharmacopsychiatry,* 23: 206–211, 1990.

2. Ishigooka J, Wakatabe H, Murasaki M, and Miura S: Phase I study of risperidone, a new antipsychotic drug of benzisoxasol derivative. *Clinical Evaluations,* 19: 93–163, 1991.

NR357 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Clinical Efficacy and Safety of Olanzapine: A New Atypical Antipsychotic Agent

Pierre V. Tran, M.D., Psychopharmacology, Lilly Research Labortorie, Eli Lilly and Com. Drop 2128, Indianapolis IN 46285; Charles M. Beasley, M.D., Gary D. Tollefson, M.D., Todd Sanger, Ph.D., Winston G. Satterlee, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to be informed about the mechanism of action, clinical pharmacology, clinical efficacy, and side effect profile of olanzapine, a new "atypical" antipsychotic agent.

Summary:

Olanzapine is a putative "atypical" antipsychotic agent that belongs to the class of thienobenzodiazepines. In vitro studies indicate that olanzapine has high affinity for D1, D2, D4, 5-HT1C, 5-HT2, muscarinic, alpha-adrenergic, and histaminic receptors. In vivo behavioral studies suggest that it possesses antipsychotic activity with low propensity to produce extrapyramidal symptoms.

In a phase II, double-blind, multicentric, randomized, placebo-controlled clinical trial, 335 patients with the diagnosis of schizophrenia were randomized to one of the five arms of the study: placebo, olanzapine low-dose range (2.5–7.5 mg), olanzapine medium-dose range (7.5–12.5 mg), olanzapine high-dose range (12.5–17.5 mg) and haloperidol (10–20 mg). The acute phase of the study lasted six weeks with evaluations performed weekly. Patients in both the medium- (–12.6) and high- (–15.2) dose ranges of olanzapine had achieved reductions of normalized BPRS-total scores that were statistically significantly better than that of patients who received placebo (–3.1) when mean changes of scores from baseline to endpoint were compared. The olanzapine high-dose range produced a reduction of mean BPRS-total score numerically superior to haloperidol (–15.2 and –12.9, respectively) although the difference was not statistically significant. When SANS-composite and SANS-summary scores were compared, the olanzapine high-dose range yielded a reduction of mean scores that were statistically better than that of haloperidol and placebo (–13.6, –6.6, and –1.9, respectively for SANS-composite and –4.1, –2.0 and –0.6, respectively, for SANS-summary). The olanzapine high- (–1.0) and medium- (–1.0) dose ranges were statistically significantly better than placebo (–0.3) when the mean changes in CGI-severity from baseline to endpoint were compared.

Patients receiving olanzapine experienced no acute dystonic reactions and minimal prolactin elevation as compared to haloperidol indicating that olanzapine was well tolerated overall.

We conclude that olanzapine is effective in treating both the positive and negative symptoms of schizophrenia and is well tolerated.

References:

1. Moore NA, Tye NC, Axton MS, Risius FC: The behavorial pharmacology of olanzapine, a novel "atypical" antipsychotic agent. *J Pharmacol Exp Ther,* 262(2):545–551, 1992.

2. Moore NA, Calligaro DO, Wong DT, Bymaster F, Tye NC: The pharmacology of olanzapine and other new antipsychotic agents. *Curr Opin Invest. Drugs,* 2(4):281–293, 1993.

NR358 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

New Evidence for the Clinical Utility of Haloperidol Plasma Levels

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the potential utility of haloperidol plasma level measurements in the management of schizophrenic patients and with the value of dose decreases in selected nonresponders.

Summary:

Schizophrenic patients who fail to improve substantially while taking a given dose of haloperidol pose a dilemma for the treating physician. Does a physician follow tradition and increase the dose, or does he or she lower the dose in light of the few studies indicating that more improvement occurs when plasma levels are within certain limits.

On the basis of blood levels following a 20 mg loading dose of haloperidol, we assigned inpatients with schizophrenia to fixed doses designed to generate steady-state plasma levels of 8 ng/ml to 18 ng/ml, inclusive ("medium") or 25 ng/ml to 35 ng/ml inclusive ("high"). After three weeks those whose BPRS scores had not improved by at least 30% over baseline were randomized to either continue at the same dose or to take an alternative dose designed to produce steady state-plasma levels in the high range (if they had previously been in the medium range), or the medium range (if they had previously had high levels).

The nine patients whose plasma levels dropped from the high range to the medium range experienced a mean 23.6% (SD = 23.4) improvement in BPRS scores (week 3 vs. week 6); the three whose plasma levels had increased from the medium to the high range experienced only a mean 4.6% (SD = 7.6) BPRS improvement (Wilcoxon rank sum test, X2 = 6.2, df = 1, p = .01). The 11 patients who remained in the high plasma level range also experienced significantly less improvement (12.2%, SD = 17.3) when compared to those who underwent a dose reduction (Wilcoxon rank sum test, X2 = 4.2, df = 1, p = .04). These results indicate that high haloperidol plasma levels may interfere with, or obscure, clinical improvement and that dose adjustments to produce lower levels may be of benefit.

References:

1. Coryell W, Kelly M, Perry PJ & Miller D: Haloperidol plasma levels and acute clinical change in schizophrenia. *J Clin Psychopharmacol* 10:397–402, 1990.

2. VanPutten T, Marder SR, Mintz J: A controlled dose comparison of haloperidol in newly-admitted schizophrenic patients. *Arch Gen Psychiatry* 47:754–758, 1990.

NR359 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Anticipation of Bipolar Disorder: May Be Influenced by the Sex of the Affected Parent

Francis J. McMahon, M.D., Psychiatry, Johns Hopkins, Meyer 3-181 600 N. Wolfe St., Baltimore MD 21287; Melvin G. McInnis, M.D., Mary C. Blehar, Ph.D., Elliot S. Gershon, M.D., John I. Nurnberger, Jr., M.D., Theodore Reich, M.D., J. Raymond DePaulo, Jr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1. understand the definition, indicators and implications of anticipation in bipolar disorder; 2. identify the major mechanisms of anticipation in psychiatric illnesses.

Summary:

Objective: We have reported that in families of probands with bipolar disorder, members of successive generations experience earlier onset and more frequent illness episodes, a phenomenon called anticipation. We now report that anticipation also appears to occur in an independent sample of families and may be influenced by the sex of the affected parent.

Method: Families (n = 85) with a bipolar I proband and at least one other bipolar I or schizoaffective first-degree relative were ascertained at sites of the NIMH Genetics Initiative. Subjects were evaluated with the Diagnostic Interview for Genetics Studies, a semistructured instrument that assesses lifetime psychopathology.

Results: The 111 members of the proband's generation (excluding probands) had 1 10-year earlier median age at onset than the 64 members of the previous generation ($p < .0001$). When parental age at onset was compared with that of a randomly selected offspring, affected father-offspring pairs showed a median 15.5-year difference in onset age, versus a median 9.0-year difference for mother-offspring pairs ($p = .038$).

Conclusions: While subject to ascertainment biases, these results confirm our previous findings and are the first indication of a parental sex effect upon anticipation in bipolar disorder.

References:

1. McInnis MG, McMahon FJ, Chase GA, et al: Anticipation in bipolar affective disorder. *Am J Hum Genet.* 53:385–390, 1993.

2. Nurnberger JI: Genotyping status report for affective disorder. *Psychiatric Genetics* 3:207–214, 1994.

NR360 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Low Serum Cholesterol and Attempted Suicide

Julia A. Golier, M.D., Bronx VA Hospital 116A, 130 West Kingsbridge Road, Bronx NY 10468; Peter M. Marzuk, M.D., Andrew C. Leon, Ph.D., Cindy Weiner, M.A., Kenneth J. Tardiff, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the strengths, weaknesses and controversies in the literature on low cholesterol and attempted and completed suicide; and demonstrate an understanding of the potential psychobiological and public health ramifications of the present study.

Summary:

Objective: Several studies suggest that low cholesterol is associated with increased mortality from suicide. This study sought to determine if low cholesterol is associated with a history of serious suicide attempts among psychiatric inpatients.

Methods: Lifetime history of attempted suicide of 649 patients, aged 18–59 and consecutively admitted to a psychiatric hospital, was assessed by semistructured interview. The seriousness of an attempt was rated on the basis of the resulting medical injury. Serum cholesterol levels, obtained from the admission biochemical profile, were divided into quartiles.

Results: Compared to men with low cholesterol (defined as less than or equal to the 25th percentile), men with a cholesterol level above the 25th percentile were less likely to have ever made a serious suicide attempt (R.R. = 0.45, 95% C.I. = 0.23–0.87), controlling for age, weight, race, socioeconomic status, alcohol use, and depression. There was no association between cholesterol level and attempted suicide in women.

Conclusion: Male psychiatric patients with serum cholesterol in the lowest quartile were more than twice as likely to have made a serious suicide attempt than those with a cholesterol level in the upper quartiles. Low cholesterol should be further investigated as a potential biological marker of attempted and completed suicide in men.

References:

1. Muldoon MF, Manuk SM, Matthews KM: Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. *BMJ* 301:309–314, 1990.

2. Lindberg G, Rastam L, Gullberg B, Eklund GA: Low serum cholesterol concentration and short-term mortality from injuries in men and women, *BMJ* 305:277–279, 1992.

NR361 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Suicidal Behavior Among Twins

Alec Roy, M.D., Psychiatry, East Orange VAMC, 140 Dwight Place, Englewood NJ 07631; Nancy Segal, Ph.D., Marco Sarchiapone, M.D., Veronika Solt, M.D., John Williams, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that these data suggest that genetic factors play a part in suicidal behavior.

Summary:

We reported 176 twin pairs in which one or both twins had committed suicide. Seven of the 62 monozygotic (MZ) twin pairs were concordant for suicide compared with two of the 114 dizygotic twin pairs (11.3% vs 1.8%, $P < 0.01$). However, no study has examined attempts at suicide among living cotwins of twin suicide victims. As part of developing a suicide research program, we collected a new series of 35 twins whose cotwin had committed suicide. Eleven of the 27 living MZ cotwins had themselves attempted suicide compared with none of the eight living DZ cotwins (40.7% vs 0% Fisher's Exact Test, one tailed, $P < 0.04$). Thus, these two studies show that MZ twin pairs have significantly greater concordance for both suicide and attempted suicide than DZ twin pairs. These data suggest that genetic factors play a part in suicidal behavior. We now plan a molecular genetic study in the living cotwins of the MS suicide victims.

References:

1. Roy A, Segal N, Centerwall B, Robinette D: Suicide in twins. *Archives of General Psychiatry,* 48:29–32, 1991.

2. Roy A: Family history of suicide. *Archives of General Psychiatry,* 40:971–974, 1983.

NR362 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Do [3H]-IMI Platelet Studies Reflect Treatment Outcome of Major Depression-Agitated Subtype?

Gary D. Tollefson, M.D., Psychopharmacology, Lilly Research Labortorie, Eli Lilly and Com. Drop 2128, Indianapolis IN 46285.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1. understand the 5-HT uptake mechanism and the related binding parameters of affinity (Kd) and density (Bmax); 2. To recognize the differential risk:benfit profile of FLU & IMI in agitated major depression; 3. to consider what role 5-HT uptake affinity might have in treatment response.

Summary:

Serotonin (5-HT), through direct or indirect mechanisms, has been implicated in agitation/activation among major depressives. A peripheral model for central 5-HT activity is characterization of the 5-HT : IMI binding complex on platelet.

We studied 80 DSM-III-R compatible major depressives with RDC criteria for an agitated subtype. Following a one-week placebo lead-in, subjects were blindly randomized to imipramine or fluoxetine for an eight-week, double-blind study period.

Efficacy was comparable across the two treatments ($HAMD_{17}$ change, baseline to endpoint). However, discontinuations due to an adverse event (e.g., nervous system) were significantly more frequent with imipramine (18/40; 45%) than fluoxetine (4/40; 10% [$p < .0001$]). Thirty-three subjects (15 IMI, 18 FLU) provided baseline and endpoint samples for [^{3}H]-IMI assay. Baseline K_d was predictive of Δ HAMD ($r = .22$; $p = .06$) and significantly to response status ($p < 0.05$). While baseline to endpoint B_{max} (fmol/mg) was similar for IMI (183 ± 329) and FLU (196 ± 401), a statistically

significant treatment difference in Δ K_d IMI .005 ± .010 versus FLU .088 ± .013 emerged (p = .004). Changes in K_d and $HAMD_{17}$ were positively correlated in FLU-treated patients (r = 0.406, p = 0.095) only. Plasma concentrations were not significantly correlated with a change in the binding profiles. Both baseline and endpoint K_d negatively trended with treatment-associated change in Agitation Rating Scale (r = –.31; p = .06) and HAMA (r = –.38; p = .02) scores in both treatment groups combined.

In conclusion, these data suggest that baseline status of the transporter complex may reflect the capacity for antidepressant response. In addition it may mark features of agitation/anxiety. Perturbation of K_d further reflected a baseline to endpoint change in depression severity that was unique to the SSRI fluoxetine. This may relate to the fact these two antidepressants act at different sites within the complex. FLU is a competitive 5-HT inhibitor at the uptake site, whereas IMI is noncompetitive at the [^{3}H] binding site. While overall treatment efficacy was comparable, the significantly better tolerance of FLU among agitated subjects was striking. Further study into the direct or indirect role of this uptake site in clinical response and selective drug effects is encouraged.

References:

1. Briley M: Imipramine binding: its relationship with serotonin In: *Neuropharmacology of Serotonin.* Ed. A.R. Green, Oxford University Press, New York, 1985. pp 50–70.

2. Nemeroff CB, et al: Marked reduction in the number of platelet-tritiated imipramine binding sites in geriatric depression. *Arch Gen Psychiatry 45:919–923, 1988.*

NR363 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

Increased Lactate Levels and Post-ECT Agitation

Marc Auriacombe, M.D., Department of Psychiatrie, University of Bordeaux, 121 Rue De La Bechande, Bordeaux, France; Jean P. Reneric, M.D., Daniel Usandizga, M.D., Francis Gomez, M.D., Isabelle Combourieu, M.D., Jean Tignol, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize post-ECT agitation and determine the appropriate therapeutic strategies.

Summary:

Objective: Restless agitation has been reported to occur in 10% of patients after electroconvulsive therapy (ECT). Management sometimes requires application of physical restraints. Swartz (1990) reported that this agitation could be representative of lactate-induced panic secondary to insufficient muscular blockade. The purpose of this prospective study was to test this hypothesis.

Method: In 255 consecutive ECT sessions, patients were monitored for one hour post-ECT for evidence of agitation. A blood sample was collected before and after the ECT-induced seizure for serum lactate levels. ECT was administered with a brief pulse constant current device under general anesthesia with muscular blockade using succinylcholine 1.0 mg/kg. EEG was monitored from the time prior to ECT through the agitation phase, until the patient was completely recovered.

Results: Agitation was observed in 7% of the ECT sessions. Mean lactate levels are presented for the Agitated vs. Nonagitated groups in the following table:

			Serum Lactate mmol/l(SD)	
	Patients	Sessions	before ECT	after ECT
Nonagitated	36	228	1.66(.55)	2.54(1.53)
Agitated	2	16	1.77(.56)	4.77(1.47)
t test			t = .44 p > .05	t = 2.8E05 p < .0000

Succinylcholine dose was increased up to 1.5 mg/kg in the post-ECT Agitated group. This resulted in cessation of post-ECT agitation and decreased lactate levels: (Serum Lactate before ECT: 1.61(.53); Serum Lactate after ECT: 2.07(.94)).

Conclusion: This study's data concur with data supporting the hypothesis that post-ECT agitation may be due to lactate-induced panic. Increasing the succinylcholine dose in the agitated group resulted in cessation of post-ECT agitation and resulted in maintaining the post-ECT increase in lactate levels to the same degree as the lactate levels in the nonagitated patient group.

References:

1. Swartz CM: ECT emergence agitation and succinylcholine dose. *Journal of Nervous and Mental Disease,* 178:445–457, 1990.

2. Devanand CP, et al: Clinical features and predictors of postictal excitement. *Convulsive Therapy* 5:140–146, 1989.

NR364 Wednesday, May 25, 9:00 a.m.-10:30 a.m.

An Asymmetric Bilateral ECT Electrode Placement

Conrad M. Swartz, M.D., Psychiatry, ECU School of Medicine, Greenville NC 27858

Educational Objectives:

At the conclusion of this presentation, the participant should be able to consider a variety of stimulus electrode placements for ECT and weigh their advantages and disadvantages for individual patients.

Summary:

Objective: In view of the ongoing dilemma between the problematic cognitive side effects of traditional bitemporal (bilateral) electroconvulsive therapy (ECT) and the low reported efficacy of unilateral ECT, a new stimulus electrode placement was constructed and an open trial conducted.

Method: Placement construction was according to expectations that cognitive side effects would be minimized by avoiding induction of seizure foci in brain regions associated with concrete neuropsychological functions, and that greater efficacy accompanies a larger volume of seizure foci. This led to anterior placement of the left-sided electrode, to above the left eye, with temporal placement on the right side. An open trial with brief-pulse stimuli of 1 msec pulsewide was conducted on 10 consecutive female inpatients with depression, mania, or mixed manic-depressive state, nine of whom showed severe cognitive impairment, psychosis, or both.

Results: All patients achieved remission, indicating efficacy as likely above 93.3% as below it, and above 74% (p < .05). No cognitive morbidity was observed on post-ECT mini-mental status score, which averaged 28.4 of 30, with an average improvement of 17.3 points, substantially better than reported for traditional bitemporal ECT. Remission was maintained at six-to-10-week followup.

Conclusions: These results justify further consideration of this new placement.

References:

1. Swartz CM: Asymmetric bilateral right frontotemporal left frontal stimulus electrode placement. *Neuropsychobiology,* in press.

2. Abrams R, Swartz CM, Vedak C: Antidepressane effects of high-dose right unilateral ECT. *Arch Gen Psychiatry* 48:746–748, 1991.

NR365 Wednesday, May 25, 12 noon-2:00 p.m.

Role Strains, Role Fit and Psychological Distress in Immigrant Muslim Women: An Exploratory Study

Pascale Des Rosiers, M.D., Psychiatry, Montreal General Hospital, 1650 Cedar, Montreal PQ H3G 1A4, Canada; Ellen

Corin, Ph.D., Cecile Rousseau, M.D., Normand Peladeau, M.Sc.

Summary:

Objectives: To explore how women raised with different cultural values deal with issues of multiple roles. In particular, this study centers on the relationship between the working status, role fit, role strains, and psychological distress in a sample of immigrant Muslim women in Montreal.

Method: 23 immigrant Muslim women were interviewed, recruited through two community centers in Montreal. The interview consisted of a sociodemographic questionnaire, the Ilfeld Psychiatric Symptom Index, a religiosity scale, a measure of role fit, and a role strains questionnaire.

Results: 1) Working immigrant Muslim women show more psychological distress than homemakers. Women in role-unfit situations also show more psychological distress than women in role-fit situation. However, the role fit is not a better predictor of distress than the working status. 2) Of all the sociodemographic factors studied, religiosity stands out as a major protective factor. 3) The role fit appears to contribute to distress via "internal" variables of role strains (personal satisfaction and wish for change), while the working status contributes to distress via " external" variables of role strains (husband's and extended family's demands).

Conclusion: In our sample of immigrant Muslim women, the working women and the women in role-unfit situations appeared at particular risk of psychological distress.

NR366 Wednesday, May 25, 12 noon-2:00 p.m.

The Identification of Culture-Specific Syndromes, as Proposed for the DSM-IV, in Children and Adolescents from Xhosa, South Africa

Brian A. Robertson, M.D., Psychiatry, University of Cape Town, 17 Parish Road, Constantia 7800, South Africa; Karin Ensink, M.A., Gerard Drennan, M.A.

Summary:

Objective: To determine whether culture-specific syndromes are found among Xhosa children and adolescents in South Africa.

Method: The first stage of the study, involving comprehensive semistructured interviews and the use of vignettes with 12 Xhosa traditional healers of different types identified five potential culture-specific syndromes. In the second stage 16 Xhosa diviners, recruited on a networking basis, were asked to systematically describe their symptoms and signs. All interviews were audiotaped, transcribed, and translated into English. The 16 sets of symptoms and signs were tabulated according to syndrome.

Results: UKUPHAPHAZELA ("fright") and school anxiety (brain-fag syndrome) demonstrated a high degree of consensus, and AMAFUFUNYANE ("possession by evil spirits") correlated with possession trance disorder. UKUPHAPHAZELA appears to be predominantly a cultural variation of sleep terror disorder, and school anxiety a cultural variant of conversion disorder.

Conclusion: There appear to be at least three culture-specific syndromes among Xhosa children and adolescents that can be classified as cultural variants of known DSM-IV disorders. UKUPHAMBANA ("madness caused by evil spirits") and UKUTHWASA (calling by ancestral shades to become a healer) are less discrete categories that may have developed indigenously to give meaning to more biologically based and more psychosocially influenced abnormal behavior, respectively.

NR367 Wednesday, May 25, 12 noon-2:00 p.m.

Race and Benzodiazepine Use Among Opioid Abusers

D. Daniel Rajna, M.D., Psychiatry, Yale Medical School, 34 Park Street, New Haven CT 06519; Juliana Pakes, Scott W. Woods, M.D., Boris Meandzija, M.D., Thomas R. Kosten, M.D., Richard S. Schottenfeld, M.D.

Summary:

In recruiting subjects from a methadone maintenance program for a benzodiazepine detoxification study, we noticed that minority study candidates appeared to be underrepresented relative to the clinic population. We therefore investigated the racial distribution of benzodiazepine use in this population.

Method: We surveyed for clinical demographic data and benzodiazepine use a database that included 94% of New Haven methadone maintenance new enrollees from July, 1990 to January, 1992, who gave at least one urine sample (n = 209).

Results: For the proportion of urines positive for benzodiazepines during the study period per patient, the mean was 18.3% for 117 white patients (2469 urines), 6.9% for 22 Hispanic patients (519 urines), and 6.5% for 70 African-American patients (1221 urines) ($F = 5.86$, $df = 2,206$, $p < .005$, Duncan's multiple range test: whites > Hispanics = African Americans).

Discussion: The data suggest lower rates of benzodiazepine use by minority patients among recent New Haven methadone maintenance enrollees compared with whites. Future research should explore the replicability of these findings in other settings.

Supported by NIDA R01 DA08265, P50 DA04060, R18 DA06190, and K02 DA00112.

NR368 Wednesday, May 25, 12 noon-2:00 p.m.

Psychological Impact of Civil War on Liberian Children

Dana L. Sanderson, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Grace L. Kennedy, M.D., Edward O. Bixler, Ph.D., John W. Getz, M.A., H. Allen Handford, M.D.

Summary:

Although natural and man-made disasters often prompt subsequent research into the psychological impact on victims, rarely do investigators have the opportunity to evaluate a sample population before and after a crisis. A major civil war began in Liberia in 1990. In 1989, prior to the outbreak of hostilities, the primary author (D.S) had the opportunity to evaluate psychologically Liberian children in their native surroundings. In 1991, subsequent to the initial onslaught of the war, a larger group of children was evaluated more extensively. Both pre- and post-war samples of children displayed similar demographics (age, sex, culture, life-style), except that post-war children had lost one or both parents during the war. In the initial group, each child was interviewed in a semi-structured format with a series of questions pertaining to mood, preferences, and home life. In evaluating the second sample, in addition to the previously utilized interview format, projective drawings were obtained and medical examinations conducted. The baseline control group of children evaluated prior to the war displayed generally positive moods, few age-appropriate fears, and appropriate behavior and functioning in their culture. In contrast, the post-war sample of children exhibited substantial symptoms of anxiety related to the war, their personal traumas, and what they had witnessed. Many of these children displayed classic symptoms of post-traumatic stress disorder (PTSD) including: nightmares, recurrent intrusive memories, flashbacks, acting-out behavior, withdrawal, avoidance, and diminished school functioning. In contrast to their ongoing psychological distress, these children had regained adequate nutritional and physical well-being as a result of relief efforts to the country. In conclusion, this study is believed to be one of the first to demonstrate that PTSD symptoms observed in children following a war-time crisis were not present prior to the crisis.

NR369 Wednesday, May 25, 12 noon-2:00 p.m.

Total Quality Management Reduces Costs of Managing High-Risk Patients

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Summary:

A dramatic increase in overtime above budgeted levels at Buffalo Psychiatric Center (BPC) in 1992 resulted in a penalty against the number of full-time equivalent (FTE) positions the facility was authorized to fill. BPC staff addressed the need to reduce overtime by using techniques learned in training designed to encourage TQM/CQI initiatives in the public sector offered by the NYS Government Office of Employee Relations. These included: designation of a project team, examination of process, use and rearrangement of data, and participation of staff at all levels. We identified key administrative and clinical factors contributing to excessive overtime, including use of special observation (33%), unscheduled absenteeism (27%), and absences due to workers compensation (13%). Use of special observations (50%), in particular SO level 1 requiring 1 : 1 supervision, accounted for the highest percentage of overtime costs. Pareto analysis showed that the Intensive treatment Unit accounted for the highest percentages of overtime and use of special observation in the facility. We then focused our interventions ont hat unit. Staff at all levels gained an understanding both of the causes and consequences of excessive overtime. We developed interventions that were successful in reducing the use of special observation as well as unscheduled absences. Absences due to workers compensation were reduced as a result of changes in union contracts. We brought overtime below budgeted levels in four months, reducing our FTE penalty while maintaining patient and staff safety and improving the quality of patient care.

NR370 Wednesday, May 25, 12 noon-2:00 p.m.

Critical Clinical Variables Mediating a Short Length of Stay

Geetha Jayaram, M.D., Psychiatry, Johns Hopkins, 600 N. Wolfe Street, Baltimore MD 21287; Patricia Sullivan, R.N.

Summary:

Objective: Diagnosis related groups, historically used by the Health Care Financing Administration for reimbursement, do not address the heterogeneity and differences in illness-severity that remain unaddressed. Our aim was to identify significant patient and severity variables influencing length-of-stay on a short-stay psychiatric inpatient unit.

Methods: We studied 108 consecutive admissions to a short-stay inpatient unit at the Johns Hopkins Hospital between November 1, 1992 and June 30, 1993, using admission, treatment, and discharge data bases. Reviewer 1 collected admission data after direct patient evaluations and chart review, which included medical and psychiatric comorbidity. Reviewer 2 collected treatment, discharge data by chart review, including intensity of nursing care, and adverse outcome events. Reviewers were blind to each other's assessments. The following instruments were used for additional patient assessments: Global Assessment Scale, Mini-Mental-State Exam, Cognitive Test Battery, Addictions Severity Index, Milwaukee Evaluation of Daily Living Skills.

Results: Length-of-stay was significantly correlated with GAS score at admission, Mini-Mental-State Exam score, diagnosis of substance abuse, score on the MEDLS, severe mental illness, treatment with antidepressants or anti-psychotic medications.

Conclusions: Further research to elucidate case-mix and disease-specific severity measures for inpatients is necessary.

NR371 Wednesday, May 25, 12 noon-2:00 p.m.

What Happens When Psychiatric Beds Are Cut by Sixty Percent?

Alex Richman, M.D., Psychiatry, Dalhousie University, 5959 Spring Garden Road #609, Halifax NS B3H 1Y5, Canada.

Summary:

Method: A province-wide, person-oriented file links psychiatric hospitalizations in Nova Scotia during 1979–1991. The file includes admissions to mental hospitals and general hospital psychiatric units. Analysis of this file shows year-to-year changes in bed supply, one-year treatment prevalence, inception of new cases, and duration of stay of discharges.

Results: During the 11-year study period, bed use decreased from 1.0 to 0.4 beds per 1,000. There were no significant changes in the annual numbers of individuals hospitalized each year, first admissions or new cases with functional psychoses. Lengths of stay per case decreased markedly. Readmission rates for new cases were stable.

Conclusions: Psychiatric bed use is discretionary and is more affected by social than clinical factors. Reduced bed supply did not affect the number of individuals seen each year. The same number of persons was seen for shorter stays and fewer readmissions. Access was not reduced for either new patients or for previously hospitalized persons.

NR372 Wednesday, May 25, 12 noon-2:00 p.m.

Referral and Non-Attendance at a Psychiatric Clinic

Rosemary M. Morrison, Ph.D., Psychiatry, Manchester University, Mathematics Tower, Oxford Road, Manchester M139PL, England.

Objective: Research has suggested that there are medical, social, and administrative reasons for nonattendance by new psychiatric outpatients. The objective of this phase of the study was to assess the circumstances of referral and consider if and how these might lead to improved attendance.

Method: Examination of the records of a consecutive series of 262 referrals to an urban psychiatric clinic in the U.K. with a nonattendance rate of 22%. Telephone calls and questionnaires to referrers of all nonattenders (58). Structured interviews with 97% of the nonattenders and a sample of attenders. The research was designed and piloted at another centre.

Key Findings: Important aspects of research on the reasons for nonattendance were borne out. There was evidence of communication failure and inadequacy of assessment at referral. Referral was unacceptable to a third of nonattenders, but only 13% had discussed their doubts: referrers recognised only 9% as being at risk of nonattendance. More nonattenders (55%) than referral letters (21%) indicated need for urgent appointments. There was some confusion about where, by whom, and why they should be seen. Risk factors identified (medical and social circumstances). Nonattenders were less well known to referrers than attenders ($p < 0.05$). Referrer/nonattender relationships were generally good. Referrals came from medical sources, mainly general practice (80%). Nonattenders came from 45% of doctors (1–3 each) making referrals in the study period. This has implications for developing a remedial strategy.

Conclusion: Sources of referral have a viable and key role to play in promoting attendance.

NR373 Wednesday, May 25, 12 noon-2:00 p.m.

Adults and Children Admitted with Adjustment Disorder Diagnoses: Clinical Correlations and Two-Year Rehospitalization

David N. Rosenfeld, M.D., Psychiatry, Bergen Pines City Hosp., 230 E. Ridgewood Avenue, Paramus NJ 07652; Eddy A. Ortega, M.D., William M. Greenberg, M.D.

Summary:

Objective: Adjustment disorders (ADs), representing a "marginal or transitional illness category," are commonly but somewhat nebulously applied in clinical practice, receiving little study, and none use DMS-III-R. We compared DSM-III-R AD admissions with controls, exploring AD subtypes, suicidality, diagnostic stability, and two-year rehospitalization outcome.

Method: We retrospectively surveyed charts of AD-diagnosed admissions during 1989 to a 220-bed acute psychiatric service, with controls matched on age and sex. We separately analyzed children and adults.

Results: Cases (54 children, 102 adults) did not differ from controls on marital status, ethnicity, religion, commitment status or discharge disposition. Withdrawal, work inhibition, and physical complaint subtypes were almost unused. Both child and adult cases had shorter hospitalizations (20 vs. 32 days, $p = 0.04$; 20 vs. 44 days, $p < 0.001$) and suicidal ideation or behavior on admission more often than controls (both $p < 0.001$). Forty percent of cases were discharged without AD diagnoses; only 6% of controls were changed to ADs on discharge. Adult but not child cases were more often substance-abuse diagnosed and had significantly fewer psychiatric readmissions and less total readmission length-of-stay than controls two years post-discharge (all $p < 0.001$). Only 18% of case readmissions were AD-diagnosed.

Conclusions: Adjustment disorders are highly associated with suicidality on admission, and with substance abuse in adults. They are unstable diagnoses, but in adults predict shorter hospitalization and less rehospitalization.

NR374 Wednesday, May 25, 12 noon-2:00 p.m.

Presurgical Psychiatric Assessment of Medically Refractory Epileptic Patients

Rahul Manchanda, M.D., Psychiatry, University Hospital, 339 Windermere Road Box 5339, London ON N6A 5A5, Canada; Betsy Schaefer, B.A., Richard McLachlan, M.D., Warren T. Blume, M.D.

Summary:

A total of 250 consecutive adult patients with a medically refractory epilepsy were assessed psychiatrically as part of a routine evaluation of epilepsy surgery candidates. A definite focus of seizure onset was determined by electroencephalographic recording with telemetry and subdural electrode placement. A total of 191 patients had temporal lobe focus (103 left-temporal, 71 right-temporal and 17 bi-temporal focus), 40 had a nontemporal focus, and 19 had generalized or multifocal abnormalities. A psychiatric diagnosis was made in 123 (49.2%) using the DSM-III-R criteria. The most common diagnosis was personality disorder in 40 (16.0%) patients, followed by anxiety disorder in 35 (14.0%), schizophrenia in 12 (4.8%), mood disorder in eight (3.2%), adjustment disorder in seven (2.8%), organic brain syndrome in seven (2.8%), impulse control disorder in six (2.4%), substance abuse in five (2.0%), and pseudoseizures in three (1.2%) patients. Further, patients were also assessed using the Present State Examination. When the 36 syndrome profiles of the PSE were examined, each group of epileptic patients scored high on worrying, social unease, loss of interest, concentration, and irritability. When the types of focus (temporal, nontemporal and generalized) and PSE syndromes were examined, no significant findings emerged. This study indicates that almost half of the candidates for epilepsy surgery have a psychiatric morbidity, but this is unrelated to their focus of epilepsy.

NR375 Wednesday, May 25, 12 noon-2:00 p.m.

Family Environment and BPD

Jody Shachnow, Ph.D., NY Hospital CUMC, 21 Bloomingdale Road, White Plains NY 10605; John F. Clarkin, Ph.D., Norman Shachnow, M.D., Cynthia Smith, M.S.W., Fran Thuraton, M.S.W., James Hull, Ph.D., Edward N. Shearin, Ph.D.

Summary:

This study examined the evidence for biparental psychopathology, disturbed climate, and disruptive/traumatic events in the family environments of female patients with borderline personality disorder, along with the relationship of these elements to each other and to borderline severity. The sample included 30 reliably diagnosed inpatients at The New York Hospital-Westchester, and their 60 biologic parents. Of 40 consecutively admitted women who met criteria, nine refused and one failed to complete the protocol.

Instruments included: The Family Experiences Interview, the Family Environment Scale, and the SCID-NP and SCID-II and the BPD Dimensional Score Interview. We found a high incidence of parental psychiatric disorders both on Axis I and Axis II. Notably, parental psychopathology and serious trauma were absent in a number of families. Both patients and parents reported deficiencies in the relational qualities of family climate and, commonly, numerous traumatic events. However, the perceptions of patients and parents were significantly different. Dysfunctional aspects of the family environment tended to cluster. Additionally, the presence of biparental psychopathology during early childhood was predictive of borderline severity. The study yielded additional clinical insights on temperament, inter-generational repetition, "trickle-down abuse" within families, and the absence of social supports. The findings underscore the importance of differential evaluation and treatment of the family environment.

NR376 Wednesday, May 25, 12 noon-2:00 p.m.

Agreement of Direct Interview and Family History of Diagnosed Personality Disorders

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Summary:

Objective: To examine the concordance between direct interview and family history assessments of personality disorders with the use of the Personality Disorder Examination (PDE) and Family History Interview for Personality Disorders (FHIPD). Concordance between direct interview patient-informant reports has been found to range from –.06–.34 for the individual personality disorder diagnoses.

Method: Subjects were 454 relatives of 179 outpatients with mood and personality disorders and 45 normal controls. PDE and FHIPD assessments were made blindly.

Results: Kappas for the individual Axis II disorders ranged from –0.1 to .28 (median = .10). Kappas were .15, .20, and .11 for Cluster A, B, and C, respectively. Kappa for any Axis II disorder was .15. Pearson r for the number of criteria ranged from .14 to .40 (median = .18). When predictors of concordance were examined, agreement on the presence of a Cluster A personality disorder in the subject was predicted by subject lie scale score, and the presence of a Cluster B personality disorder in the informant. Agreement on the presence of a Cluster B personality disorder in the subject was predicted by subject age, subject lie scale score,

the presence of alcoholism in the informant, and the presence of any personality disorder in the informant. Agreement on the presence of a Cluster C personality disorder in the subject was predicted by informant gender.

Conclusions: The results indicate that the FHIPD has comparable rates of concordance to those reported for direct-informant interviews for Axis II. Future work will address the comparative validity of informant reports and direct interviews and the optimal method of combining data from informant and direct reports.

NR377 Wednesday, May 25, 12 noon-2:00 p.m.

Asymmetrical Alpha Power in Schizotypes

Dean F. Salisbury, M.D., Psychiatry, Harvard Medical, Psych 116A 940 Belmont Street, Brockton MA 02401; Martina M. Voglmaier, Ph.D., Robert W. McCarley, M.D., Larry J. Seidman, Ph.D., Evana Goodreau, B.A.

Summary:

Objective: To examine whether DSM-III-R-diagnosed schizotypes display low values and topographic abnormalities of alpha power. Alpha waves (8–12 Hz) reflect increased brain synchronization during periods of relaxation. Alpha is reduced in schizophrenics, and increases with clinical improvement. Schizotypal personality disorder may reflect the schizotaxic diathesis, and a measure that is abnormal in schizotypy and schizophrenia may be a candidate for a genetic marker.

Method: Eleven right-handed male schizotypes (SCID II) and 12 matched controls had continuous EEG recorded for two minutes in 2.5 sec epochs, with eyes open, and again with eyes closed. Eye movements were covaried from epochs, and epochs with residual eye movement (± 50 μv) were rejected. Spectral components were computed separately for eyes open and closed. Alpha power was measured between 8 and 12 Hz from mid-coronal electrodes (T3, C3, C4, T4).

Results: Schizotypes displayed reduced alpha power over the right hemisphere, with a reversed asymmetry relative to controls. Group interacted with hemisphere (collapsed across eye condition, $p = .017$), with eyes closed ($p = .019$), and trended towards significance with eyes open ($p = .06$). Control alpha was larger over the right hemisphere than left (Collapsed: 1.58 vs. 1.41 μv^2; Eyes closed: 2.15 vs. 1.89; Eyes open: 1.01 vs. 0.93), whereas schizotypes were smaller over right hemisphere than left (Collapsed: 1.21 vs 1.44 μv^2; Eyes closed: 1.55 vs. 1.82; Eyes open: 0.87 vs. 1.06).

Conclusions: Schizotypes failed to deactivate the right hemisphere during periods of relaxation. This may reflect increased activity of the right hemisphere in schizotypes as a consequence of left hemisphere pathophysiology, which has been observed in both schizotypal personality disorder and schizophrenia.

NR378 Wednesday, May 25, 12 noon-2:00 p.m.

Cholinergic Challenge and Affective Instability in Personality Disorder Patients

Bonnie J. Steinberg, M.D., Psychiatry, Mt. Sinia School of Med., 1 Gustave L. Levy Pl. Box 1228, New York NY 10029; Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Emil F. Coccaro, M.D., Larry J. Siever, M.D.

Summary:

Objective: The purpose of this study was to examine the relationship between cholinergic supersensitivity, as indicated by dysphoric responses to cholinergic challenge, and affective instability, a characteristic of many patients with borderline personality disorder and patients with certain other personality disorders.

Method: Fourteen DSM-III-R personality disordered patients participated in a physostigmine challenge paradigm in which glycopyrrolate was administered to block the peripheral effects of physostigmine, followed by either placebo or 0.014 mg/kg of intravenous physostigmine. The Profile of Mood State (POMS) self-report measure was obtained at baseline and following placebo or physostigmine infusion, with patient and raters blind to the infusion.

Results: The physostigmine-induced change in peak POMS depression subscale was significantly correlated with the trait of affective instability ($r = 0.72$, $p < 0.01$). The placebo-corrected peak POMS depression subscale response to physostigmine of 11.0 ± 2.0 in patients with borderline personality disorder was significantly greater than the response of affectively stable personality disordered patients, 3.6 ± 6.80 ($t = $, $p < 0.01$). These same patients did not respond to serotonergic, noradrenergic or placebo challenge with a depressive response, implying relative specificity.

Conclusions: These preliminary data suggest a correlation between affective lability as a trait and mood response to physostigmine challenge, and imply that the cholinergic system may be involved in the regulation of affect in Axis II disorders as well as in Axis I mood disorders.

NR379 Wednesday, May 25, 12 noon-2:00 p.m.

Serum Cholesterol and Impulsivity in Mood and Personality Disorders

Antonia S. New, M.D., Psychiatry, Mt. Sinai Medical Center, Box 1228 One Gustave Levy Pl, New York NY 10029; Robert L. Trestman, M.D., Maki Kano, B.A., Scott Gettinger, B.S., Larry J. Siever, M.D.

Summary:

Objective: The goal of this study was to determine whether fasting serum cholesterol is reduced in personality disorder patients and whether it correlates negatively with measures of impulsivity and hostility in these subjects.

Method: As part of ongoing psychobiological studies of mood and personality disorders in patients from two medical centers, serum cholesterol was measured as part of initial medical clearance and subsequently correlated with diagnostic criteria, clinical variables, and measures of impulsivity and aggression.

Results: No differences in mean serum cholesterol were found in personality disorder subjects ($n = 40$) as compared to either normal controls ($n = 22$) or depressed subjects ($n = 32$). Subjects meeting DSM-III criteria for borderline personality disorder ($n = 5$), however, did show reduced serum cholesterol compared to normal controls ($n = 22$) ($t = 2.3$, $p < .033$). Using the Buss-Durkee Hostility Inventory (BDHI) and the Barratt Impulsiveness Scale (BIS), no correlations with serum cholesterol and total or subscale scores on BDHI ($n = 51$), nor on BIS ($n = 45$) were found. In borderline personality disorder ($n = 5$), reduced serum cholesterol tended to correlate with increased BIS subscale for motoric impulsivity ($r = -.87$, $p < .05$). In personality disorder subjects meeting the specific DSM-III criterion for borderline personality disorder of physically self-damaging acts ($n = 5$), reduced serum cholesterol correlated with increased impulsivity (BIS total score, $r = -.90$, $p < .05$), and with the BIS subscale for self-assessment of impulsivity ($r = .88$, $p < .05$). In depressed subjects ($n = 17$), a *decreased* serum cholesterol correlated with reduced hostility (BDHI total score $r = .57$, $p < .02$, BDHI indirect aggression $r = .49$, $p < .05$, and BDHI irritability, $r = .53$, $p < .03$).

Conclusions: Serum cholesterol was lower in the subpopulation of personality disorder subjects with borderline personality disorder and in those with a history of physically self-damaging acts. Low cholesterol correlated negatively with specific measures of impulsive aggression in personality disorder subjects with physically self-damaging behavior. The positive correlation with measures of hostility in depressed patients suggests that the putative relationship between cholesterol and impulsive/aggressive behav-

ior may manifest differently or be moderated by additional factors in different diagnostic groups, as has been seen in previously published data on biological correlates of impulsivity.

NR380 Wednesday, May 25, 12 noon-2:00 p.m.

The Factor Structure of Schizotypy

Andrea J. Bergman, M.D., Psychology, St. John's University, 8000 Utopia Parkway, Jamaica NY 11439; Vivian Mitropoulou, M.A., Robert L. Trestman, M.D., Larry J. Siever, M.D.

Summary:

Background: In defining the boundaries of the schizophrenia spectrum, schizotypal traits have been studied in both clinical and community populations. There is some support that the factor structure of symptoms in schizophrenia is parallel to the factor structure of schizotypal symptoms in nonschizophrenic populations (Kendler, et al., 1991). However, the factor structure of schizotypy in personality disordered patients has not been established.

Objective: The goal of this study was to examine the factor structure of both clinically rated and self-report schizotypy in subjects displaying personality disorder traits.

Method: Subjects (N = 193) were assessed as part of ongoing psychobiological studies of mood and personality disorders in two medical centers; 138 subjects met full criteria for at least one DSM-III personality disorder, while 55 subjects displayed only personality disorder traits by Structured Interview for DSM-III Personality Disorders (SIDP). Measures included the SIDP criteria for schizotypal personality disorder (SPD) and the Chapman scales of Perceptual Aberration, Physical Anhedonia, and Social Anhedonia.

Results: Varimax factor analyses were conducted separately for SPD criteria (N = 193) and the items from the Chapman scales (N = 79). Analyses for the SPD criteria yielded three factors (Deficit-related, Positive, and Paranoid). The two factors from the Chapman scales were Anhedonia (mostly social) and Perceptual aberration. Correlations between these two sets of factors indicated that the Deficit-related factor and the Paranoid factor derived from the SPD criteria were positively correlated with the Anhedonia factor derived from the Chapman scales ($r = .49$, $p < .001$; $r = .27$, $p < .02$, respectively). The Paranoid factor from the SPD criteria was also positively correlated with the Perceptual Aberration factor of the Chapman scales ($r = .30$, $p < .01$).

Conclusions: These results indicate that the basic factor structure of positive and negative symptomatology in schizophrenia persists in clinical samples of personality disordered patients. This supports the notion of a schizophrenia spectrum ranging from chronic schizophrenia to milder, schizophrenia-related personality traits.

NR381 Wednesday, May 25, 12 noon-2:00 p.m.

SPECT Imaging of Cognition in Schizotypals

Robert L. Trestman, M.D., Psychiatry, Mt. Sinai Sch of Medicine, One Gustave L Levy Pl Box 1230, New York NY 10029; Monte S. Buchsbaum, M.D., Benjamin V. Siegel, M.D., Miklos F. Losonczy, M.D., Claire Schaefer, Ph.D., Larry J. Siever, M.D.

Summary:

Objective: Schizophrenic patients have demonstrated a reduced rCBF (by SPECT) in the prefrontal cortex during activation with the Wisconsin Card Sorting Test (WCST) compared with a control task; this contrasts with normal controls, who demonstrate an increase in prefrontal rCBF (Weinberger et al 1986, 1988). Consistent with a schizophrenia spectrum hypothesis, schizotypal personality disorder (SPD) patients are hypothesized to compensate for cognitive impairment by alternative, less efficient strategies than those used by normal controls.

Method: Subjects are medically healthy males and are DSM-III-R SPD (n = 8) or normal controls (n = 6). With informed consent, subjects are studied on two days with tasks counterbalanced. An automated version of the WCST is compared with a symbol-matching task (SMT); 99mTc- HMPAO is infused and registered on a Medimatic 564.

Results: These preliminary data suggest that, compared with normal controls, SPD patients: 1) may increase flow in the dorsolateral prefrontal cortex (DLPFC) in response to WCST, particularly the left DLPFC; 2) appear to have a dissociation of performance from rCBF in the left DLPFC, while left DLPFC rCBF in normals is inversely related to rate of perseverative errors; 3) the DLPFC/occipital lobe ratio of rCBF increases significantly during the WCST compared with the SMT only in SPD patients; and 4) rCBF in the medial temporal lobe (including the hippocampus and adjacent structures) decreases on the left and increases on the right during WCST vs SMT, while the opposite pattern occurs in normal controls.

Conclusions: These results are consistent with the possibility that SPD patients use alternative, inefficient strategies to compensate for an underlying prefrontal neurocognitive deficit; these strategies may rely on increasing prefrontal rCBF.

NR382 Wednesday, May 25, 12 noon-2:00 p.m.

Depressive Experiences in Borderline Inpatients

Kenneth N. Levy, B.A., Psychiatry, Yale Psych. Inst., P.O. Box 208038, New Haven CT 06520; John Kolligian, Ph.D., Donald M. Quinlan, Ph.D., Daniel F. Becker, M.D., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To investigate the quality of depressive experiences (dependent and self-critical) in depressed patients and in depressed patients with borderline personality disorder.

Method: Forty-six (20 male and 26 female) severely disturbed adolescent and young adult inpatients (M = 19.5 years, S.D. = 5.9) diagnosed reliably with depression (major depression = 43; dysthymia = 24, comorbid major depression/dysthymia = 21) participated. Twenty-nine of the 46 subjects also were diagnosed reliably with borderline personality disorder. Subjects also completed the Depressive Experiences Questionnaire and the Symptom Checklist 90- Revised.

Results: As predicted, there were no differences between the two groups in level of impairment or severity of depression ($t[44] = 1.03$, p = ns), but phenomenologically the depressive experiences where quite different. Borderline depression was associated with anaclitic dependency ($t[44] = 2.74$, $p < .01$), characterized by feelings of helplessness, fears about separateness and rejection, and intense concerns about loss of gratification and experiences of frustration. Additionally, anaclitic dependency correlated significantly with interpersonal distress ($r = .44$, $p < .01$); self-destructive behaviors ($r = .30$, $p < .05$); and lability and impulsivity ($r = .42$, $p < .01$). Self-criticism correlated significantly with identity concerns ($r = .47$, $p < .01$).

Conclusions: These data support the hypothesis that borderline and nonborderline subjects with depression can be differentiated by the phenomenology of their depressive experiences.

NR383 Wednesday, May 25, 12 noon-2:00 p.m.

Dependent and Self-Critical Personality Disorders

Kenneth N. Levy, B.A., Psychiatry, Yale Psych. Inst., P.O. Box 208038, New Haven CT 06520; John Kolligian, Ph.D., Donald M. Quinlan, Ph.D., Daniel F. Becker, M.D., William S. Edell, M.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To investigate the relationship between anaclitic dependency and self-critical depression and DSM-III-R personality disorders.

Method: Seventy-six severely disturbed adolescent and young adult inpatients were assessed reliably with the Personality Disorder Examination and also completed the Depressive Experiences Questionnaire. Subjects were 39 males and 37 females, average age = 19.8 years (S.D. = 5.7).

Results: As predicted, anaclitic dependency was positively and significantly related to criteria met for borderline ($r = .22$, $p < .03$), histrionic ($r = .30$, $p < .02$), and dependent ($r = .39$, $p < .002$) personality disorders and significantly negatively correlated with criteria for schizoid personality disorder. ($r = -.31$, $p < .01$). Self-criticism, as predicted, was significantly related to the number of criteria met for schizoid ($r = .29$, $p < .03$), schizotypal ($r = .27$, $p < .04$), borderline ($r = .30$, $p < .01$), and narcissistic ($r = .33$, $p < .03$) personality disorders. Additionally, the differences between the correlations of these various personality disorders with anaclitic dependency and self-criticism were significant.

Conclusions: The anaclitic dependency—self-critical distinction appears to have greater generality beyond its usefulness of differentiating between two types of depression and appears to a useful basis for the conceptualization of psychopathology.

NR384 Wednesday, May 25, 12 noon-2:00 p.m.

Does Antidepressant Treatment Change Personality?

Ron G. Goldman, M.D., Psychiatry, Columbia University, Unit 35 722 West 168th Street, New York NY 10032; Patrick J. McGrath, M.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D.

Summary:

Objectives: Recent speculation about the use of new generation antidepressant drugs to change personality has gained national attention. This study investigated the effects of medication treatment on personality in depressed patients treated with fluoxetine, imipramine, or placebo.

Methods: The Tridimensional Personality Questionnaire (TPQ) was administered to 59 depressed patients before and after six weeks of double-blind treatment with imipramine or placebo. A second group of 56 patients with major depression treated with fluoxetine completed the TPQ before and after 10–12 weeks of treatment.

Results: There was a significant group-by-time interaction for harm avoidance when responders were compared to nonresponders in imipramine-treated ($p < .01$) and placebo-treated ($p < .02$) patients. Reductions in harm avoidance compared to baseline occurred only in patients whose depression improved with imipramine ($p < .001$) or placebo ($p < .08$) treatment. Fluoxetine treated patients showed a similar reduction in harm avoidance in patients who were no longer depressed after 10–12 weeks of treatment. Novelty seeking and reward dependence were not significantly affected by any treatment. Continuation of medication beyond six weeks in nine responders to imipramine resulted in a further significant reduction in harm avoidance ($p < .001$).

Conclusions: In patients whose depression improved, a concurrent decrease in harm avoidance is observed. This factor, postulated to be a stable dimension of personality, demonstrates plasticity in the face of mood change. Harm avoidance may therefore describe some aspect of depression, or antidepressants may have the capacity to "treat" more enduring "personality traits." These data support the need for further elucidation of the conceptual interface between chronic depression and personality traits.

NR385 Wednesday, May 25, 12 noon-2:00 p.m.

The Clinical Utility of Self-Defeating Personality Disorder

Lora K. Heisler, M.S., Psychiatry, 225 East 95th Street #17K, New York NY 10128; Michael J. Lyons, Ph.D., John G. Goethe, M.D.

Summary:

Objective: The purpose of this two-part study was to examine the clinical utility of the proposed diagnostic category Self-Defeating Personality Disorder (SDPD).

Method: Part 1: A prototypic case history questionnaire was mailed to American and British psychiatrists and clinical psychologists. The professionals were asked to provide a diagnosis for each case, report the percentage of their current patients with a similar condition, and the percentages of males and females. Part 2: Two SDPD self-report measures were administered to American and British undergraduates.

Results: Part 1: The most frequent diagnoses assigned to the SDPD cases by both American ($n = 42$) and British ($n = 78$) professionals were SDPD and Personality Disorder Not Otherwise Specified; no alternative diagnoses were consistently provided. More than one in two professionals reported treating patients with a condition similar to the SDPD cases, and approximately 65% of these patients were reported to be female. Part 2: Four percent of American ($n = 100$) and 3% of British ($n = 100$) undergraduates responded in a self-defeating manner on the SDPD measures. Responses did not significantly differ by sex.

Conclusion: The results suggest that SDPD is a distinct and clinically useful diagnostic category. We recommend that it be reconsidered for inclusion in the DSM.

NR386 Wednesday, May 25, 12 noon-2:00 p.m.

The Development of Psychopaths: A Cognitive Model

Robert J. Blair, Ph.D., University College London, MRC Cognitive Unit, 4 Taviton Street, London WC1, England.

Summary:

Various social animal species have been noted to inhibit aggressive attacks when a conspecific displays submission cues (Lorenz, 1966). Blair has suggested that humans possess a functionally similar mechanism that mediates the suppression of aggression in the context of distress cues. He has suggested that this mechanism is a prerequisite for the development of the moral/conventional distinction: The distinction between moral and conventional transgressions consistently found in subject's judgments from the age of 36 months (e.g., Smetana & Braeges, 1990). He has also suggested that this mechanism is a prerequisite for the development of the arousal response to the distress cues of others. Psychopaths may lack this violence inhibitor. A causal model will be developed showing how the lack of this mechanism explains the core behavioral symptoms associated with the disorder. A prediction of such a causal model is that while incarcerated controls will make the moral/conventional distinction, psychopaths will not. This prediction was confirmed. A second prediction of this model is that the psychopath should not show arousal to distress cues. The galvanic skin responses of psychopaths and incarcerated controls to distress, fear and neutral stimuli were compared. The incarcerated controls were found to show arousal to the distress and the fear stimuli. The psychopaths, in contrast, were found to only show arousal to the fear stimuli. The psychopaths processed the distress cue stimuli as affectively neutral.

NR387 Wednesday, May 25, 12 noon-2:00 p.m.

Physicians' Beliefs About Benzodiazepines

Edward K. Silberman, M.D., Psychiatry, Jefferson Medical College, 1015 Walnut Street, Philadelphia PA 19107.

Summary:

The purpose of this study was to assess the extent to which psychiatrists' and internists' beliefs about benzodiazepines reflect current knowledge, and to what extent they reflect common, but unsubstantiated concerns about therapeutic tolerance and abuse liability of these drugs.

Questionnaires assessing beliefs about benzodiazepines were sent to 1,900 members of the American Psychiatric Association and 2,000 members of the American College of Physicians in Pennsylvania. Respondents were asked to endorse or reject 13 statements related to benzodiazepine tolerance, withdrawal, misuse, and abuse.

Seven hundred fifty-eight psychiatrists (40%) and 590 internists (30%) responded. More than half the internists believed that benzodiazepines are only transiently effective and are commonly overused and abused by the general public; 25% to 45% of psychiatrists endorsed similar beliefs. Psychiatrists were significantly less negative and more knowledgeable in their beliefs than internists. Physicians who had completed training more recently were only slightly more knowledgeable than those longer out of training.

Unfounded concerns about benzodiazepines appear to be common among both psychiatrists and internists. More continuing education about these drugs may be needed for the physicians who prescribe them more frequently.

NR388 Wednesday, May 25, 12 noon-2:00 p.m.

Gender Differences in Cocaine Dependence

Kimberly A. White, M.D., Psychiatry, Med. Univ of SC, 171 Ashley Avenue, Charleston SC 29425-0742; Kathleen T. Brady, M.D., Susan Sonne, Ph.D.

Summary:

Gender differences in characteristics of substance use disorders may have important implications. To further explore this, 27 women and 60 men presenting for treatment of cocaine dependence were compared on demographics, substance use, and psychopathology. Women earned less in the past year ($p < 0.01$) and were more likely to have been unemployed ($p < 0.05$) when compared with men. There were no significant gender differences in the amount of cocaine use. On the Addiction Severity Index, women had significantly higher scores on the employment subscale ($p \leq 0.001$), but significantly lower scores on the drug and alcohol subscales ($p \leq 0.05$). While women began using cocaine at a later age than men, they attained regular cocaine use at the same age as men and, therefore, had fewer years of total cocaine use at the time of presentation for treatment ($p \leq 0.001$). Women were more likely to initiate cocaine use with crack cocaine ($p \leq 0.01$) and report shorter duration of abstinent periods since initiating cocaine use ($p \leq 0.05$). Women were more likely to have a diagnosis of PTSD ($p < 0.05$), report more suicide attempts ($p < 0.05$), and seek psychiatric treatment ($p < 0.05$). Other gender differences in psychopathology were not noted. The implications of these data for the "telescoping" of cocaine dependence in women will be discussed.

NR389 Wednesday, May 25, 12 noon-2:00 p.m.

Carbamazepine for Cocaine Dependence

Henry R. Kranzler, M.D., Psychiatry, Univ of Conn Hlth Center, 263 Farmington Avenue, Farmington CT 06030; Lance Bauer, Ph.D., David F. Hersh, M.D.

Summary:

Cocaine induces kindling in animals, an effect that is reversed by treatment with carbamazepine (CBZ). It has been hypothesized that in humans, kindling underlies cocaine-induced craving. Preliminary studies showed CBZ to be of potential utility for the prevention of relapse in cocaine-dependent subjects. To examine the drug's efficacy in relapse prevention, we conducted a randomized, double-blind, parallel groups comparison of CBZ and placebo in 40 cocaine-dependent males. Analysis of results from the active treatment period revealed no significant effect of CBZ on self-reported mean frequency or amount of cocaine use, mean frequency or amount of alcohol consumption, or mean severity of anxiety or depressive symptoms. Weekly urine tests for benzoylecgonine also failed to show an advantage for the active drug. Preliminary analysis of data from a three-month post-treatment follow-up revealed no effect of CBZ on mean frequency or amount of cocaine use or mean severity of anxiety or depressive symptoms. We conclude that at a daily dosage of 600 mg, CBZ is not efficacious for the treatment of cocaine dependence.

NR390 Wednesday, May 25, 12 noon-2:00 p.m.

Validity of the SCID in Substance Abuse Patients

Henry R. Kranzler, M.D., Psychiatry, Univ of Conn Hlth Center, 263 Farmington Avenue, Farmington CT 06030; Bruce J. Rounsaville, M.D., Howard Tennan, Ph.D.

Summary:

We evaluated the convergent, discriminant, and criterion validity of the SCID for use in the diagnosis of substance use, anxiety, and depressive disorders in 100 substance abuse patients. ANOVA revealed significant differences on the ASI alcohol scale, MAST, and quantity and frequency of alcohol use for patients who met criteria for alcohol abuse/dependence, compared with those who did not. Similar differences were evident on the ASI drug scale, DAST, and quantity and frequency of drug use for patients who met criteria for drug abuse/dependence, compared with those who did not. Convergent validity and discriminant validity were not as good for diagnoses of major depression and anxiety disorders. Criterion validity was assessed by using a Longitudinal, Expert, All Data ("LEAD") procedure. Overall kappas were >0.75 for concordance between SCID and LEAD for both current and lifetime substance use diagnoses. In contrast, overall kappas for diagnoses of major depression and anxiety disorders were 0.29 and 0.40 (current and lifetime, respectively). We conclude that while the SCID yields valid substance use disorder diagnoses in substance abuse patients, it is substantially less valid for the diagnosis of major depression and anxiety disorders in this patient population.

NR391 Wednesday, May 25, 12 noon-2:00 p.m.

Comorbidity in Adolescent Inpatient Drug Abusers

Carlos M. Grilo, Ph.D., Psychiatry, Yale Psychiatry, P.O. Box 208038, New Haven CT 06520; Kenneth N. Levy, B.A., Daniel F. Becker, M.D., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To assess the prevalence of substance use disorders (SUD) in adolescent inpatients and to examine DSM-III-R comorbidity in SUD patients.

Method: 165 patients were assessed using the K-SADS-E (Axis I) and the PDE (Axis II). Diagnoses were reliable; average kappas were .77 and .84 for Axis I and Axis II. The prevalence of SUD and the distribution of Axis I disorders in patients with SUD versus those without SUD were examined. Kappa coefficients were calcu-

lated to determine significant co-occurrence of diagnoses, beyond that predicted by base-rates in the sample.

Results: Seventy-seven patients met criteria for a SUD. Of these, 74 subjects received at least one additional Axis I diagnosis. SUD was moderately comorbid with conduct disorder (CD) ($k = .39$, $p < .001$) but not with oppositional defiant disorder (ODD) ($k = -.14$, $p < .05$). To examine this comorbidity, patients with SUD and CD were compared to patients with CD without SUD and to patients with SUD without CD. Differences between the groups on Axis II and psychiatric history variables were observed.

Conclusions: A high rate of overlap with other Axis I diagnoses was observed in SUD inpatients; comorbidity, however, was significant only for CD. Our findings support the validity of the ODD-CD distinction and the comorbid CD-SUD subgroup.

NR392 Wednesday, May 25, 12 noon-2:00 p.m.

Nicotine Stimulates Gene c-fos Expression in Human Leukocytes In Vivo

Andrew B. Norman, Ph.D., Psychiatry, University of Cincinnati, 231 Bethesda Avenue, Cincinnati OH 45267; Herbert R. Thompson, B.S., Sean P. Stanton, B.S., Brian J. McConville, M.D., Eugene Somoza, M.D.

Summary:

Nicotine administration has been reported to stimulate the expression of the immediate-early response gene c-fos in rat brain *in vivo*(1). Sensitization of the expression of c-fos in rat brain following repeated challenges with d-amphetamine(2) may represent a model of the molecular changes underlying the development of dependence. We investigated the possibility that nicotine administration to nicotine-naive subjects modulates the expression of c-fos in human cells *in vivo*. Blood was drawn from nicotine-naive subjects between 7:00 and 8:30 a.m. using Leucoprep cell separation tubes. Subjects (n = 10) then chewed one piece of Nicorette® gum (2 mg nicotine) or placebo gum (n = 6) for 30 min. At 30, 90, 150 and 270 min. following the administration of gum, additional blood samples were drawn, leukocytes were rapidly separated, washed, homogenized, and frozen. Fos protein levels were then measured by immunoblotting. For each subject the optical density of the band representing fos protein was calculated as a percentage of the pregum levels. By 90 min. following the administration of Nicorette® gum there was a significant ($p < 0.05$, one way ANOVA with repeated measures) increase (260%) in the mean optical density of the fos immunoreactivity compared with pregum levels. Fos levels had returned to baseline levels by 2.5 hours. There was no significant increase in fos levels in cells from subjects administered placebo gum. These data represent the first demonstration of an alteration in gene expression in human cells following administration of an addictive psychoactive drug. The nicotine-induced transient stimulation of c-fos expression in human cells *in vivo* could indicate the molecular mechanisms underlying the development of drug dependence.

NR393 Wednesday, May 25, 12 noon-2:00 p.m.

The Effects of Benzodiazepines, Buspirone and Placebo Treatment on Mood and EEG Activity in Alcoholics and Normal Subjects

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Summary:

Objective: To determine subjective effects (euphoria, alcohol craving) and electroencephalographic (EEG) responses to single doses of antianxiety agents in subjects with and without a history of alcohol dependence.

Method: Subjects with alcohol dependence and control subjects without a personal or family history of alcohol dependence were administered single oral doses of alprazolam (1.5 mg), diazepam (15 mg), buspirone (15 mg), and placebo; their responses to these agents were monitored over an eight-hour period. Mood changes were measured by a standardized battery of scales. EEG activity was recorded from frontal and occipital electrodes. Power spectrum was computed using Fast Fourier Transformation.

Results: Alcoholic subjects had greater euphoric responses to both alprazolam and diazepam than control subjects. Alcoholics also reported greater alcohol craving when alprazolam was compared to placebo at 2½ and 3 hours post drug. Decreases in alpha power were found to be significantly greater for alcoholics than for controls following administration of either benzodiazepine. No group differences were detected in the increase in beta power produced by these agents.

Conclusion: These results suggest that mood enhancement after a single dose of alprazolam or diazepam is greater in alcoholic subjects than controls. The nature of this change has implications for abuse liability and therapeutic interventions. EEG data suggest that there are objective neurophysiological correlates to mood effects.

NR394 Wednesday, May 25, 12 noon-2:00 p.m.

Traumatic Exposure and PTSD Symptomatology Among Substance Abusers

Patricia Ryan Recupero, M.D., Psychiatry, Brown University, 345 Blackstone Blvd, Providence RI 02906; Pamela J. Brown, Ph.D., Robert Stout, Ph.D., Jessica Wolfe, Ph.D., Sharon Morello, R.N.

Summary:

The purpose of the present study is twofold: (1) to investigate the prevalence of various traumatic events experienced by a sample of substance abusers receiving inpatient treatment; (2) to assess symptomatology indicative of post-traumatic stress disorder (PTSD). Subjects were 84 patients (48 male and 36 female) recruited from consecutive admissions to an inpatient substance abuse treatment program at a private hospital. All subjects were administered a demographic questionnaire, a trauma screening instrument inquiring about the occurrence and impact of numerous high-magnitude life stressors (e.g., physical or sexual abuse), and a self-report measure of PTSD symptomatology. Analyses showed that approximately 59% (n = 48) of the sample reported experiencing at least one traumatic event in their lifetime that caused them extreme distress at the time of occurrence. High prevalence rates were found for the following traumatic events: robbery or mugging (19%, n = 16); physical assault/abuse (27.4%, n = 23); sexual molestation/assault (excluding rape; 16.7%, n = 14); and rape (19%, n = 16). Of those patients who experienced at least one traumatic event, 35% (n = 17) presented with significant current PTSD symptomatology. Implications of these findings for routine trauma screening and treatment are discussed.

NR395 Wednesday, May 25, 12 noon-2:00 p.m.

Clinical Course of Mentally Ill Substance Abusers

Jonathan D. Berman, M.D., 6601 E. Mill Plain Blvd Ste156, Vancouver WA 98661; Roland M. Atkinson, M.D.

Summary:

Objective: This study was undertaken to determine if acceptance of abstinence-based treatment by mentally ill substance abusers is associated with a subsequent reduction in substance abuse and psychiatric hospitalization.

Method: A cohort of 199 male veterans was assessed for admission to a specialized outpatient dual-diagnosis treatment program. During a two-year follow-up interval, clinical records of all medical, psychiatric, and substance abuse treatment were reviewed for documentation of substance use and psychiatric hospitalization. Multivariate analyses were performed to evaluate the relationships between initial acceptance of treatment, subsequent hospitalization and substance abuse, and diagnostic and psychosocial variables.

Results: Patients who accepted treatment were less likely to have subsequent documented relapse to substance use and abuse-related life problems than those who rejected treatment. Relapse in turn was associated with a significantly greater likelihood of psychiatric hospitalization, but neither was significantly associated with other clinical or psychosocial variables. The proportion of the cohort hospitalized decreased progressively in each postassessment year, independent of treatment engagement or documented substance use.

Conclusions: Structured, abstinence-based treatment may be effective in reducing substance abuse in dual-diagnosis patients and may also contribute to reduced hospital utilization. Referral of chronically mentally ill individuals for substance abuse treatment appears more likely to occur during periods of relative clinical instability and high hospital utilization.

NR396 Wednesday, May 25, 12 noon-2:00 p.m.

Effect of Alpha-methyl-para-tyrosine on Response to Cocaine Challenge

Susan M. Stine, M.D., OSAC-Bldg 36, VA Medical Center, 950 Campbell Avenue, West Haven CT 06516; Ismene Petrakis, M.D., Peter I. Jatlow, M.D., John H. Krystal, M.D., Sally L. Satel, M.D., Dennis S. Charney, M.D.

Summary:

Pretreatment with alpha-methyl-para-tyrosine (AMPT), a tyrosine hydroxylase inhibitor, reduces the euphoria after amphetamine administration (Jönsson et al, 1971). We have investigated the ability of AMPT to diminish the effects of cocaine administration. It is hypothesized that AMPT may reduce cocaine-induced euphoria by decreasing dopamine (DA) synthesis and release. Subjects are medically healthy, active, nontreatment-seeking cocaine abusers with histories of intranasal cocaine use, pretreated with AMPT or Benadryl (an "active" placebo with sedative properties) then challenged with 2mg/kg cocaine intranasally. Each subject receives all four combinations of AMPT vs. Benadryl and cocaine vs. placebo in a blinded balanced-for-order design. Physiological assessments consist of blood pressure, EKG, heart rate, and respiratory rate. Psychological assessments include self-reported ratings such as high, craving, rush, sedation, anxiety, etc.. Preliminary results with five subjects have shown a diminished cocaine "high" after AMPT pretreatment when compared with placebo ($p < .058$ by ANOVA). No change was seen in psychological responses. However, AMPT pretreatment did lower physiological responses to cocaine. The observed effects are not explained by differences in serum cocaine levels after AMPT vs. Benadryl. A total of 12 subjects will be tested and presented. AMPT merits further investigation as a possible agent in the treatment of cocaine abuse and dependence.

NR397 Wednesday, May 25, 12 noon-2:00 p.m.

Reporting and Representation of Sociodemographic Groups in Cocaine Pharmacotherapy Studies

David A. Gorelick, M.D., Treatment, NIH-NIDA-ARC, P.O. Box 5180, Baltimore MD 21224; Ivan D. Montoya, M.D.

Summary:

Cocaine abuse affects all segments of the U.S. population, but the representation of various sociodemographic groups as patients in studies of cocaine abuse pharmacotherapy has never been evaluated. In light of recent FDA and NIH regulations requiring adequate representation of women and minorities in clinical trials, we assessed sociodemographic representation in 61 reports of outpatient pharmacotherapy for cocaine abuse, published in refereed, English-language journals between 1983 and 1993. Representativeness was compared with the epidemiology of frequent cocaine use in the 1990 NIDA National Household Survey of Drug Abuse (NIDA-HS). There were 41 (67.2%) open-label, 19 (31.1%) double-blind, and one (1.6%) unspecified reports, using 30 different pharmacologic treatments. Seven (11.4%) studies did not report on age, two (3.2%) omitted sample size, nine (14.7%) gender, 24 (39.3%) race, 46 (75%) education, 49 (80%) employment, 55 (91%) socioeconomic status. No article reported ethnic/cultural characteristics. There was under-representation of 12–25 year olds, Hispanics, and subjects from the South and West areas of the United States; there was over-representation of 26–35 year olds unemployed, high school or college graduates, and those form the Northeast. These findings show that important sociodemographic data are often not reported, and raise issues of quality of research reports, generalizability of results, social equity, and accessibility for certain groups in cocaine abuse pharmacotherapy research.

NR398 Wednesday, May 25, 12 noon-2:00 p.m.

Combination of Bupropion and Bromocriptine for Treatment of Cocaine Dependence

David A. Gorelick, M.D., Treatment, NIH-NIDA-ARC, P.O. Box 5180, Baltimore, MD 21224; Ivan D. Montoya, M.D.

Summary:

Bupropion (BUP) and bromocriptine (BRO) have been used separately for treatment of cocaine dependence. This eight-week open-label study used the two medications in combination with the goal of obtaining an enhanced therapeutic effect with fewer side effects. Thirteen subjects [mean (SD) age 32.9 (±5.8) years, education completed 12.5 (+1.9) years, 10 (76.9%) males, nine (69.2%) blacks, nine (69.2%) employed, mean (SD) lifetime use of cocaine 5.3 (±4.8) years, amount of cocaine used in the past 30 days 3.1 (±0.6) grams or $238 (±51)] received medication for one week or more Subjects received BUP (≤300 mg) plus BRO (≤7.5 mg) daily plus weekly individual counseling. No subject reported any serious adverse event. Mean retention time in treatment was 18.8 (±3.8) days. One patient was discharged for non-medication-related medical reasons. Comparisons between pre- and post-treatment showed a significant ($p < .01$) reduction of patients' self-reported weekly grams used and money spent on cocaine, and of Beck Depression Inventory score. Urine samples collected three times a week for qualitative and quantitative analyses showed no significant reductions in the percent of urines positive for cocaine nor the amount of benzoylecgonine in urine. These results suggest that 1) the combination of bupropion and bromocriptine is safe; 2) there is a discrepancy between self-reported drug use and urine toxicology results; and 3) this medication combination may not be efficacious for treatment of cocaine dependence at the actual doses achieved in this study.

NR399 Wednesday, May 25, 12 noon-2:00 p.m.

Obsessive Compulsive Personality in Substance Dependence

Dr. Myroslava K. Romach, Mental Health Unit, Addiction Research Fdtion, 33 Russell Street 3 West, Toronto Ontario

M1B 3L9, Canada; Howard L. Kaplan, Ph.D., Gail Somer, M.A., Edward M. Sellers, M.D.

Summary:

Numerous attempts have been made to link particular personality characteristics to risk of substance dependence. Antisocial personality disorder has been a constant association. Among chronic, therapeutic-dose benzodiazepine users (N = 131; mean age 47 years; 58% male) many self-reported OCP traits on the SCID II, with males endorsing significantly more traits than females ($p < 0.03$). Twenty-two percent of the group were diagnosed with OCP disorder (OCPD), the most common personality disorder in the group. A further 21% of the group were rated as subthreshold for this diagnosis. OCPD patients had higher scores on the obsessive compulsive subscale of the HSCL-90 ($p < 0.02$). Fifty percent of the OCPD patients had a past history of alcohol dependence, compared with 35% in the non-OCPD individuals. OCPD subjects overall showed a trend to drinking greater amounts of alcohol. There were no differences in dose of benzodiazepines used. There was no significant correlation with any other Axis I psychiatric disorder. In a separate sample of 47 alcohol-dependent individuals (mean age 43 years; 72% male) OCPD traits were prominently endorsed on self-report. SCID interviews diagnosed OCPD in 12 (26%) subjects, with another 10 (21%) almost meeting diagnosis (subthreshold). In this sample, OCPD patients showed higher rates of generalized anxiety and panic disorders ($p < 0.01$). There were no differences in alcohol consumption among the OCPD versus non-OCPD patients. OCPD patients had greater overall impairment in their functioning ($p < 0.05$). These data suggest that OCPD traits are common in subgroups of patients dependent on certain substances. Understanding such personality differences, the cognitive processing and affective states around issues of control, and how these relates to substance use may be important in designing treatment interventions that meet specific individual needs.

NR400 Wednesday, May 25, 12 noon-2:00 p.m.

Comorbidity in Drug Dependent Adoptees

Barbara M. Rohland, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive #2887 JPP, Iowa City IA 52242; Remi J. Cadoret, M.D., Edward Troughton, B.A.

Summary:

Objective: To determine and compare comorbidity of drug dependence and psychiatric disorder in two age groups in a rural population.

Method: 497 adoptees who were born and raised in Iowa were evaluated for lifetime prevalence of drug dependence and psychiatric disorder according to DSM-III-R criteria. The prevalence of psychiatric illness in young drug-dependent subjects (17–25) and older subjects (26–50) was compared with same age subjects without drug dependence.

Results: Of 271 subjects aged 17–25, 17.3% met DSM-III-R lifetime criteria for drug dependence, compared with 18.6% in the older age group. Over one half (53.4%) of young subjects with drug dependence had antisocial personality disorder (ASPD) versus 7.5% of subjects of the same age who were not drug dependent ($p = .0001$). A similar, equally significant difference was observed in older subjects. The prevalences of depression (39.1% vs 12.9%) and agoraphobia (60% vs 15.7%) were significantly different in the younger drug-dependent compared with the non-drug-dependent group and higher than in the older group.

Conclusions: Drug-dependent adolescents and young adults have increased prevalence of ASPD, depression, and agoraphobia. The relationship between ASPD and drug dependence appears to be stable over time. The frequent co-occurrence of Axis I psychiatric disorder in drug dependent adolescents and young adults suggests the importance of recognizing and treating comorbidity in this population.

NR401 Wednesday, May 25, 12 noon-2:00 p.m.

Depression in Drug Dependency

Mark S. Gold, M.D., Psychiatry, University of Florida, College of Med P.O. Box 100244, Gainesville FL 32610; Norman S. Miller, M.D., Norman G. Hoffmann, Ph.D.

Summary:

Whether depression is a symptom, primary diagnosis, pre-existing, or underlying illness in patients with drug dependency and/or alcoholism has been widely studied and debated. However, the high degree of association of depression and addictive disorders is clear. A total of 6355 patients from 41 treatment sites received a structured CATOR interview on admission. Follow-up data were gathered by a structured telephone interview (110 questions) at six and 12 months. The typical patient was middle aged (35.7), male (70.6%), white (88.9%), high school educated (84.6%), married (43.4%), employed (73.3%), income of $10,000–50,000, living alone (55.7%) using alcohol (51.3%). In the total sample of 6355, the rate of lifetime diagnosis of major depression was 43.7% and subclinical depression was 9.6%. More than half of the patients had two or more symptoms of depression and 35.9% had five or more symptoms of major depression. The abstinence rate in the total population for one continuous year was 55.4%. There were no significant differences in abstinence rates between those with and without a lifetime diagnosis of major depression. Alcohol dependence was associated with major depression significantly less than was major depression and other drug dependencies. The association of a lifetime diagnosis of major depression was greatest for opiate, prescription, and stimulant dependence. There was a significant association between the number of drugs used and frequency of drug use with a lifetime diagnosis of major depression, with daily drug users showing the greatest depression. The rates of depression were significantly greater for females than males. Depressed males (56.2%) and females (65.6%) began drinking at an earlier age (before age 14) and were more likely to be multiple drug users. Outpatients were significantly less likely to be depressed than inpatients (29.5% vs 40.4%). While depression may complicate the diagnosis, risk, and course of drug dependency, it does not appear to alter the relapse rate.

NR402 Wednesday, May 25, 12 noon-2:00 p.m.

Fenfluramine Treatment of Cocaine Dependence: Interim Analysis

Steven L. Batki, M.D., Psychiatry, UCSF-SF General Hospital, 1001 Potrero Avenue Ward 93, San Francisco CA 94110; Mark Bradley, Mark D. Herbst, M.D., Tracy Jones, Michael Markman, Allyson Washburn, Ph.D., Peyton Jacob III, Ph.D., Reese T. Jones, M.D.

Summary:

Objective: To perform an interim analysis of a controlled trial of the serotonergic agent fenfluramine in cocaine dependence.

Method: Double-blind, placebo-controlled, balanced crossover design. Ten DSM-III-R cocaine-dependent methadone maintenance (MMT) outpatients were assigned to fenfluramine (FEN) 60 mg/da or placebo (PLA) for the first four weeks, and after a one-week washout, were crossed over for the second four weeks. Measures of cocaine use included quantitative urine benzoylecgonine (BE) levels.

Results: Median urine BE was 60,140 ng/mg creatinine (Cr) at intake; 24,744 ng/mgCr for the 4 weeks of FEN; and 45,582 ng/mg Cr for the 4 weeks on PLA; 6 of 9 Ss had lower urine BE on FEN. Mean days of cocaine use was 3.9 da/wk at intake, 1.8 da/

wk on FEN, and 2.8 da/wk on PLA; 6 of 8 Ss had fewer days of cocaine use on FEN. Mean dollars worth of cocaine used was $120/wk at intake, $20/wk on FEN and $33/wk on PLA; 6 of 8 Ss reported spending less on cocaine on FEN. Mean cocaine craving was 13.4 (range 0-24) at intake, 7.5 on FEN and 8.3 on PLA; 3 of 8 Ss reported less craving on FEN.

Conclusion: Fenfluramine may be safe and well tolerated in cocaine-dependent MMT patients. More subjects must be studied to determine if FEN is significantly helpful in reducing cocaine use.

NR403 Wednesday, May 25, 12 noon-2:00 p.m.

Substance Abuse: Treatment Failure Profiles

Portia P. Belden, Ph.D., Research, Carrier Foundation, Route 601, Belle Mead NJ 08502; Helen M. Pettinati, Ph.D., Charles Ruetsch, M.S., Fran Kaplan, B.A., Bradley D. Evans, M.D.

Summary:

In the President's health care reform proposal, failing outpatient treatment for substance abuse may be a necessary criterion for obtaining inpatient rehabilitation. This presentation focuses on identifying the profile of alcohol-dependent outpatients who fail treatment. Subjects were 178 alcohol-dependent (DSM-III-R) patients admitted to inpatient or outpatient treatment at a private psychiatric hospital in N.J. These *S*s were part of a larger five-year study on the cost-effectiveness of inpatient vs. outpatient treatment. Results indicated that outpatients were four times more likely than inpatients to fail treatment (41% vs 10%, $p < .01$). Two categories of outpatient treatment failures were identified: *S*s who left treatment against medical advice (AMA) ($n = 18$), and *S*s who continued to drink while attending treatment ($n = 13$). Patient billing information showed that the treatment failures who continued to drink utilized more than twice the outpatient treatment hours (7.5 vs 16.3, respectively) at almost double the cost ($614 vs $1084, respectively) of those who left AMA. Of the treatment failures who continued to drink, 53% were referred to inpatient treatment. This study is an important step toward establishing a profile of the patient who can be treated both successfully and cost-effectively in an outpatient setting.

NR404 Wednesday, May 25, 12 noon-2:00 p.m.

Growth Hormone Response to Bromocryptine in Alcoholics and Controls

Conor K. Farren, M.D., Psychiatry, Yale Medical School, 29 Sylvan Avenue, New Haven CT 06519; Anthony W. Clare, M.D., Faiq A. Hameedi, M.D., Douglas M. Ziedonis, M.D., Timothy G. Dinan, M.D.

Summary:

There is considerable research evidence to implicate dopamine system underactivity as a major reason for the alcohol withdrawal syndrome, but there has been little research into the dopamine system in the postwithdrawal state, that is, the time by which the alcohol-dependent patient has completely recovered from the intoxicating effects of alcohol. The measurement of hormones that are released by the use of dopamine system agonists is a method of assessing the activity of the dopamine system. Growth hormone (GH) responses to the dopamine agonist bromocriptine were measured in eight DSM-III-R alcoholics who were two or more weeks post alcohol withdrawal. Their responses were compared with eight nonalcoholic healthy controls. After an overnight fast each subject received 1.25mg of bromocriptine, and serial samples of serum GH were taken over a three-hour period. Bromocriptine caused a significantly attenuated peak delta GH response in the alcoholic group relative to the controls, $t = 2.96$, $df = 14$, $p = 0.0103$. This GH response did not correlate with age of subjects, $r = -0.42$, $p = 0.10$; duration of alcohol history, $r = 0.17$, $p = 0.7$; duration of abstinence, $r = -0.21$, $p = 0.6$; severity of alcohol dependence, $r = 0.04$, $p = 0.9$, or typology of alcohol abuser, $r = -0.29$, $p = 0.47$. The results imply there is a relative dopaminergic subsensitivity in alcoholics in the postwithdrawal period, and suggests that dopamine agonists may have a part to play in alcoholism pharmacotherapy.

NR405 Wednesday, May 25, 12 noon-2:00 p.m.

Prolactin Response to d-Fenfluramine in Alcoholics and Controls

Conor K. Farren, M.D., Psychiatry, Yale Medical School, 29 Sylvan Avenue, New Haven CT 06519; Anthony W. Clare, M.D., Faiq A. Hammeedi, M.D., Douglas M. Ziedonis, M.D., Timothy G. Dinan, M.D.

Summary:

There is considerable research evidence to implicate serotonin system overactivity in the alcohol withdrawal syndrome and to indicate that serotonin deficiency may play a role in the initial development of alcoholism. The measurement of hormones released by the use of serotonin agonists is a method of assessing the activity of the serotonin system. Serum prolactin responses to the serotonin agonist d-fenfluramine were measured in 19 DSM-III-R male alcoholics, three or more weeks post alcohol withdrawal. The prolactin responses were compared with nine healthy nonalcoholic male controls. After an overnight fast each subject received 30mg of d-fenfluramine orally, and serial samples of serum prolactin were taken over a five-hour period. D-fenfluramine caused a significantly attenuated peak delta prolactin response in the alcoholics relative to the controls, $p < 0.05$. The baseline serum prolactins did not differ significantly between the two groups. The delta prolactin response did not correlate with subjects' age, $r = 0.12$, $p = 0.55$; duration of alcohol use, $r = 0.37$, $p = 0.10$; duration of abstinence from alcohol, $r = -0.04$, $p = 0.85$; severity of alcohol dependence, $r = -0.47$, $p = 0.04$ or type of alcohol, $r = 0.06$, $p = 0.7$. The results imply a relative subsensitivity of certain serotonin systems in postwithdrawal alcoholics. The results suggest a possible role for serotonin agonists in pharmacotherapy of alcoholism.

NR406 Wednesday, May 25, 12 noon-2:00 p.m.

Depression in Cocaine Abusing Opioid Addicts Treated with Buprenorphine Versus Methadone

Douglas M. Ziedonis, M.D., Psychiatry, Yale University, 34 Park Street Room 269, New Haven CT 06519; Conor K. Farren, M.D., Thomas R. Kosten, M.D.

Summary:

Depression and cocaine abuse are common problems and poor prognostic factors among opioid addicts treated with methadone. Pharmacotherapy strategies attempting to improve outcomes include the use of adjunctive antidepressants and alternatives to methadone such as buprenorphine. In this randomized, double-blind, 24-week clinical study, the impact of depression on addiction treatment outcomes was compared in 125 cocaine abusing opioid addicts who were either treated with methadone (MET, $n = 69$) or buprenorphine (BUP, $N = 56$). Thirty-three patients (26%) were diagnosed with current depression (dysthymia or major depression) and had significantly better treatment retention than nondepressed patients ($p < 0.01$); however this difference was due to those on BUP. Depressed patients on BUP ($n = 14$) did better than those treated with MET ($n = 19$), including better treatment retention, longer periods of cocaine abstinence, and further reductions in cocaine-positive urines. Depression predicted better outcomes with buprenorphine, but not with methadone. Supported

by NIDA P50-DA04060, R18-DA06190, and K02-DA0112 (TRK), and K20-DA0193 (DMZ).

NR407 Wednesday, May 25, 12 noon-2:00 p.m.

Serotonergic Function During Acute and Chronic Cocaine Abstinence

Faiq A. Hameedi, M.D., Psychiatry, Yale Medical School, 34 Park Street, New Haven CT 06517; Marc I. Rosen, M.D., Lawrence H. Price, M.D., Conor K. Farren, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

Summary:

We conducted a preliminary study using mCPP as a neuroendocrine probe to explore serotonergic function in abstinent cocaine abusers. In this pilot study with five subjects who met DSM-III-R criteria for cocaine dependence, the subjects participated in two test days during acute and two test days during chronic cocaine abstinence. On two separate days during the acute and chronic abstinence phases, the subjects received mCPP, .1 mg/kg, or placebo intravenously over a 20-minute period in a double-blind random design. Behavioral ratings and blood samples for prolactin and cortisol levels were done over 180 minutes. The prolactin response to mCPP was blunted in both one to three days and two weeks abstinence compared with normal controls (prolactin levels; normal controls > 2 weeks > 1–3 days). The cortisol response to mCPP was blunted in both one to three days and two weeks abstinence as compared to normal controls (cortisol levels; normal controls > 2 weeks > 1–3 days). These data indicate a serotenergic dysfunction during one to three days cocaine abstinence, which tends to return to normal following two weeks of abstinence. Our data support the findings from other studies by Dackis et al. (1985) and Buydens et al. (1993). The blunting of prolactin and cortisol response to mCPP could be due to decreased serotoninergic function. Data from larger sample will be presented.

NR408 Wednesday, May 25, 12 noon-2:00 p.m.

Substance Abuse and Psychiatric Illness: Psychosocial Correlates

Kevin L. Sloan, M.D., Psychiatry, Seattle VAMC, 4731 84th Avenue SE, Mercer Island WA 98040; Gail Rowe, Ph.D.

Summary:

Objective: This study examined, within a population of help-seeking substance abusers, the psychosocial correlates of having a history of any type of psychiatric treatment and being staff identified as appropriate to receive treatment from a outpatient dual diagnosis treatment program.

Method: The authors retrospectively reviewed all patients who presented for substance abuse and/or dual diagnosis treatment at a Veterans Administration hospital within a 16-month period. The sample consisted of 1303 individuals, of whom 665 described a history of psychiatric treatment and 133 were referred for outpatient dual diagnosis treatment. Data on demographics, employment and treatment histories, and recent substance use were collected at time of initial contact.

Results: Higher rates of homelessness, disconnection from social support systems, unemployment, disability, and treatment chronicity are related to a history of psychiatric treatment, with those who were ultimately referred to the dual diagnosis program having the greatest impairments.

Conclusions: Substance abuse programs should anticipate significant case management needs in addition to psychiatric support when treatment programs are expanded to include services to patients with comorbid psychiatric illness.

NR409 Wednesday, May 25, 12 noon-2:00 p.m.

Perceived Severity of Alcoholism and Relation to Self-Efficacy

Elaine Souder, Ph.D., Psychiatry, Univ. Ark Med. Sciences, 4301 W. Markham MS 529, Little Rock AR 72205; Eve J. Wiseman, M.D., Patricia S. O'Sullivan, Ed.D.

Summary:

Objective: The purpose of this study was to relate self-perception of alcoholism severity to abstinence self-efficacy.

Methods: A prospective study was conducted using 46 inpatients (mean age 50.3, SD = 10.6) in a VA alcohol rehabilitation program. The mean MAST score was 37.0 (10.6). Perceived severity of alcoholism was assessed by a visual analogue scale (VAS), in which subjects indicated on a 10 cm anchored line, to what degree they viewed alcohol as causing their current difficulties. Self-efficacy regarding anticipated abstinence similarly was assessed using a VAS.

Results: The mean VAS scores for alcoholism severity was 50 (5.2). For self-efficacy, the mean VAS of 76.6 (25.6) indicated a high degree of confidence in remaining abstinent. Perceived alcoholism severity was negatively correlated with self-efficacy ($r = -.40$, $p < .003$), after correcting for skewness.

Conclusions: These pilot data indicate that perception of severity of alcoholism is significantly related to self-efficacy. When severity of alcoholism is perceived to be low, it is accompanied by an inflated degree of confidence in remaining abstinent, which may contribute to poor investment in treatment.

NR410 Wednesday, May 25, 12 noon-2:00 p.m.

Craving and Treatment Need: A Function of Denial

Eugene Somoza, M.D. Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; R. Jeffrey Goldsmith, M.D., John Lutz, M.D., Juris P. Mezinskis, Ph.D., Sue R. Dyrenforth, Ph.D.

Summary:

Drug craving and denial of dependency are recognized as critical factors in precipitating relapses in alcohol-dependent and drug-dependent patients. The goal of this project was to study the interrelationship between craving and denial in patients with various types of addictions, and to determine how much they influence certain treatment parameters. The study population consisted of 547 patients who sought substance abuse treatment at a VA medical center over a 20-month period. All were given the Addiction Severity Index (ASI) by specially trained therapists who also determined the stage of denial and the intensity and frequency of craving. Patients were subdivided into three types of addictions according tho their usual patterns of use: alcohol alone (AA, 41%), alcohol plus other drugs (AD, 20.5%), and two or more nonalcoholic drugs (DD, 38.5%). Denial stages 4 and 5 were the most common for all addiction types. DD patients had the least denial and greatest craving. A lower degree of denial was associated with higher craving scores for all groups (e.g., $R = 0.38$, $p < 0.01$ for the AD group). Craving intensity and denial stage were both positively correlated with several ASI need-for-treatment parameters. Results indicate that the measurement of denial and craving is clinically useful for all three types of addictions studied.

NR411 Wednesday, May 25, 12 noon-2:00 p.m.

Factors Influencing Drug Craving Over Time

Sue R. Dyrenforth, Ph.D., Psychiatry, VA Medical Center, 3200 Vine Street ML 116B, Cincinnati OH 45220; Eugene C. Somoza, M.D., Juris P. Mezinskis, Ph.D., Mark W. Cohen, Ph.D.

Summary:

This study was designed to examine craving behavior specifically in relation to mood states, drug of choice, and day of inpatient treatment. The 135 patients in the combined drug and alcohol rehabilitation programs made ratings of their level of craving for all substances of abuse each day of their 28-day hospitalization. At the same time, they rated the intensity of eight specific feeling states. Nicotine was the most often and most intensely craved substance, with 77% of subjects reporting an average value of moderate, severe, or extreme craving. Alcohol was more frequently identified as the drug of first choice as well as second choice, followed by cocaine, marijuana, and opiates. Marijuana was most often listed second, while all others were most often listed as first. Analysis of the relationship between mood states and craving revealed moderate correlations: the total multiple correlation for all eight moods and all drugs ranged from .30 to .35. The drug that showed the highest relationship to mood was marijuana ($p => .01$). A discriminant function analysis failed to predict craving by feeling (Wilk's L = .80; F = .79). However, further analysis is planned. Both alcohol and cocaine craving dropped by 80% during treatment. However, there appear to be different craving profiles by drug of choice. The cocaine craving is initially higher than that of alcohol, then drops, only to peak between days 17–19. The alcohol curve generally diminishes throughout the 28-day period.

It is hypothesized that these differences reflect abstinence factors and environmental cues. Similarly, the feeling state profile appears to vary significantly by drug of choice. Cocaine users present higher ratings than others, especially on anger, irritability, impatience, and difficulty concentrating, but the overall severity scores are reduced by end of treatment, while alcoholics' severity scores did not vary or increased as treatment progressed. Findings suggest implications for treatment of craving and indicate there may be unique precipitants of craving by drug of choice.

NR412 Wednesday, May 25, 12 noon-2:00 p.m.

Cocaethylene Effects in Humans

Elinore F. McCance-Katz, M.D., Psychiatry, Yale University, P.O. Box 208038, New Haven CT 06520; Lawrence H. Price, M.D., Thomas R. Kosten, M.D., Peter I. Jatlow, M.D.

Summary:

Introduction: Simultaneous abuse of cocaine and alcohol is common. Cocaethylene, the ethyl ester of benzoylecgonine, is formed in humans during concurrent use of cocaine and ethanol. We recently obtained an IND for administration of cocaethylene fumarate (EC) by nasal insufflation. A pilot study was undertaken to evaluate the effect of EC in humans.

Methods: Four drug administration sessions were conducted in a randomized, double-blind sequence to subjects over an eight-day period. The four test days included the following drug administration schedule: EC 0.5mg/kg; EC 1mg/kg; cocaine 1mg/kg, or placebo. Physiological and subjective (visual analog scales, "High" scale) measures, plasma cocaine or EC levels were assessed.

Results: EC produced prolonged and enhanced euphoria relative to an equivalent dose of cocaine. No significant cardiovascular effects were observed. The elimination half-life of EC is about twice that of cocaine (190 min. vs. 99 min.). Peak plasma concentrations were greater for EC than for the equivalent dose of cocaine (164 ng/ml vs. 127 ng/ml) indicating increased bioavailability for EC. The effects of EC are similar to those of cocaine, but are prolonged.

Conclusion: These findings have important implications for the pathoetiology of cocaine-alcohol abuse.

NR413 Wednesday, May 25, 12 noon-2:00 p.m.

Transdermal Nicotine and Drug Craving

Eve J. Wiseman, M.D., Psychiatry, University AR Medical Sci, 4301 W. Markham Slot 554, Little Rock AR 72205; Donald E. McMillan, Ph.D., Margaret J. Briggs, L.P.N.

Summary:

Objective: The question addressed in this study was whether nicotine patches affect craving for drugs, particularly nicotine and cocaine, in subjects with nicotine dependence and recent cocaine abuse.

Method: Nineteen male inpatients were selected from a Veterans Administration drug rehabilitation program, and 15 consented and completed the study. Transdermal nicotine and placebo patches were applied in a crossover, double-blind design. Outcome was assessed by visual analog scales to measure drug craving. Subjects had a mean age of 38.5 (SD 4.3) years and had smoked cigarettes and abused cocaine an average of 22.0 (SD 6.3) and 8.4 (SD 6.0) years, respectively.

Results: Cigarette craving was significantly less for subjects with nicotine patches ($p < 0.05$): baseline 55.3 (SD 23.6), placebo 37.5 (SD 22.1), and nicotine 23.2 (SD 13.9) millimeters. Cocaine craving tended to be less for subjects with nicotine patches, but the ANOVA was not statistically significant (p 0.059). Subjects with non-zero baseline cocaine craving (27.3, SD 28.6) had significantly less cocaine craving with both the nicotine (6.7, SD 4.8) and placebo (17.0, SD 26.6) patches than at baseline ($p < 0.05$).

Conclusions: Nicotine patches significantly reduced craving for cigarettes without increasing cocaine craving. In fact, both nicotine and placebo patches reduced cocaine craving, and there was a nonsignificant trend for nicotine patches to reduce cocaine craving more than placebo patches.

NR414 Wednesday, May 25, 12 noon-2:00 p.m.

Measuring Alcoholism Severity: Relationship of DSM-III-R and Michigan Alcoholism Screening Test

Eve J. Wiseman, M.D., Psychiatry, University AR Med Sci, 4301 W. Markham Slot 554, Little Rock AR 72205; Elaine Souder, Ph.D., Patricia S. O'Sullivan, Ed.D.

Summary:

Objective: The two questions addressed in this study were (1) does the Michigan Alcoholism Screening Test (MAST) provide a valid indicator of alcoholism severity according to Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) criteria? and (2) What are the psychometric data of the DSM-III-R alcohol dependence criteria?

Method: Initially, 52 male inpatients were selected from a Veterans Administration alcohol rehabilitation program; 48 consented, and 46 completed the study. A psychiatrist interviewed subjects to evaluate presence of DSM-III-R criteria, and a research assistant coordinated collection of MAST data. Subjects had a mean age of 50.3 (SD 9.9) years and had abused alcohol an average of 21.1 (SD 10.6) years.

Results: Subjects averaged 7.6 (SD 1.5) DSM-III-R criteria and had a mean MAST score of 37.0 (SD 10.6). Pearson's r between DSM-III-R criteria and MAST was .54 ($p < 0.001$). The alpha coefficient for the nine DSM-III-R criteria was 0.59.

Conclusions: The MAST, widely used to screen for alcoholism, provides an excellent indication of alcoholism severity according to DSM-III-R critieria. Self-administered and easily scored, the MAST may assist in matching patients to appropriate treatments. Additional studies are needed to assess internal consistency of DSM-III-R criteria for alcohol dependence.

NR415 Wednesday, May 25, 12 noon-2:00 p.m.

The Effects of Morphine on Ethanol Consumption: Effect of Prior Ethanol Exposure

Michael F. Stromberg, Ph.D., Psychiatry, University of Penn., 3900 Chestnut Street, Philadelphia PA 19104; Joseph R. Volpicelli, M.D., Barbara L. Slifer, Ph.D., Steven C. Meister, B.S., Ronald R. Ulm, Ph.D.

Summary:

This experiment was designed to evaluate the effect of the prior administration of morphine, 2.5 mg/kg, on the consumption of ethanol in rats. Small doses of morphine have been shown to both increase and decrease the consumption of ethanol. A critical variable in these experiments may be whether or not the rats were pre-exposed to ethanol prior to the introduction of morphine. If morphine primarily controls ingestion, pre-exposure should not be a factor. However, if morphine's primary effect is to modulate ethanol's reinforcing properties, it might be expected that some prior exposure to ethanol is necessary for the rat to learn about these reinforcing properties. This experiment used two groups of rats, one received morphine, 2.5 mg/kg sc, simultaneously with the introduction of ethanol and again 21 days later. The second group received saline injections simultaneously with the introduction of ethanol and morphine 21 days later. Analysis of the data revealed that the administration of morphine following prior exposure to ethanol produced a significantly higher intake of ethanol than when administered with the initial introduction of ethanol. These results suggest that some prior experience with ethanol is required for morphine to potentiate consumption. This is consistent with the view that endogenous opioids contribute to modulating the reinforcing properties of ethanol.

NR416 Wednesday, May 25, 12 noon-2:00 p.m.

An Objective Measure of Nicotine Craving for Psychiatric Patients

Neil Hartman, M.D., Psychiatry, NPI (691/B1 51DT350), W. Los Angeles VAMC, Los Angeles CA 90073; George C. Mazzei, B.A., Sidney Gold, M.D., Shelly Wilkerson, R.N., Nicholas Caskey, Ph.D., Murray E. Jarvik, M.D.

Summary:

Standard questionnaires regarding nicotine craving and withdrawal are ill suited for severely impaired and often uncooperative psychiatric patients confined involuntarily on locked, smoke-free units. A completely objective, reliable, behavioral measure involving smoking topology of individual patients was reported last year at this meeting (Hartman et al., 1993). We now report another, equally reliable method, that can be applied to numerous patients simultaneously. Informed consent was obtained from 10 nicotine-addicted (more than one pack per day) patients admitted involuntarily to a highly secured unit at the "smoke-free" West Los Angeles VA Medical Center. On locked units only, each patient is permitted three postprandial cigarettes per day. After an enforced abstinence of at least six hours, verified by carbon monoxide, each was allowed to smoke successive standard filtered cigarettes to satiety. All butts were collected and the filters dissected and weighed by a blind investigator. In every case the filter from the first (abstinent) cigarette weighed the most (P = 0.0067, 2-tail t-test) with successive cigarettes weighing progresssively less. Smoking topography from videotapes of each smoking session and self-report questionnaires from cooperative patients correlate well with this easily administered, new objective measure of nicotine craving.

NR417 Wednesday, May 25, 12 noon-2:00 p.m.

The Wender Utah Rating Scale and Residual ADHD in Adult Substance Abusers

James J. McGough, M.D., Psychiatry, UCLA-NPI, 1762 Westwood Blvd Ste 440, Los Angeles CA 90024; John F. Curry, Ph.D.

Summary:

It is well demonstrated that children with ADHD are at increased risk for adult substance abuse. Identification of a subgroup of adult substance abusers with residual ADHD could lead to more effective substance abuse treatments. The Wender Utah Rating Scale (WURS), a validated self-report measure for the retrospective evaluation of ADHD in adults, was administered to 107 patients admitted to an inpatient VA alcohol/drug treatment program. Scores consistent with ADHD were obtained in 31% of the sample. The subscale for ADHD positively correlated with subscales for conduct disorder ($r = .69$; $p < .0001$), learning disorder ($r = .61$; $p < .0001$), school suspensions/expulsions ($r = .69$; $p < .0001$), somatization ($r = .33$; $p < .0004$), repeated grades ($r = .26$; $p < .006$), and negatively correlated with highest grade level ($r = -.28$; $p < .004$). Subjects meeting criteria for ADHd had significantly higher T-scores on measures of conduct disorder ($p < .0001$), learning disorder ($p < .0001$), and somatization ($p < .02$), compared with control subjects. Chi-square analysis demonstrated a significant increase in school suspensions/expulsions ($p < .0001$), and repeated grades ($p < .007$), compared with the control group. There is apparent use for the WURS in identifying a residual ADHD picture in severe substance abusers. Additional research, including diagnostic assessment with structured interviews and careful measurements of treatment outcome, should further elucidate the relationship between residual ADHD and chronic substance abuse.

NR418 Wednesday, May 25, 12 noon-2:00 p.m.

Haloperidol and Smoking Behaviors in Normals

William C. Wirshing, M.D., Psychiatry Bldg 210, VAMC West Los Angeles, 11301 Wilshire (B151H), Los Angeles CA 90073; Murray E. Jarvik, M.D., Nicholas Caskey, Ph.D., Donna Ames, M.D.

Summary:

Objective: Rate of smoking in neuroleptic-treated schizophrenic populations is among the highest of any surveyed group. This study investigated the possible interaction between neuroleptics and smoking behaviors.

Methods: Twelve psychiatrically and neurologically healthy smokers were given 2 mg of oral haloperidol and placebo (double-blind randomized dose) one week apart. Subjects were observed for six hours after dosing and allowed to smoke freely.

Results: The third intercigarette interval after dosing was significantly shorter after haloperidol dosing ($t = 2.992$, $p = .012$, two-tailed). Shiffman-Jarvik craving subscale ratings were significantly higher ($t = 2.222$, $p = .053$, two-tailed) 30 minutes after the third cigarette (mean difference – 5.5, $SD_{DIFF} = 7.79$). For eleven subjects (one subject had insufficient amount of plasma), difference in plasma nicotine levels four hours after drug ingestion was in the predicted direction (haloperidol: mean = 29.6 ng/ml, SD = 9.6; placebo: mean = 25.2, SD = 4.9) ($t = 1.22$, $p = .125$, one-tailed). There were no differences on measures of mood states or smoking satisfaction.

Conclusions: Results tentatively suggest treatment with neuroleptics may cause smoking at increased rates to attain the same level of satisfaction, perhaps mediated by dopamine blockade and a down regulation in the "hedonic sensitivity."

NR419 Wednesday, May 25, 12 noon-2:00 p.m.

SPECT Imaging of the Dopamine Transporter During Cocaine Abstinence

Elizabeth A. Wallace, M.D., Psychiatry, Yale University, 29 Sylvan Avenue, New Haven CT 06443; Robert T. Malison, M.D., Susan E. Best, M.D., Robert B. Innis, M.D., Thomas R. Kosten, M.D.

Summary:

Objective: Cocaine abuse has been a recurrent health problem during this century, and effective treatment modalities are greatly needed. Cocaine is thought to exert its effects through interaction with the dopamine (DA) transporter. The objective of this study is to investigate changes in DA transporters during cocaine abstinence using single photon emission computed tomography (SPECT) and the ligand [123I] methyl 3β-(4-iodophenyl)tropane-2β-carboxylate (or β-CIT), which binds to DA and serotonin transporters.

Methods: This is a within-subject longitudinal evaluation of β-CIT binding during cocaine abstinence. Five cocaine dependent subjects (one male, four females) have been studied to date. Each received β-CIT and SPECT imaging on admission and at two, four, or six weeks following cocaine abstinence (not all subjects were studied at all time points.) The primary outcome measure is V_3'' which is proportional to the β-CIT binding potential at the DA transporter.

Results: At two, four, and six weeks, the mean values of V_3'' decreased (from admission values) by 21.6% (n = 3), 15.26% (n = 2) and 18.21% (n = 1), respectively.

Conclusion: These preliminary data demonstrate a decrease in β-CIT binding following the cessation of cocaine use in cocaine-dependent individuals.

NR420 Wednesday, May 25, 12 noon-2:00 p.m.

Low Dose of Lorazepam Increases Psychometric Performances in Healthy Volunteers

Michel Bourin, M.D., Pharmacology, Faculty of Medicine, 7 Rue Gaston Veil, Nantes 44035, Frances; Marie C. Colombel, B.A., Myriam Malinge, M.D.

Summary:

The effects of 0.25 mg twice a day of lorazepam on several cognitive and performance tasks were investigated in nonanxious healthy students (Images test, DSST, CFF, CRT). A double-blind, independent group design was used to compare placebo and lorazepam (30 volunteers in each group). Subjects completed a battery of tests at D_0, D_3, D_7, D_{10}, D_{14}.

As it was shown in a previous study with a small number of volunteers, D_3 performances were better than or equal to placebo (Bourin et coll., in press). But a significant improvement of performances was shown at D_7, D_{10} and D_{14} in the lorazepam group compared with the control group. An increased learning effect is possible, but no practice effect was observed in the placebo group. This study clearly point out a psychostimulant effect of lorazepam at low dose in healthy volunteers. This paradoxical result leads to the hypothesis of partial inverse agonist activity of lorazepam increasing performance without any anxiogenic properties.

NR421 Wednesday, May 25, 12 noon-2:00 p.m.

Serotonergic Mechanisms and Personality Profiles in PTSD Patients

H. Constance Bonbrest, M.D., Veterans Admin. Hospital, P.O. Box 5000, Hines IL 60141; Ramesh Arora, Ph.D., Omar Nasib, M.D., John W. Crayton, M.D.

Summary:

Cloninger (1987) proposed that there are three independent, inherited dimensions of personality: Harm Avoidance (HA); Novelty Seeking (NS); and Reward Dependence (RD). In addition, each dimension was correlated with activity of a particular neurotransmitter: HA with serotonin; NS with dopamine; and RD with norepinephrine. To test this hypothesis, we administered the Cloninger Tridimensional Personality Questionnaire (TPQ) to 26 patients with post-traumatic stress disorder (PTSD) and 16 controls (C) and correlated the scores with paroxetine binding to the platelet serotonin transporter, a measure previously shown to distinguish PTSD from C (Arora, et al., 1993). PTSD patients had significantly higher scores than controls on HA (21.0 ± 8.4 vs. 9.4 ± 6.4; $p < 0.001$; mean ± S.D.) and NS (19.6 ± 5.1 vs. 14.2 ± 3.4; $p < 0.001$) and lower on RD (7.7 ± 3.7 vs. 13.1 ± 4.0; $p < 0.001$). Paroxetin B_{max} (number of serotonin transporter binding sites) was significantly correlated with HA ($r = -0.326$; $p = 0.049$) and approached significance for NS ($r = -0.288$; $p = 0.084$), but not with RD. Combining HA and NS scores yielded a higher correlation than using either score alone ($r = -0.375$; $p = 0.022$). The results partially support the Cloninger hypothesis in this population of PTSD patients. The hypothesized personality risk factor for PTSD (eg. Schnurr, et al., 1993) may be related to a serotonin-mediated substrate.

NR422 Wednesday, May 25, 12 noon-2:00 p.m.

Pilot Study of Platelet Serotonin Transporter Binding Sites in Women with Postpartum Depression

Zachary N. Stowe, M.D., Psychiatry, Emory Univ Sch of Med, 1639 Pierce Drive NE Ste 4003, Atlanta GA 30322; Michael J. Owens, Ph.D., Charles B. Nemeroff, M.D.

Summary:

Postpartum depression (PPD) represents a significant mental health problem. Despite numerous investigations, the etiology of postpartum mood disorders remains obscure. Several groups have observed a marked decrease in the number of platelet [^{3}H]-imipramine and [^{3}H]-paroxetine binding sites (Bmax) in drug-free patients with nonpuerperal major depression. The purpose of the present study was to determine if platelet [^{3}H]-paroxetine binding was altered in women with postpartum-onset major depression. All potential participants were interviewed by a psychiatrist (ZNS) and were medication-free for more than four weeks except for prenatal vitamins. Nineteen postpartum (2–20 weeks) women who fulfilled DSM-III-R criteria for major depression (HRSD 24.2 ± 4.2) and 13 postpartum (4–20 weeks) nondepressed controls (HRSD of 4.5 ± 2.3) were included in the pilot sample. Platelet [^{3}H]-paroxetine binding was determined using a modification of the procedure of Raisman and colleagues. No significant difference between the Bmax for platelet [^{3}H]-paroxetine in women with postpartum depression (Bmax 854.26 ± 231.19) and postpartum controls (Bmax 862.33 ± 158.38) was observed. Nursing did not significantly alter the Bmax or Kd of [^{3}H]-paroxetine binding in either the control (n = 8) or depressed groups (n = 7). In contrast to previous platelet binding studies in women with postpartum depressive symptoms using [^{3}H]-imipramine, we found no significant alteration in the dissociation constant (Kd). These results suggest that the biological parameter of decreased platelet serotonin transporter binding sites observed in nonpuerperal major depression may not be present in PPD, underscoring the need for further biological studies in this population.

NR423 Wednesday, May 25, 12 noon-2:00 p.m.

HPA Axis Effects on Dopamine Activity in Man

Joel A. Posener, M.D., Psychiatry, Harvard Medical School, 115 Mill St. McLean Hospital, Belmont MA 02178; Alan F. Schatzberg, M.D., Joseph J. Schildkraut, M.D.

Summary:

Objective: To investigate the effects of the hypothalamic-pituitary-adrenal (HPA) axis on dopamine activity in humans.

Method: In pilot studies, ovine corticotropin-releasing hormone (CRH) was administered IV to 10 healthy volunteers, and synthetic adrenocorticotropic hormone (ACTH) was administered IV to 12 healthy volunteers. Plasma levels of homovanillic acid (pHVA), the dopamine metabolite, were measured before and after substance administration. In a current study, 10 healthy volunteers are administered each of CRH, ACTH, hydrocortisone, and placebo in a double-blind, randomized, crossover design. Plasma cortisol, ACTH and HVA are measured at 9 AM, 4 PM, and 6:45 PM; the test substance is administered at 7 PM; the same plasma measures are then obtained every 30 minutes from 7:30 to 11 PM, and at 9 AM and 4 PM on each of the two following days.

Results: In the pilot studies, neither CRH nor ACTH produced an increase in pHVA over the 3.5 hours after substance administration. However, CRH and ACTH did produce significant rises in pHVA over the 24–55 hours following substance administration in subgroups of five and six subjects respectively. Results of the current study will suggest which HPA axis products exert independent effects on pHVA.

Conclusions: CRH and ACTH may increase dopamine activity in healthy humans. Results of the current study will suggest strategies for examining HPA axis-dopamine interactions in psychotic disorders.

NR424 Wednesday, May 25, 12 noon-2:00 p.m.

Hippocampal Lesions Enhance Vasopressin Response to Stress

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Summary:

Objective: Unexplained increases in plasma vasopressin (AVP) occur in schizophrenics following psychosis/stress, and likely contribute to life-threatening water intoxication in those with hyponatremia and polydipsia. Hyponatremic polydipsics have smaller hippocampi and DST abnormalities. The hippocampus likely suppresses cortisol response to stress by diminishing AVP secretion. We measured the neuroendocrine response of rats, with and without hippocampal lesions, to swim stress to see if we could produce changes analogous to those seen in schizophrenia.

Method: Three to four weeks following either bilateral aspiration of the hippocampus (H) or overlying neocortex (C), Long-Evans rats were placed, at 8 a.m., in water for 45 seconds, and sacrificed immediately afterwards, or at 30-minute intervals for 90 minutes.

Results: AVP at time = 0 was equal (H = 1.2 ± 0.4 pg/ml (n = 5 throughout); C = 1.7 ± 0.6), but increased, in a linear fashion, only in H (time = 90 min.: H = 4.7 ± 2.5; C = 2.4 ± 0.9; time-group interaction F = 2.63, df = 32,3 $p < .07$, linear component t = 2.6 $p < .015$). Peak ACTH and corticosterone were similar (ACTH: time = 0, H = 348 ± 219 pg/ml, C = 376 ± 101; CORT: time = 30 H = 312 ± 150 ng/ml, C = 312 ± 103) and declined to non-significantly higher levels in C (ACTH: time = 90 H = 39.5 ± 37.1, C = 99.4 ± 105; CORT: test 73.4 ± 69.2, control 181.8 ± 129). AVP was marginally, and negatively, correlated with both CORT and ACTH ($p < .02$). Mean body weight and recognized stimuli of AVP were similar across groups.

Conclusions: Hippocampal lesions increase plasma AVP response to stress, while controls, like normal humans, show no response. The mechanism is unclear and cannot be attributed to enhanced secretion of ACTH secretagogues. This animal model may assist in clarifying the pathophysiology of AVP abnormalities in schizophrenia.

NR425 Wednesday, May 25, 12 noon-2:00 p.m.

Variability of the Human Melatonin Phase Response Curve

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Summary:

Disturbances in the internal circadian pacemaker appear to produce circadian phase sleep and mood disorders. Measuring the time of onset of the pineal gland's nightly surge of melatonin production is thought to be the best determination of the phase of the internal circadian clock. Properly timed bright light exposure causes phase changes with resolution of symptoms of these circadian disorders. Exogenous melatonin was recently shown to produce phase changes in the internal melatonin rhythm (Lewy *et al.,* 1992). Since melatonin can produce consistent phase changes, it may be an effective treatment for winter depression, jet lag, and circadian phase sleep disorders, perhaps supplanting light treatment.

Therefore, we began the first study examining the variability of the human melatonin phase response curve (PRC). Melatonin (0.5 mg) was given to four subjects in 12 trials, obtaining a 24-hour PRC for each. Comparison of individual PRCs showed little variation in the crossover points between the phase delay and phase advance zones but as much as 100% variation in the amplitude of the phase shifts. Elderly subjects responded with larger phase shifts (advances and delays) than did younger subjects. Pharmacokinetic evaluations are currently being conducted.

Determining the shape and variability of the melatonin PRC will be necessary for optimizing the circadian phase-correcting effect of melatonin and maximizing its treatment potential.

NR426 Wednesday, May 25, 12 noon-2:00 p.m.

The D-Fenfluramine Challenge in Alcoholics

Mario Seguel, M.D., Psychiatry, Catholic University, Marcoleta 352, Santiago, Chile; Sergio Gloger, M.D., Rodrigo Labarca, M.D., Rafael Torres, Ph.D., Sergio Valdivieso, M.D.

Summary:

The present study assessed serotonergic (5-hydroxytryptamine, 5HT) function in 38 alcoholics (21 type I and 17 type II) and 18 healthy controls, matched by sex and age. All subjects were interviewed using SCID-P (for DSM-III-R). Alcoholics fulfilled DSM-III-R critieria for alcohol dependence only. Other physical and psychiatric disorders were considered exclusionary criteria. Cloninger's criteria for types I and II were used. At least 12 weeks of controlled abstinence was required for the challenge. Central 5HT function was assessed through plasma prolactine response (delta PRL) to D-fenfluramine (30 mg orally), a 5HT selective releasing/uptake inhibitor according to Siever's criteria.

Results/Discussion: No statistically significant difference was found in the basal PRL values among the three groups (9.8 ± 3.6 controls, 7.9 ± 3.6 type I and 8.8 ± 4.6 type II. p = n.s.). The delta PRL value was significantly higher in the control group compared with type I (12.9 ± 11.76 controls, 5.8 ± 3.6 type I and 9.6 ± 4.6 type II, $p < 0.05$). These results suggest that alcoholics may have a 5HT dysfunction that could be more severe in type I alcoholics. (Supported by FONDECYT grant 0739-91).

NR427 Wednesday, May 25, 12 noon-2:00 p.m.

MRI and Neurological Soft Signs in PTSD Veterans

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Ph.D., Hiroto Hokama, M.D., Natasha B. Lasko, Ph.D., Roger K. Pitman, M.D.

Summary:

This study reinvestigated the neurological status of a subset of seven medication-free, outpatient Vietnam veterans meeting DSM-III-R criteria for chronic post-traumatic stress disorder (PTSD), and seven non-PTSD, combat control subjects, selected from a previous study. All were without alcohol or drug dependence or abuse during the previous year. Subjects underwent a repeat, modified, videotaped examination of neurological soft signs (NSS), each scored on a 0–3 scale, and neuropsychiatric history with special attention to developmental problems and CNS insults. Mean NSS ratings were PTSD 32.8 (SD 9.7) vs. non-PTSD 15.4 (SD 4.8), $t(12) = 4.9$, $p < .001$. These findings suggest neurodevelopmental impairment as a risk factor for a chronic course of PTSD. Exploratory magnetic resonance imaging (MRI) volumetric analyses incorporating three-dimensional reconstruction of brain structures in vivo compared the above seven PTSD subjects with seven other age-matched normal control subjects taken from another study, which employed a different scanning technique. These exploratory analyses suggested enlargement of the left temporal horn of the lateral ventricle in the PTSD subjects: mean volumes PTSD 0.26 ml (SD .13) vs. normal .05 ml (SD .03). Volumetric analyses of the PTSD and combat control subjects, as well as of additional normal and schizophrenic comparison subjects, all studied with the same scanning technique, will be available at the time of the presentation.

NR428 Wednesday, May 25, 12 noon-2:00 p.m.

Plasma Tryptophan and Brain Serotonin Function in Patients Taking Cholesterol Lowering Drugs

Nicholas J. Delva, M.D., Psychiatry, Queen's University, 72 Barrie Street, Kingston ON K7L3J7, Canada; Philip J. Cowen, M.D., David R. Matthews, B.M.

Summary:

Treatments that lower serum cholesterol concentrations are associated with an increased incidence of death from accidents, suicide, or violence. Brain serotonin (5-HT) pathways are involved in the regulation of mood and aggression; it has been proposed that cholesterol-lowering treatments predispose some subjects to aggression and suicide by decreasing brain 5-HT function. This study examined the prolactin response to the 5-HT releasing agent, d-fenfluramine; and measured plasma concentrations of the 5-HT precursor, tryptophan, in 20 patients receiving cholesterol-lowering medication and 20 age- and sex-matched controls, to test the hypotheses that 1) cholesterol-lowering treatments decrease brain 5-HT function; and 2) do so by reducing the availability of tryptophan for brain 5-HT synthesis. Although patients(P) were somewhat more depressed than controls(C) (Beck Depression Rating Scale; (P) 5.45 vs (C) 2.30; $p < 0.05$), there was no difference in aggression between the two groups (Buss-Durkee: Attitude (P) 4.15 vs (C) 3.20; Motor (P) 18.45 vs (C) 18.95; both NS). There was no difference between the groups in either prolactin response (by repeated measures ANOVA or area under curve) or either free (0.77(P) vs 0.83(C), μg/ml; NS) or total (11.67 (P) vs 11.87 (C) μg/ml; NS) tryptophan. Thus no evidence was found of abnormal brain serotonin function in patients on cholesterol-lowering treatment.

NR429 Wednesday, May 25, 12 noon-2:00 p.m.

Dopamine Enhances GABA Transmission in the Hippocampus

Stephen J. Schertzer, M.D., Psychiatry, Women's College Hospital, 76 Greenville Street, Toronto ON, Canada; Liang Zhang, M.D., Peter Carlen, M.D.

Summary:

Objective: Although dopaminergic hyperactivity underlies the pathophysiology of schizophrenia, many studies have demonstrated only modest direct electrophysiological effects of dopamine (DA) in cortico-limbic structures. Our study was designed to clarify the role of DA in synaptic transmission in the hippocampus.

Method: This study used whole cell patch-clamp recordings of individual pyramidal cells in the CA1 region of the hippocampus in an in-vitro slice preparation. All drugs were bath applied in an artificial CSF solution. Near soma concentric electrode stimulation elicited a postsynaptic current in which the GABA component was pharmacologically isolated.

Results: The amplitude of this GABA current was transiently increased by DA (10uM & 30uM). A more prolonged and robust augmentation was elicited by D1 agonist SKF38393 (100nM & 1uM). This GABA current augmentation was blocked in the presence of D1 antagonist SCH23390. The D2 antagonist sulpiride (10uM) tended to increase the response to DA. The time course of these effects was consistent with a second messenger system.

Conclusions: We conclude that dopamine facilitates GABA transmission via D1 receptors by enhancing quantal release of GABA from inhibitory interneurons. It is possible that D2 blockade unmasks the inhibitory properties of DA, which may not be seen in the presence of excessive D2 receptors.

NR430 Wednesday, May 25, 12 noon-2:00 p.m.

Verapamil Versus Placebo for Acute Mania: Preliminary Results From a Double-Blind Study

Philip G. Janicak, M.D., Research, Ill. State Psych Inst., 1153 N. Lavergne Avenue, Chicago IL 60651; Ghanshayam Pandey, Ph.D., Rajiv P. Sharma, M.D., Jim Peterson, B.S., Anne Leach, M.D., John M. Davis, M.D.

Summary:

Many bipolar manic patients are intolerant, only partially responsive, or nonresponsive to lithium.

Objective: To determine whether calcium antagonists (e.g., verapamil), perhaps in part due to the similar effects these drugs and lithium have on calcium ion activity, may be effective alternative antimanic agents. Thus far, the evidence for verapamil's efficacy rests on one small study with six patients and two partially controlled studies; while one apparently well-controlled trial had a negative result.

Method: A three-week double-blind, parallel group, random-assignment, placebo-controlled trial of verapamil (dose titrated up to 480 mg/day) in hospitalized manic patients. Rescue medications are chloral hydrate or lorazepam, up to day 10 of the double-blind phase.

Results: Thus far, 15 patients (seven placebo, eight verapamil) have completed the study, averaging a total pretreatment medication washout of 15.6 days. An ANCOVA (with baseline scores as covariate) computing absolute change scores on the Mania Rating Scale at endpoint did not differ between the drug and the placebo groups ($F = .01$; $df = 1$; $p = .92$). There were no significant differences between the two groups in baseline ratings, age, sex, amount of rescue medications, and total days on treatment.

Conclusions: Preliminary results indicate no benefit for verapamil over placebo during an acute manic episode.

NR431 Wednesday, May 25, 12 noon-2:00 p.m.

Toward a Biological Classification in Psychiatry

Erwin R. John, Ph.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Leslie S. Prichep, Ph.D., Robert Cancro, M.D., Francis G. Mas, M.D.

Summary:

Normative equations for numerous quantitative EEG (QEEG) features have been described. In a "neurometric" evaluation, hundreds of QEEG features are extracted from the resting EEG and evaluated statistically relative to the normative distribution. In healthy, normally functioning individuals, the incidence of significant findings is at the chance level. In a wide variety of psychiatric and neurological illnesses, a high proportion of the values obtained in a neurometric QEEG examination are significantly deviant or statistically "abnormal."

The profile of abnormal findings is distinctive for many different disorders. Multiple discriminant functions successfully separate patients with different DSM-III-R diagnoses, achieving high accuracy on independent replications. Such discriminants use DSM-III-R as a "gold standard", defining a *training group* that serves as a template for pattern recognition.

Discriminant analysis is thus tautological, showing only that a DSM-III-R rubric has recognizable biological correlates but casting little light on the structure of pathophysiology. We have carried out uninformed cluster analysis on large samples of patients representing many DSM-III-R categories. Each category was found to contain several subtypes. Patients in several categories were often classified into the same cluster to a certain extent. The structure of pathophysiology appears to differ from the structure of present psychiatric nosology.

NR432 Wednesday, May 25, 12 noon-2:00 p.m.

Evolution of Dementia in Quantitative Electroencephalographic Subtypes of the Elderly

Leslie S. Prichep, Ph.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Erwin R. John, Ph.D., Barry Reisberg, M.D., Steven Ferris, M.D.

Summary:

Normative equations describe the maturation of hundreds of quantitative electroencephalographic (QEEG) features across the human life span. Healthy, normally functioning individuals show deviations from these normal values at the chance level. We studied a very large cohort of elderly patients, with their level of cognitive deterioration evaluated using the Global Deterioration Scale (GDS). Elderly patients with cognitive impairment display a number of characteristic QEEG abnormalities. The statistical significance of such abnormalities increases with clinical severity, reaching very high levels of correlation.

Among this cohort were a large number of patients with a clinical rating of GDS 2.0, corresponding to subjective complaints of memory loss in spite of failure to detect any objective deficit with psychometric testing. Many of these patients were recalled for repeated clinical examination after three to 10 years. Patients were divided in to three groups: 1) those who showed no change from their initial GDS score; 2) those with a one-point increase to a GDS of 3, mild senile dementia (SDAT) and 3) those with two or more points of increase to a GDS to moderate senile dementia (SDAT). The members of these three groups showed drastically different QEEG profiles at initial testing. Group 1 was essentially normal at that time, while Groups 2 and 3 had profiles of QEEG abnormalities resembling those found in more impaired patients.

NR433 Wednesday, May 25, 12 noon-2:00 p.m.

Clinical Relevance of Quantitative Electroencephalogram Subtyping

Francis G. Mas, M.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Leslie S. Prichep, Ph.D., Eric Hollander, M.D., Michael R. Liebowitz, M.D.

Summary:

A multicenter study using a quantitative electroencephalographic (QEEG) method known as neurometrics, in which QEEG data from OCD patients were compared statistically with those from an age-appropriate normative population, shows the existence of two subtypes of OCD patients within a clinically homogeneous group of patients who met DSM-III-R criteria for OCD. Following pharmacological treatment, a clear relationship can be found between treatment response and neurometric cluster membership. Cluster 1 is characterized by excess relative power in theta, especially in the frontal and frontotemporal regions; cluster 2 is characterized by increased relative power in alpha. Further, 80.0% of the members of cluster 1 are found to be nonresponders to selective serotonin reuptake inhibitors (SSRI), while 82.4% of the members of cluster 2 are found to be SSRI responders. These findings suggest the existence of at least two pathophysiological subgroups within the OCD population that share a common clinical expression, but show a differential response to treatment with serotonin reuptake inhibitors. The relationship between QEEG subtypes of panic disorder patients and treatment outcome will also be presented.

NR434 Wednesday, May 25, 12 noon-2:00 p.m.

Regional CBF Studies in Narcolepsy

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Summary:

Narcolepsy is a neurological condition manifested by a tetrad of symptoms, most commonly excessive daytime sleepiness and often by other symptoms such as sleep paralysis, cataplexy, and hypnogogic hallucinations. Sometimes symptoms of narcolepsy overlap with depression, schizophrenia-like psychosis, and attention deficit disorder, and cerebral blood flow studies have been evaluated in the latter disorders. To test the hypothesis that functional abnormalities involving the frontal or anterior temporal lobes may be present in narcolepsy, regional cerebral blood flow (rCBF) studies were performed in eight patients.

Eight drug-free patients (M = 4; F = 4) aged (18–50 yrs) were diagnosed clinically as narcoleptics by standard polysomnography and multiple sleep latency test. Each underwent 99mTc hexmethyl-propyleneamine oxime (99mTc-HMPAO) high-resolution brain SPECT imaging. Regions of interest (ROI) for analysis were defined using a reference system that defined cortical circumferential ROI at slice levels parallel to and sequentially above the canthomeatal line at +3.5cm, +5.5cm & +7.5cm. The cortex was subdivided into 12 equal angular regions using a computer-automated edge detection program. The caudate nucleus and thalami were also evaluated by reference to an anatomic scan. Regional CBF values were obtained by normalizing cortical counts to both whole brain and cerebellar counts.

A one-sample t-test revealed a significant decrease in mean rCBF of the R-anterior temporal ($p = .001$) and R-posterior frontal ($p = .043$) regions compared with normals. A two-sample t-test revealed a significant decrease in mean rCBF of the R-anterior temporal ($p = .048$) and R-posterior frontal ($p = .044$) regions of patients *with cataplexy* compared to those *without.* A similar significant decrease in mean rCBF of R-anterior temporal ($p = .043$) & R-posterior frontal ($p = .029$) was found between patients *with sleep paralysis* compared with those *without.* In conclusion, this study suggests that regional decreases in frontal and anterior temporal lobe rCBF occurs in patients with narcolepsy, and may provide a method to better understand the underlying pathophysiology.

NR435 Wednesday, May 25, 12 noon-2:00 p.m.

Cortical Gender Dimorphism in Healthy Subjects

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Summary:

Brain regions involved in determining sexual behavior have earlier been reported to differ between the sexes, but other regions have not been extensively studied. The well-established cognitive functional differences between the sexes might be reflected in higher-order cortical differences. We hypothesized that cortical regions involved in verbal behavior (which is sexually dimorphic) would differ between sexes. Using magnetic resonance imaging we assessed gray matter volumes in several cortical regions in 17 women and 43 men.

Women had 23.2% (dorsolateral prefrontal cortex) and 12.8% (superior temporal hyrus) greater gray matter percentages (corrected for overall brain size and age) than men ($p < 0.001$) in these language-related, but not in comparable visuo-spatial-related, cortical regions. There are well-documented gender differences in lability and expression of schizophrenia, a disorder of known cortical involvement. The markedly later onset of schizophrenia and fewer negative symptoms in females could possibly be explained by the larger amount of gray matter in the dorsolateral prefrontal cortex, a region pathologically affected in schizophrenic patients.

NR436 Wednesday, May 25, 12 noon-2:00 p.m.

Correlations Between Topography of Resting Metabolism and Clinical Presentation in Schizophrenia

Ruben C. Gur, Ph.D., Psychiatry, University of Penn., 3500 Spruce St. 10 Gates Bldg, Philadelphia PA 19104; Raquel E. Gur, M.D., Lyn Harper-Mozley, Ph.D., P. David Mozley, M.D., Derri L. Shtasel, M.D. Abass Alavi, M.D.

Summary:

The integration of Positron Emission Tomography (PET) methodology to schizophrenia research permits examination of the relation between clinical features and the pattern of brain activity. We measured glucose utilization using ^{18}F-fluoro-deoxyglucose (FDG) with PET in 42 unmedicated patients and 42 sociodemographically balanced healthy controls. ROIs for anatomically coregistered PET/MRI images included cortical and subcortical regions.

There were no differences in the topography of regional activity between first-episode and chronic patients or between deficit and nondeficit patients using Carpenter's classification. Correlations between regional activity and specific symptoms were modest, suggesting severity of negative symptoms to be negatively correlated with frontal lobe activity, whereas positive symptoms were positively correlated with temporo-limbic activity. However marked differences in the pattern of activity were observed between clusters of patients defined as Deficit, Paranoid and Schneiderian.

NR437 Wednesday, May 25, 12 noon-2:00 p.m.

Brain Function in First Episode Schizophrenia

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The study of first-episode (FE) patients with schizophrenia provides an opportunity to assess brain function before treatment is initiated. Furthermore, course of illness can be monitored prospectively. The goal of this series of studies was to integrate clinical measures with neuropsychological, neuroanatomic, and physiologic parameters in FE patients.

A sample of well-characterized, neuroleptic-naive patients (ranging from 20–50 per study) participated in the following studies after standardized evaluation: 1) neurobehavioral measures of a range of cognitive functions; 2) neuroanatomic studies using MRI examining whole brain as well as regional volumes in the frontal and temporal lobes; 3) neurochemistry studies using MRS; 4) metabolic studies measuring glucose metabolism and CBF applying neurobehavioral probes.

The results indicate a brain dysfunction in FE patients that implicates primarily the temporo-limbic system. New-onset patients show a similar pattern of aberration to that evident in chronic patients. The results support a neurodevelopmental perspective of schizophrenia.

NR438 Wednesday, May 25, 12 noon-2:00 p.m.

Correlates of SPECT Findings in Schizophrenics

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Summary:

Neuroimaging studies in schizophrenia have demonstrated abnormalities in frontal and temporal lobes as well as subcortical areas. In particular, SPECT studies have shown reduced small rCBF to frontal lobes in subgroups of schizophrenics; neuropsychological testing has shown cognitive deficits, in particular on frontal lobe tasks, and global deficits on standardized batteries such as the Halstead-Reitan Battery. We compared 16 patients with DSM-III-R diagnoses of schizophrenia with a community control group matched for age and sex. SPECT imaging was carried out with a Triad using TcHMPAO as the tracer. Both multiple tomographic and three-dimensional volume displays were produced. Regions of interest were determined as described by Rubin, et al. Patients received a comprehensive neuropsychological battery, which included the Halstead-Reitan Battery supplemented by the Wechsler Adult Intelligence Scale (WAIS), Wisconsin Card Sort Test, FAS Test, and the Ruff Figural Fluency Test. Compared with controls, schizophrenic subjects had significantly different rCBF to all lobes except the right temporal and right parietal lobes. For instance, hypofrontality was noted bilaterally ($p = .003$). We then tested the hypothesis that these areas of abnormality on SPECT would correlate with the appropriate neuropsychological tests. Our findings are consistent with previous reports in the literature.

NR439 Wednesday, May 25, 12 noon-2:00 p.m.

Do Neurologically Impaired Schizophrenics Have Abnormal SPECT Scans?

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Summary:

There are numerous reports of schizophrenic subjects having abnormal neuropsychological test results. We hypothesized that schizophrenics with neuropsychological abnormalities would have impairment on rCBF determined by SPECT scans. We therefore studied 16 DSM-III-R-diagnosed schizophrenics and a control group ($n = 19$) that were matched for age and sex. Schizophrenics received a neuropsychological battery that included the Halstead-

Reitan Neuropsychological Battery as well as the Wechsler Adult Intelligence Scale (WAIS), Wisconsin Card Sort Test, FAS, and the Ruff Figural Fluency Test. Both schizophrenic and control groups received a SPECT scan, which was carried out with a Triad using TcHMPAO as the tracer. Both multiple tomographic sections and a three-dimensional volume display were produced. Scans were evaluated for regions of interest using the method described by Rubin, et al. Of the 16 schizophrenics, six were impaired on the Halstead-Reitan impairment index. Compared with the HII nonimpaired group, the neuropsychologically abnormal schizophrenics were not different on any demographic or SPECT variable. Our findings raise the question of the clinical utility of these abnormal findings in schizophrenics.

NR440 Wednesday, May 25, 12 noon-2:00 p.m.

Acute Effects of Cigarette Smoking on CBF: A PET Study

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Summary:

Cigarette smoking has potent acute effects on peripheral blood flow, but its effects on cerebral blood flow (CBF) in humans remains unclear. If there is a substantial effect on CBF either acutely after smoking or upon withdrawal, such effects may confound the interpretation of CBF studies that compare schizophrenics to other groups, as the smoking rate in schizophrenia is extremely high. In order to examine this issue, we performed CBF studies on a sample of regular smokers using ^{15}O-H_2O positron emission tomography (PET).

Ten serial images were obtained over a period of approximately three hours. The only difference across each injection of ^{15}O-H_2O was the time since last cigarette, which ranged from about 12 hours (injection #'s 1 and 2) to one minute (injection #'s 3 and 8).

Preliminary results on a pilot sample of five subjects suggest a minimal acute effect on whole brain CBF after smoking, as well as a minimal withdrawal effect. The study is ongoing, and an expanded sample will be presented (anticipated N = 10), along with an examination of regional blood flow patterns in response to cigarette smoking.

This study suggests that cigarette smoking may not be an important confounder in CBF studies and may provide clues to the aspects of brain function that drive smoking behavior.

NR441 Wednesday, May 25, 12 noon-2:00 p.m.

SPECT Changes with Risperidone in the Elderly

Ileana Berman, M.D., Psychiatry, FDR VA Hospital, Mount Sinai Sch of Medicine, Montrose NY 10548; Julia Pavlov-Rachov, M.D., Mordechai Lorberboym, M.D., Claire Schaefer, Ph.D., Michael Pontecorvo, Ph.D., Miklos F. Losonczy, M.D.

Summary:

Introduction: Although there is evidence that schizophrenic patients may have altered regional cerebral blood flow (rCBF) patterns, the effect of novel antipsychotic drugs on rCBF is less clear. As part of an open-label study in a group of elderly schizophrenic patients the changes in rCBF induced by risperidone (a potent serotonin –S2 blocker) were examined using Single Photon Emission Computed Tomography (SPECT).

Method: Inclusion criteria for this study required subjects to be over age 65 and diagnosed as schizophrenic by DSM-III-R. One SPECT study was performed before the initiation of risperidone, while patients were on a typical neuroleptic that was discontinued before the initiation of risperidone. A second SPECT was performed after the patients had been treated with risperidone for at least three weeks. Both studies involved the injection of 10 mCi of HMPAO in a quiet, dimly lit room. Images were obtained using a dedicated head Tomomatic 564, which produces 8 contiguous 1.0 cm thickness slices. Photographic images were assessed by a nuclear medicine physician clinically and using an automated cortical segmentation process.

Results: Seven patients (age 66–81) completed the study. On the basis of the clinical ratings, at baseline all patients showed decreased rCBF in the frontal area. Also, these patients appeared to show rCBF asymmetry with decrease activity on the left side. Several weeks after the risperidone trial the overall clinical picture as measured by PANSS improved significantly. In addition, in all subjects, SPECT images following risperidone treatment were associated with a general reduction of rCBF in all areas relative to the most active regions (in the occipital cortex). Along with these clinical observations, additional quantitative analyses will be presented.

Conclusions: It is tempting to speculate that risperidone may enhance possible reductions of rCBF noticed at baseline in elderly schizophrenics. This could represent a possible therapeutic mechanism in which the partial compensatory reductions in frontal flow found under typical neuroleptic treatment are further decreased by risperidone. Further evidence based on larger double-blind studies are needed to address the issue.

NR442 Wednesday, May 25, 12 noon-2:00 p.m.

SPECT in Panic Disorder Pre- and Post-Treatment

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Summary:

Using single photon emission computed tomography (SPECT) and 99m Tc-hexamethylpropyleneamine oxime (HM-PAO), regional cerebral blood flow (rCBF) was assessed in seven patients with panic disorder before treatment and again following four weeks of treatment with Adinazolam. Diagnosis of panic disorder was established with the Structured Clinical Interview for DSM-III (SCID). Significant clinical improvement occurred as measured by change in the number of panic attacks/week (mean ± S.E. pretreatment = 10.1 ± 2.26; posttreatment = 1.4 ± 0.72 $p < 0.02$). SPECT images were obtained with a dedicated high-resolution multicamera system, and HM-PAO uptake was quantified for the superior frontal, inferior frontal, mesio temporal, and cerebellar regions bilaterally. The ratio of superior frontal activity/inferior frontal activity (S/I) was calculated in each subject for their pretreatment (study 1) and posttreatment (study 2) SPECT images. Subjects were independently rank ordered based on the degree of clinical improvement experienced during the study. A significant correlation was seen between the ratio of S/I study 2/S/I study 1 in the left frontal region and the independent rank order of clinical improvement (Spearman rank order correlation; $p < 0.02$). Patterns of left frontal rCBF distribution appear to differ between those subjects with the greatest clinical improvement in panic disorder and those with the least.

NR443 Wednesday, May 25, 12 noon-2:00 p.m.

Depression and Frontal Regional Cerebral Metabolic Rates of Glucose Correlate Inversely

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Summary:

Objective: To assess relationships between regional cerebral metabolic rates of glucose (rCMRglu) and clinical mood ratings.

Background: Prior studies have suggested an inverse correlation between depression ratings and frontal rCMRglu in patients with mood disorders.

Methods: Twenty-nine medication-free mood-disorder inpatients (9 UP, 8 BP1, 12 BP2) had fluorine-18 deoxyglucose positron emission tomography to measure rCMRglu while performing an auditory continuous performance task. Statistical parametric mapping (SPM) was used to assess correlations between mood ratings and normalized rCMRglu.

Results: Severity of depression as assessed by the Hamilton (for week of scan), and Bunney-Hamburg (both day of scan, and weekly mean for week of scan) depression ratings and severity of anxiety as assessed by the Spielberger state anxiety rating (for week of scan) correlated inversely with anterior mesial frontal lobe rCMRglu. Weekly Hamilton and Bunney-Hamburg depression ratings and Spielberger anxiety ratings also showed positive correlations with left posterior temporal rCMRglu.

Conclusions: Consistent inverse correlations between mood ratings and frontal lobe rCMRglu were observed across various rating instruments in a heterogeneous group of refractory unipolar and bipolar patients. This provides further evidence linking frontal lobe hypometabolism to mood disturbance in affective illness.

NR444 Wednesday, May 25, 12 noon-2:00 p.m.

Regional Cerebral Metabolic Rates of Glucose in Unipolar Versus Bipolar Depression

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Summary:

Objective: To assess differences in regional cerebral metabolic rates of glucose (rCMRglu) in depressed unipolar (UPdep) and bipolar (BP1dep, BP2dep) patients compared with healthy controls.

Background: Although studies suggest depression is associated with frontal cerebral hypoactivity, rCMRglu differences between UPdep versus BPdep remain to be demonstrated.

Methods: Twenty-three depressed, medication-free inpatients (8 UPdep, 9 BP2dep, 6 BP1dep) and age- and sex-matched healthy controls had fluorine-18 deoxyglucose positron emission tomography to measure rCMRglu while performing an auditory continuous performance task. Statistical parameteric mapping (SPM) was used to assess group differences in absolute rCMRglu.

Results: UPdep compared with controls had widespread (11,654 voxels out of 50,000 in the entire brain) decreases in frontal, posterior temporal, inferior parietal, incugulate, hypothalamic, and brainstem rCMRglu. BP2dep had sparse (34 voxels) scattered rCMRglu decreases. BP1dep had *increased* (1,675 voxels) anterior temporal, mesial occipital, and mesial frontal rCMRglu.

Conclusions: These data suggest that compared with controls UPdep is associated with regional hypometabolism (especially frontal), BP2dep with minimal rCMRglu changes, and BP1dep with anterior temporal hypermetabolism. These region and "polarity" rCMRglu differences are consistent with phenomenological, family history, and medication response differences between unipolar and bipolar depression.

NR445 Wednesday, May 25, 12 noon-2:00 p.m.

CBF After ECT for Depression

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Summary:

Objective: Studies by several groups (including ours), using brain single photon emission computed tomography (SPECT), have found deficits in regional cerebral blood flow (rCBF) localized to the left frontal cortex in depressed patients (Austin et al, 1992). This study was designed to test the hypothesis that treatment-responsive depressed patients would exhibit an increase in left frontal lobe rCBF following a full course of ECT.

Method: We have thus far examined eight acutely depressed hospitalized patients (6 women, 2 men; mean age ± SD = 53.8 ± 16.1 years). Scans using technetium labeled HMPAO (Ceretec) were performed on a high-resolution dedicated brain SPECT system 24–48 hours before the initial ECT, and follow-up SPECT studies were performed 24–48 hours after completion of a full course of ECT.

Results: Pre-ECT Hamilton Depression Rating Scale scores ± SD = 30.0 ± 4.5 and post-ECT scores ± SD = 11.75 ± 8.2 ($t = 5.73$, $df = 7$, $p < .001$). Following a full course of ECT there was a statistically significant increase in rCBF in the left frontal cortex ($t = 2.46$, $df = 7$, $p < .05$). None of the other four brain regions analyzed showed significant changes from baseline rCBF following ECT.

Conclusion: These findings, together with other studies (Kanaya et al., 1990), suggest that there is an increase in left frontal cortex rCBF following successful antidepressant treatment.

NR446 Wednesday, May 25, 12 noon-2:00 p.m.

Quantitative Morphology of the Corpus Callosum in Children and Adolescents: Effects of Age and Gender

Jay N. Giedd, M.D., Child Psychiatry, NIMH, 9000 Rockville Pike, Bethesda MD 20851; Deb Kaysen, B.S., F. Xavier Castellanos, M.D.

Summary:

Cerebral MRI scans of 50 males and 50 females, aged 5–18 years, were analyzed to evaluate the effects of age and sex on six subdivisions of the midsagittal cross-sectional area of the corpus callosum. In females all regions increased with age except the rostral body. In males only the isthmus increased significantly with age. With the exception of the isthmus, which increased steadily across all age groups (15–18 > 12–14 > 9–11 > under 9) the age effects were driven by smaller areas in the under 9 age group. The areas of the splenium and rostral body were larger in males than females, but not when corrected for total brain volume. The effects of age and sex on the morphology of the corpus callosum may be important in developmental neuroanatomical studies of normal and clinical populations.

NR447 Wednesday, May 25, 12 noon-2:00 p.m.

Symptom Activation and rCBF in OCD

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Summary:

Objective: To determine how regional cerebral blood flow (rCBF) changes in obsessive compulsive disorder (OCD) patients when symptoms intensify after combined pharmacological and behavioral challenge.

Background: Prior studies, mainly using resting-state paradigms, have implicated frontal and basal ganglia mechanisms in OCD. The mixed $5HT_{1/2}$ agonist m-CPP provokes symptoms in OCD patients, more effectively during concurrent behavioral challenge.

Methods: Five unmedicated OCD patients had Tc99m HMPAO SPECT studies after m-CPP (0.08 mg/kg i.v.) and after placebo infusion. m-CPP was given after imaginal exposure to symptom-related material, placebo after imaginal exposure to neutral material. Statistical parametric mapping (SPM) was used to assess overall within-subject changes in rCBF.

Results: After the activation procedure, rCBF increased most notably in the right medial temporal lobe, right mid-cingulate cortex, and right occipital cortex ($p < 0.05$ omnibus). rCBF decreased after activation in right and left frontal cortex. Ratings (NIMH Global OCD scale) and clinical impressions indicated that OCD symptoms and anxiety were worse after the activation procedure.

Conclusions: These preliminary findings suggest that alterations in rCBF may accompany expression of OCD symptoms. They also demonstrate the utility of high-resolution SPECT procedures for such studies.

NR448 Wednesday, May 25, 12 noon-2:00 p.m.

Intravenous Clomipramine for Clomipramine-Refractory OCD

Brian A. Fallon, M.D., Psychiatry, Columbia Univ NYSPI, 722 West 168th Street #13, New York NY 10032; Michael R. Liebowitz, M.D., Raphael Campeas, M.D., Franklin R. Schneier, M.D., Donald F. Klein, M.D., Sharon Davies, R.N.

Summary:

Background: Approximately 30% of patients with OCD do not respond or are only partially responsive to oral clomipramine (CMI). Case reports suggest that IV CMI is more effective and better tolerated than oral CMI. Preliminary results from our placebo-controlled study of IV CMI among patients with "CMI-refractory" OCD will be presented.

Methods: Refractory was defined as the persistence of clinical OCD despite an adequate trial of oral CMI. Each patient received 14 infusions on consecutive weekdays. Patients were rated by a blind evaluator at baseline, infusion #7, and infusion #14. Ratings: YBOCS, NIMH-OCD scale, HAM-D, CGI. Midway through the study, we added ratings at one week and one month post-IV.

Preliminary Results: In the double-blind phase, four of 21 (19%) patients randomized to CMI were responders vs. 0 of 17 on placebo ($p = .08$). The mean YBOCS improvement was 43% for the four IV CMI responders but only 10% for the 21 IV CMI patients as a whole. One week post-IV, five of 14 (36%) IVCMI patients were responders.

Discussion: IV CMI was safe but not helpful to most patients. Because the response increased with time, beyond the controlled design of this study definitive conclusions cannot be drawn. One in five patients, however, did seem to show sustained improvement.

NR449 Wednesday, May 25, 12 noon-2:00 p.m.

Cognitive Activation SPECT in Memory Disorders

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Summary:

Using single photon emission computed tomography (SPECT), ^{99m}Tc-HMPAO brain uptake was assessed twice. The first SPECT (base) was made during a basic condition of injection (with eyes opened). The second SPECT (activation) was carried out during the learning process of a visual memory task (MEP: Rey's Memory Efficiency Profile).

Fifteen nondemented patients (mean age = 64,7 – mean MMSE = 27,5) with memory complaints were included in the study. At the screening evaluation memory functioning was assessed with the Signoret memory battery scale (BEM). Using this test four subjects were considered to be normal and 11 to have objective memory disorders.

Regions of interest (ROI) were automatically delineated by a computer using the Talairach brain atlas. The measurement of the percent change from activation to baseline SPECT was calculated for each ROI by the index: counts per pixel (activation – base)/counts per pixel (Base) × 100.

Mean activation effect was higher in both right cerebellum and inferior temporal ROIs of the normal subjects when compared with the objective memory disorders patients. Furthermore, a positive correlation was observed between the activation effect measured by HMPAO in the in the above-mentioned ROIs and the cognitive scores (MEP and BEM).

NR450 Wednesday, May 25, 12 noon-2:00 p.m.

Personality Traits Correlate with Resting rCBF

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Summary:

Objective: To better understand the neurobiological basis for normal variants in personality.

Background: The Cloninger Tridimensional Personality Theory proposed that three dimensions of personality are functions of basal tone in distributed brain networks that are regulated by the neurotransmitters dopamine (DA), norepinephrine (NE), and serotonin (5HT).

Methods: In order to assess this theory, we used $H_2{}^{15}O$ PET to image 13 healthy volunteers at rest. We then administered the Cloninger Questionnaire, deriving total scores for novelty seeking, harm-avoidance, and reward-dependence, putatively related to DA, NE, and 5HT, respectively. PET scans were stereotactically normalized into Talairach space, analyzed using SPM, and correlations were performed between regional activity and the three personality dimensions.

Results: Resting rCBF in the brainstem and cerebellum positively correlated with higher scores on the harm-avoidance subscale ($r = .5$, $p < 0.01$). There was a trend for scores on the novelty-seeking subscale to correlate positively with rCBF in the brainstem and left caudate ($r = .3$, $p < 0.07$), i.e., areas with rich dopamine innervation.

Conclusions: These preliminary findings in healthy controls suggest there may be links between stable personality traits and rCBF at rest in regions known to be regulated by specific neurotransmitters. Functional neuroimaging techniques with flow agents or more specific neuroligands may help elucidate the neural correlates of personality.

NR451 Wednesday, May 25, 12 noon-2:00 p.m.

Magnetic Resonance Showing Basal Ganglia Volumes in Schizophrenia

Hiroto Hokama, M.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Martha

E. Shenton, Ph.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

Summary:

MR scans were obtained from 15 schizophrenics (SZ) and 15 normal controls (NCL) who were matched for sex, age (normals; mean = 38 years), handedness, and social class of origin. These subjects were part of a previous study that showed left lateralized volume reductions in temporal lobe structures, including amygdala/hippocampal, parahippocampal gyrus, and superior temporal gyrus. We here report basal ganglia volumes in this subject group. Previous studies have shown changes in overall volume in the basal ganglia in SZs; we here report the first study to evaluate subdivisions within this structure.

MR scans were obtained from a 1.5 Tesla magnet using a 3D Fourier-transform (3DFT) spoiled-gradient-recalled acquisition (SPGR). Voxel dimensions were: $0.9 \times 0.9 \times 1.5$ and the data were stored as 124 1.5-mm coronal slices. Automated segmentation procedures, 3D slice editing techniques that allowed reformatting of slices in different planes, and 3D surface rendering techniques were then applied to the data sets to create 3D representations of the basal ganglia, including the caudate nucleus, putamen, and globus pallidus. Volumes of these structures were also evaluated, and a significant increase in overall basal ganglia volume was observed in SZ ($F(1, 11.37) = 16.03$; $p \leq 0.001$; mean = 19.77 ± 2.57 for NCL; mean = 22.79 ± 2.56 for SZ). A statistically significant group X tissue interaction (subdivisions of basal ganglia-caudate, putamen, and globus pallidus) was also observed ($F(2, 2.90) = 25.37$; $p \leq 0.01$) and this was due primarily to the putamen (mean = 8.55 ml ± 1.15 for NCL; mean = 10.24 ml ± 1.01 for SZ). A significant laterality effect (left > right) was observed for both groups ($F(1, 9.2) = 25.37$; $p \leq 0.001$).

These data provide evidence for differences in basal ganglia subdivisions between groups; they are also consistent with recent reports of basal ganglia abnormalities in SZ based on MR (e.g., Jernigan et al., 1991; Lieberman et al., 1993) and post-mortem (e.g., Heckers et al., 1991) data. However, mechanisms related to increased tissue volumes are still unknown, although volume changes may be related to a disturbance in neuronal development or possibly to the chronic effect of neuroleptics.

NR452 Wednesday, May 25, 12 noon-2:00 p.m.

Three-Dimensional Brain Atlas From Magnetic Resonance Data

Hiroto Hokama, M.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Cynthia G. Wible, Ph.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

Summary:

Magnetic resonance (MR) data sets consist of two-dimensional (2D) slices that contain three-dimensional (3D) information. Radiologists traditionally analyze these 2D slices and reconstruct them mentally into 3D shapes in order to evaluate structural abnormalities. Up to now, 3D visualization techniques have not been applied to MR scans because the data were not adequate. Currently, however, with new acquisition sequences and new computer graphics methods, it is possible to analyze evaluate structures in 3D. We here present data from a project creating a human brain atlas from MR data. MR scans were obtained on a 1.5 Tesla magnet using 3D Fourier-transform (3DFT) spoiled-gradient-recalled acquisition (SPGR). Voxel dimensions were 0.9 by 0.9 by 1.5 and the data were stored as 124 1.5-mm coronal slices. Automated segmentation methods, 3D slice editing techniques that allow reformatting of slices in three different planes, and 3D surface rendering techniques were then applied to these data sets to show 3D representations of neuroanatomical regions of interest. Thus far, our human brain atlas depicts cerebral cortical gray matter (subdivided by lobe), cerebellum, brainstem structures including the pons and medulla, corpus callosum, basal ganglia structures, limbic system structures, and the ventricular system. Part of the white matter structure, including the corticospinal and the optic radiations are also reconstructed in 3D to show the proximal relationships of these brain structures. This digitized human brain atlas and features will be illustrated in a videotape as well as in photographic images. This atlas will be expanded and used to automatically register new MR data sets using nonlinear techniques ("brain warping"). This atlas also has the potential of serving as a basis for teaching neuroanatomy, since the spatial relationships can be more readily grouped when the student is able to view and rotate the structures in 3D space.

NR453 Wednesday, May 25, 12 noon-2:00 p.m.

Mood Effects on CBF Correlates with Emotional Self-Rating: ^{15}O Study

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Summary:

The effects of experimentally controlled mood states on cerebral blood flow (CBF) were studied. Quantitative brain images were acquired on a continuous slice PENN-PET scanner during four conditions while ^{15}O labeled water was infused. CBF and heart rate were measured in 18 normal subjects during standardized happy and sad mood induction, and during two nonemotional control conditions: sex differentiation and rest. Absolute CBF was calculated from counts in 54 regions that were placed on MRI scans of the subjects and transposed as a single unit onto the corresponding PET images. Region to whole brain flow ratios were analyzed. The changes in heart rate and total CBF were similar during all three activated conditions when compared with rest. Against this pattern of generalized activation there were lateralized and valence-specific effects of mood on CBF for subcortical, but not for frontal-temporal regions. CBF increased in the left amygdala and decreased in the right during sadness, relative to control conditions. These lateralized changes correlated with shifts toward negative affect. Correlations were opposite for the subcortical (negative affect associated with lower left hemispheric CBF) compared to the frontal-temporal cortical regions. The findings suggest a reciprocity between subcortical and frontal-temporal regulation of emotional experience.

NR454 Wednesday, May 25, 12 noon-2:00 p.m.

Learned Helplessness Produces Reciprocal CBF Changes in Mammillary Bodies, Amygdala and Hippocampus: A PET ^{15}O Study

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Summary:

The experimenters explored the question of whether learned helplessness is reflected in activation of discrete neuronal systems in the human brain. Learned helplessness was produced in 12 healthy humans by unsolvable cognitive problems. Solvable anagrams and resting baselines after each anagram task served as control conditions in a within-subjects design. Activation was measured by the equilibrium infusion method utilizing $H_2{}^{15}O$ PET on a continuous slice PENN-PET scanner during four conditions.

Absolute flow values were calculated from the counts in 54 regions of interest that were placed on MRI scans of the subjects and transposed as a single unit onto the corresponding PET images. Region to whole brain flow ratios were analyzed. Compared with solvable cognitive problems and rest as control conditions, helplessness resulted in a cerebral blood flow (CBF) increase to mammillary bodies and amygdala and a decrease in hippocampal activation. The solvable task condition produced a decrease in mammillary bodies activation and an increase in hippocampal activation. This suggests a cerebral network integrating negative emotion and cognition, with a reciprocal activation providing one potential neural substrate for learned helplessness and possibly depression.

NR455 Wednesday, May 25, 12 noon-2:00 p.m.

Three-Dimensional Magnetic Resonance Surface Measures of Planum Temporale in Schizophrenia

Martha E. Shenton, Ph.D., Psychiatry, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Hiroto Hokama, M.D., Ron Kikinis, M.D., Michelle Ballinger, Dorothy P. Holinger, Ph.D., Robert W. McCarley, M.D.

Summary:

We report a novel method for evaluating the planum temporale (PT) from MR scans (1.5 Tesla, 3DFT SPGR images) obtained from 15 schizophrenics and 15 normal controls who were matched for sex, age, handedness, and social class of origin (male, right-handed, mean age = 38 years). These subjects were part of a previous study that showed: 1) a 19% decrease in left anterior amygdala/hippocampus; 2) a 13% decrease in volume in left parahippocampal gyrus (vs. 8% on the right); and 3) a 15% decrease in volume in left superior temporal gyrus, with decreases in the latter being correlated r = −0.81 with amount of thought disorder. Here we evaluate the superior temporal gyrus more closely by focusing on the planum temporale, a region of the brian known to be an important substrate of language. This new method involved using well-established automated segmentation methods, 3D slice editing techniques that allow reformatting of slices in different planes, and 3D surface rendering techniques to create 3D representations of the cortical surface of the temporal lobe. "Computerized surgical cutting tools" were then used "to cut" the surface of the 3D rendered temporal lobe in order to separate the PT from the rest of the temporal lobe. This method is reliable and reduces the labor-intensive measurements of MR volume from serial slices. Moreover, preliminary data suggest differences in the PT between groups and indicate the utility of this method.

NR456 Wednesday, May 25, 12 noon-2:00 p.m.

Neuroimaging of Reaction Time Crossover with PET Reveals Cingulate Involvement

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Summary:

Reaction time "crossover" refers to a subject's inability to benefit from regular prepatory intervals (PI) compared to irregular PI's. This phenomenon has been observed in patients with schizophrenia as well as in their family members. In order to determine whether this phenomenon is associated with activation in discreet areas of the brian that may be relevant to schizophrenia, we studied regional cerebral blood flow (rCBF) in 11 normal male subjects under different conditions of the Shakow "crossover" reaction time (RT) task. This consists of three repetitions of a baseline motor task, an RT task with regular PI's and RT with irregular PI's. rCBF data were obtained over 1.5 minutes using bolus intravenous infusion of oxygen-15 radiolabeled water and positron emission tomography.

Scan data were assessed using statistical probability mapping software that stereotacticly normalizes images to allow statistical comparisons in groups of subjects under different cognitive activation conditions.

When comparing images form the irregular with the regular PI conditions, the first five subjects showed a major focus of activation in the anterior cingulate region. This focus was confirmed in the subsequent six subjects.

The results of this study suggest that RT "crossover" task may be promising in the study of schizophrenia, especially for assessing cingulate gyrus dysfunction.

NR457 Wednesday, May 25, 12 noon-2:00 p.m.

Neuroanatomical Correlates of Normal Human Emotion

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Summary:

Positron emission tomography (PET) was used to study 12 healthy female volunteers during three target emotions (happy, sad, and disgust) and three control conditions induced externally by six silent film clips and internally by recall of six autobiographical scripts. PET images of cerebral blood flow (CBF) were obtained using 40 mCi injections of ^{15}O-water, 60 second scans, and an interscan interval of 10–15 minutes. The three control scans were collectively subtracted from the average of the three emotion scans to compare and contrast the CBF patterns associated with external vs. internal emotion elicitation.

Film- and recall-generated emotion were both associated with CBF increases in medial frontal cortex and thalamus and decreases in right lateral prefrontal and parietal cortex, structures that could be involved in common experiential or expressive aspects of the elicited emotions. In comparison to recall-generated emotion, film-generated emotion was associated with greater symmetrical CBF increases in visual and heteromodal association areas, amygdala, hippocampal formation and lateral cerebellum, and greater decreases in anterior cingulate gyrus, structures that could participate in investing exteroceptive sensations with emotional significance. This study demonstrates neuroanatomical correlates of externally and internally generated human emotion.

NR458 Wednesday, May 25, 12 noon-2:00 p.m.

PET Measurement of Cerebral Metabolism with Acute Tryptophan Depletion in Remitted Major Depression

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Summary:

Objective: Studies using positron emission tomography (PET) and [F-18]2-fluoro-2-deoxyglucose (FDG) have shown a decrease in glucose metabolism in cingulate, caudate, and prefrontal cortex in patients with major depression at baseline. We have previously shown an increase in depressive symptomatology following acute tryptophan depletion in patients with major depression remitted on the serotonin reuptake inhibitor, fluoxetine. The purpose of this study was to measure glucose metabolism with PET FDG following acute tryptophan depletion and placebo in patients with major depression remitted on a serotonin reuptake inhibitor.

Methods: Patients were administered a 24-hour low tryptophan diet followed by a tryptophan-depleting drink or placebo. A 60-minute PET scan with eyes open was performed six hours after administration of the drink, MRI scans were obtained for coregistration using a surface matching program running on Analyze®, and behavioral ratings were obtained with the Hamilton Depression Scale and other measures. Regions of interest were defined based on specific criteria developed in conjunction with a neuroradiologist, drawn on the MRI, and templates transferred to the coregistered PET.

Results: Glucose metabolism decreased following tryptophan depletion in comparison to placebo in 4/5 patients in bilateral caudate, bilateral thalamus, bilateral putamen, left cingulate, and right prefrontal cortex, and in 3/5 patients in right cingulate, and left prefrontal cortex. Less robust changes were seen in occipital and temporal cortex. Patients who relapsed following tryptophan depletion (N = 2) had a decrease in metabolism in all regions following tryptophan depletion, while the one patient with a relapse on placebo increased metabolism in all regions following tryptophan depletion.

Conclusions: These findings suggest that the combination of PET and the tryptophan-depletion paradigm may represent a useful approach to the study of the neurobiology of depression.

NR459 Wednesday, May 25, 12 noon-2:00 p.m.

Functional MRI Shows Dynamic Deployment of Neural Resources

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Summary:

Functional MRI (FMRI) is a new technique for brain imaging with particular promise for studying psychiatric illnesses. In addition to its unparalleled anatomic resolution, FMRI has a three-second time resolution enabling assessment of relatively rapid changes in brain state. Moreover, since subjects are not exposed to radiation, they can be studied under different experimental or clinical conditions. Full application of FMRI to clinical issues, however, requires development of standardized methods of task presentation and data analysis that can evaluate dynamic aspects of brain function. We report here evidence that: 1) simple presentation of words in a passive listening task produces localized activation of the posterior superior and transverse temporal gyri (auditory receptive cortex); 2) activation is lateralized, with left usually greater than right; and 3) the area of activation expands as the rate of word presentation increases. Words were presented through headphones at rates of 10, 50, 90, or 130 per minute. Images were obtained using an echoplanar imaging sequence with 3.75 or 7.5 sec repetition time and 50 msec gradient echo time with a 2.1T Bruker Biospec spectrometer. Two (four subjects) or four (two subjects) axial-oblique, contiguous 5 mm thick slices were obtained with in-plane resolution of 3 × 6 mm. Activated voxels were identified by T-test comparison of signal intensity before and during word presentation.

NR460 Withdrawn

NR461 Wednesday, May 25, 12 noon-2:00 p.m.

Cerebral Perfusion in Heroin Addicts: A Tc-99m Exametazime SPECT Study

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Summary:

Evidence is accumulating that there has been a significant increase in the use of heroin in the United States. Surprisingly, little information is available on the effects of opiates on CBF and cerebral metabolism. The purpose of the present study was to determine whether CBF alterations are associated with heroin addiction and if these alterations persist during abstinence. Ten physically healthy male heroin addicts admitted to an inpatient drug rehabilitation unit were used as subjects. Each patient had a Tc-99m HMPAO SPECT scan twice during his inpatient rehabilitation, at one week after opiate discontinuation and two weeks later. The initial scans in nine out of 10 patients demonstrated significant, often discrete, cerebral blood flow defects, especially in the frontal and parietal cortices. Data quantification was achieved by calculating, in the midsagittal plane, the Tc-99m HMPAO uptake in discrete cortical regions and in the cerebellum, used as a standard. Repeat SPECT scans, done two weeks later, showed increased tracer uptake in the areas previously affected in the same nine patients as well as increased cerebral/cerebellar uptake ratios. All 10 subjects had normal CT scans or MRI imaging. This study demonstrates that opiates, like cocaine and alcohol, have a significant effect on cerebral blood flow. This study also reports a significant improvement in CBF after three weeks of abstinence. The degree of CBF reversibility needs to be assessed with a longitudinal study.

NR462 Wednesday, May 25, 12 noon-2:00 p.m.

Three-Dimensional Brain MRI Position Standardization

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Summary:

A method was designed to standardize the position of three-dimensional magnetic resonance brain images for reconstruction and morphometry. The method was implemented using GE MrX magnetic resonance imaging software. An estimated line connecting the anterior to the posterior commissaries (est. AC-PC line) was used as the target for position standardization. The original positions of a series of brain landmarks relative to the absolute scanner coordinates were used to define the estimated midsagittal plane and the AC-PC line. The deviation between the original scan position and the absolute position is defined as the angles of each of the axes: anterior-posterior (Z axis), transverse (X axis) and vertical (Y axis). The procedure can be described as a "picture frame" protocol consisting of two steps: (1) aligning the midsagittal plane of the brain to the standard sagittal plane of the MR coordinate system (Y-Z plane); (2) based on the corrected images from step 1, an estimated AC-PC line is drawn from additional landmarks by regression and used to calculate and correct rotation around the transverse axis. Validity and reliability of the method was tested. Rotational data from the three axes based solely on identification of selected landmarks was input into the MrX program for automatic reformatting into a standard position. This method enhances regional definition and improves the sensitivity of current morphometry methods.

NR463 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Religiosity in Liver Transplant Patients

Shimon S. Waldfogel, M.D., Psychiatry, Jefferson Med. College, 1020 Sansom Street, Philadelphia PA 19107; Lisa Marcucci, M.D., Michael J. Moritz, M.D., S.A. Westerberg, M.D.

Summary:

Background: The religiosity of the medical patient has been shown to have an impact on their well-being. It has been suggested that addressing the religious dimension of the patient would lead to improved well-being and enhanced satisfaction with life.

Objectives: To ascertain the role the various dimensions of religion play in the subjective well-being and life satisfaction of patients in a liver transplant program.

Methods: A questionnaire consisting of questions about beliefs, ritual, social, experiential, and consequential dimensions of religion was completed by 15 patients in the liver transplant program at a university hospital. The patients' responses were correlated with 1. Satisfaction With Life Scale (SWLS) and 2. RAND 36-item Medical Outcome Study (MOS).

Results: 14 of the 15 patients agreed that they believe in God. Most employ religious ritual in their coping. Most find contact with a clergy beneficial. While most do not believe their illness was the will of God, they believe that the transplant was the will of God.

Conclusion: Our preliminary findings indicate that religiosity is important to most of the patients in the study. In specific cases specific dimensions of religion play an important role in coping with severe liver disease.

NR464 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Predicting Depression in HIV Disorders

J. Hampton Atkinson, M.D., Psychiatry, Univ. Calif. San Diego, 9500 Gilman Drive 0603, San Diego CA 92093; Thomas L. Patterson, Ph.D., James L. Chandler, M.D., Igor Grant, M.D., Andres Sciolla, M.D., HNRC Group

Summary:

Objective: To determine two-year risk and predictors of major depression in human immunodeficiency virus (HIV) HIV-infected (HIV+) men and (HIV–) seronegative controls.

Methods: HIV+ (N = 136) and HIV– (N = 44) men participating in a longitudinal cohort study were examined annually for personal and family history of mood disorder (Structured Clinical Interview for DSM-III-R [SCID]; Family history RDC), neuropsychological (NP) status, magnetic resonance imaging (MRI), coping (Ways of Coping), and marked life adversity (Brown & Harris). Likelihood of major depression was computed by survival analysis and predictors were determined from a Cox proportional hazards model.

Results: Kaplan-Meier plot for time to major depression indicated overall (HIV+ and HIV–) risk of 7% for each six-month interval on study. Time to episode of depression was related to premorbid history of major depression (logrank test, $p < .001$) and avoidant coping ($p < .01$) with life circumstances in the six months preceding the depressive episode, but not to serostatus, NP or MRI, abnormality, or family history or life adversity. The two years cumulative risk was 48% for those with past history vs. 19% for those without prior major depression.

Conclusion: Careful psychiatric history-taking and coping assessment is crucial to identifying "high risk" for mood disorders in HIV.

NR465 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Clinical Efficacy and Tolerance of Paroxetine Therapy in HIV/AIDS Patients: 12-Month Experience of an HIV/AIDS Psychiatry Clinic

Jonathan L. Worth, M.D., Psychiatry, Mass General Hospital, Fruit St. Wang 812, Boston MA 02114; Mark H. Halman, M.D., Naomi M. Hamburg, B.A., Kathy M. Sanders, M.D., Anne D. Emmerich, M.D.

Summary:

Objective: To determine the clinical efficacy and tolerance of paroxetine therapy in HIV/AIDS patients.

Method: A retrospective chart review of all consecutive ambulatory HIV/AIDS patients begun on a paroxetine trial during the calendar year of 1993. Clinical response was classified according to symptom resolution. Patients underwent a semi-structured interview by a psychiatrist, Beck Depression Inventory (BDI), and a computer-based screening test for HIV-associated cognitive deficits.

Results: 4/23 (17%) patients did not return after the initial evaluation. Of the remaining 19 their mean age (SD) was 36 (7) years; 18 men and one woman. HIV/AIDS risk factors were homo/bi= sexual sex (n = 17) and injection drug use (n = 2). Classification by stage of HIV disease (CDC, 1992): asymptomatic = 6; non-AIDS-defining symptoms = 7; and AIDS-defining conditions = 6. Mean CD4+ lymphocyte count (SD) = 260 cells/μL (249). Ten were on either no HIV/AIDS medications or only treated with an antiretroviral; 9 were on ≥ 2 medications for AIDS-defining conditions. *DSM-III-R* (1987) disorders included: major depression (n = 13) (68%) and organic mood disorder (n = 4) (21%). Mean BDI score (SD) prior to pharmacotherapy = 24(9). 5/19 (26%) patients discontinued paroxetine after ≤3 weeks, all due to side effects, which was significantly associated (Fisher's exact) with concurrent treatment with ≥2 medications for AIDS-defining conditions (p = .011).

Of the 14 patients whose trial was ≥4 weeks 8 (57%) had either a moderate-full or complete response ("responders"). Of the six "non-responders" two (14%) discontinued paroxetine due to side-effects or poor response. Responders had significantly higher (ANOVA) mean group CD4+ cell counts (SD) and daily paroxetine doses (SD), as compared to non-responders: 462 (193) cells/μL vs. 143 (211) cells/mL ($p < .02$); and 22 (8) mg/day vs. 13 (4) mg/day ($p < .05$). Response was significantly associated with: early staged HIV disease (X^2; p = .02), and treatment with either no HIV/AIDS medications or only an antiretroviral (Fisher's exact; p = .001).

Conclusions: These findings suggest that paroxetine can be effective and well tolerated in HIV/AIDS patients. However, patients who are at advanced stages of HIV disease or who are on medications for AIDS-defining conditions may experience dose-limiting side effects or a less than full response.

NR466 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Pain and Psychological Distress in Intravenous Drug Users with AIDS

William Breitbart, M.D., Psychiatry, Memorial Hospital, 1275 York Avenue Box 421, New York NY 10021; Barry Rosenfeld, Ph.D., Steven D. Passik, Ph.D., Russell Portenoy, M.D., David Hewitt, M.D., Margaret McDonald, B.S., Kathy Grummon, M.A., Francisco Gil, M.A.

Summary:

Aims: To compare pain experience and associated psychological distress in intravenous drug users (IVDU's) with AIDS to that of non-IVDU's with AIDS.

Methods: 262 ambulatory patients with AIDS were surveyed. Assessment measures included: 1) Brief Pain Inventory (BPI), 2) Beck Depression Inventory (BDI), 3) Brief Symptom Inventory (BPI), 4) Beck Hopelessness Scale (BHS), 5) Sociodemographic and AIDS-related Medical Data, 6) Substance Abuse Classification.

Patient Characteristics: Mean age: 39; gender: 81% male, 19% female; race: 46% white, 31% black, 21% hispanic, 2% other; AIDS risk behavior: 44% non-IVDU (n = 116), 56% IVDU (n = 146); substance abuse status: 54% methadone maintenance (n =

79), 33% inactive IVDU (n = 47), 13% active IVDU (n = 18); 85% met 1993 CDC criteria for AIDS (n = 205).

Results: IVDU's and non-IVDU's were comparable (no significant differences) as to number of pains reported (2.5), pain prevalence (67% vs. 57%), average pain intensity (BPI-VASPI 6.1 vs. 5.5), pain relief and pain interference. IVDU's reported more psychological distress (BSI = 116.6 vs. 100.7, $p < .005$), depression (BDI = 20.1 vs. 15.9, $p < .005$), and hopelessness (BHS = 7.9 vs. 6.2, $p < .05$) than non-IVDU's. Both IVDU's and non-IVDU's with pain reported more psychological distress (BSI, $p < .005$) and depression (BDI, $p < .001$) than patients without pain.

Conclusion: Despite comparable pain experience, IVDU's with AIDS report significantly greater levels of psychological distress and depression than non-IVDU's with AIDs.

NR467 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Anatomic Correlates of Cerebral Blood Flow Abnormalities in HIV

Renee M. Dupont, M.D., Psychiatry, VAMC, 3350 La Jolla Village Drive, San Diego CA 92161; Terry Jernigan, Ph.D., Patricia Lehr, Ph.D., Guy Lamoureaux, M.D., Samuel Halpern, M.D., Igor Grant, M.D.

Summary:

Background: The etiology of cerebral perfusion abnormalities (CPA) in HIV infection reflects vascular, cortical, and/or subcortical pathology. We hypothesized that perfusion defects represent, in part, a cortical deafferentation correlating with the extent of white matter pathology. The extent of regional CPA, as well as their clinical correlates were assessed.

Methods: 66 HIV positive (+) individuals were studied using IMP SPECT imaging and magnetic resonance (MR) imaging. SPECT images were process using a cortical mapping method (Lamoureaux et al 1990), with quantitation of absolute and relative regional cortical activity. Standard MR images were processed using a method for quantitation of pixels meeting criteria for cortical and subcortical grey matter, cortical and subcortical fluid, and abnormal white matter (hyperintensities) (Jernigan et al, 1991). To determine relationships between the SPECT and MR data sets, a single canonical correlation using all variables from each set was performed.

Results/conclusion: Three significant canonical correlations were produced. The first strongly implicates contributions from white matter abnormalities to frontal, parietal, and temporal CPA. The second suggests lenticular volume loss correlates with frontal CPA, and the third that thalamic volume loss is associated with temporal CPA. Clinical data demonstrating that frontal perfusion abnormalities are more prevalent in advanced disease, and are strongly associated with global neuropsychological will be presented.

NR468 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Cerebrovascular Response in HIV Infection

Renee M. Dupont, M.D., Psychiatry, VAMC, 3350 La Jolla Village Drive, San Diego CA 92161; Patricia Lehr, Ph.D., David Yeung, M.D., Samuel Halpern, M.D., Guy Lamoureaux, M.D., Igor Grant, M.D.

Summary:

Cerebral perfusion abnormalities (CPA) in HIV positive (+) individuals are largely attributed to neuronal dysfunction. However disturbance of vascular structure and function is reported in HIV infection. We hypothesized that independent cerebrovascular dysfunction contributes to CPA. We predicted that response to acetazolamide (a vasodilatory stimulus) would be abnormal in HIV positive (+) individuals.

Methods: 11 HIV+ and 11 HIV negative (–) subjects were studied. No subject had a history of intravenous drug use or stimulant abuse. All subjects were injected with the blood flow tracer Tc-99 HMPAO under two conditions: (1) In an eyes closed, quiet state without acetazolamide and (2) 25 minutes following the injection of 1000 mg of acetalozamide 1000 mg. Data were analyzed using a cortical uptake mapping method (Lamoureaux, et al 1990).

Results: Based upon preliminary analysis of seven controls subjects and 10 HIV positive subjects, increases in tracer uptake were seen in all controls except one, but only 5/110 HIV + subjects. HIV+ individuals demonstrated a lower mean increase in tracer uptake than controls 10.4% vs 25.6% $p < .025$). The T4% correlated positively with response to acetazolamide in HIV+ subjects ($r^2 = .6$; $p < .02$).

Conclusion: Abnormal response to acetazolamide is associated with early stages of HIV infection. Possible etiologic mechanisms include maximal vasodilation at rest "rest" and/or aberrant cerebrovascular response to a chemical stimulus. Results implicate primary vascular pathology as one contributing etiology for CBF defects.

NR469 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

HIV and Tuberculosis Among the Homeless Mentally Ill

Mary R. Stock, M.S.W., Psychiatry, LSU Medical School, 1542 Tulane Avenue Room 125, New Orleans LA 70112; Mark H. Townsend, M.D., Irma J. Bland, M.D., Kathleen W. McCaffery, M.S.W.

Summary:

The prevalence of HIV and tuberculosis (TB) among the homeless mentally ill population is unknown. Some have suggested that the mentally ill homeless are at higher risk of acquiring HIV and TB than those homeless persons without a diagnosed mental illness. In order to test this hypothesis, we reviewed 337 medical records of a municipal homeless clinic in a large southern city. Seventy-eight were those of all patients with a diagnosed mental illness, and the remaining charts were randomly selected. Regarding HIV, 65% (N = 51) of the mentally ill patients were tested and 5 (9.7 %) were positive; 50% (N = 129) of the non-mentally ill patients were tested and 8 (6.2%) were positive. Thirty-five percent (N = 27) of the mentally ill were tested for TB, and five were positive (18.5%); Forty-three percent (N = 112) of the non-mentally ill were tested, of whom 32 were positive (28.6%). Among other variables, the homeless mentally ill were more likely to be local residents ($p < 0.01$), and were less likely to be currently using alcohol or street drugs ($p < 0.001$). In conclusion, the prevalence of HIV and TB in our samples was equivalent between both groups. The mentally ill population appeared much less mobile and less likely to be using drugs or alcohol.

NR470 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

HIV Disease and Sexual Functioning in Intravenous Drug Using Men

Heino F.L. Meyer-Bahlburg, Ph.D., HIV Center, NYS Psychiatric Inst., 722 West 168th Street, New York NY 10032; Curtis L. Dolezal, Ph.D., Theresa M. Exner, Ph.D., Anke A. Ehrhardt, Ph.D., Wafaa El-Sadr, M.D., Stephan J. Sorrell, M.D.

Summary:

Objective: To evaluate longitudinally sexual functioning in HIV+ injected-drug using (IDU) men.

Method: Between December 1988 and 1989, N = 144 IDU men, 83 HIV+ and 61 HIV– (excluding patients with AIDS), mostly African-American and Hispanic, were recruited from two hospital settings in Manhattan for a three and a half year study of the

natural history of HIV disease. A comprehensive battery of medical and behavioral assessments was administered every six months; it included a systematic sexual history interview. All categories of sexual dysfunctions listed in *DSM-III-R* were assessed (as continuous variables rather than diagnoses) along with several global ratings and composite scales of functioning. The two HIV groups were compared over time.

Results: Significantly more HIV+ men than HIV– men reported difficulties with sexual desire, sexual pleasure, and erectile functioning. Only few men reported marked specific dysfunctions other than sexual desire, and the corresponding group differences were not significant. There was no significant decline of sexual functioning over time. Those who subsequently died functioned less well than the surviving HIV+ men.

Conclusions: Asymptomatic and low-symptomatic HIV disease in IDU men is associated with increased rates of difficulties in sexual functioning, especially of sexual desire.

NR471 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Evaluation of Factors Related to Retention of HIV-Positive Patients in Ambulatory Psychiatric Treatment

Cheryl Ann Kennedy, M.D., Psychiatry, UMDNJ-NJ Med School, 185 S. Orange Avenue MSB-E501, Newark NJ 07103; Joan H. Skurnick, Ph.D., Monica M. Lintott, Ph.D.

Summary:

Injecting drug use and heterosexual behavior account for over 60% of HIV transmission in NJ. Our purpose was to examine factors influencing retention of ambulatory HIV-positive patients referred for psychiatric care. Subjects were 164 patients enrolled in a mental health clinic established for HIV/AIDS patients. Of these, 88% reported prior substance use and 60% reported active use at intake. Patients were 75% black, 18.6% Hispanic; 61% were male; average age was 36 (range 21–60 years). All patients were enrolled in individual psychotherapy and/or psychopharmacology as needed.

Results: As of December 1993, 95 (58%) had dropped out of treatment (i.e., not appearing for appointments nor responding to two letters and phone calls). Being male ($p = 0.007$), reporting past substance use ($p = 0.002$), or current use ($p = 0.02$) predicted which patients were more likely to drop out of treatment.

Discussion: Psychological distress and substance use are known to affect sexual behavior. These data suggest that successful mental health treatment must specifically address substance use especially in a population at risk for transmitting of HIV. Further investigation to determine factors which account for why some substance users stay in treatment is warranted.

NR472 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Compliance Patterns in a Child Psychiatry Outpatient Consultation/Liaison Unit

Ilisse R. Perlmutter, M.D., Psychiatry, NYU Medical Center, 178 East 80th Street Apt PH-F, New York City NY 10021; Suellen Carney, Psy.D., H. Paul Gabriel, M.D., Richard Oberfield, M.D., Raul Silva, M.D.

Summary:

Objective: Children's increasing mental health requirements necessitate appropriate referrals to child psychiatry. Noncompliance impedes service delivery. This study examined referral and compliance patterns between outpatient pediatrics and outpatient consultation/liaison psychiatry.

Method: Charts of 285 patients ages 2 to 18 years old consecutively referred by ambulatory pediatrics to the attached child psychiatry consultation/liaison clinic at Bellevue Hospital were retrospectively reviewed for: 1) gender, 2) age, 3) ethnicity, 4) referral source, 5) reason for referral, 6) pediatric diagnosis, 7) *DSM-III-R* Axis I diagnosis, and 8) compliance with psychiatric evaluation. Data analysis included frequency statistics and chi-square analyses.

Results: 28.1% of patients were noncompliant with psychiatric evaluation. Regarding reasons for referral, there were significant differences in compliance between patients referred for somatic complaints and those referred for suicidality ($X^2 = 4.21$, $p = 0.04$). 41.9% of somaticizing patients were noncompliant, compared to 12.5% of those with suicidal ideation. A marginally significant difference among referral sources occurred between child life specialists and social workers ($X^2 = 2.31$, $p = 0.10$). Social workers referred the highest rate of noncompliant patients (43.8%); while child life referred the lowest (16.7%).

Conclusions: Reason for referral and referral source discriminated noncompliers. The implications of suicidality may encourage compliance with psychiatric intervention. In contrast, somaticizers may deny psychiatric components of illness, possibly explaining high noncompliance rates. We discussed how a consultation/liaison clinic within pediatrics may increase service delivery based on proximity and accessibility which may help promote compliance.

NR473 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Major Depression and Irritable Bowel Syndrome: Is There a Relationship?

Prakash Masand, M.D., Psychiatry, SUNY HSC, 750 E. Adams Street, Syracuse NY 13210; David Kaplan, M.D., Sanjay Gupta, M.D., Amar N. Bhandary, M.D., George Nasra, M.D., Mark Kline, M.D.

Summary:

Irritable bowel syndrome (I.B.S.) has been reported in 10% to 22% of adults. Seventy percent to 90% of patients with I.B.S. who seek medical attention have psychiatric comorbidity most commonly major depression. In contrast, very few studies have looked at the prevalence of I.B.S. among psychiatric patients. Using a structured clinical interview to look at the prevalence of irritable bowel syndrome, we compared 58 patients seeking treatment for depression to an age- and sex-matched control group of patients who were seeking treatment in a general physicians office for other medical illnesses. The control group did not have any Axis I disorders. I.B.S. was diagnosed according to the criteria of Drossman et al. Fifty percent of the patients with major depression met criteria for I.B.S. in contrast of 2.5% of the control group ($p < .00001$). Patients with major depression and irritable bowel syndrome were more likely to report symptoms of weakness ($P = .009$), heartburn ($P = .009$), and nocturnal bowel movements ($P = .005$). There were no differences between the study group and the control group or the two subgroups of patients with major depression (those with and without I.B.S.) on other demographic variables.

NR474 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Ovarian Cancer Risk: Adherence to Recommendations

Kathleen N. Franco, M.D., Psychiatry, Cleveland Clinic, 9500 Euclid Avenue Desk P68, Cleveland OH 44195; Jerome Belinson, M.D., Graham Casey, Ph.D., Marion Piedmonte, M.S., Sarah Plummer, B.S.

Summary:

Ovarian cancer has become the fourth leading cause of cancer-related deaths in women. Although not all ovarian cancer is inherited, the most important known risk factor is a strong family history.

The gene BRCA-1 on chromosome 17_q21, carries a lifetime risk of nearly 90% by age 70.

Women often experience distress when learning about their familial risk. In addition to the Brief Symptom Inventory (BSI), Death Anxiety Scale (DAS), and Multidimensional Health Locus of Control (MHLC), a questionnaire was mailed to 127 women of the Familial Ovarian Cancer Registry to assess health care practices and early detection recommendations.

Of the 83 (65%) who responded, 73% (n = 59) had physical examinations, 75% (n = 61) PAP testing, 59% (n = 47) mammograms, 48% (n = 39) breast self-exams, or 22% (n = 18) all at recommended intervals. An elevated DAS score was associated with failure to have a gynecological examination (p = 0.029). Increased influence by a powerful other (MHLC) was correlated with obtaining a mammogram (p = 0.012) at the recommended time, as well as having a gynecological examination and PAP smear along with the mammogram (p = 0.05). Women with higher levels of education scored significantly lower on 11 scales/subscales of distress. Those women who currently reported feeling anxious, experiencing behavioral symptoms of anxiety, or attending a support group scored significantly higher on many subscales. Generally, psychiatric distress (BSI) was higher than nonpatient norms, but lower than psychiatric outpatients.

Women were generally well adapted, although there were those with greater levels of anxiety needing additional support. Locus of control may influence adherence and help identify diverse approaches for individual patients to promote healthy self-care.

NR475 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Medical Evaluations of Emergency Psychiatric Patients

James M. Schuster, M.D., Psychiatry, Allegheny General, 320 East North Avenue, Pittsburgh PA 15212; Ole J. Thienhaus, M.D.

Summary:

The necessity of medical evaluation of all emergency psychiatric patients has never been evaluated. Patients with concurrent medical and psychiatric complaints typically receive medical as well as psychiatric evaluations in emergency settings. However, patients with solely psychiatric complaints often do not receive medical evaluations in emergency settings. This study compared the rate of medical complications noted after admission to psychiatric units in two different institutions. In one institution all psychiatric patients receive medical evaluations in the emergency department. At the other institution only patients who present with concurrent medical complaints receive medical evaluations prior to their admission to the psychiatric units. Review of admissions from both institutions found no difference in the number of patients who required transfer to a medical unit from the psychiatric unit. In addition, there was no difference in the number of concurrent medical problems among the two populations. The results suggest that patients with schizophrenic spectrum illnesses as well as organic mental disorders were more likely to suffer medical complications after admission to a psychiatric unit and the medical status of patients with those disorders should receive closer scrutiny in emergency settings.

NR476 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Alcohol Level at Head Injury and Subsequent Psychotropic Treatment During Trauma Critical Care

Peggy E. Chatham-Showalter, M.D., Psychiatry, Legigh Valley Hospital, 1243 S. Cedar Crest Blvd #2800, Allentown PA 18103; Wayne E. Dubov, M.D., Michael Rhodes, M.D., Maria C. Barr, Pharm.D., Jyh-Ming Sun, B.S., Thomas Wasser, M.Ed.

Summary:

Alcohol intoxication at the time of trauma presents vexing and serious complications in treating patients with traumatic brain injury (TBI). Prior studies have shown that intoxicated TBI patients are more agitated and require longer ventilatory support. Psychiatrists are called to consult on agitation in these complex patients. This is the first reported data on psychotropic medication dosages administered to TBI patients in the critical care setting. The assessment method was concurrent record review of all patients 15 years or older with TBI as a primary or secondary diagnosis and a blood alcohol level (BAL) drawn before admission to trauma critical care. BAL positive patients (n = 14) had a mean BAL of 210.7 mg%, were older (p = .095), had lower admission Glascow Coma Scores (p = .031), and spent more days on respirators (p = .125), with longer trauma critical care stays (p = .160) than the BAL zero patients (n = 21), which makes our population similar to others reported. The BAL positive group received more days of narcotics and benzodiazepines and received markedly higher average daily doses. For these differences to be statistically significant at a power of 0.8, a sample size of approximately 80 per group would be necessary. These initial results are a basis for future studies examining the relationships between treatment variables and outcomes for TBI patients and the development of specific medication guidelines.

NR477 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychiatric Problems in Left Ventricular Assist Device Patients

Peter A. Shapiro, M.D., Psychiatry, Columbia University, 622 W. 168th Street Box 427, New York NY 10032

Summary:

Objective: To describe clinical problems encountered by the psychiatrist in the care of patients treated with the left ventricular assist device (LVAD) as a bridge to heart transplantation.

Method: Retrospective review of clinical course and psychiatric intervention in a consecutive series of severely ill patients who received a LVAD. All patients were initially screened by a psychiatrist as part of their evaluation for transplantation. Outcomes of interest included psychiatric diagnoses and predominant issues in psychotherapy with LVAD patients and their families.

Results: Twelve patients received a pneumatically powered LVAD, and two an electrical LVAD. There were two early deaths (one pneumatic LVAD, one electric LVAD patient). Psychiatric diagnoses made in the follow-up period were: adjustment disorder (seven cases), organic mental disorder (five cases), and major depressive episode (two cases). Significant family distress prompted psychiatric counseling for family members in four cases. Some patients had more than one problem requiring intervention, and in only three cases was there no psychiatric intervention. Five patients underwent heart transplantation; of these, one had postoperative psychiatric complications.

Conclusions: Symptoms of psychiatric disorder are common in patients treated with a LVAD for severe heart failure, but may be ameliorated with treatment.

NR478 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Desipramine Deaths May Be Adrenergic

Charles W. Popper, M.D., McLean Hospital, Harvard Medical School, 115 Mill Street, Belmont MA 02178

Summary:

Four unexplained cases of sudden death in children during desipramine treatment have raised concerns about its routine use in children, and brought puzzlement about why imipramine

(metabolically converted to desipramine) has not been associated with sudden deaths. Although the relevance of overdose data to sudden death in children during desipramine treatment is speculative, the risks of fatality following overdose with different tricyclic antidepressants were calculated, using single drug ingestion and mortality figures in the national poison control database (1985–1992). In children (ages 6–17), the risk of fatality following desipramine overdose is 1.04%, compared to 0.22% for desipramine ($p < 0.0005$). A comparable differential risk between desipramine and imipramine was also found in adults (1.04% vs 0.40%, $p < 0.0005$). The lethality of desipramine overdose was not greater in children than adults. Overdose lethality profiles for eight antidepressants were then compared to their relative neuropharmacological, neuroreceptor, and cardiotoxic effects. Direct myocardial and neuroreceptor properties showed only weak correlations. A strong significant correlation was found with norepinephrine reuptake inhibition. These data suggest that there is an excess overdose mortality of desipramine over other tricyclic antidepressants in both children and adults, and that sympathetic overstimulation of the heart may be a relevant mechanism.

NR478-A Wednesday, May 25, 3:00 p.m.-5:00 p.m.

A Fifth Case of Sudden Death in a Child Taking Desipramine

Brian Zimnitzky, M.D., Department of Psychiatry, Children's Hospital, 300 Longwood Avenue, FEGAN 8, Boston, MA 02115; Charles W. Popper, M.D.

Summary:

Although antidepressants are generally viewed as safe when used as prescribed, three cases of sudden death in children taking desipramine were reported in 1990. The children, ages 7 and 8, were being treated with ordinary doses of desipramine, were believed to have received adequate medical monitoring, self-injury was not suspected, and there was no evidence of overdose. A fourth case, reported in 1993, has led to increased concern about the routine use of desipramine in child psychiatry. Clinical information of these cases is sparse, but three of the four cases are known to have involved death during or just after physical exertion.

This poster will describe the fifth case of non-overdose sudden death in a child. Clinical history, neurological and medical status, cardiac monitoring, and circumstances of death will be reported, based on public documents (coroner's report, autopsy report, and postmortem toxicology), medical records, and interviews of family members will be presented.

All 5 reported cases of sudden deaths during treatment with tricyclic antidepressants in children have invloved desipramine. Further investigation is needed to uncover possible additional cases of sudden death in children being treated with tricyclic antidepressants, so that risk assessment can be more accurately addressed.

NR479 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Prediction of Psychiatric Outcome in Liver Transplantation

Marian Fireman, M.D., Psychiatry, Portland VA Med. Center, 3710 SW Veterans Hospital Road, Portland OR 97207; Roland M. Atkinson, M.D., John M. Rabkin, M.D., C. Wright Pinson, M.D.

Summary:

Objective: This study examines the results of psychiatric evaluations of liver transplant candidates, the incidence of psychiatric diagnoses in pre and postoperative transplant patients and which preoperative psychiatric diagnoses predicted postoperative psychiatric complications.

Method: All 121 patients evaluated since the liver transplant program at the Portland VA Medical Center was established received psychiatric assessment, including record review, patient interview, and mental status evaluation. All patients transplanted were followed by the psychiatric consultant pre and postoperatively.

Results: 105/121 (87%) patients had one or more psychiatric diagnoses, including substance use disorders (79), delirium (40), personality disorders (17), PTSD (11), major depression (9), and adjustment disorders (3). Eighty-seven were accepted for transplant and 48 have been transplanted to date. Psychosocial factors were important in 11 of 17 cases in which transplant was denied; intractable psychosis, severe nonreversible cognitive deficits, and active substance abuse were present in these patients. Postoperative psychiatric consultation was requested for 30 patients (63%) for issues including affective disorders, delirium, PTSD, adjustment disorders, cognitive disorders, and anxiety disorders.

Conclusions: The prevalence of preoperative psychiatric diagnoses and incidence of postoperative psychiatric complications in liver transplant patients exceeds 60%. Analysis of the data shows no clear predictors of postoperative psychiatric complications on the basis of preoperative psychiatric diagnosis but some trends are noted. Patients with histories of affective disorders, delirium, and PTSD may be at increased risk for development of similar disorders postoperatively.

NR480 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Age, Gender and Post-Ethanol Acetate Metabolism

Thomas P. Beresford, M.S., Psychiatry, University of Colorado, VAMC 116 1055 Clermont Street, Denver CO 80220; Joseph Schwartz, M.D., Michael R. Lucey, M.D.

Summary:

In earlier human studies, we noted that, compared to younger subjects, non-alcoholic elderly subjects are 1) more sensitive to ethanol, and 2) demonstrate cerebral blood flow alterations in relation to ethanol but not acetate blood concentration This study assessed acetate metabolism differences in relation to age and gender as a partial explanation of these findings.

Method: 57 subjects (28 male, 29 female) were studied, 28 in the young (21 to 40 years) and 29 in the old (>60 years) cohort. Hypochlorhydric subjects were excluded as were those with gastric or intestinal pathology or slowed gastric emptying. All subjects received ethanol (0.3 grams/kg) on three occasions: 1) orally after an overnight fast, 2) orally after a standard breakfast, and 3) IV after a standard breakfast. Blood acetate was represented by area under the curve (AUC) in 240 minutes.

Results: Average AUC's for old and young females were strikingly different in all three metabolic states (old > young, $p < 0.002$). In contrast, blood acetate AUC's did not separate old from young males. Viewed by gender, elderly women reached acetate levels 22% to 34% higher than elderly men. Differences were most striking in the oral non-fed state ($p < 0.002$) but were significant in the other metabolic states as well (oral fed, $p < 0.04$; IV non-fed, $p < 0.02$). Young females did not differ from young males in acetate AUC.

Conclusions: These data suggest an influence of age on acetate metabolism that appears specific for elderly females. The mechanism underlying this age/gender effect probably reflects altered enzymatic metabolism of acetate that may be genetically determined. Phenomenologically, high acetate levels may in part account for lessened alcohol use among non-alcoholic elderly women.

NR481 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Correlation of Age at Onset of Dementia with Regional Cerebral Glucose Metabolism in Alzheimer's Disease

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Summary:

AD is probably a disease of heterogeneous etiology. In an effort to identify subgroups of AD based upon AAO of AD and regional brain metabolism, we used 18-FDG PET (Scanditronix PC-1024-7B, 6mm FWHM) to measure rCMRglc in 57 screened healthy patients with possible or probable AD diagnosed according to NINCDS-ADRDA criteria (23 female, 34 male). The AD patients had a mean AAO of AD = 62.7 ± SD9.6 years (range 40–79), mean duration of illness to time of evaluation = 5.4 ± SD2.9 years, mean Folstein Mini Mental Status Exam (MMSE) = 16.6 ± SD8.1. Patients were scanned at rest (eyes patched, ears occluded). Absolute values of rCMRglc were referenced to the mean of sensorimotor and calcarine regions. There was no significant correlation of dementia severity, MMSE score, education, or duration of illness with AAO of AD. In spite of a difference in AAO of AD between sexes ($t(55) = 2.23$; $p < 0.05$), a multiple regression analysis for each brain area showed no significant interaction of sex by AAO of AD. We therefore collapsed across sexes to examine the relationship of AAO of AD to rCMRglc. There was a highly significant positive correlation of AAO of AD with rCMRglc of left ($r = 0.342$, $p < 0.01$) and right ($r = 0.389$, $p < 0.003$) superior temporal cortex and left ($r = 0.504$, $p < 0.0001$) and right ($r = 0.402$, $p < 0.002$) parietal cortex, but not with prefrontal or premotor cortex, basal ganglia, thalamus, motor cortex, or primary sensory cortex. Moreover, all four subregions of the parietal cortex measured showed a significant positive correlation with AAO of AD, suggesting greater dysfunction throughout the parietal cortex in those with earlier onset of AD. These results confirm our previous finding of lower parietal lobe metabolism in early onset AD, compared with late onset AD, and extends this finding to the superior temporal region. These findings suggest that some characteristic of posterior association cortex in younger brain results in greater vulnerability to the neuropathology of AD.

NR482 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Site Variability in a Geriatric Depression Trial

Gary W. Small, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles CA 90024; Lon S. Schneider, M.D., Susan Holman, M.S., Alexander Bystritsky, M.D., Barnett S. Meyers, M.D., Charles B. Nemeroff, M.D.

Summary:

Objective: A recent multicenter clinical trial for geriatric depression found no significant difference in $HAMD_{17}$ change scores and a significantly greater remission (last $HAMD_{17} \leq 8$) rate for fluoxetine compared to placebo (31.6% vs. 18.6%, $p < 0.001$). Such industry-sponsored trials routinely use multicenter designs, and clinical site variability may influence outcome but is generally overlooked.

Methods: Data were analyzed from each of 30 sites of a double-blind, placebo-controlled, six-week trial of fluoxetine 20 mg daily. After a one-week placebo lead-in, 671 patients were randomized. Outpatients were ≥60 years, met *DSM-III-R* criteria for unipolar major depression, and had baseline $HAMD_{17}$ scores ≥16. Effect size (ES), expressed as mean difference between effects divided by the pooled SD of the effects, was calculated for each site.

Results: ES ranged from −0.57 (favoring placebo) to 1.36 (favoring fluoxetine) for $HAMD_1$;7 % change scores, and from −0.91 to 1.84 to % remitters. Large, positive ESs ($d \geq 0.80$) based on mean $HAMD_{17}$ % change was found at only three sites, moderate ES (0.40 to 0.79) at eight, and minimal ES (0 to .39) at six; ESs favored placebo at 12 of the 30 sites. For % remission, ESs were distributed similarly. University sites showed a fluoxetine ES only half that of private clinics.

Conclusions: Considerable heterogeneity among clinical sites could account in part for modest overall active drug response in this trial. Lack of interrater reliability, "blindability," research site, and financial incentive could contribute to such heterogeneity.

NR483 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Depressive Symptoms in Alzheimer's Disease and Multi-Infarct Dementia

William E. Reichman, M.D., Psychiatry, UMDNJ-RWJMS, 667 Hoes Lane P.O. Box 1392, Piscataway NJ 08855; Andrew C. Coyne, Ph.D.

Summary:

Depressive symptoms accompanying dementia can lead to enhanced subjective distress, excess functional disability, and increased caregiver burden. We examined the prevalence of major depression, depressed mood/anhedonia, and subjective and neurovegetative symptoms of depression that were unaccompanied by depressed mood/anhedonia in patients with clinically-diagnosed Alzheimer's disease and multi-infarct dementia. The specificity of subjective and neurovegetative depressive symptoms for depressed mood in dementia was examined. One hundred five dementia diagnostic clinic outpatients who met *DSM-III-R* criteria for Alzheimer's disease (AD) ($n = 67$) or multi-infarct dementia (MID) ($n = 38$) were screened for the presence of major depression, depressed mood/anhedonia, and other depressive symptoms in the absence of depressed mood. Depressed mood/anhedonia was frequently noted in both the AD (40.3%) and MID (34.2%) groups. One or more depressive symptoms, not accompanied by depressed mood/anhedonia, were also common in AD and MID (49.3% and 36.8%, respectively). Major depression was relatively uncommon in AD (10.5%) but was noted more frequently in MID (29.0%). Among AD patients, neurovegetative symptoms of depression were not any more common in patients with depressed mood/anhedonia than in those without depressed mood/anhedonia. Subjective symptoms of depression in AD patients were also not significantly associated with depressed mood/anhedonia. The study highlights the importance of viewing major depression, depressed mood/anhedonia, and other depressive symptoms (subjective and neurovegetative) as separate entities in AD and MID.

NR484 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Presentation of OCD in the Elderly

Robert Kohn, M.D., Psychiatry, Brown University, Butler Hosp 345 Blackstone Blv, Providence RI 02906; Robert J. Westlake, M.D., Steven A. Rasmussen, M.D., Richard T. Marsland, R.N.

Summary:

Objectives: There has been no systematic study of the clinical features of obsessive compulsive disorder (OCD) in the elderly. This study describes the patterns of OC symptoms and comorbidity with other psychiatric and medical disorders in 32 patients age ≥60 meeting OCD *DSM-III-R* criteria.

Methods: To study the clinical presentation of this disorder among elderly, we examined 633 patients presenting to an OCD clinic. The YBOCS, NIMH OCD Scale, and a 41-item current symptom questionnaire were administered. Age was investigated as a continuous and categorical measure.

Results: The elderly had later onset (x = age 33.6) compared to younger patients ($x = 20.4$, $p < 0.05$). No differences were found

in severity of symptoms on YBOCS. Elderly had more ($p < 0.05$) concerns about symmetry, fear of sinning, need to know, and counting rituals. Hand washing was less common ($p < 0.05$). Increasing age was ($p < 0.05$) associated with symmetry, magical thinking, need to know, re-reading, dressing or washing rituals, ordering, and touching compulsions. Axis I comorbidity was high (p = ns).

Conclusion: There are few differences in clinical features of OCD due to aging. Clinicians need to be alert to the possibility of diagnosing OCD in elderly patients presenting with anxiety or depression.

NR485 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Cognitive Decline and Olfaction in Older Depressives

Diane L. Amend, Ph.D., Psychology, University of Arizona, Room 312, Tucson AZ 85721; Iris R. Bell, M.D., Alfred W. Kaszniak, Ph.D., Josh Miller, Ph.D., Jacob Selhub, Ph.D.

Summary:

Objective: This prospective study compared elderly depressives with and without baseline olfactory identification dysfunction to evaluate cognitive change at six months and possible relationships to elevated cortisol and an excitotoxic amino acid (Sapolsky 1992). Olfactory dysfunction may be a nonspecific early finding in Alzheimer's disease. Many late-onset depressives progress over time to irreversible dementias, but previous research has not identified specific markers for such decline.

Method: Subjects were 30 community dwelling elderly (mean age 77 ± 6 yrs; 77%F/23%M) recruited by newspaper advertisement with and without depression and cognitive difficulties. At baseline and six-month follow-up, subjects completed the Geriatric Depression Scale (GDS), the Alzheimer's Disease Assessment Scale (ADAS), the Folstein Mini-Mental State Examination (MMSE), the Cain Olfactory Identification Test, baseline 8 am plasma cortisol levels (CORT), a 0.5 mg. dexamethasone suppression test (DST), and plasma homocysteine (HC). 29/30 completed all cognitive measures at follow-up, and 27 completed both cognitive and blood measures.

Results: Subjects were divided into four groups based on baseline scores on the GDS (≥15 vs <15) and Cain test (≥8 vs <8): depressed with and without impaired olfaction (DEP/IMP OLF; DEP ONLY) and nondepressed with and without impaired olfaction (IMP OLF only; NORMALS). Groups were compared with analyses of covariance, controlling for age. There were significant main effects for depression group on baseline MMSE ($p = 0.03$) and ADAS ($p < 0.0001$) as well as a main effect for olfaction group on baseline ADAS ($p = 0.04$). DEP/IMP OLF were the most cognitively impaired at baseline on both measures (MMSE: $p = 0.04$; ADAS: $p = 0.09$). On follow-up, the DEP/IMP OLF tended to demonstrate the greatest cognitive loss (ADAS difference score: $p = 0.056$). The groups with impaired olfaction had higher baseline cortisol (18.9 vs 17.1; $p = 0.05$) and a trend toward more HC (12.9 vs 8.6; $p = 0.06$).

Conclusions: Depressed elderly with olfactory deficits show the greatest baseline cognitive dysfunction and the largest six-month loss of cognition. Poor olfaction is associated with relative elevations of both CORT and HC, perhaps consistent with neurotoxic damage in olfactory pathways.

NR486 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Depression and Suicide in Old Age: A Tragedy of Neglect

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Summary:

Objective: To investigate the incidence and treatment of depression in geriatric suicide.

Method: All coroners' records, autopsy, and police reports for suicides aged 65+ in Ontario (n = 540) in 1989, 1990 and 1991 were examined.

Results: Over 86% of those diagnosed as depressed were untreated. 13.1% received antidepressants (84% tricyclics, 0% SSRIs). 19.3% were treated with tranquilizers. Females were three times as likely to be treated as were males and those seeing psychiatrists were four times more likely to be treated with antidepressants than those seeing GPs. Few of those suffering from terminal illnesses (2.6%), cancer (5.6%), heart attacks (3.9%) or strokes (7.7%) were treated for depression.

Conclusions: Over 70% of elderly suicides received no psychiatric referral and although 33.5% had been diagnosed as depressed, only 13.1% received antidepressants. Tricyclics, which are lethal in overdose, were the drugs of choice. None were treated with the safer SSRIs. Few of the medically ill were treated for depression. These findings strongly indicate early geropsychiatric assessment and vigorous treatment could prevent many suicides in old age.

NR487 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Risperidone in Elderly Psychotic Patients

Ileana Berman, M.D., Psychiatry, FDR VA Hospital, Mount Sinai Sch of Medicine, Montrose NY 10548; Julia Pavlov-Rachov, M.D., Kammalama Duvvi, M.D., Amalia Merson, M.D., Michael Pontecorvo, Ph.D., Miklos F. Losonczy, M.D.

Summary:

Introduction: Previous trials have shown that risperidone is an effective antipsychotic agent causing minimal anticholinergic and parkinsonian symptoms. There are no studies, however, that looked at the safety and tolerance of risperidone in elderly patients. The present study is an open-label trial designed to assess the safety and tolerance of risperidone in a group of elderly patients.

Method: Twelve psychotic patients (age 66 to 81, mean of 71) entered the study. Ten patients met the *DSM-III-R* criteria of schizophrenia. They received placebo for one to five days and then risperidone which was increased from 2 mg to 6 mg daily over three days. The patients were assessed psychiatrically and cognitively before risperidone and during the treatment using Positive and Negative Symptom Scale (PANSS), Clinical Global Improvement (CGI), and cognitive tests such as Minimental Examination (MME) Digit Symbol Test (DST), Digit Span (DS), and verbal fluency.

Results: The patients tolerated risperidone well. All patients tolerated up to 6 mg of risperidone and had stable vital signs, no significant ECG changes or drug induced laboratory abnormalities. Two months after the treatment one patient developed SIADH which resolved after the drug discontinuation. Our patients showed minimal clinical change after one week but ANOVA results suggested significant improvement in PANSS and CGI after three weeks of treatment ($p = 0.003$ and, respectively, $p = 0.05$); the positive and general symptoms seemed to improve more than the negative symptoms. Also, the patients showed significant improvement of MME ($p = 0.002$), verbal fluency ($p = 0.03$), DST ($p = 0.02$), and DS ($p = 0.05$).

Conclusions: According to this open-label study it appears that risperidone is a safe drug in elderly patients. In addition, the patients' psychiatric condition seemed to improve along with the cognitive tests. This is, however, an open-label trial and other controlled studies are necessary to support the present findings.

NR488 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Late-Life Dysphoria in Nursing Home Residents

Andrew Satlin, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Adam Burrows, M.D., Carl Salzman, M.D., Kenneth W. Nobel, M.D.

Summary:

Objective: To determine the rate and characterize the nature of untreated depressive syndromes among elderly patients in long-term care facilities.

Method: The 495 residents without advanced dementia in a 725-bed academic long-term care facility (mean resident age = 88) were screened for daily depressive symptoms by nurses using a standardized instrument. Of the 110 subjects identified, 58 were not receiving antidepressants. Twenty-one of these were excluded for the following reasons: severe dementia (n = 9); acute medical illness (4); aphasia (3); uncooperative (2); died before interview (2); schizophrenia (1. The remaining 37 subjects and their primary nurse caregivers were videotaped during a structured clinical interview, and were independently rated by four trained clinicians using the Cornell Scale for Depression. We recorded separate scores for the caregiver and patient interviews. A geriatric psychiatrist assigned *DSM-III-R* diagnoses.

Results: Eight subjects met criteria for major depression (MAJOR), six had no affective diagnosis (ND), and 23 were a heterogeneous group, with depressive syndromes not meeting criteria for major depression (MINOR). Cornell scores showed large differences between the groups on the patient-rated scores (ND = 3.8 ± 1.6; MINOR = 7.0 ± 2.6; MAJOR = 16.5 ± 3.5), but smaller differences for caregiver ratings (ND = 9.6 ± 6l6; MINOR = 10.1 ± 4.3; MAJOR = 12.4 ± 3.5). There were no significant differences in Mini-Mental State scores among the groups, suggesting that depressive symptoms in the MINOR group could not be accounted for by overlap with dementia features.

Conclusions: Our findings suggest that nursing assessment may identify a large number of untreated nursing home residents with depressive symptoms, and that many of these have atypical affective syndromes that require further diagnostic classification and therapeutic trials.

NR489 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Impact of a Geriatric Delirium Service

Martin G. Cole, M.D., Psychiatry, St. Mary's Hospital, 3830 Lacombe, Montreal Quebec H3T 1M5, Canada; Francois J. Primeau, M.D., Robert F. Bailey, M.D., Michael J. Bonnycastle, M.D., Filippo Masciarelli, M.D., Frank Engelsmann, Ph.D.

Summary:

We conducted a randomized clinical trial to determine if systematic detection and intervention in elderly medical inpatients with delirium was effective in reducing cognitive impairment, abnormal behaviors, functional disability, length of hospital stay, and mortality. Patients aged 75 or over admitted to the medical services of a primary acute care hospital were screened within 24 hours of admission. 88 patients with delirium (*DSM-III-R* criteria) were detected and enrolled in the trial: 42 were randomly allocated to the treatment group and 46 to the control group. Patients in the treatment group received a geriatric specialist consultation and follow-up by a liaison nurse. Cases were assessed on enrollment and 1, 2, 4, and 8 weeks later using the Short Portable Mental Status Questionnaire (SPMSQ) and the Crichton Geriatric Behavioral Rating Scale (CGBRS). The beneficial effects of detection and intervention were very small. There was a significant difference in SPMSQ scores between treatment and control groups at two weeks, but differences of other measures between treatment and control groups were not statistically significant. Cases without dementia or with a specific causal factor were more likely to improve. In future trials, the effect of detection and intervention procedures might be increased by two strategies: improved targeting of patients most likely to benefit or increased intensity of intervention.

NR490 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Clinical Correlates of Postmortem Brain Serotonin Levels in Alzheimer's Disease

Brian A. Lawlor, M.D., Psychiatry, St. James Hospital, James's Street, Dublin-8, Ireland; Linda M. Bierer, M.D., Theresa M. Ryan, B.S., Vahram Haroutunian, Ph.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Post-mortem neurochemical abnormalities have been described in the serotonin (5-HT) system in Alzheimer's disease (AD). To explore the clinical correlates of these 5-HT changes in AD, the relationship between levels of 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) in temporal cortex and clinical symptoms prior to death was examined in 23 patients with autopsy confirmed AD. There was a significant negative correlation between the degree of cognitive impairment, as measured by the Alzheimer's Disease Assessment Scale (ADAS), and the level of 5-HT in Brodmann area 21. However, no significant correlations were found between behavioral measures (ADAS subscales for agitation, psychosis, and depression) and the level of 5-HT or 5-HIAA in temporal cortex. These data suggest that decrements in the level of 5-HT in temporal cortex are associated with the degree of cognitive, but not behavioral disturbance in AD.

NR491 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Plasma MHPG and Clinical Symptoms in Alzheimer's Disease

Brian A. Lawlor, M.D., Psychiatry, St. James Hospital, James's Street, Dublin-8, Ireland; Linda M. Bierer, M.D., Theresa M. Ryan, B.S., Lizette L. Williams, B.A., Peter J. Knott, Ph.D., Richard C. Mohs, Ph.D.

Summary:

Post-mortem findings point to significant abnormalities in central noradrenergic function in Alzheimer's disease (AD) which may be reflected by changes in peripheral markers. In this study, the relationship between the peripheral noradrenergic marker, plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) and clinical symptoms was examined in 26 patients with probable AD. All patients were placed on a low MAO diet for at least three days prior to testing. Plasma MHPG was measured at 10:45 and 11:00 a.m. after an overnight fast, and the basal MHPG calculated as the average of these two baseline samples. Subjects were rated using the Alzheimer's Disease Assessment Scale (ADAS). Basal MHPG levels correlated significantly with increased cognitive impairment ($r = 0.61$, $p = 0.001$), controlling for age, age of onset, and gender, but not with the degree of behavioral disturbance in AD. These results suggest that plasma MHPG increases as cognitive function in AD deteriorates, possibly mirroring noradrenergic neuron fallout associated with disease progression.

NR492 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Caregiver Assessment of Depression in Patients with Probable Alzheimer's Disease

Bernardo Arias, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue Ste 702, Miami FL 33136; Miguel Alfonso, M.D., Steven Sevush, M.D.

Summary:

It has been suggested that caregivers of patients with probable Alzheimer's disease (PAD) overestimate patient depression because: a) they project their own depressed mood onto the patient; and b) they place undue weight on dementia-related vegetative signs. We examined these possibilities by: a) comparing caregiver assessments of patient depression with caregiver self-assessments of their own mood (N = 154); and b) determining the relative contributions of ideational vs. vegetative signs to the caregivers' assessment of patient depression (N = 40). Caregiver assessments of patient depression utilized a seven-item quantitative questionnaire. The CES Scale for Depression was used to measure caregiver depression.

Results: Caregiver assessments of patient depression did not correlate with caregiver CES scores (Pearson R = .05, p = .5). Caregiver assessments of patient depression correlated more strongly with ideational measures (pessimism, R = .41; helplessness/hopelessness, R = .58; low self-esteem, R = .59) than with vegetative measures of patient depression (psychomotor retardation, R = .26; impaired sleep, R = .26; impaired appetite, R = .29). These results support the validity of caregiver assessments of PAD depression by suggesting that caregivers neither project their own depression onto patients nor base their assessment of patient depression unduly on dementia-related vegetative signs.

NR493 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Cortical Metabolic Deficits are Related to Subcortical Pathology in Vascular Dementia

David L. Sultzer, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles CA 90024-1759; Jeffrey L. Cummings, M.D., Michael E. Mahler, M.D., Wilfred G. Van Gorp, Ph.D., Charles Brown, M.D., William H. Blahd, M.D.

Summary:

Objective: To examine the relationship between structural subcortical pathology and cortical metabolism in patients with vascular dementia.

Method: Eleven elderly patients with vascular dementia who demonstrated *no* lesion involving the cerebral cortex on MR image underwent ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) to assess cortical metabolism. Subcortical lesions on MR images (periventricular hyperintensities, deep white matter hyperintensities, and subcortical lacunar infarcts) were measured using a visually-guided graded scale of severity. Mean FDG uptake in each cortical lobe and global mean uptake within the hemisphere were calculated using the PET image maps of regional FDG uptake.

Results: Patients with unilateral subcortical lesions had ipsilateral reductions in cortical FDG uptake. Two patients with subcortical lesions that predominantly affected the posterior subcortical white matter had associated reductions in biparietal or bitemporal metabolism. Mean cortical hemispheric FDG uptake was associated with extent of periventricular hyperintensities in ipsilateral anterior subcortical regions (p = .01). Patients with lacunar infarcts of the basal ganglia or thalamus had lower mean metabolic rates in the frontal lobe compared to patients without such lesions (p = .13).

Conclusions: Cortical metabolic dysfunction is related to subcortical pathology in patients with vascular dementia; lesions of subcortical nuclei may have a specific effect on metabolism in the frontal cortex. The profile of psychiatric symptoms in patients with vascular dementia likely reflects subcortical pathology.

NR494 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Self-Awareness of Memory Impairment

Hilary T. Hanchuk, M.D., Geriatric Psychiatry, COPSA UMDNJ-RWJ Med., CMHC 667 Hoes La P.O. Box 1392, Piscataway NJ 08855-1392; Andrew C. Coyne, Ph.D., William E. Reichman, M.D., Neil Cederbaum, B.S.

Summary:

Essential to psychiatric evaluations is assessment of judgment, insight, cognitive impairment and self-image. Disturbance in self-awareness of severity of one's own cognitive impairment is not only common but also contributes to inappropriate treatment. This study examined the correlates of impaired self-awareness. Charts of 109 outpatients in a dementia clinic were reviewed. Seventy-one (65.1%) patients had a diagnosis of Alzheimer's disease (AD); 5 (4.6%) vascular dementia (VaD); 19 (17.4%) mixed dementia (AD plus VaD); and 14 (12.8%) received other diagnoses. Females comprised 72.9%; average age 74.3 (±8.5); average Folstein MMSE 16.0 (±6.2). Sixty-five percent of all AD patients whereas 40% of VaD had no awareness of their memory deficits. Patients were categorized to those with **some insight** into their deficits and those with **no insight.** The two groups did not differ in average age, duration of illness, or years of education (p's > .05). Patients with some insight displayed significantly higher MMSE, $t(107) = -3.15$, $p < .01$; lower Blessed Dementia Rating, $t(83) = 3.89$, $p < .001$; and lower Clinical Dementia Rating (CDR), $t(42)$, $p < .01$. Chi-square analyses indicated that there were no significant differences across the two insight groups as to gender distribution, visuospatial skills, or previous history of depression (p's > .05). Whereas among patients with insight, mood disorders were more prominent while among those with no insight, delusional disorders were more frequent $X^2 = 6.51$, $p < .05$. These findings emphasize that issues of self awareness of deficits (impaired in 2/3 of all AD patients) must be kept in mind by all health care providers.

NR495 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Agitation in Alzheimer's Disease and Vascular Dementia Patients

Enid Rockwell, M.D., Psychiatry, University of Calif., 3350 La Jolla Village Dr 116A, San Diego CA 92161; Edward Jackson, M.D., Dilip V. Jeste, M.D.

Summary:

Introduction: Agitation is one of the most disabling concomitants of dementia. To our knowledge no published large-scale study has ever examined the difference between Alzheimer's disease (AD) patients and Vascular dementia (VD) patients with respect to agitation.

Methods: 1,552 outpatients evaluated at nine university-based research centers in California from 1985 to 1992 were diagnosed with probable AD and 283 with VD, using *DSM-III* and NINCDS-ADRDA criteria. All patients underwent extensive psychiatric, neurologic, neuropsychological, and social evaluations in addition to the usual dementia workup. Minimum Uniform Dataset Manual was used, and every attempt was made to standardize and operationalize all definitions. Agitation was assessed on the basis of intake examination of the subjects.

Results: The point prevalence of agitation was higher in the VD group (36.0%) than in the AD patients (32.6%), (p < 0.0001, McNemar chi-square). Agitation was most common (68.5% in AD and 79.5% in VD) in patients with both delusions and depression, while it was least common (18.5% in AD and 19.6% in VD) in patients without either delusions or depression. In both dementia groups, patients with agitation performed worse on Mini-Mental State and Blessed Examinations (p < 0.002) than nonagitated patients.

Comment: This large-scale outpatient study showed that approximately a third of the patients with dementia have agitation at a given point in time. We will discuss the possible psychopathological and therapeutic implications of the observed associations of agitation.

NR496 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychiatric Symptoms of Dementia: Results in a Population-Based Sample

Isabelle M. Paquette, M.D., Psychiatric Geriatric, Hosp. Louis H Lafontaine, 7401 Rue Hochelaga, Montreal QC H1N 3M5, Canada; Bernadette Ska, Ph.D., Yves JoAnette, Ph.D., Francine Giroux, M.Sc.

Summary:

Objective: Non-cognitive symptoms of dementia have important diagnostic and management significance both for patients and their caregivers. Recent clinical studies suggest a high prevalence of delusions, hallucinations, and depression in dementia. Epidemiological data, however, are still uncommon. In this study, depressive symptoms, hallucinations, and delusions were investigated in a population-based sample of demented subjects.

Method: The subjects originate from the Montréal segment of the Canadian study on health and aging, designed to determine prevalence of Alzheimer's type dementia (DAT). A random population-based sample of 720 subjects over 65 were screened for cognitive impairment using the 3MS (Modified mini-mental state. A score below 79 (N = 121) led to an extensive clinical examination (medical, neurological, and neuropsychological); caregivers were administered a CAMDEX questionnaire. Delusions, hallucinations, *DSM-III-R* criteria and diagnosis of depression were identified.

Results: Thirty-seven cases of dementia, including 25 DAT, were identified. Nineteen percent had psychotic symptoms; 19.4% had depressed mood; other criteria for depression were frequent but nonspecific and did not suggest a mood disorder except for one subject.

Conclusions: Even in an epidemiological sample of subjects with dementia, psychiatric symptoms are frequent and therefore should not be considered atypical. More research is needed to characterize these manifestations in unselected samples.

NR497 Withdrawn

NR498 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Folate and Dementia

David A. Casey, M.D., Psychiatry, University of Louisville, Norton Psych Clin Box 35070, Louisville KY 40232; Charles A. Class, M.D., Tony A. Bouldin, B.S.

Summary:

A retrospective chart review examination of 210 inpatients admitted to a geriatric psychiatry ward during the span of 12 months in 1992 and 1993 was performed. Each chart was examined for demographic information, Axis I, Axis II, and Axis III diagnoses, and CBC indices. This information was found primarily in the lab work-up contained in each chart. Of the 210 inpatients examined, 120 had Axis I diagnosis of dementia and subsequently their folate and B-12 levels were monitored upon admission. Only four (3.3%) of the 120 patients diagnosed as demented were found to have low levels of blood folate. In no cases could the dementia be clearly established to be caused by the folate deficiency. In light of the relatively low frequency of folate deficiency among geriatric patients with diagnoses of dementia found in this study, the cost effectiveness of the routine administration of the folate blood examination with such patients should be more closely examined.

NR499 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Beta-Amyloid Peptide Fragment Channel Formation in the Etiology of Alzheimer's Disease

Bruce L. Kagan, Ph.D., Psychiatry, UCLA Medical School, 760 Westwood Plaza, Los Angeles CA 90024; Tajib Mirzabekov, Ph.D., Meng Chin Lin, B.S., Peter J. Marshall, B.A., Ivan Lieberburg, M.D.

Summary:

Significant evidence implicates the β-amyloid peptide (Aβ) in the etiology of Alzheimer's disease (AD). Aβ is found in the hallmark senile plaques and neurofibrillary tangles of AD and can be toxic to neurons in culture, perhaps by dysregulation of intracellular Ca^{+2} levels. Aβ can be produced in vivo by processing the amyloid precursor protein APP. We have found in preliminary studies that a neurotoxic Aβ fragment (Aβ 25–35) can form channels in lipid bilayer membranes. These channels are voltage-dependent and are permeable to a wide variety of ions, including sodium, potassium, calcium, and chloride. Ionic disturbances resulting from channel formation might lead to neuronal cell death. We propose that the channel-forming properties of Aβ 25–35 may play a role in the etiology of AD.

NR500 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Older Age and the Under Reporting of Depressive Symptoms

Jeffrey M. Lyness, M.D., Psychiatry, University of Rochester, 300 Crittenden Blvd, Rochester NY 14642; Christophe Cox, Ph.D., Jennifer Curry, B.A., Yeates Conwell, M.D., Deborah A. King, Ph.D., Eric D. Caine, M.D.

Summary:

There have been suggestions that older people underreport depressive symptoms. Several studies have noted only a modest degree of correlation between examiner-rated and self-reported standardized depressive symptom scales. To our knowledge no published studies specifically focused on age effects. We examined this issue in 97 psychiatric inpatients, ages 21 years and older, with *DSM-III-R* major depression, using the Beck Depression Inventory (BDI) as the self-report measure and the Hamilton Rating Scale for Depression (Ham-D) as the examiner-rated assessment. Age was not significantly correlated with Ham-D. However, age was independently and negatively associated with BDI. Gender, education, age of onset of depressive illness, and medical illness burden were not independently associated with BDI. Examination of depressive symptom subtotals (psychologic/affective versus somatic/neurovegetative) revealed that only the self-reported psychologic/affective subtotal was significantly associated with age. We conclude that some older patients with clinically significant major depression underreport their symptoms. When asking older patients about depressive symptoms, clinicians should view negative responses only within larger clinical context. Similar concerns must temper interpretation of research that relies on subject self-report to study depression in late life.

NR501 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Treatment of Psychosis in the Non-Demented Elderly

Carolyn M. Mazure, Ph.D., Psychiatry, Yale University Sch 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.

Summary:

Low neuroleptic doses have been the standard for treating acute psychosis in the elderly due to concern about the potential for

adverse reactions. Yet, it remains unclear if low dose treatment is effective in the *non-demented* elderly with psychotic illness, and in what period of time acute response might be expected. The current work is one of the first preliminary examinations of acute response to fixed low dose neuroleptic in this population. All patients (median age = 72; range = 65–82) were non-demented (as assessed on MMSE; WAIS-R), hospitalized for recent onset psychosis (median episode duration = 28 days) and scored >3 on at least one of three BPRS psychosis items (median pretreatment BPRS total = 34). *DSM-III-R* diagnoses were: schizophrenia (N = 5), manic psychosis (N = 6), psychotic depression (N = 13), delusional disorder (N = 3). Method: 20 consecutive patients were given 0.15 mg/kg/day of perphenazine (median dose = 9 mg) for 10 days; a subgroup of eight patients who failed to respond to 0.15 mg/kg/day were increased to 0.3 mg/kg/day for an additional 10 days; and a third group of seven consecutive patients received 0.3 mg/kg/day (median dose = 16 mg) for 10 days to determine if a higher dose would affect 10-day response rate. Results: (1) In the 0.15 group, 10-day response rate was poor (25%) and significantly lower than the 10-day response rate (54%) in an historical control group of 66 younger patients given 0.5 mg/kg/day of PPZ (Fisher Exact Test = .01). (2) Seven of eight patients who failed to respond to 0.15 mg/kg/day and were increased to 0.3 mg/kg/day for 10 days showed a good response. (3) In the 0.3 group however, only two of seven met response criteria in 10 days. These pilot data suggest that response to neuroleptic develops over a three-week period in the *non-demented* elderly compared to a shorter duration in the non-elderly, and that an increase in dose from 0.15 to 0.3 mg/kg/day does not appear to speed acute response.

NR502 Withdrawn

NR503 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Temazepam 7.5 mg: Sleep Effects in Elderly Insomniacs

Anthony Kales, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Alexandros N. Vgontzas, M.D., Edward O. Bixler, Ph.D., David Myers, B.A., Anthony Centurione, M.A.

Summary:

The literature on efficacy and side effect profiles of benzodiazepines in the elderly is limited, particularly in light of the extent of their use in this patient population. In the elderly, the use of benzodiazepines at dose levels similar to those used for the non-elderly is associated with a much higher frequency of adverse reactions. There is a clear need in the elderly for a hypnotic drug that is effective in the lowest possible dose and produces a minimum of adverse reactions. Accordingly, we evaluated a reduced dose of temazepam (7.5 mg) in the sleep laboratory in eight elderly insomniacs using a 14-night protocol (four placebo-baseline nights, seven drug nights, and three placebo-withdrawal nights). With short-term use, temazepam was found to be effective, producing a significant improvement in total wake time from baseline. With continued drug administration, total wake time remained below baseline but not significantly so. During drug administration, there were no major CNS and behavioral side effects reported such as daytime sedation, amnesia, and other cognitive impairments of hyperexcitability (daytime anxiety). Following drug withdrawal, there was no significant increase in wakefulness, i.e., no rebound insomnia. In summary, temazepam 7.5 mg is effective in elderly subjects with short-term use and has a minimum of side effects. Use of hypnotic drugs is an adjunctive therapy which should be for a short-term period with subsequent short-term intermittent use as needed. Temazepam can be effectively used in this intermittent manner because of its low propensity for producing hyperexcitability states (daytime anxiety during drug use and rebound insomnia following withdrawal).

NR504 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Managing Disruptive Behavior in the Elderly

Elaine Souder, Ph.D., Psychiatry, Univ. Ark Med. Sciences, 4301 W. Markham MS 529, Little Rock AR 72205; Kim Heithoff, Sc.D., Patricia S. O'Sullivan, Ed.D.

Summary:

Objective: This study was designed to examine the relationship between rankings of the severity of 36 disruptive behaviors given by experts and rankings of behaviors in terms of actual time required to manage. Disruptive behaviors were defined as observable actions that had negative consequences and were socially unacceptable or isolating.

Methods: A prospective study was conducted using a sample of 153 institutionalized VA patients, mean age = 72.6 (10.8). Data regarding time to manage 36 behaviors were collected over 21 consecutive shifts for each patient. 26 geropsychiatric experts ranked the severity of 36 disruptive behaviors, and demonstrated high interrater agreement (ICC = .97). Expert rankings were statistically associated with mean time to manage each behavior.

Results: Overall, average time to manage a disruptive behavior was 23.4 minutes (range 5–211 minutes, SD = 33.5). Kendall's tau, a nonparametric coefficient of agreement, was .16 (p = .16). For example, one of the least disruptive behaviors identified by experts, "talks constantly," ranked sixth in actual time to manage with an average of 27 minutes.

Conclusion: This degree of discrepancy suggests further studies are needed to determine 1) the basis experts are using to frame their estimates, and 2) the appropriateness of interventions ∴at patients are receiving.

NR506 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Lithium Augmentation in Geriatric Major Depression

Paul A. Kettl, M.D., Psychiatry, Penn State Hershey, P.O. Box 850, Hershey PA 17033

Summary:

Since DeMontigny, et. al.'s classic article[1] on the usefulness of lithium augmentation for the treatment of resistant major depression, a variety of studies have more closely examined the usefulness of this technique. However, little information is available on its use in geriatric patients.

We reviewed the usefulness of one week of lithium augmentation of an existing antidepressant in treatment of *DSM-III-R* major depression in 14 patients hospitalized in a university-based geriatric psychiatry unit. All had failed at least 12 days treatment of another antidepressant. Lithium 300 mg po qhs was added to nine patients on an SSRI, two on buproprion, two on nortriptyline, and one on selegiline. The patients ranged in age from 63 to 91 with an average age of 76. 64% were female.

Seven of the 14 patients improved within one week, and a remarkable five of the seven demonstrated a dramatic improvement or "light switch response" within the first 48 hours of lithium therapy. Responders were no different in age or sex from non-responders. Of the nine patients on SSRI's, 2/3 did not respond to lithium augmentation. Seven of the 14 patients had mini-mental status exam scores less than 24 and six of these did not respond to lithium augmentation. Three patients could not tolerate lithium—one had a GI bleed, one experienced a delirium (with a lithium level of 0.6), and one developed myoclonic jerks. Thus, lithium augmentation is an effective treatment for geriatric patients as well, and is most effective in those not cognitively impaired.

NR507 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Depression and Adherence to Advance Directives

David M. Smith, M.D., Psychiatry, Portland VA Med. Center, 116A P.O. Box 1034, Portland OR 97207; Melinda Lee, M.D., Linda K. Ganzini, M.D., Darien Fenn, Ph.D.

Summary:

Fifty elderly, depressed veterans and a control group of 50 non-depressed veterans, all of whom were inpatients, were asked their preferences regarding life-sustaining interventions in hypothetical situations. 97/100 cases were followed up three years later. An investigator, blind to the results of the original interview, reviewed the charts for information regarding clinical decisions during subsequent hospitalizations, adherence to advance directives, and use of life sustaining interventions such as CPR, transfusions, NG tube feedings, dialysis, intensive care, and mechanical ventilation. At follow-up, 47% of depressed patients had died compared to 22% of controls. Depressed patients were twice as likely as controls to have a DNR order in their charts. A majority of both groups received life sustaining interventions such as transfusions, NG tube feedings, intensive care, and mechanical ventilation. There was a correlation between original response regarding the use of dialysis and subsequent decision against dialysis. Although a majority of both groups did not have advance directives in their charts, opposition to CPR in original scenarios showed a significant correlation with eventual DNR orders for both depressed and non-depressed patients.

NR508 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychiatric Medications in Chronic Elderly Inpatients

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Summary:

Few recent studies have investigated psychiatric medication use in chronic geropsychiatric inpatients. We surveyed medication administration in 699 inpatients at a public psychiatric center. Medication data represent average daily dosage received for the week of study.

Surprisingly, 23.6% of patients received no psychiatric medications at all, 64.7% received neuroleptics either alone or in combination with other drugs, and 11.75% received non-neuroleptic medications only. The percentage of patients receive no psychiatric medications was similar across major diagnostic groups. Sixty-eight percent of *DSM-III-R* schizophrenic patients, 54.4% of affective disorder patients, and 54.6% of dementia patients received neuroleptics alone or in combination with other medications. The equivalent dosages of neuroleptic medications did not differ among the diagnostic groups (100–183.7 mg/day for patients receiving neuroleptics only, and 257.1–421.1 mg/day for those receiving neuroleptics and other psychiatric medications). The most commonly prescribed antipsychotic was haloperidol. Seventeen percent of affective disorder patients, 6.1% of dementia patients, and 3.3% of schizophrenic patients received mood stabilizers, with or without other psychiatric medications.

Regardless of diagnosis, most patients in this survey received moderate doses of neuroleptics, or received no psychiatric medication at all. The use of multiple neuroleptics or polypharmacy was quite rare. The small number of patients treated for affective disorder will be discussed.

NR509 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychiatric Predictors of Medical Readmissions

Jennifer Fetner, B.A., Psychiatry, Mt. Sinai Sch of Med., 1 Gustave Levy Pl Box 1228, New York NY 10029; George Fulop, M.D., Peter Tafti, David Huertas, M.D., Karen Pasternak, James J. Strain, M.D.

Summary:

We attempted to replicate an earlier study which reported that current or past alcohol use was associated with increased likelihood of multiple readmissions to a geriatric medicine unit. We tested for the presence of psychiatric comorbidity in a random sample of 467 elderly medical/surgical inpatients and observed the readmission rate over a three-year follow-up. All 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).

Half the inpatients had a single admission. The 232 readmitted patients comprised 834 multiple admissions to the hospital: one—40%, two—23%, three—10%, four—8%, or five—7% readmissions. Multiple admits (MAs) compared to single admits (SAs) were, respectively: male 45% vs. 45%; white 45% vs. 55%, black 60% vs. 40%, or hispanic 54% vs. 46%; education 10.9 vs. 11.6 years; and, mean age of 75 vs. 75 years (All p = NS). MAs also had no significant difference in marital status, outpatient psychiatric treatment (19% vs. 17%). MAs vs. SAs had significantly more positive psychiatric family history for alcohol abuse (20% vs. 14%), but not current (13% vs 15%) or past (28% vs. 27%) alcohol use, major affective (16% vs 16%), psychotic (9% vs 9%), or anxiety/panic (5% vs. 5%) disorders.

Conclusion: We did not replicate our previous finding that alcohol use was associated with MAs on a geriatric medicine unit to the general medical/surgical elderly population. Reasons for the differences between studies include: substantial differences in minority admission rates, increased proportion of males, and a 10-year younger elderly sample encompassing surgical cases, and chemotherapy versus medical admissions only. Secondary analyses will be presented that identify subpopulations with psychiatric comorbidity who are at increased risk for medical rehospitalizations.

NR510 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Effect of ECT on Mortality and Clinical Outcome in Elderly Patients

Larry L. Richards, D.O., Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52242; Robert A. Philibert, M.D., George Winokur, M.D.

Summary:

Recent reports have called into question the safety and effectiveness of electroconvulsive therapy (ECT). In order to investigate these claims, the effects of ECT on clinical outcomes were examined as part of a retrospective, naturalistic study of 193 geriatric patients consecutively admitted between 1980 and 1987 to a large midWestern tertiary care center for the treatment of depression. Mean age of the patients at index admission was 71 years. Data were analyzed by both Chi square and ANOVA analysis. No significant differences in underlying medical conditions were found. However, when intention to treat analysis was performed, patients initially treated with ECT were more likely to be rated as completely improved and less likely to be rated as not improved by their discharging physician than those not treated with ECT. Furthermore, those treated with initially with ECT, were somewhat more likely, though not statistically significantly more likely (66% vs 55%), to be alive at the time of follow-up than those not treated with ECT during hospitalization. These results confirm previous studies demonstrating the superior efficacy of ECT as compared to chemotherapeutic treatment, and demonstrate its safety in long-term follow-up and suggest (but do not prove) an effect on longevity.

NR511 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Effect of Emotion on Retention in Old Age

Avraham Calev, Ph.D., Psychiatry, SUNY at Stony Brook, Stony Brook NY 11794

Summary:

It is well known that normal aging effects memory and that the deterioration affects certain memory functions more than others. Emotionality is a factor reported to contribute to memory on one hand, and not to be affected by aging as much as memory is affected, on the other. Emotionality may thus be of benefit for memory performance in the old. Two experiments are presented showing that this indeed is the case. In experiment 1, middle-aged subjects (N = 60) were tested on immediate and 48 hours delayed recall of two emotional and one neutral, word lists. Whereas the rate of forgetting of neutral materials was inversely correlated with age, no such trend was observed on emotional tasks. In experiment 2, young (in their 20's) and old (in their 60's) subjects were presented with the same procedure. Old subjects again showed selective forgetting of the neutral more than the emotional lists, unlike the young. It is suggested that emotional processing enhances recall in old age because it is a faculty which remains relatively intact. When emotion is absent, retention decreases.

NR512 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Educational and Current Reading Level in the Elderly

F.M. Baker, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Janice T. Johnson, Susan A. Velli, B.A., Cynthia Wiley, B.S., Patricia Langenberg, Ph.D.

Summary:

Because the current cohort of persons age 65 and older are known to have had limited educational opportunities, a study was done to determine whether the elder's reported education was congruent with the elder's current reading level. Eighty-two percent (47 of 57) of the sample was black with a mean current reading level of 5.8 grades. Eighteen percent of the sample was white (10 of 57) with a mean reading level of 7.1 grades, a statistically significant difference ($p < 0.001$). When the effects of education, race, and the covariance of education and race upon current reading level were assessed by ANOVA, only race was identified as significant ($p = 0.057$). Alcohol abuse/dependence did not affect current reading level ($p = 0.11$). Current reading level is important in comprehending written information, completing forms (Medicare, Social Security), reading directions for medications, and providing informed consent. These results suggest that some frequently used forms may need to be revised for better comprehension of their content by the current cohort of elderly persons.

NR513 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Reliability of the Geriatric Depression Scale and the Center for Epidemiologic Studies of Depression Scale in the Elderly

F.M. Baker, M.D., University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Cynthia Wiley, B.S., Susan A. Velli, B.A., Janice T. Johnson

Summary:

In order to establish the reliability and validity of the 15-item Geriatric Depression Scale (GDS) and the Center for Epidemiologic Studies of Depression Scale (CES-D) as screening instruments for depression in older, black and white persons, these instruments were administered to 30 psychiatric patients with affective illness. All patients referred with a diagnosis of depression completed a Structured Clinical Interview for the *Diagnostic and Statistical Manual-Third Edition* (SCID) as the reference standard. The sample was composed of 31% black women, 33% white women, 8% black men, and 11% white men. Sixty-seven percent of the sample had a diagnosis of major depressive disorder by the SCID. Eighty-three percent of the sample were age 60–79. Of the 14 African American elders with depressive illness, nine had CES-D scores of 16 or higher, resulting in a sensitivity of 64%. Deleting mild cases of depression (two cases of Adjustment disorder with depressed mood), nine of 12 older, black patients screened positive; a sensitivity of 75%. Of the 16 white Americans with depressive illness, 15 had CES-D scores of 16 or higher; a sensitivity of 94%. With the GDS only six of 14 depressed, older, African Americans were identified as having depressive symptoms; a sensitivity of 43%. Of the 12 older, depressed white patients, eight were identified by the GDS, a sensitivity of 75%. Based upon these preliminary data from an ongoing study, the CES-D is an effective screening instrument for screening for depressive symptoms in black and white elderly. The GDS was found to be less effective as a screening instrument for depression in both racial groups.

NR514 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Qualitative Assessment of Brain Morphology in Geriatric Depression

Blaine S. Greenwald, M.D., Psychiatry, Hillside Hospital, PO Box 38 Lowenstein Res Bldg, Glen Oaks NY 11004; Elisse Kramer-Ginsberg, Ph.D., Bernhard Bogerts, M.D., Manzar Ashtari, Ph.D., Peter Aupperle, M.D., Luis G. Allen, M.D., David Zeman, M.D., Mahendra Patel, M.D.

Summary:

Structural brain abnormalities have been implicated in geriatric depression, and more particularly, in late-onset (LO) geriatric depression.

Objective: The purpose of this study was to evaluate brain morphology seen with magnetic resonance imaging (MRI) by *qualitative* assessment in geriatric depressives and age-matched normal controls.

Methods: Elderly *DSM-III-R* depressives (n = 30) and controls (n = 36) underwent T-1 and T-2 weighted MRI scans of the head. MRI scans were qualitatively evaluated in random order by an expert research psychiatric (BB) trained in neuroanatomy and radiologic assessment, blind to diagnosis. Parameters assessed: T-1 (4-point scales): ventricular enlargement, cortical atrophy, mesio-temporal atrophy, basal ganglia size. T-2 (modified Fazekas criteria): periventricular (PVH) and deep white matter (DWM) hyperintensities, and subcortical gray matter lesions.

Results: Significant differences between depressed and control groups were not demonstrated for any brain region assessed. Late-onset (LO) geriatric depressives had significantly more abnormal left basal ganglia ($p < .04$) and left mesio-temporal ($p < .05$) ratings than early-onset (EO) counterparts of similar age. Although not reaching statistical significance, all patients (n = 3) with severe hyperintensity ratings (i.e. PVH extending into deep white matter or large confluent DWM areas) were depressed.

Conclusions: Findings: (1) indicate both non-specificity and lack of homogeneity of qualitatively measured structural brain changes in geriatric depression; (2) suggest that pathology of specific brain regions may be implicated in a subgroup of LO elderly depressives; (3) lend limited support to prior observations implicating the basal ganglia and severity of hyperintensities in late-life depression. Quantitative morphometric analyses of this sample are in progress.

NR515 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Hypothyroidism in Geriatric Psychiatric Patients

Irl L. Extein, M.D., 1050 NW 15th Street Ste 115, Boca Raton FL 33486

Summary:

Objective: The objective of this study was to determine the prevalence and type of thyroid dysfunction in a geriatric psychiatric population. Hypothyroidism (particularly subclinical hypothyroidism) becomes increasingly common with aging, and may have treatment implications for prescription of thyroid hormones, particularly in depression.

Method: Thyroid history and T4, T3-uptake, and TSH were obtained in 166 consecutive patients over 65 in a private psychiatric practice in South Florida—117 women/49 men, mean age 75, 39 inpatients/127 outpatients. 109 had a primary depressive disorder, nine bipolar, and 19 a primary organic mental disorder. TSH greater than 4.0 uIU/ml was considered elevated and defined subclinical hypothyroidism.

Results: 38 (23%) were receiving thyroid hormone supplementation for previously diagnosed hypothyroidism at the time of initial psychiatric assessment. Of these, four had dosages increased due to elevated TSH. Of those not on thyroid hormones, five (3%) had elevated TSH, of which three were started on thyroid hormones. Only one patient had a low T4 and one an elevated T4.

Conclusions: This 26% prevalence of hypothyroidism is twice that reported for healthy elderly. The finding that most of the study patients with hypothyroidism had been previously diagnosed and treated probably reflects the fact that most were followed by local internists. TSH levels were much more helpful than T4 levels in identifying hypothyroidism. Identification of elevated TSH led to the addition of thyroid hormone medication in a significant number of cases. Adequacy of thyroid hormone supplementation and relationship of subclinical hypothyroidism to depression in geriatric psychiatric patients needs to be studied further.

NR516 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Criteria to Enroll End-Stage Dementia Patients Into a Hospice

Mark J. Alexakos, B.A., Psychiatry, University of Chicago, 5841 S. Maryland Ave MC 3077, Chicago IL 60637; Patricia H. Hanrahan, Ph.D., Daniel J. Luchins

Summary:

Alzheimer's disease is the fourth leading cause of death, yet less than 1% of patients enrolled in hospice have a primary diagnosis of dementia. (Hanrahan, Luchins & Segneri, 1992; Luchins & Hanrahan, 1993). The major obstacle to enrolling dementia patients in hospice is the inability to predict whether or not the patient will die within six or seven months. This study extends our pilot study which established criteria to enroll end-stage dementia patients into hospice and showed that the average survival time for 11 patients was 6.6 months. Our criteria for enrollment includes patients having the characteristics of end-stage dementia and a history of medical complications related to their dementia. So far, 15 patients have been enrolled with an average length of stay in hospice of 5.26 months. Five of the 15 patients have died with an average survival time of one month and a range of five days to two months. Of the 10 surviving patients, the average length of stay has been 7.4 months. Updated survival data and information on costs, enrollment criteria, and service data will be presented.

NR517 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Mechanisms for Outcome in Psychiatric Intervention Studies in the Medically Ill: A Reanalysis

James J. Strain, M.D., Psychiatry, Mt. Sinai Sch. of Med., 1 Gustave Levy Place Box 1228, New York NY 10029; Albert Diefenbacher, M.D., Mary Eichmann, Ph.D., Mimi Fahs, Ph.D., John Lyons, Ph.D., Jeffrey S. Hammer, M.D.

Summary:

Introduction: Psychiatric interventions are cost effective in the medical/surgical setting and improve psychiatric morbidity and diminish rehospitalization post discharge in elderly hip fracture patients. (1). The mechanism of the intervention is not understood.

Methods: 113 intervention patients (who went home two days earlier than controls) were divided into five intervention groups: 1) Patient consultation/staff intervention/medications; 2) medications and staff intervention only; 3) patient intervention only; 4) no intervention; 5) refusers (refused to consent to enter study). Statistical analyses: T-tests, chi square, ANOVA (significance .05).

Results:

GROUP	NUMBER	MEAN (DAYS)	S.D.
1	27	29,7	19,98
2	42	17.36	5.27
3	23	15.70	3,84
4	11	15.18	6.15
5	35	19.86	8.66

All other orthopedic disorders and the mean of all hospital admissions had increased length of hospital stay during the intervention year when hip fractures decreased by two days.

Conclusion: Mechanism for the intervention effect may require a greater specification of the intervention than is generally reported in CL studies. Different interventions were associated with different lengths of stay.

NR518 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Weekly Psychiatric Review of Nursing Home Patients

Suhayl J. Nasr, M.D., Nasr Psychiatric, 901 Lincolnway Ste 312, Laporte IN 46350; Lori C. Gilmore, B.A.

Summary:

We assessed 32 patients over a nine-month period at a local nursing home. Patients were interviewed and observation of their general behavior on the unit was recorded. Alteration in diagnosis and prescriptions of patients were made as needed and adjustments were made on weekly follow-up. Initially 28 patients were diagnosed with schizophrenia, three with Alzheimer's, and one with mental retardation. Twenty-seven of the patients were on antipsychotic medications with a mean dose of 410 mg ± 334.7 of chlorpromazine equivalents. At the end of this study period 11 were diagnosed with schizophrenia, nine with major depression, recurrent with psychotic features, eight with bipolar disorder, and two with mental retardation. Nineteen patients were on antipsychotic medications with a mean dose of 275 mg ± 226.82 of chlorpromazine equivalents. More dramatic than the alteration in the diagnoses and prescription medications for these patients was the social and psychological changes that were noted. The patients become more self-caring, and took responsibility for daily hygiene and for helping one another. These findings indicate that many patients were misdiagnosed and their treatment was subsequently inadequate. It is our general impression that the quality of life for these patients greatly improved.

NR519 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Effect of Naloxone on Stress-Induced Immunosuppression

Choong-Han Yoon, M.D., Yong-In Mental Hospital, 4 Sanghari Kusungmyun, Yong-In Kun, Kyung-Gido 449-910, South Korea; Byung-Hwan Yang, M.D., Kwang-Il Kim, M.D., Kim Jung-Mogg, M.D.

Summary:

The present experiment addressed the effects of stress on opiate-mediated immunosuppression. In this experiment, male Sprag-Dawley rats were used as subjects. Animals were separated into five groups such as home cage control group, Skinner box control group, conflict group, and two pretreatment groups with naloxone. Home cage control group had no stress condition and Skinner box control group was immobilized without electric shock. Conflict group received psychological conflict stress with electric shock depending on the coping behavior. Pretreatment group had received naloxone intraperitoneally and 15 minutes later received psychological conflict stress like conflict group. And the natural killer cell cytotoxicity (NKCC) against YAC-1 murine lymphoma cells, proliferation of rat splenic lymphocytes stimulated with mitogen such as concanavalin-A and plasma concentration of corticosterone were measured. The results showed that there was significant decrease in NKCC and lymphocytes proliferation of conflict group compared with those of normal and Skinner box control group, which were reversed by naloxone. And there was significant increase in plasma concentration of corticosterone of conflict and pretreatment groups compared with those of normal and Skinner box control group.

In conclusion, this study suggests that opioid system may play a major role in the modulation of the stress-induced immunosuppression.

NR520 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Immunity in Young Adults with Major Depressive Disorders

Steven J. Schleifer, M.D., Psychiatry, UMD-NJ Medical School, 185 South Orange Avenue, Newark NJ 07103; Jacqueline A. Bartlett, M.D., Beverly Delaney, M.D., Diane Zeitlin, B.A., Haftan Eckholdt, Ph.D., Steven E. Keller, Ph.D.

Summary:

Immunologic studies in patients with major depressive disorder (MDD) have reported inconsistent results. We previously reported an age related association between MDD and immunity, with decreased mitogen responses in older depressed patients and either no change or elevated lymphocyte reactivity in younger patients. We now report on 21 new ambulatory medication-free young adults (age 18–33; 15/21 female) with SCID-*DSM-III-R* unipolar MDD compared with 21 matched controls suing an extended quantitative and functional immune battery. Consistent with previous findings, mitogen responses did not differ between the depressed young adults and controls, except for *increased* responses at the highest PHA dose ($p < 0.03$). MDD patients had increased total leukocytes and decreased monocytes ($p < 0.05$), and possibly increased granulocytes ($p < 0.1$). They also had lower circulating CD56+ (NK) cells ($p < 0.05$), but did not otherwise differ from controls in standard lymphocyte subsets. The depressed young adults had *lower* natural killer (NK) cell activity ($p < 0.05$), which could not be accounted for statistically by the decreased circulating NK cells. These findings are consistent with previous studies of decreased NK activity in MDD as well as age-dependent alterations in lymphocyte mitogen responses. Exploratory analyses suggested further that the immune differences in MDD are restricted to patients without comorbid anxiety disorder.

NR521 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Localization of Stem Cell Factor mRNA in Rat Brain

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Summary:

Stem cell factor (SCF) is a potent cytokine, known to affect the growth and differentiation of hematopoietic cells. It has been previously shown that SCF mRNA is present in brain, particularly in the thalamus during development and also in adulthood. It is still unclear if in adult brain SCF mRNA is localized in other important structures, such as hippocampus. We conducted this work to carefully ascertain the localization of SCF mRNA in adult brain, using *in situ* hybridization histochemistry with an ^{35}S-labeled antisense riboprobe; a sense riboprobe was used as control. We localized SCF mRNA abundantly in thalamus, and also in cortex, hippocampus, and cerebellum. Control experiments with the ^{35}S-labeled sense riboprobe yielded only background hybridization. At the cellular level we found that SCF mRNA was expressed predominantly in neuron-like cells. Dyskeratosis congenita is a rare disorder causing anemia, abnormal calcifications, skin alterations, and mental retardation. It has been postulated that a dysregulation of SCF function is the key pathophysiological feature in dyskeratosis congenita. If that is the case, we speculate that a dysfunction of SCF in brain may be related to the biological basis of the mental retardation associated with that disorder.

NR522 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Distribution of Interleukin-1 Receptor Type I mRNA in the Brain

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Summary:

Interleukin-1 (IL-1) is a potent cytokine, thought to be involved in the pathophysiology of severe psychiatric disorders, such as Alzheimer's disease, major depression, anorexia nervosa, and AIDS dementia. Systemic IL-1 results in clear biological effects mediated through the central nervous system (CNS), such as fever, anorexia, and activation of the hypothalamic-pituitary-adrenocortical (HPA) axis. IL-1 acts via specific cell-surface receptors. Given the multiple central effects of IL-1 in rat, it would be expected that IL-1 receptors ought to be present in rat brain. However, no previous studies have localized IL-1 receptor or its mRNA in rat brain, possibly due to the fact that interspecies probes were used in previous studies. The recent cloning of the rat IL-1 type-I receptor (IL-1R1) has permitted us to conduct an *in situ* hybridization study using a species-specific, ^{35}S-labeled antisense riboprobe to localize IL-1 receptor mRNA in rat brain. We localized IL-1RI mRNA in hippocampus, choroid plexus, and cerebellum. At the cellular level we found IL-1RI mRNA in low to moderate levels in hippocampal neurons and in Purkinje cells of the cerebellar cortex, and in high levels in the endothelium of postcapillary venules and in glial cells surrounding arterioles throughout the brain. This pattern of localization provides support to the concept that IL-1 may cross the blood-brain barrier. Future studies are needed to clarify how the expression of the gene encoding IL-1RI is regulated in brain tissue.

NR523 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Aggression and Immunity

Jacqueline A. Bartlett, M.D., Psychiatry, UMD-NJ Medical School, 185 South Orange Avenue, Newark NJ 07103; Steven E. Keller, Ph.D., Melissa K. Demetrikopoulos, Ph.D., Steven J. Schleifer, M.D.

Summary:

Research has demonstrated relationships between many psychosocial factors and immunity. However, little research has investigated associations between aggression and immunity. Previously we reported preliminary findings of increased immunity associated with aggression. We investigated immunity and aggressive behaviors in 350 inner city adolescents, hypothesizing that both functional and ennumerative measures of immunity would be increased with aggression. Aggression was conceptualized as aggression towards the self, i.e., inward directed or aggression directed externally toward objects or people. Utilizing a modified aggression scale, subjects were classified into three groups, those reporting no aggressive behaviors (NA), those with aggression directed outward (AO), and those with both self and outward directed aggression (AOI). All analyses controlled age, gender, and race. Significant findings included the following: the % of B (CD 20) cells was highest in the AO group, lowest in the AOI group; while % of T inducer of help cells (CD45RA) was highest in the NA and lowest in the AO group. Further, response to pokeweed mitogen was higher in both AO and AOI compared to the NA, at each dose. These data support the construct that aggressivity is associated with increases in some ennumerative and functional immune measures and may influence PNI relationships.

NR524 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Medical Status, Depressed Mood and Immune Function

Steven E. Keller, Ph.D., Psychiatry, UMD-NJ Medical School, 185 South Orange Avenue, Newark NJ 07103; Steven J. Schleifer, M.D., Jacqueline A. Bartlett, M.D., Melissa K. Demetrikopoulos, Ph.D.

Summary:

Considerable research has been conducted on the relationship between major depressive disorder (MDD) and immunity. A comprehensive meta-analyses of the pertinent literature has demonstrated several reliable immune-depression associations, including decreased lymphocyte functioning with increasing severity of depression and greater age. Decreased NK cell activity has been consistently found in association with MDD. However, there have been few studies which examine the relationship between depressive symptoms per se and immunity. Depressive symptoms apart from syndromal depression is ubiquitous and therefore, immune consequences could have major public health implications.

The present study examined depressive symptoms—immune relationships within the context of medical health, which has been postulated as a critically important co-factor in PNI studies. 331 adolescents were studied. The healthy group and the group with medical problems showed "baseline levels" of immune function while the minor medical ill group showed elevated parameters of immunity. hen these relationships were examined in connection with depressed mood the group with medical problems showed marked immuno-suppression with increasing severity of depressive symptoms. Basic principles of PNI as well as immune reserve issues will be discussed in light of these findings.

NR525 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Temporo-Limbic Epilepsy and Dream-Like States

R. Andrew Schultz-Ross, M.D., Psychiatry, University of Hawaii, 1356 Lusitana St. 4th Floor, Honolulu HI 96813

Summary:

Objective: The nature of the behavioral symptoms of persons with temporo-limbic epilepsy (TLE) has been controversial. This pilot study measured whether persons with TLE have experienced a dream-like state, a symptom to be considered characteristic historically, but less described in more recent neuropsychiatric literature.

Methods: Questionnaires were distributed to persons with TLE and to controls. Ninety-four were received from patients, 15 from controls. The patients and controls were asked to describe whether they had "felt as though I was in a dream while I was actually awake" by rating themselves on a four-point scale.

Results: A T-test for independent samples showed that the persons with TLE reported this symptom significantly more than the control group ($t = 3.55$, $df = 106$, $p < .01$).

Conclusions: Determining likely symptoms of TLE may aid in its detection in psychiatric populations. This result, if verified, may mean that patients are more adept than previously recognized at reporting altered states of consciousness. Also, a higher incidence of dream-like symptoms would raise new concerns in the difficult differential diagnosis between TLE and dissociative disorders.

NR526 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Psychopathology in Psychophysiological Insomnia

Silvio Scarone, M.D., Psychiatry, IRCCS H. San Raffaele, Via Prinetti 29, Milano 20127, Italy; Orsola Gambini, M.D., Marco Zucconi, M.D., Arturo Campana, M.D., Luigi Ferini-Strambi, M.D., Salvatore Smirne, M.D.

Summary:

Psychophysiological insomnia (PI) represents about 15% of all insomniacs diagnosed in sleep disorders centers (according to ICSD, 1990). The exclusion of psychiatric disorders according to *DSM-III-R* criteria is one of the essential characteristics for the diagnosis. However, few studies considered *DSM-III-R* diagnoses obtained by means of psychiatric structured interview and polysomnographic data to examine young patients at first clinically diagnosed as psychophysiological insomnia. The present study evaluates 35 outpatients (mean age 31±6) first classified as PI at the sleep disorder center. *DSM-III-R* interview, PDQR and clinical interview were used for psychiatric diagnosis. Subjects underwent two consecutive home night sleep recordings (Oxford Medilog 9000). Sleep and clinical data were compared with those of 10 healthy subjects. Twelve out of 35 (34%) patients had past axis I diagnoses and five (14%) had axis II diagnoses. Compared to controls, sleep data showed a reduced sleep efficiency (SE), an increased number of stage-shifts/hour, and an increased St.1NREM% in PI patients vs controls. Among the group with, without psychiatric diagnoses and controls St.1NREM and number of stage-shifts/hour were significantly different. No significant difference was found between PI subjects with and without psychiatric diagnosis.

NR527 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Long-Term Efficacy of Uvulopalatopharyngoplasty for Sleep Apnea

Edward O. Bixler, Ph.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Alexandros N. Vgontzas, M.D., Ernest Manders, M.D., Rocco L. Manfredi, M.D., Anthony Kales, M.D.

Summary:

Previous studies have examined the short-term efficacy of uvulopalatopharyngoplasty (UPP), with most studies evaluating the period of 30 to 180 days following the procedure. In this study, the long-term effectiveness of UPP for the treatment of obstructive sleep apnea (OSA) was assessed in 29 patients. The patients were evaluated pre-UPP and at 30 days and two years post-UPP. Efficacy was defined as a greater than 50% reduction in the apnea/hypopnea index (AHI). The success rate during short-term follow-

up (30 days post-UPP) was approximately 60%. At two years post-UPP, about 40% showed continued response to UPP. Of those patients who initially responded, almost half lost effectiveness over the two-year period, while of those who did not initially respond, approximately 20% met the criteria for success after two years. Patients who had a successful UPP at the two-year follow-up showed an improvement both in terms of hypoxia and sleep disturbance. In contrast, the patients who had unsuccessful UPP at the two-year follow-up did not show any improvement in their sleep quality, while their hypoxia levels were somewhat improved. Age, severity of apnea, and degree of obesity did not predict long-term outcome. Our data suggest that UPP is initially associated with a moderate success rate and that this success rate is somewhat lower after two years. From a clinical standpoint, these findings show that long-term follow-up of UPP is essential, Finally, further investigation is needed to identify predictors of successful UPP outcome.

NR528 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Delta Sleep-Inducing Peptide in Normals and in Sleep Apnea and Narcolepsy

Alexandros N. Vgontzas, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Theodore Friedman, M.D., George Chrousos, M.D., Edward O. Bixler, Ph.D., Antonio Vela-Bueno, M.D., Anthony Kales, M.D.

Summary:

Delta sleep-inducing peptide (DSIP) is an endogenous neuropeptide with a possible role in the homeostatic or circadian model of sleep/wakefulness. Sleep apnea and narcolepsy are two sleep disorders characterized by abnormal sleep/wakefulness patterns. To examine potential alterations of circulating DSIP in these sleep disorders, we measured the morning plasma concentrations of this hormone by specific radioimmunoassay in nine patients with sleep apnea, 10 patients with narcolepsy, and 11 normal controls. Comparisons between the three groups showed no significant differences, although there was a trend in the narcoleptic group, particularly in patients not using medications, to be associated with low levels of DSIP-like immunoreactivity (DSIP-LI). To assess for effects of circadian variation of DSIP levels, we measured morning and evening plasma levels of this hormone in a second group of 11 normal controls and eight patients with sleep apnea. Again, no differences were found between normal controls and sleep apneics in morning or evening plasma DSIP-LI levels. Also, there was no clear correlation between DSIP levels and slow-wave sleep (SWS) or REM sleep. Our findings do not support a pathophysiologic association between DSIP and sleep apnea. Further, our results on DSIP levels and SWS, which differ from previous studies, suggest that the definition of a potential relationship between plasma DSIP and slow-wave sleep would require a larger sample and the use of more precise measures of slow-wave sleep, such as power density in the delta band.

NR529 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Association of Tumor Necrosis Factor Microsatellite Polymorphisms with Narcolepsy

Charles Rivers, B.S., Microbiology, UAB, 1808 7th Avenue Room 802, Birmingham AL 35294; Rodney Go, Ph.D., Shashidhar M. Shettar, M.D., Bracie Watson, Ph.D., Chotip Vanichanan, M.D., Mei-Ling Tseng, Ph.D., Yan Qui, B.S., Ronald Acton, Ph.D.

Summary:

Although narcolepsy has been reported associated with HLA-DR2 and DQw1, some patients do not possess either of the phenotypes. In order to further define the genetics of narcolepsy, we have looked for an association with other polymorphisms within this region of chromosome 6p. CA/GT repeat TNFa polymorphisms were assessed in narcoleptic and ICNSH patients. TNFa is located 875kb telomeric of the DRα gene. A significant increase in the a7 allele ($p = 0.006$, Odds Ratio (O.R.)=3.2) was found in African Americans (AAs) ($n = 41$) compared to healthy controls ($n = 46$). The association is independent of the presence or absence of cataplexy. A significant association ($p = 0.001$, O.R. = 2.4) of the a11 allele was observed only in cataplexy positive Caucasian Americans (CAs) ($n = 61$) vs. healthy controls ($n = 87$). The association was stronger when comparing cataplexy positive ($n = 61$) to negative ($n = 46$) CA patients ($p = 0.0003$, O.R. = 4.0). Association of ICNSH with a TNFa allele was not observed for either race. All of the AA a7 positive patients and 96% of the CA a11 narcoleptic/cataplexy positive patients who were HLA typed were DR2 or DQw1. This suggests strong linkage disequilibrium between the TNFa DR and DQ alleles.

NR530 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

A Sleep Disorder Questionnaire Subscale for Chronic Fatigue Syndrome

Alan B. Douglass, M.D., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor MI 48109-0116; Jon K. Zubieta, M.D., Mark A. Demitrack, M.D., N. Cary Engleberg, M.D.

Summary:

Chronic fatigue syndrome (CFS) includes persistent fatigue, non-restful sleep, daytime sleepiness, diffuse pain, and other somatic complaints. The sleep complaints could be confused with narcolepsy, sleep apnea, and nocturnal periodic limb movement disorder (PLMD). A diagnostic scale for each of these has been derived from the Sleep Disorders Questionnaire (SDQ), and also for major depression (MDD). We sought a method of differentially diagnosing CFS sleep complaints using this questionnaire.

Using multivariate procedures, we compared the SDQ responses of CFS patients ($n = 60$) to the original SDQ reference groups: narcolepsy ($n = 73$), sleep apnea ($n = 158$), PLMD ($n = 96$), MDD ($n = 108$), and healthy controls ($n = 84$). The SDQ responses did not differ significantly between Subsyndromal CFS patients ($n = 14$) and those with the full CDC syndrome ($n = 46$). The multivariate analysis was highly significant ($p < .0001$) id identifying CFS patients. The derived CFS subscale contained 10 items (SDQ no. 27, 29, 48, 58, 72, 88, 91, 137, 153, 174) with $r \geq 0.60$ to the CFS canonical variable. These items relate to nocturnal muscle pain bruxism and headaches, removal of tonsils, abnormally small jaw, good psychosocial function, high level of education, daytime sleepiness, and long night sleep. CFS sleep complaints can be distinguished by SDQ questionnaire from those in other major sleep disorders.

NR531 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

More Cortisol Suppression in Depressed Cacosmics: DST Evaluation of Chemically-Sensitive Older Adults

Iris R. Bell, M.D., Psychiatry, Univ. of Arizona, 1501 N. Campbell Ave RM 7402, Tucson AZ 85724; Diane L. Amend, Ph.D.

Summary:

Objective: The present study compared post-dexamethasone cortisols and depression in elderly with and without self-reported illness from environmental chemicals (cacosmia). Cacosmia is a core symptom of several controversial syndromes, including multiple chemical sensitivity (MCS), the recent "Gulf War Illness," and chronic fatigue syndrome (CFS). Elderly cacosmics report

more depression, nasal allergies, breast cysts, hypothyroidism, irritable bowel, and migraine headache.

Method: Subjects were community-dwelling elderly (mean age 77 ± 6 yrs, 77%F/23%M), recruited for a study of depression and cognitive loss. At baseline and six-month follow-up, subjects completed the Geriatric Depression Scale (GDS), Mini-Mental State Examination (MMSE), the Cain Olfactory Identification test, a 0.5 mg dexamethasone suppression test (DST) with 8 am cortisols, and a Cacosmia Scale (total # out of 10 possible chemicals endorsed as causing illness).

Results: Subjects were divided into two groups, Cacosmic (CAC, n = 10, Cacosmia scores 4.0 ± 1.3) and Noncacosmic (NONCAC, n = 19, Cacosmia scores 0.3 ± 0.5). At baseline, CAC were significantly younger ($p = 0.008$), more depressed (GDS 16 vs 9, $p = 0.02$), and lower in post-dexamethasone cortisol (2.8 vs 5.7, $p = 0.03$), with a trend toward better olfactory ability (8.1 vs 6.3, $p = 0.12$), but were not different for gender distribution ($p = 0.4$), baseline cortisol (17.8 vs 17.8, $p = 1.0$), or MMSE (26.1 vs 26.2, $p = 0.9$) compared with NONCAC. After covarying for age and GDS, the cacosmia score differences persisted ($p < 0.0001$), and the post-DST cortisol finding became a trend ($p = 0.12$). At follow-up the original groups did not differ significantly on depression scores (11 vs 8, $p = 0.2$), MMSE, or cortisols; CAC had significantly better olfactory ability ($p = 0.039$), after controlling for age and 6-month GDS. The two Cacosmia scores correlated well ($r = 0.7$, $p < 0.0001$).

Conclusions: Cacosmic elderly may exhibit stable cacosmia, but a state depression-dependent, heightened cortisol suppression by DEX, consistent with a previously hypothesized biological overlap of MCS and CFS with post-traumatic stress disorder, possibly mediated by time-dependent sensitization (Bell et al., 1993).

NR532 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Memory and EEG in Chemically-Sensitive Young Adults

Gary E. Schwartz, Ph.D., Psychology, University of Arizona, Room 312, Tucson AZ 85721; Iris R. Bell, M.D., Anne M. Herring, Ph.D., Julie M. Peterson, B.S., Alfred W. Kaszniak, Ph.D.

Summary:

Objective: Young adults who report illness from low level chemical odors (cacosmia) rate themselves with increased concentration and/or memory problems. Cacosmia has received recent attention as a symptom of the poorly-understood polysymptomatic illnesses that developed in a subset of Gulf War veterans during and after their service. This study examined nonveteran young adults for baseline neuropsychological test performance and quantitative EEG responses to test chemical exposures in the laboratory.

Method: Subjects were college students of both sexes drawn from an introductory psychology course (N = 800), representing the top and bottom 15% on self-ratings of illness from five chemicals. All subjects underwent baseline testing with the California Verbal Learning Test (CVLT) and Continuous Visual Memory Test (CVMT), as well as quantitative EEG recordings during one-minute blinded inhalations of a perfume constituent (galaxolide), an indoor air pollutant (n-butanol), and placebo vehicle controls.

Results: The cacosmics (n = 33) performed significantly more poorly than did noncacosmics (n = 33) on the delayed recognition component of the CVMT ($p = 0.01$). Cacosmics recalled more correct items with cues ($p = 0.04$), but made more perseveration errors after a short delay on the CVLT ($p = 0.05$). on qEEG, cacosmics had more alpha blocking over the left temporal, central, and right temporal-parietal regions than did the noncacosmics during chemical exposures, after subtracting changes during placebos ($p < 0.05$).

Conclusions: Young adults who rate themselves with heightened sensitivity to environmental chemicals show complex baseline differences on memory tests in comparison with their noncacosmic peers, i.e., worse delayed recognition visual memory, better delayed/cued verbal memory, but more perseveration on the verbal task. Cacosmics also exhibit EEG evidence of exposure-dependent decreases in alpha activity bilaterally over regions involved in memory and olfactory processing. Further research is now indicated in patient populations.

NR533 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Irritable Bowel Syndrome and Psychiatric Illness: A Family Study

Catherine L. Woodman, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52240; Kevin Breen, M.D., Russell Noyes, Jr., M.D., Carol Moss, B.A., Robert Fagerholm, R.N., Robert Summers, M.D.

Summary:

Irritable bowel syndrome is the most common gastrointestinal disorder, yet it has no clearly established pathogenesis or treatment, and the diagnosis remains one of exclusion without a biological marker. IBS had been associated with psychiatric illness, predominantly anxiety and depression, in 50% to 100% of patients who consult a physician. This study is a preliminary effort to evaluate whether the relationship between IBS and psychiatric illness is a true association by comparing the first-degree relatives of patients with IBS with the first-degree relatives of patients who had laproscopic cholecystectomy (i.e. patients with gastrointestinal pathology that is not associated with IBS symptoms). If there is an association between IBS and psychiatric illness, then there should be an increased prevalence of both psychiatric illness and IBS in the first-degree relatives of IBS probands.

Structured interviews were administered to probands and their first-degree relatives to obtain lifetime psychiatric and gastrointestinal histories. IBS probands had significantly higher lifetime psychiatric illness than cholecystectomy patients (18/20 or 90% v. 9/20 or 45%, $p = .002$). While the first-degree relatives of IBS probands have significantly higher lifetime psychiatric illness than the first-degree relatives of cholecystectomy probands (54/101 or 55% v. 38/113 or 34%, $p = .0001$), the lifetime prevalence of IBS was not significantly different between the two groups (8/101 or 8% v. 4/113 or 3.5%).

Several studies have suggested that patients with IBS who also have psychiatric illness are more likely to seek treatment, and that patients who meet criteria for IBS but do not seek treatment are no more likely to have psychiatric illness than the nonaffected population. This preliminary study supports this hypothesis by failing to find an association between IBS and psychiatric illness in the first-degree relatives of IBS probands.

NR534 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

High Frequency of Somatization in Benzodiazepine Dependents

Herminio Martinez-Cano, M.D., Psychiatry, Autonomous University, Camino De Vinateros 12 8F, Madrid 34 28030, Spain; Antonio Vela-Bueno, M.D., Rolando Pomalima, M.D., Mariano Iceta, M.D.

Summary:

Data on the psychological features of benzodiazepine dependent patients are scarce and non-systematically obtained. This presentation reports on the personality patterns of a population of benzodiazepine dependent patients evaluated with the Minnesota Multiphasic Personality Inventory (MMPI). There were 153 patients (98 women and 55 men), of a mean age of 46.9 years who

were taking different benzodiazepines at various dose levels for an average of 4.6 years. Benzodiazepine dependence was diagnosed according to *DSM-III-R* criteria.

A total of 147 patients successfully completed the MMPI and obtained a valid profile. One or more scales were elevated a pathological degree in 122 subjects (83%). The scales most elevated were, in order, 2 (depression), 1 (hypocondiasis), 3 (conversion hysteria), 8 (schizophrenia) and 7 (psychastenia). Also the most frequently MMPI code was the 3-2-1 type, present in 44 patients (30%) of the total sample.

These data suggest a high frequency of somatization among benzodiazepine dependent subjects. We conclude the subjects with a somatization-repressive personality profile are at high risk for development of benzodiazepine dependence and should be closely monitored by their physicians for early signs and symptoms of this disorder.

NR535 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Development of an Inventory for the Multidimensional Assessment of Sex and Aggression

Robert A. Prentky, Ph.D., J.J. Peters Institute, 260 S. Broad Street Ste 220, Philadelphia PA 19102-3814; Raymond A. Knight, Ph.D.

Summary:

The impetus for the development of an inventory that tapped sexual and aggressive thoughts and fantasies derived from our programmatic work on taxonomic models for classifying sexual offenders. The general area of sexualization, covering both aggressive and nonaggressive as well as paraphilic (i.e., deviant) and nonparaphilic fantasies and behaviors, not only was theoretically important, but posed the most difficult and challenging structural and dimensional problems for our model. Since archival data on offense-related and non-offense related sexual fantasies are often poorly represented or nonexistent, we needed to supplement the file data to more accurately evaluate the taxonomic import of sexualization.

To accomplish this we needed a more accurate and complete assessment of this domain on a wide range of subjects. We set out to develop an efficiently administered, psychometrically sound, self-report evaluation of these crucial yet inadequately examined domains on a large portion of our sample. We sought to develop a psychometric instrument that would serve the dual purpose of providing detailed information on sexual fantasies and behavior as well as serving as a classification interview.

We administered this inventory to 127 sexual offenders and repeated administration after a six-month interval on a subsample of 35 offenders. The high internal consistencies, high test-retest reliabilities, and the reported incidence of sexualization in these scales indicates that the inventory achieved its major purpose, and these scales will be extremely useful in adjusting and concertizing the criteria in our classification system for rapists. In our presentation we will discus the development of the inventory, its component scales and their internal consistency, test-retest reliability, and preliminary analyses on concurrent validity.

NR536 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Adolescent Murderers: Follow-Up and Typology

Louis Morissette, M.D., Psychiatry, Institute Pinel, 10905 Est Henri-Bourassa, Montreal Quebec H1C 1H1, Canada; Jean Toupin, Ph.D., Juan E. Labadie, M.D.

Summary:

Objective: Evaluate the long-term prognosis of adolescent murderers.

Method: In Montréal, Canada, all juveniles (n = 63) who killed between 1975 and 1987 were compared to 46 aggressive adolescents and 61 property offenders (chart review) and the three groups are being followed for their official criminal recidivism all across Canada.

Results: At 138 months follow-up (33 to 246 months) (February 1993), 41% of the murderers re-offended, 73% of the aggressive, and 72% of the property offenders.

On a yearly basis, the property offenders re-offended the most (.86), the murderers, the least (.45), and the aggressive are at .81.

On a yearly basis, the aggressive group had more violent crimes (.26), the murderers, the least (.07), and the property offenders had .17 violent crimes/year.

The murderers group seemed heteregenous and consequently they were classified according to the typology proposed by Cornell et al. (1987).

The adolescents who killed while committing another crime (n = 23) recidivate more often (61% vs 23%), with more crimes/year (.53 vs .11) and more violent crimes/year (.11 vs .01) than adolescents who kill in the context of an interpersonal conflict (n = 26).

Conclusion: 1. The adolescent murders constitute an hetegenerous group (clinically and outcome).

2. The adolescents who kill while committing another crime have the worst prognosis.

NR537 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Machine Learning of Back-Ward Violence Patterns

Cheryl K. Cantrell, M.D., Psychiatry, Delaware State Hospital, 1901 N. Dupont Highway, New Castle DE 19720; David A. Pensak, Ph.D.

Summary:

Objective: This investigation uses machine learning algorithms to analyze atypical patterns of violent behavior and sequences of precursor events in a population of 40 very chronic state hospital inpatients whose patterns of behavior are difficult to discern intuitively.

Method: Daily data were gathered over a period of 550 days encompassing 369 distinct violent incidents in a state hospital ward where "unpredictable" violence had been a serious problem. Several classification and learning algorithms were applied to these data, utilizing sliding time windows of different lengths to classify violent episodes according to agitation sequences over previous days, all as a function of diagnosis.

Results: Utilizing the C4.5 suite of programs, a marked difference was discernable in the patterns of agitation between groups of patients as separated by diagnosis. A greater than 80% correct prediction rate was achieved despite significant missing data. Machine elucidation of these discriminants is required because the patterns are both complex and non-intuitive.

Conclusion: Artificial intelligence systems can be used to analyze complex or incomplete data sets such as hospital records and patient acuity reports and identify non-obvious patterns.

NR538 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Atypical Violence Patterns in Back-Ward Patients

Cheryl K. Cantrell, M.D., Psychiatry, Delaware State Hospital, 1901 N. Dupont Highway, New Castle DE 19720; Eric S. Cole, Ph.D., D. Erik Everhart, B.A.

Summary:

Objective: Although numerous studies have examined the correlation between psychiatric diagnosis and assaultiveness, conflicting results abound. This investigation examines patterns of

violence among subgroups of patients with coexisting diagnoses on a chronic state hospital unit.

Method: Thirty-three of 40 patients were assigned to one of two diagnostic categories: Axis I psychosis only or Axis I psychosis plus an organic mental disorder. All incidents of agitation and physical assaultiveness were recorded for a period of 550 days. These were tabulated and analyzed.

Results: Dually diagnosed patients were more violent than the psychotic patients (20.8 vs. 8.0 episodes/pt.). They also showed more days with multiple aggressive events (4.8 vs. 1.4 episodes/pt.). The expected "crescendo" pattern of agitation in the five days prior to physical assaults was present in only 56% of the 335 violent episodes observed. In 20% of each group, no agitated events were recorded on either the day of or the day prior to the assault.

Conclusions: Dually diagnosed chronic inpatients show more than twice the rate of physical violence as patients with psychosis alone. Almost half of all violent episodes in this entire population occurred without any readily observable precursor events.

NR539 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Training and Experience of Psychiatric House Staff with Domestic Violence Identification

Glenn W. Currier, M.D., Psychiatry, Yale University, 66 Dowing Street, New Haven CT 06513

Summary:

Objective: To characterize psychiatric resident experience with recognition, referral, and treatment of domestic violence victims, as well as to define educational needs on that topic.

Methods: Questionnaire distributed to all adult psychiatry residents at four psychiatry residency training programs in the U.S. (N = 221). Survey questions concentrate on the following aspects of domestic violence: clinical experience, screening practices, and educational needs.

Results: Over 71% of 145 respondents recall no training in domestic violence identification or treatment in medical school or in residency. Only 13% of residents recall any such training in medical school. Eighty-seven percent of residents reported contact with one or more documented cases of domestic violence within the year prior to the survey. In total, 21/145 (14.5%) of respondents reported having previously suspected at least one case of domestic violence but not asking the patient about it. Overall, 65.6% of residents were unable to list a local community agency that specifically serves victims of domestic violence. Prior training on the topic was the best predictor of domestic violence case identification and referral to specialized agencies, and 92% of residents felt they need further training on violence-related issues.

Conclusions: A preponderance of psychiatric residents sampled receive minimal training in recognition and clinical management of domestic violence victims, contributing to reduced case identification and missed opportunities for intervention.

NR540 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Adjunctive Propranolol and Nadolol in Aggression and Akathisia

Edward R. Allan, M.D., Psychiatry, FDR VA Hospital, Box 100, Montrose NY 10548; Murray Alpert, Ph.D., Gabriel Laury, M.D., Cecile E. Sison, Ph.D.

Summary:

Management of aggressiveness is very important in any psychiatric facility. Beta blockers have been suggested as an adjunct to neuroleptic medication for this indication. A link between aggressiveness and akathisia has also been suggested. We compared two beta blockers and placebo to control aggressiveness, and examined the relationship between aggressiveness and akathisia in a double-blind study of adjunctive use of nadolol, 80 mg. and propranolol, 120 mg. (in long-acting form). Subjects were either schizophrenic or schizoaffective psychiatric inpatients. Measures included daily blood pressure and pulse readings for safety and the BPRS, Global Assessment Scale, and NOSIE, and modified versions of the Barnes Akathisia Scale and Simpson-Angus PS Scale for efficacy.

Only one subject (on nadolol) was discontinued due to persistent low blood pressure. The efficacy data indicate improvement in the BPRS activation factor score for both active medications during the first week ($p. < .04$). Propranolol by itself was significantly superior to placebo ($p. < .05$). Propranolol showed significantly more improvement than nadolol or placebo in a global akathisia rating.

Stepwise multiple regression analysis was done to test whether changes in BPRS and akathisia share pharmacodynamic mechanisms. The relationships of BPRS and the global akathisia rating in the modified Simpson-Angus was significant only for propranolol treatment, suggesting a shared mechanism for the two indications that is affected by a centrally active beta-adrenergic blocker.

NR541 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Deployment and Dysfunction

Ronald Koshes, M.D., Military Psychiatry, Walter Reed Army, Institute Research, Washington DC 20307-5100; Joseph M. Rothberg, Ph.D., John Shanahan, Ed.D., Karl Christman, M.Ed.

Summary:

The conventional wisdom among mental health professionals is that military deployments are stressful and that soldiers make more use of services in and around such times of stress. Rates of alcohol and drug use, marital problems, unit disciplinary actions, and other dysfunctional behaviors have been seen to increase in soldiers returning from war. We undertook a study of the use of selected services (social work service, alcohol and drug program) on a U.S. Army post before, during, and after Operations Desert Shield/Desert Storm to quantify the changes associated with those events, thereby providing data for mental health manpower and staffing decisions. The major finding are: 1) in the time before the start of Operation Desert Shield, the problem rates were higher in units which deployed than in units which did not; 2) during the deployment, the problem rate in the non-deployed units was lower than either before or after the deployment; 3) there were relative increases in the problem rate at the time of Desert Storm for the non-deployed units and at the time of re-deployment for the deployed units; and, 4) there were differences in the age and race of members of those units which were deployed to Southwest Asia as compared to those units which did not.

NR542 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Negative Symptoms and Serotonin in PTSD

Christopher G. Fichtner, M.D., Psychiatry, Loyola University, Hines VA Biol. Sect. 116A7, Hines IL 60141; Francine L. O'Connor, R.N., Hock C. Yeoh, B.S., Muhammad O. Nasib, M.B., Ramesh C. Arora, Ph.D., John W. Crayton, M.D.

Summary:

In previous studies exploring markers of possible serotonergic dysregulation in post-traumatic stress disorder (PTSD), we have found a lower number of binding sites (B_{max}) and a lower dissociation constant (K_D) for the binding of ^{3}H-paroxetine to blood platelet serotonin (5-HT) uptake sites in PTSD patients compared to normal controls. To assess whether this alteration in 5-HT transport relates more specifically to particular aspects of PTSD symptom-

atology, we have now studied 41 Vietnam veterans with SCID-diagnosed combat-related PTSD who completed the Mississippi Scale for Combat-Related PTSD (MS-PTSD) at the time of the platelet ^{3}H-paroxetine binding assay. Specific PTSD symptom patterns were determined using the MS-PTSD items in four ways: (a) a face-valid phenomenological breakdown reflecting the three distinct symptom clusters identified in *DSM-III-R,* i.e., reexperiencing (R), avoidance (A) and hyperarousal (H); (b) subtotals based on a previously published factor analysis yield a three-factor solution including the factors reexperiencing/numbing (RN), anger/lability (AL), and social alienation (SA); (c) subtotals based on a recent factor analysis yielding a four-factor solution including the factors reexperiencing/situational avoidance (RSA), numbing/withdrawal (NW), arousal/loss of control (ALC), and self-persecution (SP); (d) an emotional numbing (EN) subscale developed at the National Center for PTSD. The results indicated that B_{max} correlated inversely with A ($r = -0.37$; $p = .018$), SA ($r = -0.40$; $p = .0095$), NW ($r = -0.32$; $p = .042$), and EN ($r = -0.39$; $p = .012$), but not with other components of the MS-PTSD. No relationship was found between the K_D of ^{3}H-paroxetine binding the MS-PTSD. These findings suggest that the negative symptoms of emotional numbing, withdrawal, and avoidance may be more closely related than other PTSD symptoms to alterations in the 5-HT system.

NR543 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Sleep Disturbance Related to Hurricane Andrew

Thomas A. Mellman, M.D., Psychiatry, Miami VA Medica Center, 1201 NW 16th Street, Miami FL 33125; Daniella David, M.D., Renee Kulick-Bell, B.A., Joanne R. Hebding, Psg.T., Bruce Nolan, M.D.

Summary:

Sleep disturbance, which is an important dimension of chronic PTSD, has been less well characterized in acute responses to traumatic stressors. Hurricane Andrew caused widespread devastation in South Florida. Sleep was affected by the storm's threat and subsequent disruptions to environments and routines.

Sixty-one, mostly non-clinical subjects (M-14, F-47, age 40.4 ± 12.3), with significant hurricane impact, were evaluated with structured interviews and self-report ratings. The Pittsburgh Sleep Quality Index (PSQI) was included and modified to retrospectively inventory sleep disturbances prior to the hurricane and at the time of the evaluation (six months to a year post-hurricane). A subset of symptomatic subjects (n = 12), and controls without major hurricane impact (n = 8), received overnight sleep laboratory evaluations.

Global ratings for post-hurricane sleep disturbance were increased, most significantly in subjects with positive psychiatric morbidity. There was a trend ($p < .06$) for subjects with active morbidity to have, on average, increased, but sub-pathological threshold, ratings for pre-hurricane sleep disturbance.

Laboratory findings include increased entries to stage 1 and micro-awakenings in the symptomatic subjects; positive correlations of REM eye movement density and PTSD re-experiencing symptoms ($R = .7$, $p < .05$), and non-specific distress (SCL-90 global index) ($R = .78$, $P < .01$); and (in contrast to chronic disorders) a trend toward increased slow wave sleep in subjects with active symptoms.

The role of sleep in post-traumatic morbidity and recovery merits further investigation.

NR544 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Trauma as a Predictor of Dual Diagnosis

Juris P. Mezinskis, Ph.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Eugene C. Somoza, M.D., Mark W. Cohen, Ph.D., Sue R. Dyrenforth, Ph.D.

Summary:

The purpose of this study was to examine the relationship between trauma and chemical dependence. Previous studies suggest that the existence of either of these two variables is predictive of the other. Patients seeking treatment for substance abuse at the Cincinnati VA Medical Center (N = 260) were administered both the Traumatic Events Screen Inventory (TESI) and the Addiction Severity Index (ASI). A factor analysis of TESI results produced four highly independent factors: lifetime experience of traumatic stress, recent experience of trauma, homelessness with sexual and physical abuse, and a combination of being homeless and seeing others being victimized. Further statistical analysis (multiple regression) of the data determined which ASI variables most accounted for the TESI factors. Factor 1 was highly related to depression ($p \leq .001$), violence ($p \leq .001$), drug use, and attempted suicide. Factor 2 correlated with legal problems ($p \leq .01$), drug use ($p \leq .01$), and employment difficulties. Factor 3 related to suicidal thoughts and attempts ($p \leq .001$), hallucinations ($p \leq .02$), and psychiatric disorders. Factor 4 correlated with suicide attempts ($p \leq .05$), and employment problems ($p \leq .05$). TESI factors and the "need for treatment" in various areas as determined by the ASI will also be discussed as well as preferential coping strategies of patients who have experienced various degrees of trauma.

NR545 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Trauma Related Symptoms in Bosnian Refugees

Steven M. Weine, M.D., Psychiatry, Yale University, 184 Liberty Street, New Haven CT 06520; Daniel F. Becker, M.D., Thomas H. McGlashan, M.D., Dori Laub, M.D., Steve Lazrove, M.D., Dolores Vojvoda, M.D.

Summary:

Objective: To describe the psychiatric assessments of Bosnian Muslim refugees of "ethnic cleansing" recently resettled in the United States.

Method: Twenty refugees referred from an agency managing refugee resettlement underwent systematic, trauma-focused clinical interviews that included using standard assessment scales for post-traumatic stress disorder (PTSD), depression, and general psychiatric symptoms.

Results: The traumatic experiences of "ethnic cleansing" were massive in scope and genocidal in nature. The number of traumatic experiences was correlated with age. PTSD was diagnosed in 65% of the refugees and depression in 35%. PTSD severity scores were correlated with number of types of traumatic events experienced. Most refugees are highly symptomatic across 17 traumatic stress symptoms and three symptom clusters of PTSD. There is a higher frequency of reexperiencing and avoidance symptoms, and a lower frequency of hyperarousal symptoms.

Conclusions: The study shows that "ethnic cleansing" results in serious, severe psychiatric symptoms upon initial presentation. We found a high rate of PTSD and depression, consistent with the retrospective studies done among other groups of traumatized refugees. The finding that PTSD is more prevalent in older refugees appears to be a consequence of their having suffered more types of traumatic experiences. The unique profile of symptom clusters suggests that the survivors of "ethnic cleansing" might be suffering from a subtype of PTSD or from a trauma-related syndrome that has characteristics beyond that contained in the *DSM-IV* PTSD construct.

NR546 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Evoked Response Indicators of Attention in Disaster Survivors With and Without PTSD

Svein Blomhoff, M.D., Psychosomatic, National Hospital, Pilestredet 32, Oslo N0027, Norway; Ivar Reinvang, Ph.D., Ulrik F. Malt, M.D., C. Nielsen

Summary:

Objective: To study evoked response indicators of attention to various types of stimuli in survivors of a major disaster in relation to their mental health status after the disaster.

Method: 21 survivors of a passenger-vessel fire killing 159 persons were assessed by the CAPS-L and several self-report instruments, including the IES. Based on these assessments the subjects were classified as PTSD, other psychiatric syndrome, or no psychopathology cases. Auditory evoked response paradigm (p3-oddball distractor) was performed blindly to the psychiatric status of the patient with a standard tone (60% trials), target tone (20% trials), and distractor stimulus (20% trials). The distractor stimuli were digitized speech consisting of reversed (meaningless), positive content, or negative content words. Three blocks of 200 trials each were run in fixed order (reversed, positive, and negative distractors).

Results: PTSD patients showed higher amplitude and shorter latency of P3 to distractor words. Differences in P3 were also observed to target tones.

Conclusion: The findings indicate that electrophysiological markers of attention show specific features in PTSD patients which differ from healthy and psychiatric comparison groups.

NR547 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Are Long Delayed Traumatic Memories Accurate: An Independently Verifiable Case

Susan Mirow, M.D., Psychiatry, University of Utah, 73 G. Street, Salt Lake City UT 84103

Summary:

A Navajo teenager was raped and then witnessed the shooting of two tribal policemen who were later murdered.

Because of amnesia for these events she was unable to provide information to authorities about the incident. She presented for psychiatric care four years after the incident with symptoms of post-traumatic stress disorder (PTSD), dissociation, and major depression. She was seen on an intermittent basis and given pharmacotherapy and psychotherapy. This resulted in a moderate improvement in PTSD symptoms, depression, and dissociative symptoms. However, she continued to have amnesia for the events of that night.

During one visit, six years after the incident, her amnesia lifted when she noticed a peyote rattle which coincidentally was in my office. She suddenly and immediately recovered complete and highly detailed memories for that night. These memories proved to be precisely accurate by independent corroboration with federal investigators.

This demonstrates that delayed recovery of dramatic memories in a dissociative patient can be highly accurate.

NR548 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Biases in Mixed Models for Analysis of Clinical Trials

Zhengyu Wang, M.S., Research, Ill. State Psych Inst., 1153 N. Lavergne Avenue, Chicago IL 60651; John M. Davis, M.D.

Summary:

Most clinical trials include patients who do not complete the trial because of either dramatic improvement with treatment or because of clinical deterioration. Recently, mixed model (random regression) methods have been used to deal with such missing data problems.

Objective: We will evaluate mixed model methods in various clinical situations using both actual data from clinical trials and simulated data to see if this method can deal adequately with nonrandom missing data.

Method: We mathematically calculate the biases in mixed model estimations in common distributions. Using a large number of simulations, we quantitatively evaluate such bias. We also analyze empirical data from some of the classic double-blind studies of psychiatric drugs and compare the mixed model with other methods.

Results: From both mathematical and simulation approaches we find if the assumption of data missing at random is not true, the mixed model method produces biased results. Analysis of actual clinical trials by mixed models where missing data is due to clinical improvement or deterioration gives a markedly biased result.

Conclusions: Since mixed models can yield biased results in clinical trials with nonrandomly missing data, they should be used with caution.

NR549 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Outcome of Inpatient Psychiatric Care Over Time

Charles J. Rabiner, M.D., Comm. Research Foundation, 444 Camino Del Rio S. Ste 219, San Diego CA 92108; William B. Hawthorne, Ph.D., Michele W. Chadwick, Ph.D., Daniel C. Cohen, M.S.W.

Summary:

Objective: To delineate the outcome of inpatient psychiatric are over time.

Methods: The study employs a single-group repeated measures design. Selection includes every adult admission with a diagnosis other than primary substance related. Instruments are administered and data collected at admission, discharge, and quarterly thereafter for a one-year follow-up period. Instruments include: the Brief Symptom Inventory (BSI, Derogatis, 1982), the Medical Outcome Survey Short Form (SF-36, Ware & Sherbourne, 1992), the Behavior and Symptom Identification Scale (BASIS-32, Eisen, Dill, & Grob, 1987), the Client Satisfaction Questionnaire (CSQ-8, Attkisson & Zwick, 1982) at discharge only, and the Derogatis Psychiatric Rating Scale (DPRS, Derogatis, 1974).

Results: Findings ($n = 90$) included elevations well above the mean of the inpatient standardization sample on all BSI and BASIS-32 scales. Significant improvements in functioning and reductions in symptoms were found on all scales of the BASIS-32, ($p < .01$). Significant improvements in functioning were also found on all scales of the SF-36 except physical functioning, pain, and general health ($p < .05$). Poor responses from psychiatrists currently preclude analysis of DPRS data. Results, including follow-up data not currently available, will be presented.

Conclusions: Findings thus far suggest major impairment at admission, and, after treatment, a clear trend toward improved psychological and social functioning as well as symptom reduction.

NR550 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Predictors of Abstract Publication

Robert G. Stern, M.D., Psychiatry, Mount Sinai Med. Center, One Gustave Levy Place, New York NY 10029; Lora K. Heisler, M.S., Idan Sharon, M.D.

Summary:

Objective: This review attempted to identify design and outcome features of reports of schizophrenia treatment trials presented at conferences that are predictive of subsequent journal publication. The following hypotheses were tested: (1) Studies reporting a positive-result are more likely to be subsequently published than studies reporting a negative result; (2) Double-blind studies are more likely to be subsequently published than open-label studies;

and (3) Double-blind studies reporting a positive result are more likely to be subsequently published than all other studies.

Method: Ninety-five schizophrenia treatment trials not sponsored by pharmaceutical companies were identified through a review of abstracts of presentations at major conferences between 1986–1991. The type of design, outcome, and number of subjects in each study were recorded. Subsequent journal publication was ascertained by searches on Medline and PsychLit.

Results: Abstracts reporting positive results from double-blind studies (33/42) were published significantly more often than all other abstracts ($x^2 = 4.30$; df = 1; $p < .05$). However, positive-result trials were not more likely to be published (55/76) than negative-result trials (8/11), and double-blind studies were not more frequently published (37/48) than open-label studies (26/39).

Conclusion: We found fewer predictors of subsequent journal publication than we expected. The search for such predictors is important because it provides means to investigate publication bias, and to monitor trends in current research.

NR551 Wednesday, May 25, 3:00 p.m.-5:00 p.m.

Methodological Issues in Clinical Drug Trials in Schizophrenia

Robert G. Stern, M.D., Psychiatry, Mt. Sinai School Med., 130 W. Kingsbridge Road, Bronx NY 10468; Michael Davidson, M.D., James Schmeidler, Ph.D.

Summary:

This investigation examined the statistical design of controlled treatment studies in schizophrenia sponsored by academic researchers (not pharmaceutical companies). Interrelationships among four aspects of statistical design: statistical power, sample size (n), level of significance (alpha), and effect size, were examined.

A Medline search covering 1988–1992 identified 10 double-blind, placebo-controlled parallel treatment studies in schizophrenia. The number of subjects and outcome measurements/hypotheses tested were determined. For comparison purposes, conventional values were assigned for level of significance, power, and effect size. Level of significance was adjusted by the Bonferroni procedure for number of tests. Calculations were performed assuming one hypothesis per study. The following variables were calculated: a) Effect size required to achieve a statistical power of 0.80 for the actual n; b) Statistical power if the effect size was 0.5, or 1.0 for the actual n; and c) Number of subjects required to achieve statistical power of 0.8 if effect size was 0.5, or 1.0. These calculated values were then compared to actual values. The mean ±SD number of subjects per group was 16.4 ± 16.3, and of outcome criteria was 20.7 ± 12.0. The mean effect size (hypothesizing a statistical power of 0.80) was 1.6 ± 0.5, and the power (hypothesizing an effect size of 0.5, or 1.0) was 0.1 ± 0.1, and 0.4 ± 0.2, respectively. The number of subjects per group required to achieve a statistical power of 0.80 for an effect size of 0.5, or 1.0) were 105.73 ± 12.84, and 28.08 ± 3.42, respectively. The average calculated effect size was significantly higher than 1.0. Even for an effect size of 1.0 the average calculated powers were significantly lower than the conventional minimum requirement of 0.8. The corresponding values were calculated if only one hypothesis per study was tested: a) 1.05 ± 0.28 for the effect size; b) 0.37 ± 0.17, and 0.76 ± 0.15, respectively, for the statistical power; and c) 50.19, and 13.15, respectively, for the number of subjects. When one hypothesis was tested the calculated average effect size was significantly higher than 0.8. The average calculated power for an effect size 0.8 was significantly lower than the conventional minimum of 0.8. The average actual sample size was significantly smaller than those calculated to be necessary for effect size of 0.5. Almost all parallel, controlled treatment studies in schizophrenia, not sponsored by pharmaceutical companies appear to be designed in a manner which would allow them to identify only very large effect sizes. For the identification of moderate (0.5) treatment effect sizes, much larger numbers of subjects would be necessary.

NR552 Withdrawn

NR553 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Does Alcoholic Liver Disease Indicate Alcohol Dependence?

Thomas P. Beresford, M.D., Psychiatry, University of Colorado, VAMC 116 1055 Clermont Street, Denver CO 80220; Michael R. Lucey, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should understand the validity characteristics of alcoholic cirrhosis as a marker for alcohol dependence.

Summary:

Objective: Medical practitioners commonly regard the signs and symptoms of alcoholic liver disease as primary evidence of alcohol dependence and use these data to label alcoholics. Alcoholism researchers, however, diagnose alcohol dependence (AD) on behavioral criteria. No one, to our knowledge, has studied whether and to what extent the two sets of criteria converge.

Method: In prospective fashion we observed two subject groups made up of patients seeking liver transplant. The first included 82 subjects with clinically diagnosed alcoholic cirrhosis (AC) who were subsequently evaluated for alcohol dependence by standard criteria (both *DSM-III-R* and *DSM-IV-R*) and a converse group of 110 subjects diagnosed as alcohol dependent who were then assessed for alcoholic cirrhosis. Cirrhosis and AD assessments were done in a blinded manner. We then compared the concordance of the two diagnoses.

Results: AD occurred in 79% of those with alcoholic cirrhosis while alcoholic cirrhosis was diagnosed in 73% of those with AD. The two diagnoses were highly sensitive (95% and 83%, respectively) but nonspecific (44% and 41%).

Conclusion: Alcoholic cirrhosis and dependence co-occur only in about three cases in every four. This is true whether AD or alcoholic cirrhosis is diagnosed first. These data question the use of alcoholic cirrhosis as an indication of alcoholic dependence both in research studies and in clinical use. This is especially important in settings such as liver transplant in which misdiagnosis may result in withholding lifesaving treatment.

References:

1. Lucey, ML, Beresford, TP: Can We Triage Alcoholics With End-Stage Liver Disease? *American Journal of Gastroenterology* 88:1314–1315, 1993.

2. Beresford, TP, Schwartz, J, Wilson, D, Merion, RM, Lucey, MR: The Short Term Psychological Health of Alcoholic and Non alcoholic Liver Transplant Recipients. *Alcoholism, Clinical and Experimental Research* 16:996–1000, 1992.

NR554 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Evaluation of Bupropion Versus Placebo for Treatment of Nicotine Dependence

Linda H. Ferry, M.D., Preventive Medicine, J.L. Pettis Mem. VA Hosp., 11201 Benton Street, Loma Linda CA 92391; Raoul J. Burchette, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1) recognize characteristics of high risk smokers (depression, etc) 2) list the outcomes of previous antidepressant trials for smoking 3) explain the role of dopamine reward mechanism in nicotine dependence 4) examine smoking histories of smokers to stratify for treatment options 5) treat chronic smokers with bupropion to improve cessation.

Summary:

Previous trials have shown modest or no effect using antidepressants for smoking cessation. To evaluate the efficacy of bupropion, a randomized, placebo-controlled, double-blind study was conducted using 190 non-depressed male and female veterans. All subjects smoked ≥1 packs of cigarettes daily and had failed multiple attempts to cease. Bupropion (300 mg per day) was given for 12 weeks. All subjects attended a one-week group smoking cessation class and biweekly relapse prevention meetings for 16 weeks with a follow-up visit at six months.

Self-reported 48-hour quit attempts were observed in 67% of the bupropion group and 41% of the placebo group ($p < 0.0003$). Abstinence ≥1 week was achieved in 57% of bupropion group and 32% of placebo group ($p < 0.0001$). Four-week abstinence during medication phase (main a-priori efficacy variable) was achieved in 40% of bupropion group and 24% of placebo group ($p < 0.02$). Continuous abstinence until the end of medication group phase was achieved in 28% of the bupropion group and in 21% of the placebo group ($p < 0.05$). Salivary cotinine levels confirmed all self-reported cessation ≥1 week.

Bupropion shows significant efficacy in smoking cessation in heavily addicted cigarette smokers.

References:

Breslau N, Kilbey M, Andreski P: Nicotine dependence and major depression. New evidence from a prospective investigation. *Arch Gen Psychiatry* 50:31–35, 1993.

Glassman AH, Covey LS, Dalack GW, et al: Smoking cessation clonodine, and vulnerability to nicotine among dependent smokers. *Clin Pharamarcol Ther* 54:670–679, 1993.

NR555 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Predictors of Response to Paroxetine Therapy in OCD

Martin Steiner, Ph.D., Clinical Development, Smith Kline Beecham, P.O. Box 1510, King of Prussia PA 19406; Rosemary Oakes, M.S., Ivan P. Gergel, M.D., David E. Wheadon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the effectiveness of paroxeting in the treatment of OCD and that baseline characteristics may be predictive of response to therapy is possible.

Summary:

The selective serotonin reuptake inhibitors (SSRIs) are distinguished from other classes of antidepressants in that they have demonstrated efficacy in the treatment of obsessive-compulsive disorder (OCD). For example, the SSRI paroxetine has been shown in controlled clinical trials to be effective in the treatment of both major depressive disorder and OCD. While demographic variables as predictors of response to therapy have been widely studied in depression, they have been less so in OCD.

Objective: This analysis examines the outcomes of paroxetine treatment for OCD as a function of baseline demographic and disease characteristics.

Method: In this 12-week, fixed-dose, multicenter study, 348 patients meeting *DSM-III-R* criteria for OCD were randomized in a double-blind fashion to receive either 20mg paroxetine, 40mg paroxetine, 60mg paroxetine or placebo. Endpoint analysis of the mean change from baseline in Yale-Brown Obsessive-Compulsive Scale (YBOCS) total score revealed statistically significant improvement for the two higher paroxetine dose groups as compared to placebo. The response to therapy was examined by: gender, co-morbid psychiatric diagnosis, duration of disease, and severity of illness.

Results: In this analysis, males, patients who presented without co-morbid psychiatric illness, and patients with longer disease histories showed greater improvement with paroxetine treatment. While the female population did not exhibit a statistically significant response to paroxetine compared to placebo, this may be due in part to the small sample size (owing to a restriction on women of child-bearing potential) and a higher placebo response. For those patients with less severe OCD symptoms (YBOCS ≤ 26), 40mg paroxetine was significantly better than placebo, whereas patients with more severe OCD symptoms (YBOCS > 26) showed a greater response to the 60mg dose.

Conclusions: These results demonstrate the effectiveness of paroxetine in the treatment of OCD and suggest that baseline characteristics may be predictive of response to therapy.

References:

1. Yonkers KA, Kando JC, Cole JO, Blumenthal S: Gender differences in pharmacokinetics and pharmacodynamics of psychotropic medication. *Am J Psychiatry* 149:587–595, 1992.

2. Wheadon DE, Bushnell WD, Steiner M: A fixed dose comparison of 20, 40, or 60 mg paroxetine to placebo in the treatment of obsessive-compulsive disorder. Presented at the 1993 Annual Meeting of the American College of Neuropsychopharmacology; Honolulu, HI; December 14, 1993.

NR556 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Effect of Cognitive/Behavioral Therapy on Twenty-Four Hour Food Intake in Bulimia Nervosa

Theodore E. Weltzin, M.D., Psychiatry, University of Pittsburgh, E-725 3811 O'Hara Street, Pittsburgh PA 15213; Lee-Keung G. Hsu, M.D., Madelyn Fernstrom, Ph.D., Burt Bolton, B.S., Walter H. Kaye, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize cognitive/behavioral therapy, with or without nutritional counseling, helps to normalize total caloric intake and decrease fat intake in women with bulimia nervosa.

Summary:

It has been demonstrated by a number of studies that cognitive/behavioral therapy (CBT) significantly decreases bulimic behavior as assessed by patient report. However, to our knowledge the effect of CBT on feeding behavior has not been confirmed in a laboratory setting designed to measure feeding behavior in humans.

In this study we assessed feeding behavior before and after 14 weeks of psychological treatment in 52 women with bulimia nervosa (weight: 130 ± 18 lbs; age 25 ± 7 years; binge frequency: 10 ± 8/week; and vomit frequency 11 ± 9/week). Feeding behavior was assessed during a 24-hour interval when subjects lived in a laboratory setting designed to characterize feeding behavior in humans. Subjects participated in one of four different psychological treatments: 1) CBT, 2) nutritional counseling (NC), 3) support group (SG), and 4) CBT + NC. Treatment significantly decreased total caloric intake (5428 ± 4439 vs. 3314 ± 2362 kcal/day, $t = 3.79$, $p < .001$) and fat intake (33.1 ± 6.2 vs. 29.6 ± 10.3% fat,

$t = 2.26$, $p < .05$) for the whole group. We also examined the effects of different treatments on feeding behavior. Bulimic subjects who were treated with CBT showed a significant decrease in total caloric intake [CBT: 7779 ± 6133 vs 3015 ± 1761 kcal/day, $t = 3.25$, $p < .01$; CBT + NC: 4934 ± 3260 vs 3093 ± 2513 kcal/day, $t = 2.94$, $p < .01$]. Caloric intake was not significantly decreased in the SG or NC groups.

To our knowledge, this study is the first to report the effects of psychological treatment for bulimia nervosa on feeding behavior as measured in a laboratory setting. Furthermore, these data confirm that CBT, with or without NC, helps to normalize total caloric intake and decrease fat intake in women with bulimia nervosa.

References:

1. Weltzin TE, Hsu LKG, Pollice C, Kaye WH: Feeding patterns in bulimia nervosa. *Biol Psych* 30:1093–1110, 1991.

2. Kaye WH, Weltzin TE, McKee M, McConaha C, Hansen D, Hsu LKG: Laboratory assessment of feeding behavior in bulimia nervosa and healthy volunteer women: methods for development of a human feeding laboratory. *Am J Clin Nutr* 55:372–380, 1992.

NR557 Thursday, May 26, 9:00 a.m.–10:30 a.m.

A Four-Year Follow-Up Study of Eating Disorders and Medical Complications in Young Women with Insulin-Dependent Diabetes Mellitus

Anne C. Rydall, B.Sc., Psychiatry, The Toronto Hospital, 200 Elizabeth Street, Toronto Ont. M5G 2C4, Canada; Gary M. Rodin, M.D., Marion P. Olmsted, Ph.D., Robert G. Devenyi, M.D., Denis Daneman, M.B.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the clinical features, including insulin omission, of eating disorders in young women with insulin-dependent diabetes mellitus and to appreciate the consequences in terms of metabolic control and long-term complications.

Summary:

Insulin-dependent diabetes mellitus (IDDM) and eating disorders such as anorexia nervosa and bulimia nervosa are both relatively common conditions in young women. The association of eating disorders with IDDM may lead to impaired metabolic control and to more long-term diabetes-related complications.

Objectives: We conducted a four-year follow-up study of 107 young women with IDDM to determine the course of eating disorder symptoms, and whether a suspected eating disorder or initial assessment would be associated with medical complications at follow up.

Method: Ninety of the original 107 subjects (84%) were assessed by: i) self-report questionnaire, ii) Eating Disorder Examination interview, and iii) medical evaluation, including fundus photography to identify diabetic retinopathy, and urinary albumin excretion, an indicator of diabetic nephropathy. Mean age of subjects at follow-up was 19.4 ± 1.7 years, and mean duration of IDDM was 10.7 ± 4.1 years.

Results: The following disturbed eating symptoms present on initial evaluation persisted at four-year follow-up: binge eating ($p < .0001$), self-induced vomiting ($p < .005$), and dieting for weight loss ($p < .005$). Insulin manipulation to lose weight increased from 13.8% to 33.3% ($p < .005$), self-induced vomiting increased from 8% to 17% ($p = .06$), and dieting increased from 40% to 53.9% ($p < .05$) over the four-year period. Diabetic retinopathy was present in eight of nine (88.9%) young women with a previously suspected eating disorder compared to only 14 of 56 (25%) without an eating disorder ($p < .0005$). Microalbuminuria was present in three of the nine (33.3%) subjects with a previously suspected eating disorder, compared to 17 of 62 subjects (27.4%) without (ns).

Conclusions: These findings suggest that disturbed eating behaviours are relatively common and persistent in young women with IDDM, and that such individuals may be at increased risk for some long-term diabetes-related complications.

References:

1. Rodin G, Daneman D: Eating disorders and IDDM: A problematic association. *Diabetes Care* 15:1402–1414, 1992.

2. Rodin G, Craven J, Littlefield C, Murray M, & Daneman D: Eating disorders and intentional insulin undertreatment in adolescent females with diabetes. *Psychosomatics* 32:171–176, 1991.

NR558 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Optimal Phase Advancement for Resolution of SAD

Katherine H. Thomas, M.D., Psychiatry, Oregon Health Sci., 3181 SW Sam Jackson Park Road, Portland OR 97201; Alfred J. Lewy, M.D., Vance K. Bauer, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should know that bright light suppresses human nighttime melatonin production, bright light shifts circadian rhythms according to a phase response curve, and can be used to treat circadian sleep and mood disorders. The participant will also recognize the clinical symptoms of winter depression and plan treatment regimes.

Summary:

As seasonal affective disorder (or winter depression) has become established as a diagnosis, etiology and appropriate treatment regimes have become clarified. Terman *et al.* (1989) reviewed pooled data from multicenter analyses evaluating the effectiveness of light therapy trials of 332 patients, concluding that morning bright light treatment was consistently more effective than bright lift scheduled at other times. By using the melatonin onset as a marker of circadian phase, we found that individuals with winter depression are phase delayed compared with normals *and that morning light is more antidepressant than evening light* (Lewy *et al.*, 1987). Improvement in clinical symptoms with morning bright light treatment is correlated with an advance in the onset of nighttime melatonin production.

To further clarify the interrelationship between phase advances in circadian rhythms and the resulting antidepressant response, we examined the dim light melatonin onsets (DLMOs) and antidepressant responses of 48 winter depressives following two hours of morning bright light treatment (2500 lux). The majority of winter depressives demonstrated clinical improvement following a phase advance of one hour in the timing of their melatonin onset. An advance in circadian rhythms of more than one hour appeared to reduce the antidepressant effect of bright light.

Determining the optimal phase advance in circadian rhythms will help plan treatment for maximum clinical response.

References:

1. Lewy AJ, Sack RL, Miller LS, Hoban TH: Antidepressant and circadian phase-shifting effects of light. *Science* 235:352–354, 1987.

2. Terman M, Terman JS, Quitkin FM, et al: Light therapy for seasonal affective disorder: a review of efficacy. *Neuropsychopharmacology* 2:1–22, 1989.

NR559 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Paroxetine Dose: Experience in Clinical Practice

Ivan P. Gergel, M.D., Clinical Development, Smith Kline Beecham, P.O. Box 1510, King of Prussia PA 19406; David E. Wheadon, M.D., James P. McCafferty, B.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that a daily dose of 20 mb of paroxetine is effective in treating depression.

Summary:

Placebo-controlled trials established the safety and efficacy of paroxetine in treating major depression. The recommended starting dose is 20 mg/day with provision to titrate up to 50 mg/day.

Objective: The object of the present study was to assess the therapeutic response to paroxetine in a clinical practice setting when the initial dose of 20 mg is maintained for at least six weeks.

Methodology: The study was a randomized, open-label, multicenter trial of eight-weeks duration. Eligible for entry were adult outpatients with a diagnosis of major depression who in the judgment of the treating psychiatrists warranted treatment with antidepressant medication. Patients were randomized in a 4:1 ratio to receive either paroxetine or one of two comparators: fluoxetine or nortriptyline. Dosing for patients receiving one of the comparator drugs followed the approved labeling for the respective agents. Paroxetine therapy was started at 20 mg/day with no increases permitted until after six weeks of treatment.

Results: Clinical evaluations were available for 1087 paroxetine, 200 fluoxetine, and 49 nortriptyline patients. In the paroxetine group, 14% withdrew due to an adverse event, and/or lack of efficacy, 18% were classified as nonresponders, and 68% were rated much improved or very much improved while being treated with 20 mg. Approximately 220 paroxetine patients had the dose increased after week 6, and of these 78% achieved a status of much improved or very much improved. These rates were comparable to rates observed for the fluoxetine group (78%) and higher than for the nortriptyline group (59%). The incidence of adverse events associated with paroxetine was comparable to or less than that reported during placebo-controlled trials.

Conclusions: These observations in the clinical practice setting support previous results indicating that a daily dose of 20 mg of paroxetine is effective in treating depression.

References:

1. Dunbar GC, Cohn JB, Fabre LF, et al: A comparison of paroxetine, imipramine and placebo in depressed out-patients. *Br J Psychiatry* 159:394–398, 1991.

2. Dunner DL, Dunbar GC: Optimal dose regimen for paroxetine. *J Clin Psychiatry* 53(2,suppl):21–26, 1992.

NR560 Thursday, May 26, 9:00 a.m.–10:30 a.m.

The Pharmacology of Antidepressants: Characteristics of the Ideal Drug

Elliott Richelson, M.D., Mayo Clinic Jacksonville, 4500 San Pablo Road, Jacksonville FL 32224.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to define many pharmacological properties of antidepressants from their *in vitro* synaptic pharmacology and, from this information, to define some of the characteristics of the ideal antidepressant.

Summary:

Objective: To define many pharmacological properties of antidepressants from their *in vitro* synaptic pharmacology and, from this information, to define some of the characteristics of the ideal antidepressant.

Method: 1) Inhibitor constants for uptake blockade were obtained from competitive uptake studies with [^{3}H]norepinephrine, [^{3}H]5-hydroxytryptamine (5-HT), and [^{3}H]dopamine in rat brain synaptosomes prepared from hippocampus, frontal cortex, and striatum, respectively. 2) Radioligand binding assays were used to determine equilibrium dissociation constants for antidepressants at histamine H_1, muscarinic, α_1-adrenergic, and dopamine D_2 receptors. For sources of receptors, normal human brain tissue was obtained at autopsy with IRB approval.

Results: Newer, second-generation antidepressants were more potent and selective for blocking uptake of serotonin than uptake of norepinephrine. Rank order of potency at blocking uptake of norepinephrine was: clomipramine > paroxetine >> venlafaxine > sertraline > fluoxetine > fluvoxamine > nefazodone > bupropion. For these drugs, rank order of potency at blocking uptake of serotonin was: paroxetine >> sertraline > clomipramine > fluvoxamine > fluoxetine > venlafaxine > nefazodone >> bupropion. Serotonin selectivity for the most potent 5-HT uptake inhibitors was: fluvoxamine > sertraline > paroxetine > trazodone > fluoxetine > venlafaxine > clomipramine > nefazodone. In general, the newer compounds were weak antagonists at all four receptor sites. This receptor blocking profile predicts a side-effect profile for the newer compounds different from that of the older antidepressants.

References:

1. Richelson E: Antidepressants and brain neurochemistry. *Mayo Clinic Proceedings* 65:1227–1236, 1990.

2. Preskorn SH: Recent pharmacologic advances in antidepressant therapy for the elderly. *Am J Med* 94:2S–12S, 1993.

NR561 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Fluoxetine Versus Placebo: Long-Term Treatment of Major Depressive Disorder

Patrick McGrath, M.D., NYSPI, 722 West 168th Street Unit 35, New York NY 10032; Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D., Jay D. Amsterdam, M.D., Jan A. Fawcett, M.D., Frederick Reimberr, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be familiar with the largest available clinical trial data set documenting the efficacy of fluoxetine in continuation/maintenance treatment of major depression.

Summary:

At five sites, patients with major depressive disorder (MDD) and an initial modified 17-item Hamilton Rating Scale for Depression (HAM-D-17*) score ≥ 16 were treated openly with fluoxetine 20 mg/day for 12 weeks. Patients who experienced full remission (HAM-D-17* total score ≤ 7 for three consecutive weeks and no MDD) entered a double-blind discontinuation phase. Patients were randomized to one of four parallel treatment groups: fluoxetine 20 mg/day for 50 weeks (N = 102), fluoxetine 20 mg/day for 38 weeks followed by placebo for 12 weeks (N = 100), fluoxetine 20 mg/day for 14 weeks followed by placebo for 36 weeks (N = 97), and placebo for 50 weeks (N = 96). Relapse or recurrence of depression was defined as either meeting criteria for MDD (including two-week duration) at any visit or achieving a HAM-D-17* score ≤ 14 for three consecutive weeks. For the patients randomized to double-blind treatment (N = 395), data are presented for relapse rates at study week 50 (38 weeks post-randomization) for all those continued to that point or who relapsed on active treatment compared with relapse rates for those randomized to placebo. The relapse rate on active treatment was 56% (79/141) compared with that on placebo of 81.4% (57/70; $p < .001$).

References:

1. Montgomery SA, Dufour H, Brion S, et al: The prophylactic efficacy of fluoxetine in unipolar depression. *Br J Psychiatry* 153(Suppl 3):69–76, 1988.

2. Frank E, Kupfer DJ, Perel JM: Three-year outcomes for maintenance therapies in recurrent depression. *Arch Gen Psychiatry* 47:1093–1099, 1990.

NR562 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Imipramine Plasma Levels: Response Curves in Panic

Matig R. Mavissakalian, M.D., Psychiatry, Ohio State University, 473 West 12th Avenue, Columbus OH 43210; James M. Perel, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the importance of plasma level determination for both the parent compound and its active metabolite in panic disorder with agoraphobia patients treated with imipramine.

Summary:

Plasma concentrations of imipramine (IMI) and N-desmethylimipramine (DMI) were assessed in 48 panic disorder with agoraphobia patients who completed an eight-week, randomized, double-blind, dose-ranging study with imipramine hydrochloride: low dose (0.5 mg/kg/day, n = 17), medium dose (1.5 mg/kg/day, n = 17), and high dose (3 mg/kg/day, n = 14). Assessments included panic diaries, patient- and clinician-rated symptom scales of panic and phobias, as well as operationalized criteria of response. Analysis included correlational and dose-response stratifications with total, IMI, and DMI concentrations as well as multiple linear regression and logistic regression analysis with total, IMI, and DMI levels as predictors of symptom severity and response.

Results revealed a sigmoidal (clinical) or linear (diary) relationship between total plasma levels and response in panic measures. The dose response curve with IMI and DMI levels mirrored that obtained with total plasma levels. On the other hand, a curvilinear relationship of phobic response was associated with the highest concentrations of DMI, while the IMI-response curve remained linear or sigmodial. The results have practical implications vis-á-vis the selection of optimal plasma levels in the acute treatment of panic disorder with agoraphobia and likewise suggest separate and different mechanisms for imipramine's antipanic and antiphobic effects.

References:

1. Mavissakalian M, Perel J, Michelson L: The relationship of plasma imipramine and n-desmethylimipramine to improvement in agoraphobia. *J Clin Psychopharmacol* 4(1):36–40, 1984.

2. Mavissakalian M, Perel J: Imipramine dose-response relationships in panic disorder with agoraphobia: preliminary findings. *Arch of Gen Psychiatry* 46(2):127–131, 1989.

NR563 Thursday, May 26, 9:00 a.m.–10:30 a.m.

Estrogen Plus Fluoxetine for Geriatric Depression

Gary W. Small, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles CA 90024; Lon S. Schneider, M.D., Susan Holman, M.S., Alexander Brystritsky, M.D., Barnett S. Meyers, M.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will know of potential interactions between estrogen replacement therapy and antidepressant effects in geriatric depression.

Summary:

Objective: The estrogen deficiency of the postmenopausal state may be a factor in both the pathogenesis of late-life depression and in therapeutic response. Studies of euthymic, asymptomatic postmenopausal women given estrogen replacement therapies (ERT) suggest improved psychological functioning. Despite estrogen's neuromodulatory effects, including down regulation of beta-adrenergic and serotonergic receptors, ERT has not been shown to affect antidepressant response in severely depressed postmenopausal women.

Methods: We examined the therapeutic response in 72 elderly depressed women receiving ERT compared with 295 not receiving ERT who entered a randomized, placebo-controlled, double-blind, multicenter trial of fluoxetine (20 mg/d) for six weeks. Outpatients met DSM-III-R criteria for unipolar major depression, were age ≥ 60 years and had baseline $HAMD_{17}$ scores ≥ 16.

Results: There was a significant interaction between ERT status and treatment effect ($p = 0.015$). Patients on ERT who received fluoxetine had substantially greater % change in $HAMD_{21}$ scores compared with patients on ERT who received placebo (40.1% vs. 17.0%, respectively). There was only a slight benefit for fluoxetine over placebo for non-ERT patients (36.1% vs. 30.4%). ERT patients and non-ERT patients did not differ significantly with respect to race and baseline $HAMD_{17}$ scores, but ERT patients were significantly younger (66.1 ± 4.8 vs. 68.3 ± 6.0 yrs, $p = 0.003$). Discontinuation for an adverse event or any reason did not differ between ERT and non-ERT patients in either fluoxetine- or placebo-treated groups.

Conclusions: ERT use predicted greater clinical improvement with fluoxetine, possibly augmenting its effect, and suggesting that ERT status be considered in geriatric clinical trials.

References:

1. Schmidt PJ, Rubinow DR: Menopause-related affective disorders: a justification for further study. *Am J Psychiatry* 148:844–852, 1991.

2. Zohar T, Shapira B, Oppenheim G, et al: Addition of estrogen to imipramine in female-resistant depressives. *Psychopharm Bull* 21:705–706, 1985.

NR564 Thursday, May 26, 12 noon–2:00 p.m.

Clinical Psychopharmacologic Trials: Cost of Patient Recruitment

Naresh P. Emmanuel, M.D., Psychiatry, Medical University, 171 Ashley Avenue, Charleston SC 29425; Michael R. Ware, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

Summary:

Recruitment of patients is a vital, expensive, and unpredictable aspect of conducting clinical pharmacology trials. Adherence to strict inclusion criteria, use of placebo, and overestimating the number of potential subjects entering a study often contribute to poor recruitment. The Clinical Research Section (CRS) of the Department of Psychiatry, Medical University of South Carolina, regularly employs newspaper, radio, and television advertising to enroll outpatients into clinical psychopharmacology studies in anxiety and mood disorders. We tracked 492 telephone calls received by the CRS from July to September 30, 1993. We then examined the specific media sources of which the patients became aware of the study. We were interested in determining the media cost per patient recruited from the different media used for advertising.

Results: 449 responses were directly attributable to media advertising. Radio was least expensive and the least effective. It took 40 radio spots, six television spots, and 0.5 newspaper spots to recruit one subject. Out of 475 subjects evaluated by telephone screens, 58% were given appointments for a structured clinical interview with a 38% enrollment rate. The cost of recruitment and alternative methods to improve recruitment will be discussed.

NR565 Thursday, May 26, 12 noon–2:00 p.m.

Factors That Influence the Length-of-Stay on an Inpatient Psychiatric Unit

James M. Schuster, M.D., Psychiatry, Allegheny General, 320 East North Avenue, Pittsburgh PA 15212; Ester Mandelker, Ph.D., Kenneth L. Goetz, M.D.

Summary:

During the past several years the average length of stay has decreased significantly on many inpatient psychiatric units. This change is undoubtedly due at least in part, to utilization review by managed care companies. Their efforts may have affected the care of all patients by changing physicians' practice patterns.

This study examined 81 patients on a general psychiatric unit with a diagnosis of major depression. It evaluated many demographic factors and clinical findings as well as whether or not the patient's stay was reviewed to try to determine factors which influence length of stay. Data were evaluated using stepwise multiple regression. Factors which were found to be significant included the severity of the patient's illness at the time of admission (as measured by the Beck Depression Inventory and the Global Assessment Scale) as well as the patient's age. Patients with concurrent utilization review had a shorter length of stay than other patients, but this difference was not great enough to be statistically significant.

NR566 Thursday, May 26, 12 noon–2:00 p.m.

Biopsychosocial Traits of General Hospital Patients

Gail A. Mallory, Ph.D., Nursing, Shadyside Hospital, 4006 Murray Avenue, Pittsburgh PA 15217; Jeremy S. Musher, M.D., Jess D. Amchin, M.D.

Summary:

The purpose of this study was to describe the biopsychosocial characteristics and associated costs of health care delivered to general hospital patients with concurrent psychiatric and non-psychiatric diagnoses. There is increasing evidence of higher costs associated with non-psychiatric patients in the general hospital who have a secondary psychiatric diagnosis. In this descriptive, case-control study, 1,537 medical records of general hospital patients with psychiatric co-morbidity and 314 general hospital patients without psychiatric co-morbidity matched on DRG, age, gender, and severity of illness were reviewed. Results found:

	PSYCHIATRIC CO-MORBIDITY	MATCHED GROUP
LOS	9.4 days	7.2 days
Psychiatry consult	30%	1.6%
Psychology consult	4%	2.8%
Social Service	79%	67.5%
Pastoral Care	83%	79%
Sitter	10%	0.6%
Restraints	14%	1.9%

Financial data are being calculated. The findings from this study demonstrate the increased resources used to provide care to general hospital patients with psychiatric co-morbidity. These findings are essential in planning and evaluating programs designed to maximize clinical and financial outcomes of general hospital patients with psychiatric co-morbidity.

NR567 Thursday, May 26, 12 noon–2:00 p.m.

Do Nice Patients Drive Out Difficult Cases?

Alex Richman, M.D., Psychiatry, Dalhousie University, 5959 Spring Garden Road #609, Halifax NS B3H 1Y5, Canada; Cyril Nair, M.A., Leonard MacLean, Ph.D.

Summary:

Should the Clinton Health Plan cover unlimited visits for psychiatric care? Would 30 visits per year be overly restrictive? Would costs be controlled with patients paying 50% of the fee?

Canadian NHI has not limited psychiatrists' care. From a five-year longitudinal analysis of unrestricted psychiatrists' care in one Canadian province, we have some relevant information. Over the five-year period, half the patients had three of fewer visits. However, one-half the psychiatrist hours were used by 5% of the patients. On the average, over a five-year period, the same 31 patients used half a psychiatrists' time. Social selection is also marked. Over half of the prolonged-therapy cases were women aged 15 to 44 and/or residents in the highest income areas.

We believe that provision of 30 visits per year would result in "nice" patients driving out difficult cases, the reverse of Gresham's Law (bad money drives out good). A co-insurance fee of 50% would be regarded as a subsidy to socially-selected cases, rather than a deterrent to longer-term therapy. It seems that the current mental health care reform plan provides a subsidized "psychotherapy annuity" to high-cost providers.

NR568 Thursday, May 26, 12 noon–2:00 p.m.

Efficacy of Drugs Used in Psychiatry Versus Internal Medicine

John M. Davis, M.D., Research, Ill. State Psych Inst., 1153 N. Lavergne Avenue, Chicago IL 60651.

Summary:

Medicine is becoming so prohibitively expensive that even wealthy societies cannot afford the costs. This reality is reflected in managed care programs, President Clinton's health care reform, etc. Thus, each medical specialty will need to justify its treatments to continue receiving reimbursement.

Objective: Our purpose is to present a meta-analysis of all controlled studies on classic antipsychotics, clozapine, and risperidone; various classes of antidepressants; mood stabilizers; anti-obsessive-compulsive disorder agents; antipanic agents; antidepressant augmentation strategies; antidepressants for cocaine abuse; and naltrexone for alcoholism.

Method: Efficacy will be calculated using the Mantel-Hanszel method and the DerSimonian-Laird method and will then be compared to the outcome of similar analyses of classic antibiotics; drugs used for heart disease and hypertension; anticancer therapies; and for certain surgical procedures.

Results: The efficacy of drugs used in psychiatry is usually double or even triple the percent of patients with good response over that seen with placebo. This is similar to the efficacy of drugs for a variety of medical conditions.

Conclusions: The average efficacy of psychiatric drugs compares quite favorably to the benefit achieved with drugs used in internal medicine, such as antibiotics and cardiotropic agents.

NR569 Thursday, May 26, 12 noon–2:00 p.m.

Inhibited and Uninhibited Temperament at Age Two: Psychophysiology and Behavior Twelve Years Later

Carl E. Schwartz, M.D., Psychiatry, Harvard Medical School, 74 Fenwood Road, Boston MA 02115; Jerome Kagan, Ph.D., Joseph J. Schildkraut, M.D., Rachel J. Kramer, Ph.D., Nancy Snidman, Ph.D.

Summary:

This project seeks to understand the relationship between infant temperament and outcome at adolescence. Two of the most stable temperamental dimensions in children are the tendency to show inhibited or uninhibited behavior with unfamiliar people, objects, and procedures. We studied 76 children age 13 to 14 categorized in the second year of life as inhibited or uninhibited. Studies have suggested that inhibition may be a risk factor for the development of childhood psychopathology.

Psychophysiological assessments included the Stroop Interference Test and measurements of urinary catecholamine output, orthostatic reactivity of diastolic blood pressure, heart rate, and salivary cortisol. Adolescents who were inhibited in the second year of life could be distinguished from those who were uninhibited (aggregate physiological index: inhibited boys = +.10 vs. uninhibited boys = −.12, t = 1.67, p = .05; inhibited girls = +.12 vs. uninhibited girls = −.15, t = 1.81, p = .04). The Stroop data show that 12 years after initial selection, adolescents who were inhibited as young children demonstrated a vulnerability to becoming affectively aroused by information that has threatening symbolic meaning (mean difference score threat minus positive words: inhibited adolescents = +.68 vs. uninhibited adolescents = −.58, t = 1.92, p = .03). Similar findings have been observed in studies of adults with anxiety disorders, which we hypothesize inhibited infants are at risk for developing in later life. Blind direct psychiatric interviews of subjects will further test this hypothesis.

NR570 Thursday, May 26, 12 noon–2:00 p.m.

Effect of Methylphenidate on Signal Detection Indices in Behavior Disordered Adolescent Inpatients

Daniel F. Becker, M.D., Yale Psychiatry Inst., P.O. Box 208038, New Haven CT 06520; William S. Edell, Ph.D., Kenneth N. Levy, B.A., Terry Ann Fujoika, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To examine the effect of methylphenidate (MPH) on signal detection indices in behavior disordered adolescent inpatients.

Method: Eighteen inpatients with disruptive behavior disorders (conduct disorder, oppositional defiant disorder, and/or ADHD) received a perceptually degraded form of a visual continuous performance test (CPT), while in a medication-free state. Signal detection theory indices were calculated from the raw (hit rate and false alarm rate) scores; these were *perceptual sensitivity* (d'; the ability to distinguish signal from non-signal stimuli) and *response criterion* (β; the amount of perceptual evidence required to respond to a stimulus as a signal). All subjects were subsequently treated with MPH, up to 40 mg. per day. Based on behavioral ratings from ward and classroom settings, patients were designated by their medicating physicians as MPH-responders ($n = 12$) or non-responders ($n = 6$). Independently, subjects received a CPT reassessment while on MPH.

Results: At baseline assessment, there was no significant difference between responders and non-responders with regard to either d' or β. On MPH, there continued to be no difference between groups for β, but responders had significantly higher d' values than non-responders ($p < .005$).

Conclusions: These results indicate that clinical response to MPH in this patient popuiation is associated with improved perceptual sensitivity—thus suggesting a specific psychophysiologic action for stimulant therapy in behavior disordered adolescents.

NR571 Thursday, May 26, 12 noon–2:00 p.m.

Attentional and Intellectual Deficits in Unmedicated Behavior Disordered Adolescent Inpatients

Daniel F. Becker, M.D., Yale Psychiatry Inst., P.O. Box 208038, New Haven CT 06520; William S. Edell, Ph.D., Terry Ann Fujioka, Ph.D., Kenneth N. Levy, B.A., Thomas H. McGlashan, M.D.

Summary:

Objective: To examine the hypothesis that impairments in attention and verbal intelligence are associated with seriously maladaptive social behavior in behavior disordered adolescents.

Method: Twenty-five unmedicated adolescent inpatients with disruptive behavior disorders (conduct disorder, oppositional defiant disorder, and/or ADHD) were rated during a one-month period for frequency of severe disruptive episodes, or "critical incidents" (CI); these included assaults, behavior resulting in the use of restraints, etc. All subjects independently received intelligence testing and continuous performance testing (CPT) of visual vigilance.

Results: Based on CI scores, subjects were divided into a high-CI group (CI > 5; $n = 9$) and a low-CI group (CI < 4; $n = 16$). On the CPT, the high-CI group showed more impairment in perceptual sensitivity (d'; an index of the ability to distinguish signal from non-signal stimuli). The high-CI group also had lower verbal IQ scores. (Both findings were significant at the $p < .05$ level.) The latter result was largely due to differences in Comprehension subtest scores ($p = .001$).

Conclusions: These results support the hypothesis. The inverse relationship between d' and CI confirms previous observations that inattention is associated with behavioral dyscontrol, and may have implications for the mechanism of effect of stimulant medications in these patients. The negative association between CI and verbal comprehension may have implications for the role of verbal intelligence in the accurate perception of social cues.

NR572 Thursday, May 26, 12 noon–2:00 p.m.

Predictors of Length-of-Stay for Children's Psychiatric Hospitalization

Dinohra Munoz-Silva, M.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Raul Silva, M.D., Richard Perry, M.D., Christine Pappas, Sunil Khushalani, M.D.

Summary:

With the proposed reforms and recent changes taking place in the health care field, as well as efforts to control costs via managed care, the identification of factors that contribute to length of hospital stay (LOS) in child psychiatry becomes imperative. The purpose of this study is to identify variables that may predict LOS for children's psychiatric hospitalization in an inner city public hospital.

Subjects: This sample consisted of 152 children (119 males, 33 females), ages ranged from 2.2 to 11.8 years (mean 7.7 ± 2.6).

Methods: This study is a chart review of all consecutive admissions to Bellevue Hospital's Children Psychiatric Inpatient Unit during a two-year period. Twenty-three variables were identified in a review of the literature and abstracted from patient charts. In order to ascertain the initial significance of possible predictive variables, a one-way analysis of variance was performed, using LOS as the dependent variable and each of the other variables as independent variables. Those variables which were then significant were entered into a multiple regression analysis (MRA) in order to ultimately determine each individual factor's predictive value while controlling for the other factors (remaining independent variables).

Results: MRA demonstrated that only four variables (number of psychotropic agents utilized, place of residence prior to hospital-

ization, level of suicidality, and full-scale IQ) significantly predicted LOS. The multiple correlation between these four variables and LOS was R = .87, which accounted for 75.2% of the variance of LOS.

Conclusions: The significance of these findings and the impact of limitations on LOS by regulatory agencies via reimbursement policies are discussed.

NR573 Thursday, May 26, 12 noon–2:00 p.m.

Adolescent Attachment and Psychopathology

Diana S. Rosenstein, Ph.D., Psychology, Institute of Penn. Hosp., 111 N. 49th Street, Philadelphia PA 19139; Harvey A. Horowitz, M.D.

Summary:

Objective: To explore associations between attachment and psychopathology in adolescents.

Method: 120 consecutive adolescent admissions to a private psychiatric hospital were asked to participate; 63 agreed and 60 completed the study. The mothers of the first 44 subjects were asked to participate. Twenty-seven completed the study. The Adult Attachment Interview classified the attachment of both mothers and adolescents either as secure (Autonomous) or insecure (Dismissing, Preoccupied, or Unresolved). Adolescent psychopathology (Axis I & II) was measured by a semistructured clinical interview. Two self-report inventories assessed symptoms and personality dimensions.

Results: A high match between maternal and adolescent primarily insecure attachment classification was found. Adolescent dismissing attachment was associated with conduct and substance abuse disorders, and narcissistic, antisocial and histrionic personality traits. Adolescent preoccupied attachment was associated with affective disorders, and avoidant, dependent, schizotypal, and dysthymic personality traits.

Conclusions: Predicted relationships between adolescents' attachment organization and psychopathology were found. Relationships between attachment histories and clinical presentation first observed by Bowlby (1944) have been empirically validated. The findings will be discussed in terms of styles of regulating distress and defensive adaptation that emerge from internal working models of attachment, leading to treatment methods based on attachment organization.

NR574 Thursday, May 26, 12 noon–2:00 p.m.

Predisposing Factors for Epidemic Dissociation Among School Girls in Thailand

Umaporn Trangkasombat, M.D., Psychiatry, Chulalongkorn University, 53 SOI 37 Lad Prao Road, Bangkok 10310, Thailand; Umpon Su-Ampun, M.D., Vera Churujikul, M.D., Orawan Nukaew, M.S., Vilailuk Haruhanpong, M.S., Kamthorn Prinksulka, M.D.

Summary:

Objective: In September 1993, at a school in the south of Thailand where belief in superstition is still prevalent, an outbreak of illness suddenly afflicted 34 girls aged 9 to 14 years. The symptoms were dissociative in nature: headache, being "in a daze" and unresponsive to stimuli, screaming, shaking, visual hallucination of the spirit, and amnesia. Rapid resolution of symptoms, no abnormal physical findings, and failure of an epidemiological investigation to detect an organic cause indicated epidemic hysteria. A case-control study was done to investigate psychological and environmental factors which predisposed a child to the illness.

Method: Psychiatric evaluation was done on 32 cases and 34 matched controls (students in the same class who did not develop any symptom). Parents were interviewed regarding the child's dissociative experiences.

Results: Among the cases there were significantly higher rates of psychiatric disorders (O.R. = 3.86, 95% C.L. = 1.16–13.23), anxious and fearful character (O.R. = 6.57, 95% C.L. = 1.79–25.53), and history of trance-like states (O.R. = 5.41, 95% C.L. = 1.18–28.11). The history of traumatic experiences and exposure to spirit possession ceremony were more frequent in the case than in the control group but these were not significant.

Conclusion: Although cultural factors have much influence on the symptom expression in epidemic hysteria, a strong relationship exists between children's intrinsic vulnerability and the development of the illness.

NR575 Thursday, May 26, 12 noon–2:00 p.m.

EEG and Dynamic Brain Mapping in Conduct Disorders

Atilla Turgay, M.D., Psychiatry, Wayne State University, 3219 Bloomfield Shore Drive, West Bloomfield MI 48323; Edward Gordon, M.D., Martin Vigdor, Ph.D.

Summary:

This prospective study involved 53 children under age 16, with chronic, treatment-resistant conduct disorders, diagnosed according to *DSM-III-R* diagnostic criteria, with a length of stay of longer than two years in psychiatric and residential treatment institutions. EEG and dynamic brain mapping (DBM) findings were compared to an age- and gender-matched comparison group from a data pool, consisting of over 700 healthy subjects. Only nine out of 53 patients with conduct disorder (16.98%) had normal DBM findings. A total of 44 out of 53 patients (83.02%) presented various DBM pathology: 14 (26.42%) showed slowing, 18 (33.96%) had generalized or petit mal paroxysmal activities, 12 (22.64%) presented temporal lobe pathology.

The DBM findings of the patients on psychoactive medication were not statistically different than the children who were not on medication ($p > 0.05$). The use of psychoactive medication alone could not explain the extensive EEG and DBM pathology and some of these abnormal findings seemed to be associated with the primary biological dysfunction in this disorder. DBM showed statistically higher significant pathology than the routine EEG reports ($p < 0.001$) and found to be more sensitive in identifying well documented seizure disorder cases.

NR576 Thursday, May 26, 12 noon–2:00 p.m.

Lethal Learning Problems: New Findings in Adolescent Suicide

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Summary:

Objective: To investigate the hypothesis that learning disabilities may be a predisposing factor in completed adolescent suicide.

Method: All available suicide notes (n = 27) from 267 consecutive completed adolescent suicides in Ontario, Canada, during 1987, 1988, and 1989 were analyzed for spelling and handwriting errors. The suicide notes were dictated to learning disabled adolescents (LD) and non-learning disabled adolescent (Non-LD) controls. All suicide notes were then rated for spelling errors and handwriting ability by four raters blind to group membership. The suicide notes were also compared to all available suicide notes (n = 9) from 184 consecutive completed older suicides in Ontario, Canada, during 1989.

Results: The results found that 89% of adolescent suicide completers had significant deficits in spelling and handwriting similar

to learning disabled adolescents and were significantly more impaired than both non-learning disabled adolescents and older adult suicides (65%).

Conclusions: The data supported a possible relationship between learning disabilities and adolescent suicide. Early identification and intervention with learning disabled adolescents could prevent many adolescent suicides.

NR577 Thursday, May 26, 12 noon–2:00 p.m.

Atypical Depression in Suicidal Adolescents

Thomas A. Hunter, M.D., Psychiatry, University of Miami, P.O. Box 016960, Miami FL 33101; Daniel Castellanos, M.D.

Summary:

Adolescents do not respond to traditional pharmacologic interventions for depression that successfully treat adults. One hypothesis to explain this different response rate is that adolescent major depression is dissimilar to typical adult major depression. The *DSM-III-R* recognizes that adolescents who are depressed may present with a predominantly irritable mood as opposed to the depressed mood seen in adults. Adolescents also appear to maintain higher degrees of mood reactivity than typically depressed adults. Adolescents who have "atypical" depressive features have been shown to respond poorly to tricyclic antidepressants and that they tend to be younger than the typically depressed adult.

Objective: Adolescent depression, not so far demonstrably responsive to TCAs, may be similar to, or on a continuum with, adult atypical depression. The purpose of this study was to estimate the prevalence of atypical depressive features in severely depressed adolescents.

Method: 43 consecutive adolescents (age 13 to 17 years) who presented at a community mental health center crisis unit for evaluation of suicidality were, as part of their routine diagnostic evaluation, screened for depression, conduct disorder and anxiety. Those with significant depressive symptoms (HAM-D > 16, n = 19) were screened for atypical depression using the Atypical Depressive Disorder Scale.

Results: Fifty-eight percent of this significantly depressed group were found to meet definite or probable criteria for atypical depression.

Conclusions: This suggests, at least in suicidal, seriously depressed adolescents, that atypical depressive symptoms are common and that the use of antidepressants other than TCAs should be investigated in this population.

NR578 Thursday, May 26, 12 noon–2:00 p.m.

Left-Right Asymmetries of Quantitative Electroencephalogram in Abused Children

Yutaka Ito, M.D., Psychiatry, Harvard Medical McLean, 115 Mill Street, Belmont MA 02178; Martin H. Teicher, M.D., Carol A. Glod, R.N., Erika Ackerman, B.A.

Summary:

Objective: We recently proposed that early childhood abuse may alter the course of limbic system or cortical development. It was supported by a chart review of psychiatric inpatients, which showed that abused patients had a greater incidence of electrophysiological abnormalities compared to non-abused patients (54.4% vs. 26.9%), predominantly in left anterior. We measured intracortical coherence as an index of right versus left cortical development.

Method: Fifteen inpatients (mean age 10.7 yr) with a history of intense abuse and 15 normal controls (10.1 yr) with no history of neurological disorders were recruited. Electroencephalography (EEG)s were obtained using a QSI-9000 (19 electrodes, 10-20 system, linked ears). Artifact free awake EEGs (40 seconds) were analyzed for coherence between F1, F2, F7, F8 and other leads in the alpha bands (8–13.6Hz).

Results: Intrahemispheric coherences was greater in abused children in left hemisphere leads (F7: $p < .02$; ANOVA). Abused children showed relatively greater left side coherence while controls showed relatively greater right hemisphere coherence ($p = .052$).

Conclusions: These findings suggest that childhood traumatic experience may alter the rate and right-left pattern of cortical development.

NR579 Thursday, May 26, 12 noon–2:00 p.m.

Children on Antidepressants: Orthostatic Changes

Nancy B. Campbell, M.D., Kobacker, Medical College, P.O. Box 10008, Toledo OH 43699; Marijo B. Tamburrino, M.D., Kathleen N. Franco, M.D., Cynthia L. Evans, M.D.

Summary:

Tricyclin antidepressants are noted to cause cardiovascular side effects in children, including blood pressure and pulse changes, but monitoring guidelines rarely address orthostatic pressure changes accompanied by pulse increases.

The purpose of this study was to explore orthostatic pressure and pulse changes of children on antidepressant medications. Over a two-year period, charts of 36 children on an inpatient psychiatric unit were retrospectively examined. There were 26 children taking imipramine, seven children on fluoxetine, and three children on sertraline. Twenty-eight boys and eight girls between the ages of five and 12 were included in the study.

Orthostatic blood pressure changes (>10mm/Hg) were noted in 54% (N = 14) of children on the tricyclics. Of these same children, 81% (N = 21) had a corresponding increased pulse rate (>10 beat/min) upon standing. Blood pressure and pulses were monitored to determine changes within three days after dose changes to a maximum of 30 days after first dose of meds. The children on fluoxetine and sertraline showed very similar results.

This study found that children do have blood pressure and pulse changes orthostatically on antidepressants. An interesting question is whether in children pulse increases serve as a compensatory mechanism to minimize orthostatic blood pressure drops.

NR580 Thursday, May 26, 12 noon–2:00 p.m.

Adolescent Sexual Activity, Axis I and Personality Disorders

Roger C. Burket, M.D., Psychiatry, University of Florida, P.O. Box 100234 UFHSC, Gainesville FL 32610; Wade C. Myers, M.D.

Summary:

Objective: Axis I and personality disorder diagnoses in sexually active adolescent psychiatric inpatients were compared to their sexually abstinent peers.

Method: Fifty-six subjects completed a sexual activity questionnaire and were assessed for *DSM-III-R* disorders using 1) the Diagnostic Interview for Children and Adolescents (DICA-R-A); and 2) the Structured Interview for *DSM-III-R* Personality Disorders (SIDP-R).

Results: Thirty-eight (68%) of the subjects (11 males and 27 females) were sexually active, while 18 (8 males and 10 females) were not. There were no significant differences between the sexually active group and the abstinent group in terms of average age, gender distribution, socioeconomic status, or mean IQ. The presence of any disruptive behavior disorder and passive aggressive personality disorder were significantly more common in the sexually active group. In sexually active females, the presence of any anxiety disorder and borderline personality disorder were

significantly more common than in the sexually active males. There was also a trend for overanxious disorder, phobias, oppositional defiant disorder, and paranoid personality disorder to be more frequent in these females. Conduct disorder and the presence of any disruptive behavior disorder were significantly more common in sexually active male subjects. There were no significant diagnostic differences between the males and females in the sexually abstinent group.

Conclusions: These findings suggest a relationship between sexual activity and certain Axis I and II disorders.

NR581 Thursday, May 26, 12 noon–2:00 p.m.

Childhood Psychopathology in 40 Adult Bipolar Patients

Gary Sachs, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114; Beny Lafer, M.D., Amy Thibault, M.D., Christine Truman, B.A.

Summary:

Objective: To identify predictors of bipolar mood disorder by assessing childhood psychopathology in bipolar adults.

Methods: Childhood psychopathology was assessed using the Kiddie-SADS-E and DICA-R in 40 unselected, SCID-diagnosed bipolar patients. Patients with early onset (EO) of mood disorder (before age 19) were compared to those with later onset (LO). Differences between the groups were tested by Chi Square test.

Results: EO patients (n = 25) met criteria for significantly more comorbid diagnoses than those in the LO (n = 15), (mean = 1.9 ± 1.6 vs. 0.47 ± 1.3) group. The EO patients suffered a significantly higher frequency of childhood anxiety disorders ($p < .008$) (separation, overanxious, or avoidant) as well as disruptive behavior ($p < .05$) (attention deficit hyperactivity, conduct, or oppositional) disorders than LO subjects. All observed cases of elimination disorders (enuresis and encopresis) ($p < .065$) and alcohol abuse ($P < 0.004$) occurred among EO patients.

Conclusion: The likelihood of childhood nonaffective psychopathology is significantly higher for bipolar patients with early onset of mood disorder. Particularly among children at risk for bipolar mood disorder, anxiety, disruptive, and elimination disorders may be a marker of increased risk for the early onset of bipolar illness and alcohol abuse.

NR582 Thursday, May 26, 12 noon–2:00 p.m.

Characterization of the Pregnant Adolescent

Catherine A. Martin, M.D., Psychiatry, University of Kentucky, 820 South Limestone Annex 4, Lexington KY 40536; Kelly S. Kearfott Hill, M.D.

Summary:

Objective: The objective of this study was to further characterize the pregnant adolescent with a particular focus on depression, major losses, and high-risk behaviors.

Method: Thirty-six pregnant adolescents (mean age 17.1 years) underwent a psychiatric interview and completed the Children's Depression Inventory (CDI) and the Modified Personal History Questionnaire (MPHQ), which is a structured questionnaire investigating high-risk behaviors (nicotine, alcohol and drug use, sexual activity, and delinquency). A series of questions regarding major losses were also asked.

Results: Eighty-one percent had experienced a major loss. Sexual activity significantly correlated with other high-risk behaviors, including drug ($p \leq 0.05$), alcohol ($p \leq 0.01$), and nicotine ($p \leq 0.05$) use, and conduct-disordered behaviors ($p \leq 0.05$) in this population. In addition, the CDI correlated with sexual activity ($p \leq 0.01$), losses ($p \leq 0.05$), alcohol ($p \leq 0.01$), and drug ($p \leq 0.001$) use, and delinquency ($p \leq 0.001$). Losses also significantly correlated with alcohol and drug use ($p \leq 0.05$).

Conclusion: Adolescent pregnancy is associated with significant personal and societal consequences. The physician's awareness of the adolescent's history of loss and vulnerability to high-risk behaviors may be the first step in helping the adolescents deal constructively with their pregnancy. Further characterization of the adolescent who is at risk for pregnancy could lead to more effective preventative efforts.

NR583 Thursday, May 26, 12 noon–2:00 p.m.

A Pilot Study of School-Based Mental Health Clinics in Special and Regular Education Settings

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Summary:

Objective: Our goal was to explore characteristics of referral, psychopathology, and treatment in school mental health clinics.

Method: Students were assessed during intake and at the end of school year through standardized instruments (Youth Self Reports, BPRS-C), clinical interviews, and questionnaires. Data analysis consisted of T-test, x^2, multiple correlation, and ANOVA procedures.

Results: (a) Special education students (N = 33; age $\bar{x}$ = 13.3 years; 67% black; 100% male) were referred mostly for emotional and behavioral problems. Fifteen percent had no past treatment. Disruptive behavior disorders were the most prevalent *DSM-III-R* diagnoses. Most students reported somatic complaints and aggressive behavior. Participants attributed their problems primarily to external factors. Most subjects and therapists reported academic and behavioral improvement due to treatment. Individual therapy was perceived as the most helpful modality. (b) Regular education students (N = 30, age $\bar{x}$ = 14.6 years; 72% black; 80% female) were referred mostly for emotional problems. Two thirds had no past treatment. Adjustment disorders were the most common *DSM-III-R* diagnoses. Most subjects reported somatic complaints. Students attributed their problems primarily to internal processes. Most youngsters reported improvement in family and behavioral problems due to treatment. Most therapists reported emotional and behavioral improvement. Group therapy was perceived as the most helpful modality.

Conclusions: School mental health clinics appear to be helpful to special and regular education students, many of whom have had no prior treatment.

NR584 Thursday, May 26, 12 noon–2:00 p.m.

Diagnostic and Referral Patterns of School and Mental Health Services

H. Allen Handford, M.D., Psychiatry, Penn State University, 500 University Drive, Hershey PA 17033; Dana Sanderson, M.D., Richard Mattison, M.D., Edward O. Bixler, Ph.D.

Summary:

This study compares two populations of children who have undergone child psychiatric evaluation with respect to referral patterns and diagnostic issues. A sample of over 500 consecutive psychiatric evaluations completed by the primary author (D.S.) in mental health settings (20%) and in the schools (80%) over the last three years (1991, 1992, and 1993) was analyzed. These evaluations were conducted in a similar format, including a semi-structured interview of the child, an interview with a parent or primary caregiver, and a review of written background information. In addition, the school-based evaluations included interviews with

school staff involved with the child being evaluated. Males were far more likely to be referred through the schools, whereas the mental health population was more balanced as to gender. Diagnostically, the school-referred population displayed more disruptive behavior disorders, including over twice as many oppositional and conduct-disordered children. Serious and acute emotional disorders (e.g. major depression, post-traumatic stress disorder, and adjustment disorders) were more frequent in the mental health population; however, chronic depression (dysthymia) was equally represented in the two groups. These findings strongly suggest different modes of identification of psychopathology in the two settings. In the schools, the primary reason for referral is external (i.e. disruptive classroom behavior), while referrals to the mental health system are prompted primarily by internal emotional distress (e.g. anxiety and depression). These findings raise concern regarding the underrepresentation of girls, as well as of children in general with more emotionally and less behaviorally based disturbances. This appears to be due to failure to identify and refer these children from the school population.

NR585 Thursday, May 26, 12 noon–2:00 p.m.

Parent and Child Agreement on DICA Diagnosis in Conduct Disordered Psychiatric Inpatients

Richard P. Malone, M.D., Psychiatry, Hahnemann University, MS 403 Broad and Vine Streets, Philadelphia PA 19102; Krista A. Biesecker, B.A., James Luebbert, M.D., Mary White, M.D., Mary A. Delaney, M.D.

Summary:

The aim of this study was to compare independent parent and child reports of *DSM-III-R* diagnoses made employing a structured interview (the Diagnostic Interview for Children and Adolescents—Revised; DICA-R; Reich and Welner, 1990). Parent/child agreement employing the *DSM-III* diagnostic schedule has been reported (eg., Vitiello, Malone et al., 1990), but there is a paucity of research on agreement for *DSM-III-R* diagnoses, particularly with inpatients. Subjects were twenty-five inpatients (20 males) enrolled in a study of aggressive conduct disorder, aged 9.83 to 16.57 years (mean = 12.34 ± 1.69), with IQ's ranging from 67 to 109 (mean = 85.5 ± 13.9). During the study the child and parent were interviewed independently by a trained DICA-R interviewer. Diagnoses made with the child and parent interview were compared for percent agreement and the *kappa statistic.* Results for diagnoses that occurred at least five times were as follows [Diagnosis (parent/child agreement, *kappa*)]: attention deficit hyperactivity (52%, .09); oppositional defiant (72%, .27), conduct disorder (84%, .41); separation anxiety (80%, –.11); overanxious (80%, –.11); phobias (68%, .31); enuresis (80%, .37); encopresis (88%, .00); psychotic symptom (88%, .52). The *kappa* values indicate that there is poor to moderate agreement for these diagnoses in this population. This result underscores the need for using multiple sources of information in making psychiatric diagnoses in children.

NR586 Thursday, May 26, 12 noon–2:00 p.m.

Stability of Major Depression in Child Psychiatry Inpatients

Richard P. Malone, M.D., Psychiatry, Hahnemann University, MS 403 Broad and Vine Streets, Philadelphia PA 19102; Mary A. Delaney, M.D., Krista A. Biesecker, B.A., James Luebert, M.D., Mary White, M.D.

Summary:

While major depressive disorder (MDD) occurs in children, responsiveness to antidepressants has not been demonstrated. To investigate whether this apparent lack of medication response may be due to higher reactivity to the presence of psychosocial stressors in the home environment, the stability of *DSM-III-R* MDD and depressive symptomatology was investigated in 26 children (11 males) hospitalized for MDD and/or a suicide attempt. Subjects ranged in age from 10.16 to 17.77 years (mean = 14.52 ± 2.32), with IQ's ranging from 63 to 128 (mean = 81.7 ± 14). At admission and weekly for two weeks, all were administered the depression section of the DICA-R (Reich and Welner, 1990). Depressive symptomatology was rated on the HAM-D, Beck Depression Inventory (BDI), and the Children's Depression Inventory (CDI) at the same points and on day 3. Sixteen subjects (61.5%) met DICA criteria for MDD at admission. Of these, 12 (75%) 10 received no psychotropics, one received neuroleptic, and one methylphenidate) did not meet DICA-R MDD criteria at subsequent ratings. Similarly depressive symptom ratings decreased significantly (ANOVA repeated measures) from the first to second rating, and second to third rating. The 75% "cure rate" exceeds drug or placebo response in controlled studies (Ambrosini et al, 1993; mostly outpatient) and supports the notion environment can maintain depressive symptoms. Implications regarding "biologic" depression and drug trials will be discussed.

NR587 Thursday, May 26, 12 noon–2:00 p.m.

The Effect of Lithium Treatment for Aggression on Measures of Cognition

Patrick W. McGuffin, Ph.D., Psychiatry, Hahnemann University, MS 403 Broad and Vine Streets, Philadelphia PA 19102; Richard P. Malone, M.D., Cornelius Fergueson, B.A., James Luebbert, M.D., Krista A. Biesecker, B.A., Mary A. Delaney, M.D.

Summary:

While lithium is a promising drug for treating aggressive behavior in children, it is important to investigate whether lithium is associated with normal development. The purpose of this study was to investigate the cognitive effects of lithium in a double-blind, placebo-controlled study in aggressive conduct disorder employing the WISC-R Mazes Test (Mazes) and the Trail Making Test, Forms A and B (Trails A and B). In all, 14 subjects, four females and 10 males, aged 10.4 to 14.58 years (mean = 12.31 ± 1.4) participated in this study. Seven were treated with lithium (serum lithium levels of 0.97 to 1.3 mEq/L; mean = 1.06 ± 0.11), and seven with placebo. A MANOVA repeated measures was performed separately for the Mazes and Trails A and B comparing scores from baseline and end of treatment. No significant differences were found between lithium and placebo groups. However, in six of seven subjects treated with lithium, Maze scaled scores improved by four or more points, while this occurred for only one placebo subject. Thus, lithium was not shown to be associated with any adverse cognitive effect, and there was a suggestion of improvement on the Mazes. Differences between these and the results of Platt and associates (1984) will be discussed.

NR588 Thursday, May 26, 12 noon–2:00 p.m.

Which Sexually Abused Children are Recommended for Follow-Up?

Gail A. Edelsohn, M.D., Jefferson Med College, 1201 Chestnut Street #1501, Philadelphia PA 19107; Ruth P. Zager, M.D., Irena C. Haughton, M.D.

Summary:

In a specially designed pediatric-child psychiatry clinic (SAFUC) for the follow-up of children/adolescents seen at the TJUH-ER, we reviewed specific variables believed to be important for clinical outcome or increased chance of referral. They included gender, age, family configuration, child symptoms, parent response and behavior, type of abuse, and past history of the child. A total of

506 children (413 females, 93 males), from age three to 17 years were seen in the SAFUC. A total of 32% received no follow-up recommendations. No differences were found for boys, girls, age, type of abuse, child symptoms, or parental behavior and responses. Family configuration was not significant for follow up except for a small subgroup of children living in a father-headed home. Highly correlated with follow-up referral was the child having a history of previous difficulties (e.g., school problems or developmental delays) that were unrelated to the sexual abuse. We conclude that children with a previous history of difficulties may be more vulnerable to the trauma of sexual abuse, less adaptive to the stress, and recover less quickly than their peers without prior problems. Such children receive more follow-up referrals when evaluated by a trained child psychiatrist.

NR589 Thursday, May 26, 12 noon–2:00 p.m.

Aggression in Child Psychiatric Hospitalization

Stuart L. Kaplan, M.D., Psychiatry Center, Rockland Children's, Convent Road, Orangeburg NY 10962; Joan Busner, Ph.D., Timothy Skahen, M.A.

Summary:

Objective: This study's objective was to determine whether and in what direction changes occur in the frequency of aggressive incidents as a function of time in child and adolescent hospitalization.

Method: The 4,609 seclusions, restraints, stat medication administrations, and patient to patient fights that had occurred with patients admitted to and discharged from a New York state child and adolescent psychiatric hospital between 4/1/91 and 3/31/93 were first coded by whether each had occurred in the initial, middle, or final third of the 534 involved patients' hospitalizations, and then analyzed for changes across hospitalization thirds.

Results: As revealed by four separate repeated measures analyses of variance, with time as the repeat factor, there were significant main effects for seclusions, F (2,724) = 20.32, $p < .0001$, and for stat medications, F (2,768) = 11.20, $p < .0001$. In both cases episode frequency was significantly higher in the first than in the third hospitalization segment, and in the second than in the third hospitalization segment (paired t-tests p's $< .005$). There were no significant effects for restraint or patient to patient fight episodes.

Conclusions: Although some improvement occurred in indices of mild aggression, there was no improvement in indices of more severe aggression.

NR590 Thursday, May 26, 12 noon–2:00 p.m.

Family Assessment in Adolescent Inpatients

Susan R. Borgaro, M.A., Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; David L. Pogge, Ph.D., John M. Stokes, Ph.D.

Summary:

Objective: Family involvement is often critical to success in the treatment of adolescent inpatients. The adolescent patient's participation in family interventions is, however, influenced by his or her perception of the functioning of their family. Moreover, the adolescent's agenda when participating in family-based treatments is likely to be determined in part by the extent and nature of the differences they perceive between their family as it is and their family as they would ideally like it to be. For this reason, assessment of the teenage patient's perception of his or her family, characterization of what he or she sees as the "ideal" family, and estimation of the discrepancy between these two is likely to prove quite useful for those intending to implement family-based interventions. A simple and cost effective measure of both the perceived "real" and "ideal" family is the Family Adaptability and Cohesion Evaluation Scale (FACES-III) developed by Olson and his colleagues (Olson, et al., 1985). Across a variety of settings, both clinical and non-clinical, the psychometric properties of this theoretically-based instrument have been established. To date, however, no investigator has examined its applicability and psychometric coherence in an adolescent psychiatric population. This study examines the adequacy of this measure in an adolescent inpatient population.

Method: A diagnostically diverse sample of 698 consecutive admissions to the adolescent service of a private psychiatric hospital completed the FACES-III within the first 10 days of their hospitalization, and were asked to characterize their "real" and "ideal" families.

Results: These data were factor analyzed to determine their concordance with the two-factor (Cohesion & Adaptability) Circumplex Model of family functioning upon which this measure is based. The existence of a four-factor solution, together with the specific factor loadings of items, particularly on Factors I and II, suggests that this measure, while not inconsistent with Olson's model, behaves in a more complex fashion in adolescent inpatients than with other clinical and non-clinical samples. Additional analyses suggest that adolescent patients tend not to rate their families as pathologically lacking in structure or as overly rigid, but would prefer an objectively dysfunctional lack of structure as their ideal. At the same time, they view their families as dysfunctionally detached, and would ideally choose a family with a healthier but not excessive level of emotional intimacy.

Conclusions: These findings suggest that the FACES-III and the Olson Circumplex Model can, with some modifications, be applied to this patient population, and imply the need for further work examining the efficacy of family interventions as a function of the discrepancies between adolescents' perceptions of their "real" and "ideal" family within this framework.

NR591 Thursday, May 26, 12 noon–2:00 p.m.

Adolescent Health Promotion in Central Texas

Jack D. Burke, Jr., M.D., Psychiatry, Texas A&M University HSC, 2401 S. 31st Street, Temple TX 76508; Kimberly C. Burke, M.S., Jenny Hurt, B.S., M. Kay Psencik, Ed.D.

Summary:

Objective: Adolescent Health Promotion in Central Texas was undertaken to prospectively follow a cohort of adolescents through high school in order to document the presence of mood disorders, substance use disorders, age at onset of disorders, social support, and functional status. This project was undertaken based on knowledge that mental disorders commonly begin in adolescence and based on a need for studies with sizeable minority populations.

Methods: All eighth grade students in the Temple, Texas Independent School District (TISD) completed an assessment battery which included the Beck Depression Inventory, the Alcohol Use Disorders Identification Test (AUDIT), the Perceived Social Support-Friends, the Perceived Social Support-Family, and the Rand Health Survey 1.0. Of the 556 students enrolled in three TISD middle schools, 541 completed the assessment package (97% response rate).

Results: Based on the Beck Depression Inventory, 18% of the adolescents received a score indicative of mild to moderate depression possible and 20% received a score in the moderate to severe depression likely category. For substance use, 19% of the adolescents reported first using substances before the age of 10 years. Results indicated a low level of perceived social support both from friends and family members. In terms of functional status, the adolescents reported scores lower than those scores reported by adults, with energy/fatigue and role limitations due to emotional problems being the scales the students scored lowest

on. Black and Hispanic students comprise 50% of this class. Results indicate that these students are more likely to have problems with substances and depression compared with white students.

Conclusion: These baseline results indicate that among a group of adolescents in a rural area, the presence of depressive symptoms and substance use are notable, especially for Hispanic students. These results will continue to be used for comparison as a subgroup of students are followed prospectively over the next several years.

NR592 Thursday, May 26, 12 noon–2:00 p.m.

Comorbidity in Conduct Disordered Adolescents

Dwain C. Fehon, Psy.D., Yale Psychiatric Inst., P.O. Box 12A, New Haven CT 06520; Daniel F. Becker, M.D., Kenneth N. Levy, B.A., Carlos M. Grilo, Ph.D., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To examine the comorbidity of conduct disorder (CD) with other *DSM-III-R* axis I and axis II disorders in a consecutively evaluated series of hospitalized adolescents.

Method: One hundred sixty-five inpatients ages 13 to 18 were given the K-SADS-E to assess axis I disorders, and the PDE to assess axis II disorders. Assessments were reliable (average kappa for axis I and axis II diagnosis = .77 and .84, respectively). Kappa coefficients were calculated to determine co-occurrence of diagnoses beyond that expected by chance, given the base-rates in this sample.

Results: Seventy-nine patients met criteria for CD, and 86 did not. For axis I, CD was significantly comorbid with attention-deficit hyperactivity disorder (ADHD) and substance use disorders (SUD). For axis II, CD was significantly comorbid with passive-aggressive personality disorder (PAPD) and antisocial personality disorder (ASPD)—with age criteria excluded (kappa coefficients are all significant at the $p < .05$ level).

Conclusions: Using a conservative definition of "comorbidity," significant associations are found between CD and ADHD, SUD, PAPD, and ASPD. These findings support the view that CD is a complex diagnosis composed of diverse axis I and axis II characteristics, questioning any notions that CD is a discrete and specific diagnostic entity.

NR593 Thursday, May 26, 12 noon–2:00 p.m.

Outcome of 18 Months of Clozapine Treatment for 100 State Hospital Patients

William H. Wilson, M.D., Psychiatry, Oregon Health Sci. Univ., Box 38 Dammasch Hospital, Wilsonville OR 97070.

Summary:

Background: The atypical antipsychotic medication clozapine is an effective treatment for refractory psychosis; however, the efficacy of clozapine when used in public mental health programs has yet to be fully characterized. This study assessed the outcome of clozapine treatment in a state hospital.

Methods: We reviewed the medical records of the first 100 patients to receive clozapine in a state hospital, beginning six months before clozapine treatment and continuing for 18 months after the first clozapine dose.

Results: The 55 men and 45 women had long-term psychosis which responded poorly to treatment with conventional antipsychotic medication. Eighteen months after beginning clozapine, 45 patients were much improved and 18 were somewhat improved. All except one of these improved patients was continuing clozapine treatment. Forty patients were living in community settings, fifty-nine remained hospitalized, and one had died of illness unrelated to clozapine. Violence decreased markedly during the first six months of clozapine treatment. Of 13 patients who had seizures while taking clozapine, six had histories of seizures prior to clozapine treatment. Twelve of the patients who seized on clozapine had only one or two seizures and continued clozapine treatment; one patient discontinued clozapine following status epilepticus. One patient developed agranulocytosis and one developed leucopenia; each recovered uneventfully after clozapine was discontinued.

Conclusions: Clozapine is an effective treatment for refractory psychotic disorders when given as a part of routine state hospital treatment. Nine to 12 months of treatment are required to identify patients who will respond.

NR594 Thursday, May 26, 12 noon–2:00 p.m.

Addition of Lithium to Haloperidol in Nonaffective Antipsychotic Nonresponsive Schizophrenia

William H. Wilson, M.D., Psychiatry, Oregon Health Sci. Univ., Box 38 Dammasch Hospital, Wilsonville OR 97070; Arvilla M. Claussen, M.S.

Summary:

This double-blind, placebo-controlled, parallel design clinical trial compared the therapeutic effects of the addition of lithium or placebo to haloperidol in 21 seriously ill state hospital patients with *DSM-III-R* schizophrenia, who did not have concurrent affective disorders and who had not responded to previous trials of conventional antipsychotic medication. During a baseline period of six weeks, patients were switched to a stable dose of haloperidol (mean ± sd dose = 13.6 ± 8.1 mg/d). Patients were then randomized to receive either lithium or placebo in addition to haloperidol for eight weeks (mean ± sd lithium level = 0.98 ± 0.13 mEq/1). Symptoms and side effects were assessed weekly. Improvement in symptoms correlated with the nonblind adjustment of antipsychotic dose, but not with lithium or placebo treatment. Side effects ratings did not differ between the two groups, but one patient developed a reversible delirium associated with combined lithium/haloperidol treatment. For these long-term severely ill patients, combined treatment afforded no advantage over treatment with haloperidol alone.

NR595 Thursday, May 26, 12 noon–2:00 p.m.

CSF Predictors of Clozapine Response

Samuel Craig Risch, M.D., Psychiatry, Medical Univ. of SC, 171 Ashley Avenue, Charleston SC 29425; C.A. Haden, Jane Caudle, R.R.J. Lewine, Ph.D.

Summary:

Approximately two thirds of otherwise neuroleptic refractory patients with schizophrenia sustain considerable clinical improvement with the atypical neuroleptic clozapine. However, at least one third of patients do not benefit from clozapine treatment. It would be useful to predict, a priori, those patients most likely to benefit from clozapine treatment. We have previously reported pilot data, replicating the original finding of Pickar, et al, (Archives of General Psychiatry, 1992), that a low cerebrospinal fluid (CSF) homovanillic acid (HVA) to 5-hydroxyindoleacetic acid (5HIAA) ratio (CSF HVA:5HIAA ratio) prior to clozapine treatment is associated with increased therapeutic benefit from clozapine. We now report data suggesting that an *increase* in the CSF HVA:5HIAA ratio over 42 weeks of clozapine treatment is also associated with therapeutic benefit from clozapine. Eight refractory schizophrenic patients had research lumbar punctures prior to clozapine treatment and after approximately 42 weeks of clozapine treatment. In the group as a whole, the CSF HVA:5HIAA ratio was unchanged. However, there was a significant *increase* in the CSF HVA:5HIAA ratio in the subjects sustaining significant clinical benefit from

clozapine therapy, while those subjects who did not improve or worsened on clozapine had no change or a decrease in the CSF HVA:5HIAA ratio. These results suggest that both baseline and change from baseline in the CSF HVA:5HIAA ratio may be useful predictors of clozapine efficacy. These preliminary data add credence to the hypothesis of Meltzer and others that CNS serotonergic and dopaminergic interactions may be mechanistically important in atypical antipsychotic efficacy.

NR596 Thursday, May 26, 12 noon–2:00 p.m.

Acetazolamide in Bipolar Affective Disorders

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Summary:

Acetazolamide is a carbonic anhydrase inhibitor used for a variety of purposes, including adjunctively in the management of various types of epilepsy. A previous study on its psychotropic effects suggested the possibility of efficacy in atypical psychotic states, especially those characterized by cyclicity. In the present investigation, 16 patients with refractory affective symptomatology were treated with acetazolamide in a prospective open trial after exhaustive trials with antidepressants, lithium, carbamazepine, divalproex, and other anticonvulsants. Seven of the 16 (44%) responded positively, in some cases dramatically, for as long as two years. Analysis revealed that all of the responders were either in a depressive phase, or in a rapid-cycling phase, of a bipolar illness, and that all had experienced partial positive response to at least one other anticonvulsant and were being maintained on anticonvulsant therapy when the response occurred. Salient theoretical issues are explored.

NR597 Thursday, May 26, 12 noon–2:00 p.m.

A Placebo Controlled Double-Blind Study of Naltrexone for Trichotillomania

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Summary:

Objective: Trichotillomania (TM) has been recently postulated as belonging to a group of obsessive compulsive spectrum disorders having in common pathological grooming compulsions and belonging to a continuum of self-injurious behavior (SIB). Canine acral lick (CAL), which involves self-injurious depilation by licking, has been proposed as an animal model for both OCD and TM. Similar to these disorders, CAL responds to serotonin reuptake inhibitors. CAL also responds to the opiate antagonist naltrexone (NAL), as do some forms of SIB in humans. This study investigates the utility of NAL for the treatment of TM.

Method: Seventeen patients with TM were randomized to six-week treatment with placebo (N = 10) or 50 mg/d NAL (N = 7) in a double-blind parallel design.

Results: NAL subjects demonstrated a statistically significant reduction in the primary assessment variable NIMH TM Severity Scale (TS) ($p = .02$). There was a trend toward improvement in the NIMH Physician Rating Scale score ($p = .11$) for the NAL group. Results were in the predicted direction but did not approach significance for number of hair-pulling episodes ($p = .16$) and NIMH TM Impairment Scale ($p = .22$) but not estimated number of hairs pulled ($p = .35$). Three (43%) of the NAL subjects vs. none of the placebo group experienced a >50% reduction is TSS (survival analysis, $p = .03$). Neither changes in pain detection nor changes in displacement behaviors as assessed by observation during a stressful task accounted for Naltrexone's superior effects.

Conclusions: Naltrexone may be a useful medication in the treatment of a subgroup of trichotillomanics.

NR598 Thursday, May 26, 12 noon–2:00 p.m.

Startle and Alprazolam in PTSD and Panic Disorder

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Summary:

Delayed habituation of the acoustic startle response has been found in post-traumatic stress disorder (PTSD) patients but not in control patients suffering from other anxiety disorders (1). Clonazepam has not been found to alter delayed habituation in PTSD patients (2). We studied habituation of skin conductance (SC) and orbicularis oculi electromyogram (EMG) responses (Rs) to 15 consecutive, 500-msec., 95-dB, 1000-HZ, zero-rise-time binaural tones in patients with PTSD ($n = 9$) vs. panic disorder (PD) ($n = 8$), before and after treatment with alprazolam. Habituation was defined for SCR by number of trials required to reach two consecutive SCRs <.05 μS, and for EMG by number of trials required to reach two consecutive EMGRs <.1 μS. Mean trials to habituation in the PTSD group before treatment was 8.0 (SD 6.0) for SCR and 7.8 (SD 6.2) for EMGR, and after two weeks' alprazolam treatment 8.8 (SD 6.5) and 7.9 (SD 6.1), respectively. Mean trials for the PD group before treatment was 10.9 (SD 5.5) for SCR and 7.3 (SD 6.4) for EMGR, and after alprazolam 3.5 (SD 5.6) and 1.8 (SD 2.1), respectively. For trials to SCR habituation, ANOVA for repeated measures yielded a treatment main effect of $F(1,15) = 5.8$, $p < 0.03$ and a treatment × diagnosis interaction of $F(1,15) = 8.9$, $p < 0.01$. For EMGR, the treatment main effect was $F(1,15) = 4.5$, $p < 0.05$ and treatment × diagnosis interaction $F(1,15) = 4.9$, $p < 0.04$. These data suggest that the pathophysiological mechanism underlying phasic arousal differs in PTSD and PD.

NR599 Thursday, May 26, 12 noon–2:00 p.m.

Safety of Combination Clozapine and ECT Therapy

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Summary:

The safety of combined clozapine and ECT has been open to question. The purpose of this retrospective study was to examine the potential adverse effects of concurrent clozapine and ECT therapy.

Method: A total of four patients, ages 27 to 68, were identified who had received either inpatient or outpatient ECT while taking clozapine in the past two years. All patients met *DSM-III-R* criteria for schizoaffective disorder. Charts were examined for unusual or adverse effects related to the combined treatments.

Results: Patients received from three to 11 ECT treatments while on clozapine during the initial inpatient series. Two also received maintenance outpatient ECT and/or repeated courses for a total of 36 and 72 treatments, respectively. Two patients were taking clozapine prior to the ECT series, and two initiated clozapine therapy during an ECT series. Maximum clozapine dose was 500 mg qd. Combined treatment was well tolerated by all patients. Only one event was identified as unusual. Patient #3 had a prolonged seizure (175 seconds) on ECT treatment #5 following the first dose of clozapine. Prolonged seizure duration was not observed in patient #4 following the first clozapine dose, but the patient was also treated concurrently with valproic acid.

Conclusion: ECT treatments may be safely administered to patients on clozapine therapy. Initiation of clozapine during an ECT

series may be associated with increased seizure duration on the treatment following clozapine initiation.

NR600 Thursday, May 26, 12 noon–2:00 p.m.

A Double Blind Study Comparing Idazoxan to Bupropion

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Summary:

Idazoxan, a potent and selective alpha-2 adrenoreceptor antagonist, has been shown to be effective in treating a small number of bipolar depressive patients. In this study we expand upon these data, comparing the clinical effects of idazoxan to bupropion in a randomized double-blind study of bipolar depressed outpatients at Friends Hospital. Following a two-week drug washout period, Patients with a *DSM-III-R* diagnosis of bipolar depression, determined by a SCID and minimum Hamilton Depression score of 16, were randomly assigned to treatment with either idazoxan (240 mg./day) or bupropion (450 mg./day). Weekly assessments, including the Hamilton Depression Inventory, Mania Rating Scale, BPRS, vital signs, and side effects were completed during the six-week trial. Patients treated with idazoxan and bupropion showed significant clinical improvement in depression by the sixth week, with reductions in Hamilton scores from $\bar{X}$s of 21 (SD = 4.12) and 22 (SD = 10.10) to $\bar{X}$s of 10 (SD = 5.15) and 13 (SD = 2.24), respectively. Patients tolerated idazoxan without significant side effects or changes in vital signs. This is the first study comparing idazoxan to an accepted standard treatment, demonstrating idazoxan to be a well-tolerated drug with a novel mechanism of action effective in treating bipolar depression.

NR601 Thursday, May 26, 12 noon–2:00 p.m.

Effects of Fluoxetine on Symptoms of Insomnia in Depressed Patients

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Summary:

This study evaluated the effects of fluoxetine (F) vs. placebo (P) on symptoms of insomnia among depressed patients. Two clinical subgroups were evaluated: melancholia (per *DSM-III-R*) and patients (pts.) with baseline sleep disturbances. Fluoxetine is an efficacious antidepressant, but its selective efficacy on symptoms of insomnia has been less thoroughly explored.

Eighty-nine pts. who fulfilled *DSM-III-R* criteria for major depression completed two nights of polysomnography, and were stratified by the presence or absence of reduced REM latency. All pts. were assigned to either (F) 20 mg/day or (P) by an adaptive randomization scheme. The two subgroups were: melancholia and pts. with baseline sleep disturbance [defined as a HAM-D sleep total (the sum of HAM-D items 4, 5 and 6) of ≥4 at baseline]. Within both melancholic and sleep disturbed patients, treatments were compared with respect to baseline to endpoint changes in HAM-D sleep total, 14-item HAM-D (HAM-D 17 total without sleep items), and one-week changes in HAM-D sleep total. Statistical analysis was conducted using (one sided) Bayesian methodology.

Melancholic pts. treated with (F) had a statistically significant greater improvement in depression (on the 14 item HAM-D scale) than those given (P). A similar result was seen in pts. who had sleep disturbance. Both (F) treated melancholics and (F) treated pts. with baseline sleep disturbance had numerically greater decreases in HAM-D sleep total versus pts. on (P).

Statistically significantly fewer melancholic pts. treated with (F) demonstrated an increase in their sleep disturbance scores at one week versus pts. on (P). Numerically fewer pts. treated with (F) who had baseline sleep disturbance had an increase in their sleep disturbance scores at one week versus pts. on (P). Thus, within these subgroups (F) does not exacerbate sleep disturbance prior to its onset of antidepressant activity.

(F) was shown to be more effective than (P) within both melancholic and sleep disturbed pts. at improving non-sleep related HAM-D items. Numerical improvements in HAM-D sleep disturbance scores were also seen for (F) versus (P). (F) also did not exacerbate sleep disturbances either early during therapy or at endpoint. The clinical significance of these findings include that fluoxetine (a non-sedative antidepressant) is effective in patients with baseline sleep disturbance.

NR602 Thursday, May 26, 12 noon–2:00 p.m.

Desipramine Augmentation of Selective Serotonin Reuptake Inhibitor Treatment of Refractory OCD Patients

Linda C. Barr, M.D. Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Wayne K. Goodman, M.D., Amit Anand, M.D., Lawrence H. Price, M.D.

Summary:

Clomipramine is widely recognized as an effective treatment for obsessive compulsive disorder (OCD). Clomipramine's principal metabolite, desmethylclomipramine, is a potent inhibitor of norepinephrine reuptake. We investigated a possible role for the combined inhibition of serotonin and norepinephrine reuptake in the treatment of refractory OCD by adding the primarily noradrenergic agent desipramine (DMI) or placebo tot he treatment of 23 OCD patients whose YBOCS scores remained greater than 16 after at least 10 weeks of treatment with either fluvoxamine or fluoxetine. Nine men and 14 women (mean ± SD age = 38.0 ± 6.9) received DMI (N = 10) (mean final dose = 162 mg QD) or placebo (N = 13) in addition to ongoing SSRI treatment for six weeks. Blind weekly assessments of both depressive and obsessive compulsive symptoms were obtained. ANOVA of YBOCS ratings revealed significant treatment X time interactions for total YBOCS ($F = 2.18$; $df = 1,6$; $p = .049$) and the YBOCS compulsions subscale ($F = 3.43$; $df = 1,6$; $p = .004$) when active DMI was compared to placebo. 3/10 patients treated with DMI and 0/13 patients treated with placebo had greater than 25% reductions in total YBOCS scores. There were no significant treatment by time interactions for YBOCS obsessions subscale scores, or HAMD scale scores. These data suggest that the combination of serotonin and norepinephrine reuptake be beneficial in some patients refractory to SSRI treatment alone. However, further studies will be needed to clarify the clinical significance of this effect.

NR603 Thursday, May 26, 12 noon–2:00 p.m.

Effects of Tryptophan Depletion on Mood During Fluoxetine Treatment of Healthy Subjects

Linda C. Barr, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Wayne K. Goodman, M.D., George R. Heninger, M.D., Lawrence H. Price, M.D.

Summary:

Fluoxetine's potential to improve mood and functioning even in those without a depressive syndrome has recently been suggested in the lay literature. We investigated this possibility by administering fluoxetine 20 mg/day to individuals without a prior personal or family history of psychiatric illness and assessing

mood and quality of life weekly for six weeks. We also investigated whether a neurobiological correlate, i.e., behavioral response to tryptophan depletion (TD), might also be altered by fluoxetine. Tryptophan depletion (TD) produces a relapse in 60% of previously depressed patients who have recovered with antidepressant treatment. Four men and two women without history of psychiatric illness participated in two test sessions: (1) TD (24-hr. low-tryptophan diet followed the next morning by a 16-amino acid drink without tryptophan) and (2) sham depletion in random order before and after six weeks of fluoxetine. Blind ratings of mood were obtained during TD and sham depletion and on a weekly basis during fluoxetine administration. In these initial six subjects, no clinically significant changes in POMS subscale items or quality of life subscales were seen during the course of fluoxetine administration. Thus, fluoxetine does not appear to possess marked thymoleptic activity in those without symptoms or history of depressed mood. No subject experienced clinically significant mood worsening (as assessed by the depression subscale of the POMS or by HAM-D) during TD either before or during fluoxetine administration. Thus, fluoxetine administration itself does not appear to produce vulnerability to the depressant effects of TD observed in fluoxetine-treated depressed patients.

NR604 Thursday, May 26, 12 noon–2:00 p.m.

Neuroleptic-Induced Psychopathology

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Summary:

Background: Neuroleptics may be less safe and less antipsychotic than the multigenerational traditions of their usage suggest. Neuroleptic-induced psychopathology (NIP) corresponds to rebound mental changes consequent to chronic neuroleptic exposure, as tardive dyskinesia corresponds to consequent movement disorders. This study aimed to describe NIP by comparing selected patients on and off neuroleptics.

Method: Selection was of four patients newly hospitalized for uncontrolled symptoms, taking neuroleptics continuously for over three years, and showing either excellent premorbid adjustment or a clear-cut current sense of initiative. Such clear-cut cases have been rare. Symptoms of depression, anxiety, obsessionalism, compulsivity, psychosis, and dyskinesia were prospectively recorded on admission and daily.

Results: While taking neuroleptics, each showed psychosis, paranoia, passivity, and dependency, and met criteria for schizophrenia. Each also had obsessions or compulsions, apathy, and dysphoria, symptoms not previously included in NIP. In an open study, in response to neuroleptic termination and treatment with lithium and sertraline in sequence, each patient experienced abrupt disappearance of psychopathology. The hyperpromptness of response was consistent with medication-induced symptoms.

Conclusions: NIP can include obsessions, compulsions, apathy, or dysphoria, besides psychosis. Some apparently neuroleptic-resistant schizophrenia may be NIP. NIP can sometimes be treated without neuroleptics.

NR605 Thursday, May 26, 12 noon–2:00 p.m.

Increased Risk of Periodic Leg Movements During Sleep with Use of Fluoxetine

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Summary:

Insomnia has been reported to occur in 7% to 22% of patients (1) treated with fluoxetine. Objective assessment of the effect of fluoxetine on sleep has not been described in detail. The mechanism by which fluoxetine results in sleep disturbance is unclear. Evidence suggests that tricyclic antidepressants can disrupt sleep continuity by causing periodic leg movements during sleep (2).

Nine patients who were treated with fluoxetine and no other medication (mean + SC, 23 ± 8 y.o.) and eight unmedicated, depressed patients (mean + SD, 25.5 ± 7 y.o.) were studied polysomnographically. Patients treated with fluoxetine reported insomnia (n = 2), morning fatigue (n = 5), or both (n = 2). All 17 recordings were subjected to blind ratings by two independent raters for presence or absence of clinically significant periodic leg movements (>30 total myoclonic movements or myoclonus index >5 events per hour of sleep).

There was a significantly higher incidence of PLMs in all fluoxetine recordings than in recordings of depressed control patients ($X^2 = 4.64$, $p < .05$). Four of the nine fluoxetine patients (44%) were rated as having clinically significant PLMs by both raters in comparison to none of the eight in the control group. All myoclonus indices for the four patients were low (mean myoclonus index = 10 events per hour). No significant difference was found between the myoclonus index ratings of the two raters.

In summary, treatment with fluoxetine is associated with an increased incidence of periodic leg movements, in young, depressed adults. The complaint of insomnia and morning fatigue in patients treated with fluoxetine may be due, in part, to an increase in PLMs. The relatively low myoclonus indices suggest that other mechanisms of sleep disruption also may be important.

(1) Cooper GL: The safety of fluoxetine—an update. *British J Psychiatry* 153 (suppl. 3):77–86, 1988.

(2) Ware JC, Brown FW, Moorad PJ, et al: Nocturnal myclonus and tricyclic antidepressants. *Sleep Res* 13:72, 1984.

NR606 Thursday, May 26, 12 noon–2:00 p.m.

Trial of the Novel Noradrenergic Antidepressant ABT-200

Neal R. Cutler, M.D., Calif. Clin. Trials, 8500 Wilshire Blvd. 7th Floor, Beverly Hills CA 90211; Jerome F. Costa, M.D., John J. Sramek, Pharm.D., Kenneth B. Kaskin, M.D., Jack A. Grebb, M.D., Sara S. Kennedy.

Summary:

ABT-200, developed at Abbott Laboratories as a potential antidepressant, antagonizes both norepinephrine uptake and presynaptic alpha-2 receptors. Patients who met *DSM-III-R* criteria for major depressive disorder and continued to meet all inclusion criteria, including HAM-D (24 items) ≥20 following a one week placebo lead-in, were randomized to receive ABT-200 60 to 140mg qd (n = 46; 34 M, 12 F) or placebo (n = 45; 26 M, 19 F) for eight weeks. During the first three weeks of the study, the dosage was titrated from 60mg qd (week 1), to 100mg qd (week 2), to 140mg qd (week 3), as tolerated. Although total HAM-D change from baseline to end of week 8 was not significant (–9.2 or 32.6% decrease on drug versus –7.4 or 24.9% decrease on placebo, $p > .05$), HAM-D core items were significantly ($p < .05$) decreased by week 1 and continued to demonstrate significance by the end of treatment (–3.0 or 38% decrease on drug versus –1.2 or 15.2% decrease with placebo, $p < .02$). The most common (≥10%) treatment adverse events with ABT-200 were headache, myalgia, dizziness, and insomnia; however, of these, only insomnia occurred at a significantly greater incidence than placebo (19.6% versus 4.4%, $p < .05$). In this preliminary study, ABT-200 was well tolerated and suggested a potential antidepressant response. Additional studies using higher doses, which are given in the morning to minimize insomnia, are currently in progress.

NR607 Thursday, May 26, 12 noon–2:00 p.m.

Trial of a Cholecystokin$_B$ Antagonist in Panic Disorder

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Summary:

A CCK_B antagonist developed at Merck Research Laboratories, L-365,260, has been shown to completely prevent CCK-4 induced symptoms of panic attack in single-dose (50 mg), placebo-controlled studies in patients with panic disorder. The present report is one site (n = 38) from a multicenter study (n = 83) designed to assess the preliminary efficacy and safety of L-365,260 in patients meeting *DSM-III-R* criteria for panic disorder, with or without agoraphobia. In order to participate, male and female patients were between 18 and 55 years of age and in good physical health. Following a one-week, single-blind, placebo lead-in, patients were randomized to 30 mg qid of L-365,260 (n = 18; 7 M, 11 F) or placebo (n = 20; 9 M, 11 F) for six weeks. At the end of the study, the frequency of panic attacks decreased more on drug (–4.3 points) than placebo (–2.7 points) compared to baseline scores, but the result was not significant (p = .36) and the groups differed markedly in their baseline frequency. Overall Physician's Global Improvement Scale was not significant. The difference in total HAM-A scores (including panic attack symptoms) was also not significant, but inter-panic HAM-A ratings showed a trend (p = .066) favoring L-365,260 (–4.4 points or 20.3% decrease) compared to placebo (–0.8 points or 4.6% decrease). L-365,260 was well tolerated; the most common drug-related adverse events were lightheadedness, headache, and nausea. Five patients were prematurely discontinued from the study, one on L-365,260 due to elevated liver enzymes, and four on placebo due to elevated liver enzymes, headache, leg cramps, and a change in the ECG. The reasons for lack of efficacy with L-365,260 will be discussed.

NR608 Thursday, May 26, 12 noon–2:00 p.m.

Desipramine Desensitizes Platelet Adenylyl Cyclase

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Summary:

Objective: To determine the effects of desipramine (DMI) on catecholamine metabolism and blood cell adenylyl cyclase (AC) activity in depressed patients.

Method: Catecholamines and metabolites in 24-hr urine collections and 8 am plasma specimens as well as measures of AC in platelets and mononuclear leukocytes (ML) were compared in antidepressant drug-free outpatients (N = 15) at baseline and after four and six weeks of treatment with DMI.

Results: After four and six weeks of DMI, there were statistically significant increases in 24-hr urinary norepinephrine ($p < .01$) and normetanephrine ($p < .04$) and decreases in MHPG ($p < .04$) and VMA ($p < .001$); similarly, plasma norepinephrine was significantly increased ($p < .02$) and MHPG was significantly decreased ($p < .04$). After six weeks of DMI, we also observed statistically significant heterologous, agonist-nonspecific receptor (prostaglandin D_2, prostaglandin E_2, alpha$_2$-adrenergic) and postreceptor (AlF_4 - ion and GTPγS) desensitization of AC in platelets but not in ML isolated from the same blood specimens.

Conclusions: DMI altered both catecholamine metabolism and platelet (but not ML) AC activity. In platelets, the stimulatory G-protein G_s and the inhibitory G-protein G_i regulate AC, whereas in ML, G_i (though present) does not modulate the stimulation of AC by G_s (Motulsky, et al., 1987). Thus, tonic inhibition by G_i may be needed to develop heterologous desensitization of AC during treatment with DMI.

NR609 Thursday, May 26, 12 noon–2:00 p.m.

Clozapine Plasma Levels and Therapeutic Response

Carol Vander Zwaag, M.D., Research, John Umstead Hospital, 12th Street, Butner NC 27509; Mark F. McGee, M.D., Joseph P. McEvoy, M.D.

Summary:

Objective: To determine the relationship between clozapine plasma levels and therapeutic response by *prospective randomization* of patients to 12 weeks of *double-blind* treatment at one of three non-overlapping clozapine plasma level ranges (50–150, 200–300, 350–450 ng/ml).

Method: At present, 17 inpatients with treatment-resistant schizophrenia have completed this ongoing study at John Umstead Hospital. Utilizing three-day turnaround time on clozapine plasma levels, the non-blind physician adjusted each patient's dose so as to reach and stay in his or her assigned plasma level range. A blind physician completed the BPRS at baseline an after six and 12 weeks of treatment.

Results: The (n = 6) patients assigned to the low plasma level range showed significantly less change in *BPRS total score* from baseline to week 12 (mean 60.7 to 58.2) than did the (n = 5) patients assigned to the middle range (mean 56.6 to 40.0) and (n = 6) patients assigned to the high range (mean 56.3 to 40.5) ($F = 3.07$, 4,28 df, $p = .032$).

Conclusions: Clozapine plasma levels of 200–300 ng/ml are associated with significantly greater therapeutic response than lower levels, with no additional benefit apparent at higher levels.

NR610 Thursday, May 26, 12 noon–2:00 p.m.

Desipramine with Paroxetine or Sertraline

Jeffrey A. Alderman, Ph.D., Center Research, Pfizer, 235 East 42nd Street, New York NY 10017; Janet Allison, M.D., Menger Chung, Ph.D., Wilma Harrison, M.D., David J. Greenblatt, M.D.

Summary:

In vitro studies have shown both fluoxetine and paroxetine to be more potent inhibitors than sertraline of the desipramine-metabolizing enzyme, cytochrome P450 2D6 (CYP2D6). Clinical work has also demonstrated that desipramine coadministered with fluoxetine (20 mg/day) leads to higher plasma desipramine levels than with sertraline (50 mg/day). The present crossover study examines the pharmacokinetics of desipramine coadministered with either sertraline or paroxetine. Twenty-four healthy volunteers (extensive metabolizer CYP2D6 phenotype) received desipramine (50 mg/day) for 23 days in each phase. Baseline desipramine levels were measured on day 7. Concomitant with desipramine, 12 volunteers were randomly assigned to receive paroxetine (20 mg/day on days 8–17, then 30 mg/day on days 18–20), and 12 to receive sertraline (50 mg/day on days 8–17, then 100 mg/day on days 18–20). Treatments were switched after a seven-day washout between phases. Preliminary results are reported here based on plasma samples collected four hours postdose. On the last coadministration day with the lower SSRI dose, paroxetine increased desipramine levels to a 6.4-fold greater extent than sertraline. After SSRI doses were increased for three days, no further changes in desipramine levels were observed with either treatment. These preliminary results suggest that paroxetine inhibits desipramine metabolism more strongly than sertraline and that this relationship is unaltered at the increased SSRI doses.

NR611 Thursday, May 26, 12 noon–2:00 p.m.

Use of Lamotrigine in the Treatment of Bipolar Disorder

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Summary:

Many anticonvulsants are effective treatments for bipolar disorder. Lamotrigine, a glutamate release inhibitor, is a novel anticonvulsant available in Europe and currently awaiting FDA approval as add-on therapy for the treatment of partial seizures with or without generalized tonic-clonic seizures. Two treatment-refractory bipolar patients were treated with lamotrigine. Both had histories of treatment failure with lithium, antidepressants, anxiolytics, anticonvulsants, and other agents. The first (77 YOWF) had failed maintenance ECT and remained in a catatonic depression. Lamotrigine was added to levothyroxine. Over several weeks, her mood steadily improved. The second patient (43 YOWM), a rapid cycler (8 cycles/year) with a predominance of depressive symptomatology, was markedly ill (mixed state) prior to adding lamotrigine to his treatment regimen (lithium, bupropion, and levothyroxine). Rapid clinical improvement was noted in the first two weeks of treatment. Cycling was reduced in frequency and intensity. After five and seven months of treatment, respectively, both patients continue to show clinically significant improvement over their pre-treatment condition of CGI, patient, and family ratings. Depressive symptoms, the predominant pre-treatment feature for both of these patients, have significantly improved. The response of these patients suggests that lamotrigine could be an important treatment option for bipolar disorder; studies are warranted.

NR612 Thursday, May 26, 12 noon–2:00 p.m.

Kindling with Clozapine

Duane Denney, M.D., Psychiatry, Oregon Health Sci. Univ, 3181 SW Sam Jackson Park Road, Portland OR 97210; Janice R. Stevens, M.D.

Summary:

Objective: Seizures occur in 3% to 5% of patients treated with clozapine (1). Acute administration of clozapine induced myoclonus in rats (2). These experiments were undertaken to determine whether repeated low doses of clozapine would provoke myoclonic or generalized seizures.

Design: Gently restrained rats were given subthreshold doses of clozapine (1 mg/kg) intraperitoneally on alternate days or once weekly. Control animals received vehicle alone. The number of myoclonic jerks following each injection was recorded electronically.

Results: Animals receiving clozapine showed no myoclonic jerks (MJs) initially. On subsequent days, increasing numbers of (MJs) were observed after each injection, reaching a peak rate of nearly 150 per hour. Control animals did not develop myoclonus. No generalizes seizures occurred.

Conclusions: A fixed low dose of clozapine, which initially provoked no response, when given on alternate days or weekly, induced increased numbers of myoclonic jerks on subsequent injections. This result is consistent with chemical "*kindling*" of myoclonus. Kindled increases of excitability in critical brain areas may be an important aspect of the therapeutic effect of clozapine, other neuroleptics, and electroconvulsive therapy. It is possible that intermittent low doses of clozapine could be used clinically to avoid some dose related complications of treatment.

NR613 Thursday, May 26, 12 noon–2:00 p.m.

Male Sexual Dysfunction Induced by Buproprion Sustained Release

Mark D. Fossey, M.D., Psychiatry, VA Medical Center, 109 Bee Street, Charleston SC 29401; Mark B. Hamner, M.D.

Summary:

Sexual dysfunction secondary to antidepressants can significantly interfere with patients' quality of life and may result in poor compliance. Buproprion has previously been described as an antidepressant free of sexual side effects in males. This open-label study examined the effects of buproprion sustained release (SR) on sexual functioning in 30 male veterans treated for depression. The mean age was 48.6 ± 8.5 years and the mean baseline Ham-D score was 26.2 ± 6.4. All patients received buproprion SR for at least one week. The mean duration of treatment was 51.7 ± 39.9 days and the mean dose was 283.3 ± 35.6 mg/day. Eight patients (26.7%) complained of erectile problems which they attributed to buproprion SR. Of these, four requested that they be taken off the study drug because of the erectile problems. Significant improvement in erectile function was noted in two individuals when the dose of buproprion SR was decreased from 300 mg/day to 200 mg/day. In another individual receiving 300 mg/day, improvement in symptoms was noted over time although complete resolution did not occur. This study suggests that buproprion SR may cause significant erectile problems in some individuals. Double-blind, placebo-controlled studies are indicated to specifically compare the relative frequency of sexual side effects of various antidepressants.

NR614 Thursday, May 26, 12 noon–2:00 p.m.

Risperidone: A One-Year Open-Label Study

Alan I. Green, M.D., Psychiatry, Harvard Med. School, 74 Fenwood Road, Boston MA 02115; Risperidone Study Group.

Summary:

The new antipsychotic drug risperidone was administered to 262 patients (in 20 sites) with *DSM-III-R* diagnoses of schizophrenia for up to one year following a double-blind study of four doses of risperidone (2 mg, 6 mg, 10 mg, and 16 mg/day), haloperidol (20 mg/day), or placebo. Following the conclusion of the double-blind study, the dose of risperidone was adjusted by the treating clinician; the allowable range was 2–16 mg/day. Anticholinergic medications and lorazepam were allowed; no other psychiatric medications were permitted. Patients were rated longitudinally with the Positive and Negative Syndrome Scale (PANSS), the Clinical Global Inmpressions (CGI) scale, the Extrapyramidal Symptom Rating Scale (ESRS), and for drug side effects. A total of 83 (32%) of the 262 enrolled patients completed one year of the open-label study with the drug. The reasons for early termination included adverse experience (7%), insufficient response (38%), and other (23%). The average dose during the open-label period was 8.5 mg/day. Data analysis is underway. The findings from this open-label study of risperidone will be presented at the meeting.

NR615 Thursday, May 26, 12 noon–2:00 p.m.

Lithium in the Treatment of Bipolar Depression

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Summary:

There are different types of lithium usage in bipolar depression: only lithium, added to an unresponsive antidepressant, or in com-

bination with antidepressants. Despite common use of the latter, there is no controlled and systematic study of it. The aim of this study is to investigate the role, model, time of action, and other characteristics of lithium in bipolar depression treated with imipramine. The study was performed in an inpatient unit. After three days of wash-out, a double-blind, placebo-controlled, randomized design was used. Thirty-five patients (22 women, 13 men) were studied. Imipramine-lithium combination was found superior to the imipramine-placebo combination in many ways. All of the patients in lithium group were recovered from depression by full remission or manic switch at the end of six weeks. While three cases were in partial remission, and four cases were unresponsive in the placebo group. Remission or manic switch occurred earlier in the lithium group (20.6 ± 7.5 days) than in the placebo group (33.8 ± 10.2 days). Significantly lower imipramine and additional drug (anxiolytic, hypnotic) doses were needed in the lithium group. Lithium has an impact on antidepressant efficacy, particularly during the first and fourth weeks of treatment and particularly in severe and/or melancholic patients.

NR616 Thursday, May 26, 12 noon–2:00 p.m.

Serotonin Depletion in Paroxetine: Treated Panic Disorder Patients

Pedro L. Delgado, M.D., Psychiatry, University of Arizona, 1501 N. Campbell Avenue, Tucson AZ 85704; Alan J. Gelenberg, M.D., Linda Bologna, R.N.

Summary:

Brain serotonin (5-HT) content is dependent on plasma levels of the essential amino acid, tryptophan (TRP). Depletion of plasma TRP causes a transient depressive relapse in most depressed patients treated with selective 5-HT reuptake inhibitors (SSRI's) (Delgado et al., 1990). The present study investigates the effects of TRP depletion on mood and anxiety in paroxetine-treated patients with panic disorder.

Method: In an ongoing pilot study, five patients with panic disorder (DSM-III-R) having had a remission of both panic attacks and depression (3/5 also were in a major depressive episode prior to treatment) after at least six weeks of open-label paroxetine (15–30 mg/day) were administered TRP depletion testing (final sample will be N = 15). Testing involved two two-day tests: a TRP-free, 15-amino acid drink and a follow-up day, in a double-blind, placebo-controlled (TRP depletion and control testing), crossover fashion. Paroxetine was continued throughout testing. Behavioral ratings (Hamilton Depression and Anxiety Scales (Ham-D, Ham-A), and panic attack inventory) and plasma (for TRP levels) were obtained prior to, during and after testing.

Results: The two patients without prior depression had no change in Ham-D or Ham-A during TRP depletion. The three with panic and pretreatment depression had an increase in Ham-D (mean 6 ± 3 before to 26 ± 6 after the drink) and Ham A (mean 6 ± 4 before to 17 ± 6 after the drink) scores, and two of these three had panic anxiety. None had significant depressive or anxiety symptoms during control testing.

Implications: These preliminary results suggest that the antidepressant and antianxiety properties of paroxetine (in some but possibly not all patients) may be mediated through similar neurobiologic mechanisms involving the 5-HT system. More testing is necessary to confirm these preliminary findings, and the results from a larger sample of patients will be presented.

NR617 Thursday, May 26, 12 noon–2:00 p.m.

Risperidone in the Treatment of Neuroleptic-Refractory Schizophrenic Patients

Jean-Pierre Lindenmayer, M.D., Bronx Psychiatric, 1500 Waters Place, Bronx NY 10461; George M. Simpson, M.D.

Summary:

The efficacy and safety of risperidone, a novel antipsychotic with serotonin $5HT_2$ and dopamine D_2 receptor antagonism, have been demonstrated in several controlled trials in schizophrenic patients. In the present open study, 12 hospitalized patients with DSM-III-R schizophrenia or schizoaffective disorder received 3 mg of risperidone twice daily for six weeks. Patients were included in the study if (1) in two drug trials they had been refractory to the equivalent of 1000 mg/day of chlorpromazine or had shown intolerance to two or more neuroleptics despite efforts to ameliorate side effects; and (2) they had a total BPRS score of 43 or above (1–7 scale) with a score of moderate or above on the items unusual thought content, conceptual disorganization, hallucinations, or suspiciousness. Treatment responders were defined as patients showing a 20% decrease in total BPRS scores or final CGI change scores of 2 or 1 (much or very much improved). Six patients were treatment responders and six were nonresponders (intent-to-treat analysis). Three patients dropped out of treatment prematurely. Among the treatment completers, five were responders and four were nonresponders. It is concluded that risperidone appears to be an effective treatment for schizophrenic patients refractory to or intolerant of other antipsychotics.

NR618 Thursday, May 26, 12 noon–2:00 p.m.

Clinical Efficacy of Risperidone in a Patient with Severe Tardive Dyskinesia

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Summary:

Based on results from double-blind, placebo- and haloperidol-controlled studies, risperidone has been suggested to possess an antidyskinetic effect in schizophrenic patients. The authors present the case of a 57-year-old male with moderate mental retardation whose extremely severe TD (rated as 8 [extremely severe] on the CGI subscale of severity of TD on the ESRS) and severe tardive dystonia (rated as 7 [severe] on the CGI subscale of dystonia on the ESRS) improved significantly with risperidone. On the fourth day of risperidone treatment, at a dose of 2 mg p.o. daily, the patient developed generalized urticaria-like lesions. Risperidone was immediately discontinued and the skin rash resolved after 72 hours. The patient was later rechallenged with risperidone using a slower dose titration regimen. Following a total of four weeks with risperidone, at a dose of 2 mg p.o. twice daily, a marked improvement was noted on the ESRS scale with a rating of 5 (moderately severe) on the CGI for TD and a rating of 5 (moderately severe) on the CGI for dystonia. The improvement in TD severity was also observed by both the nursing staff and the patient whose behavioral disturbance ceased. After four months, the patient's mental state and TD status remain improved. Since there was no recurrence of a skin rash, rechallenging patients who develop this uncommon adverse effect may be warranted in view of the potential treatment benefits of risperidone.

NR619 Thursday, May 26, 12 noon–2:00 p.m.

Alexithymia, Depression and Treatment Outcome in Bulimia Nervosa

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Summary:

The present study was designed to assess for alexithymia, e.g. diminished emotional awareness, among women with bulimia

nervosa (BN), to evaluate the inter-relationship between alexithymia, depression, and somatic symptoms, and to determine whether an intensive group psychotherapy program contributes to a reduction in the degree of alexithymia.

Method: Thirty-one of 50 BN women (62%) who completed the Toronto Hospital Day Hospital Program for Eating Disorders were administered pre- and post-treatment questionnaires. Findings from this clinical sample were compared with those of 20 non-eating-disordered women who completed the same battery.

Results: Using the Toronto Alexithymia Scale (TAS), significantly more BN women were alexithymic at pre- (61.3%) and post-treatment (32.3%) than were the comparison group (5.0%), even when depression was controlled for. At discharge, abstinence from binge/purge episodes was associated with a significant reduction in alexithymia, although there was a significant correlation between TAS scores, depression and vomit frequency.

Conclusions: Alexithymia among BN women is not simply a concomitant of disordered eating. Its partial reversibility following an intensive psychotherapy program may be a direct effect of the treatment and/or may be secondary to a reduction in depressive and/or binge/purge symptoms.

NR620 Thursday, May 26, 12 noon–2:00 p.m.

Fluvoxamine Treatment of Binge Eating Disorder: A Multicenter, Placebo-Controlled Trial

James I. Hudson, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Susan L. McElroy, M.D., Nancy C. Raymond, M.D., Scott Crow, M.D., Paul E. Keck, Jr., M.D., Jeffrey M. Jonas, M.D.

Summary:

Binge eating disorder is a newly recognized diagnostic entity for which no pharmacologic treatment has been shown effective (although one study suggests that the similarly defined condition, non-purging bulimia nervosa, may respond to desipramine).

We performed a nine-week, double-blind trial of fluvoxamine (a novel serotonin reuptake inhibitor) vs. placebo in 67 patients with binge eating disorder (62 women, 5 men; mean age 42.5 years). The dose of fluvoxamine ranged from 50mg to 300mg in a flexible-dose regimen.

At the end of nine weeks of treatment, subjects treated with fluvoxamine showed a significantly greater percentage decrease in the frequency of binge eating than subjects treated with placebo (median 75% vs. 45%, $p < .05$) and a greater degree of clinical global improvement ($p < .05$). Adverse events were mild and infrequent.

We conclude that fluvoxamine appears to be an effective and well-tolerated new treatment for binge eating disorder.

NR621 Thursday, May 26, 12 noon–2:00 p.m.

m-chlorophenylpiperazine Challenge in Bulimia Nervosa

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Summary:

Prior research has indicated that patients with BN may exhibit abnormalities in CNS serotonergic neurotransmission. This is of theoretical importance in that serotonin plays a key role in satiety mechanisms in the brain, and has been implicated in disorders of mood and impulsivity, all of clinical relevance in BN patients.

Using a double-blind, placebo-control paradigm, we administered intravenously the serotonin receptor agonist MCPP (0.1 mg/kg), or normal saline, on consecutive days to six normal controls and seven patients with BN. On each day blood samples were taken at regular intervals for prolactin, growth hormone, and cortisol. Subjects also reported subjective responses to each challenge using a visual analogue scale of 10 different mood states. Preliminary result suggest that BN patients have blunted responses to MCPP challenge compared with controls, as measured by change in prolactin levels, in ug/l, from baseline (−1.0 vs. + 6.3 at 30 mins.; −0.1 vs. + 8.3 at 60 mins.; −0.4 vs. + 7.5 at 90 mins., BN vs. controls). A number of side effects, including head throbbing and a sense of mild disorientation, were reported following MCPP but not saline in most subjects, with controls reporting greater symptoms. Other biochemical and subjective results are pending. These preliminary results are consistent with blunted serotonin function in BN patients.

NR622 Thursday, May 26, 12 noon–2:00 p.m.

Child Sex Abuse and Bulimia Nervosa in the United States, Austria and Brazil

Harrison G. Pope, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Barbara Mangweth, M.A., Andre B. Negrao, M.D., James I. Hudson, M.D., Taki A. Cordas, M.D.

Summary:

We assessed the prevalence and correlates of childhood sexual abuse among 33 women with bulimia nervosa in Boston, MA; 33 women in Innsbruck, Austria; and 25 women in Sao Paulo, Brazil. Detailed histories of sexual abuse, obtained at the conclusion of a comprehensive evaluation interview, were prepared and translated into English, then rated by a blinded investigator.

"Narrowly defined" childhood sexual abuse was reported by 24%–36% of women in the three countries, although only 15%–32% of women reported abuse occurring prior to the onset of bulimia nervosa. There were no significant differences between countries in rates of abuse. These rates appear no greater than those reported in studies of women in the general population. The data also did not support the hypothesis that bulimic subjects had endured more several sexual abuse than other women, nor did we find a significant association between history of childhood sexual abuse and severity of bulimic symptoms.

These findings add to the weight of evidence suggesting that childhood sexual abuse is not a risk factor for bulimia nervosa.

NR623 Thursday, May 26, 12 noon–2:00 p.m.

Serotonin Function in Bulimia Nervosa

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Summary:

Objective: Clinical studies suggest that impaired satiety responses may play a role in binge eating behaviors in bulimia nervosa. Initial investigation of neurotransmitter function in bulimia nervosa indicates that decreased central serotonin function could contribute to impaired satiety responses and binge eating behaviors. To follow-up on this hypothesis, patient and control responses to placebo-controlled pharmacological challenge with the indirect serotonin agonist d,l-fenfluramine were compared.

Method: Subjects included 19 medication-free, normal-weight outpatients (age 23 ± 2 years, mean ± s.d.) meeting DSM-III-R criteria for bulimia nervosa, with a binge frequency of 8 ± 5 episodes per week, and 20 healthy female controls (24 ± 4 years). Subjects were studied after overnight fast and bedrest on a clinical research unit. Behavioral and neuroendocrine measures were assessed at baseline and following administration of 60 mg fenfluramine or placebo.

Results: Baseline serum prolactin concentration was lower for patients than controls ($p < 0.001$). Prolactin response to fenflura-

mine, measured as area-under-the-curve, was significantly lower in patients than in controls ($p < 0.05$). Prolactin responses were not correlated with body weight or ratings of depression or anxiety.

Conclusions: These results provide new evidence for decreased responsiveness of central serotonergic pathways in patients with bulimia nervosa, and are consistent with suggestions that treatment response to antidepressant medication may be related to increased efficiency in serotonin function.

NR624 Thursday, May 26, 12 noon–2:00 p.m.

Body Dysmorphic Disorder: Comorbidity Study

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Summary:

Body dysmorphic disorder is defined as preoccupation with an imagined defect in physical appearance and is currently classified as a somatoform disorder. Previous studies have indicted significant comorbidity of body dysmorphic disorder with anxiety disorders, especially obsessive compulsive disorder (OCD) and social phobia, thus raising the possibility that body dysmorphic disorder represents an epiphenomenon accompanying these conditions rather than an independent diagnostic category. To expand on previous investigations we examined the prevalence of body dysmorphic disorder in 261 patients with primary diagnoses of OCD (n = 53), social phobia (n = 54), generalized anxiety disorder (GAD) (n = 32), panic disorder (n = 47), major depression (n = 42), and normal controls (n = 33). Patients were evaluated using the Structured Clinical Interview (SCID) for DSM-III-R, and a SCID-like module for body dysmorphic disorder. The sample consisted of 156 females and 105 males with a mean age of 37 ± 11 years. We found that body dysmorphic disorder aggregates primarily in patients with social phobia (11%) and OCD (8%), compared with patients with panic disorder (2%), GAD (0%), major depression (0%), and normal controls (0%). The differences reached significance in patients with social phobia ($x^2 = 4.02$, df = 1, $p = 0.045$) when compared with normal controls, with a difference approaching significance in patients with OCD ($x^2 = 2.6$, df = 1, $p = 0.11$). Our data suggest that body dysmorhpic disorder may indeed represent a clinically relevant epiphenomenon of social phobia and obsessive compulsive disorder.

NR625 Thursday, May 26, 12 noon–2:00 p.m.

The Effect of Naloxone on Twenty-Four Hour Luteinizing Hormone Secretion in Bulimia Nervosa

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Summary:

As many as 50% of women with bulimia nervosa have a history of menstrual abnormalities. Endogenous opioid systems have been shown to stimulate food intake and inhibit luteinizing hormone (LH) secretion. Therefore, increased opioid activity could contribute to disturbances of appetite and menstrual function in bulimia. In this study we determine if an infusion of naloxone, an opioid antagonist, increases LH secretion in bulimic women with menstrual dysfunction compared to control women.

Thirteen bulimic women with menstrual dysfunction and six control women matched for age (17 ± 2 vs. 19 ± 2) and weight (97 ± 7 vs. 101 ± 10% ABW) were studied during two consecutive 24-hour intravenous infusions of naloxone (10 mg bolus + 30 ug/kg/hr for 24 hours) and saline. Control subjects were studied during the early follicular phase (days 2–5 after the onset of menstrual bleeding). LH secretion was determined by blood sampling every 15 minutes during the entire 24-hour test periods. LH secretion was significantly increased on the naloxone day in both bulimic (secretory pulses/24 hours 12.5 ± 6.4 vs. 9.9 ± 6.5, $t = 3.28$, $p < .01$) and control subjects (LH secretory pulses/24 hours: 15.2 ± 2.4 vs. 10.0 ± 3.3, $t = 4.54$, $p < .01$) compared with the saline day. The naloxone-induced increase in LH secretion was the same in both groups. There was a trend toward naloxone infusion increasing LH secretion in a subgroup of bulimic women who had reduced LH secretion (n = 5, LH pulses/24 hours: 6.4 ± 6.7 vs. 2.8 ± 3.6, $t = 2.51$, $p = .07$). However, LH levels in this group remained significantly lower than in controls even during the naloxone infusion.

Opioid inhibition of LH secretion has been shown to be increased in bulimics studied during the luteal phase of the menstrual cycle (Coiro et al., 1990). Our data suggest that while opioid systems may play a role in menstrual dysfunction in bulimia, other factors may also contribute to reduced LH secretion in this disorder, an naloxone does not normalize reduced LH secretory levels in bulimics with abnormal LH secretory patterns.

NR626 Thursday, May 26, 12 noon–2:00 p.m.

CSF Isatin (Purified Tribulin) in Bulimia Nervosa

Timothy D. Brewerton, M.D. Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29451; Joseph J. Zealberg, M.D., R. Bruce Lydiard, M.D., V. Glover, M.D., M. Sandler, M.D., James C. Ballenger, M.D.

Summary:

Objective: Isatin (IS), the purified form of tribulin, is an endogenous indole that inhibits monoamine oxidase (MAO). Elevations in central ISA levels in animals have been reported in association with several stress-induced experimental paradigms. Although CSF ISA levels have been studied in patients with affective/anxiety disorders, they have not been studied in patients with eating disorders, such as bulimia nervosa (BN), who are known to engage in stressful behaviors such as dieting, binge-eating, and purging.

Methods: To investigate this area we measured CSF ISA levels in drug-free female patients with DSM-III-R defined BN and normal controls (NC's). After four days of a low monoamine diet and overnight bedrest, CSF was obtained (12th-26th cc) from seven female bulimic patients and eight age-matched NC's.

Results: BN patients had significantly higher CSF levels of ISA (0.040 ± 0.015 ug/ml) than NC's (0.025 ± 0.008 ug/ml, $p \leq 0.03$, unpaired t-test). ISA levels were inversely correlated with weekly binge frequency (n = 7, rho = 0.77, $p = 0.04$) and positively correlated with the ineffectiveness subscale score of the Eating Disorders Inventory (EDI) (rho = 0.89, $p \leq 0.02$). ISA levels were not significantly correlated with other EDI subscale scores, age, % average body weight, frequency of vomiting, or ratings of depression and anxiety. In the combined group of BN patients and NC's, there was a significant inverse correlation between CSF levels of ISA and cholecystokinin octapeptide (n = 15, rho = 0.55, $p \leq 0.04$), which is also significantly lower in BN patients. There was a trend for CSF ISA levels to be inversely correlated with CSF levels of the 5-HT metabolite, 5-hydroxyindoleacetic acid (5-HIAA) (n = 14, rho = 0.51, $p = 0.06$). CSF ISA levels were not significantly correlated with CSF MHPG, HVA, beta-endorphin, or dynorphin levels.

Conclusions: These results are based on very small sample sizes and are considered preliminary, but further research is indicated to determine the role of central ISA function in the pathophysiology of BN and related psychiatric disorders.

NR627 Thursday, May 26, 12 noon–2:00 p.m.

Do Adolescents with Anorexia Nervosa Share Alexithymia with Their Parents?

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Summary:

Alexithymic features' frequency in eating disorders, especially in anorexia nervosa, is known. If these features are related to illness or transmitted as a cognitive model of mentalisation in some families is unknown.

Objectives: To measure alexithymia in adolescents with anorexia nervosa and their parents, and to evaluate correlations through generations.

Method: Alexithymia was assessed using the Toronto Alexithymia Scale (TAS) in 18 adolescents with anorexia nervosa, after at less six months of evolution, and their parents, and compared to nine control families.

Results: Mean of the TAS score in adolescents with anorexia nervosa is 70.2. However, among 18 adolescents, 10 have a score >74 (alexithymia) and three have a score between 62 and 74 (nonconclusive). Among the nine control adolescents, mean of TAS score is 66.1, only two adolescents presenting a score > 74. Among 18 mothers of anorectics, mean is 60.7, with only 2 > 74. Among nine control mothers, mean is 59.3; no control mother exhibits a score >74. Among 17 fathers of anorectics, mean is 65.3 fathers have a score >74 and three fathers a score between 62 and 74. Among eight control fathers, mean is 58, with only one father >74.

Correlations: A Strong correlation ($p < 0.001$) is found between the total TAS score of adolescents with anorexia nervosa (mean = 69) and the score of their fathers (65).

Discussion: These results confirm the clinical impression concerning alexithymia in anorexia nervosa and the other studies. Regarding the question of relation of alexithymia features to the illness or to the family model of thinking, our results reveal a link through generations, in particular between fathers and daughters. This correlation focuses interest on the family cognitive processes working in anorexia nervosa.

NR628 Thursday, May 26, 12 noon–2:00 p.m.

A Rare Case of Bulimic Purging Through Blood Donation

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Summary:

Bulimic patients with body image distortion may resort to various forms of purging to restrict their calorie absorption and control their weight. The following is a rare and unusual case of bulimia with frequent blood donations perceived as a "deep cleansing" of the "rotten inside" in a 32-year-old woman. Her bulimia began at age 13 and it included binging, laxative abuse, and periodic vomiting. Since 10 years ago she has also been attending the Red Cross blood donor clinic to donate "the filthy blood" and to be able to generate "fresh and clean" blood. She felt relieved and even mildly elated each time she donated blood. Blood donation became a cleansing ritual that she practiced on an average of once every three months despite of her frailty. She would skillfully conceal from the Red Cross nurse the truth about her bulimia, malnutrition, and the medications that she was taking. On a few occasions she was refused the chance to give blood due to her low hemoglobuline. While the blood was being collected at the Red Cross, she would be fascinated to observe the flow of blood running away from her body and hoped that she would disappear in the process. She associated her concept of dirty blood to her binging behavior, which required a complete "purification." The possibility of a childhood sexual abuse by an alcoholic father remained an enigma. Psychodynamic and clinical implications of this severe and unusual case of normal weight bulimia will be discussed.

NR629 Thursday, May 26, 12 noon–2:00 p.m.

Eating Disorder and OCD Comorbidity: Analysis of SPEM Impairment

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Summary:

SPEM studies have became a focal point of attention in psychiatric research because of the relationship found between this kind of alteration and some psychopathological states. In particular, SPEM impairment has been documented in schizophrenia and obsessive compulsive disorder (OCD), but there are no data about SPEM characteristics in eating disorders (ED). A sample of 50 outpatients (25 OCD, 25 ED) has been tested on a clinical (EAT, Y+BOCS BPRS) and a neurophysiological assessment (SPEM). We have recorded intrusive saccades in 71% of patients with ED/OCD comorbidity, whereas these have not been shown in 'pure' ED subjects. It has been also delimited in an ED subgroup showing a significant number of anticipatory saccadic eye movements: this characteristic can only be related to the coexistence of an OCD disorder. Neurophysiological data seem to substantiate the presence of a subgroup of ED patients strictly related to obsessive compulsive disorder.

NR630 Thursday, May 26, 12 noon–2:00 p.m.

Clinical Diagnoses in Community Psychiatry: Accuracy and Cost

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Summary:

Objective: 250 psychiatric outpatients in a community clinic were interviewed with the Structured Clinical Interview for DSM-III-R (SCID) to determine (1) how SCID diagnoses compared with those made by psychiatrists in this setting and (2) the cost of diagnostic errors.

Method: Patients received SCID interviews by psychiatric nurses. Follow-up interviews were conducted by study psychiatrists or psychologists to verify diagnoses. Computerized records of service usage over the previous 19 months were obtained from the clinic computer database.

Results: The resulting DSM-III-R Axis I primary diagnoses were compared with those made by clinic psychiatrists prior to the SCID interview resulting in a Kappa coefficient of .42 across patients. A comparison of diagnoses made by nurses using the SCID and those rendered by study clinicians yielded a Kappa coefficient of .75 on primary Axis I diagnoses. Service usage patterns and costs compared in patients for whom clinic diagnoses agreed and disagreed with the SCID showed that diagnostic agreements in schizophrenics tended to be associated with 56% fewer treatment contacts and 52% fewer procedures, and affective disorders tended to be associated with 9% more contacts, but 6% fewer procedures, when compared with patients in which the diagnosis disagreed.

Conclusions: SCID demonstrates clinical applicability in a community setting. Improvement in diagnosis is associated with lower service usage and reduced cost of care.

NR631 Thursday, May 26, 12 noon–2:00 p.m.

Managed Care and Global Assessment of Functioning

Sally Caldecott-Hazard, Ph.D., Psychiatry, Florida Hospital, 601 E. Rollins Street, Orlando FL 32803; Richard C.W. Hall, M.D.

Summary:

Objective: This pilot study examined the interrater reliability of the Global Assessment of Functioning (GAF) test and developed a modified GAF that would have greater reliability for use in managed care situations.

Methods: Two groups of psychiatric professionals each rated the same intake histories and discharge summaries of 16 inpatients and assigned GAF scores for illness severity on hospital admission and discharge. One group rated using the original GAF and the other group used the modified GAF. Intraclass correlation coefficients (ICCs) measured interrated reliability for the original and modified GAF scores.

Results: ICCs for admission GAF scores were higher for raters using the modified GAF (.81) compared with the original GAF (.62). ICCs for discharge GAF scores were similar and higher than admission scores (.90 original GAF, .95 modified GAF).

Conclusions: The modified GAF may be particularly useful in situations (such as managed care evaluations for hospital admission) where interrate reliability needs to be maximal or where persons of varying skills and employment backgrounds must rate patients without having had much GAF training. Because of the increased structure, the modified GAF may also be more resistant to rater bias reported in managed care situations.

NR632 Thursday, May 26, 12 noon–2:00 p.m.

Psychiatric, Personality and Cognitive Factors in Mitral Valve Prolapse During Panic Disorder

Bonnie R. Aronowitz, Ph.D., Psychiatry, Mount Sinai QHC, 82-68 164th St N. Bldg 5th Fl, Jamaica NY 11432; Charles Swencionis, Ph.D., Eric Hollander, M.D.

Summary:

There is a high incidence of mitral valve prolapse (MVP) in panic disorder (PD) patients. This study examined the MVP-PD relationship via medical/cardiac, psychiatric, personality, and cognitive evaluations in 30 MVP echocardiography outpatients, 30 matched "rule-out MVP" (R/O MVP) subjects (receiving parallel procedures yielding negative MVP findings), and 39 asymptomatic controls.

R/O MVP subjects had mildly, but nonsignficantly higher rates of DSM-III PD. Both cardiac groups had comparable rates of DSM-III-R PD and significantly higher rates of simple phobia, separation anxiety disorder, affective disorders, chest pain, and avoidant personality disorder in comparison with controls. However, R/O MVP subjects had significantly higher rates of somatization disorder, histrionic, dependent, and self-defeating personality disorders, cardiac symptoms, anxiety sensitivity, agoraphobic cognitions, and body sensation sensitization compared with MVP and control subjects. Finally, R/O MVP subjects interpreted evens as significantly more catastrophic, probable, and costly than did both MVP and control subjects. Thus, individuals suspected of, but without, MVP, although similar in panic/anxiety and affective disorder rates, had more personality disorders, somatization, and cognitive biases, possibly influencing interpretation of their diagnoses. The study failed to support the relationship between MVP, per se, and PD, but delineated contributions of cardiac patienthood, as well as psychiatric, personality, and cognitive factors in their relationship.

NR633 Thursday, May 26, 12 noon–2:00 p.m.

Neuropsychology of OCD: Preliminary Findings

Bonnie R. Aronowitz, Ph.D., Psychiatry, Mount Sinai QHC, 82-68 164th St N. Bldg 5th Fl, Jamaica NY 11432; Eric Hollander, M.D., Concetta M. Decaria, M.S., Lisa Cohen, Ph.D., Dan J. Stein, M.D., Daphne Simeon, M.D.

Summary:

Neuropsychological studies in obsessive compulsive disorder (OCD) have yielded inconsistent findings. In addition to methodological problems within studies, inconsistencies may be due to implicit task performance variables and to the heterogeneity of the disorder. This study examined both specific functions hypothesized to be impaired in OCD and more generalized task performance variables that may underlie such compromised function. Selected neuropsychological variables were examined in 31 OCD patients and 22 age- and sex-matched normal controls. Since males may represent a homogeneous OCD subgroup with a more severe neurological form of the disorder, these variables were likewise examined in 20 male OCD patients in comparison with 10 age- and sex-matched male normal controls. OCD patients performed significantly more poorly than controls on visual recall and visual discrimination tasks as well as on set shifting/tracking tasks, e.g., time-accuracy trade-off. Male OCD patients demonstrated further impairment on visuoconstructional and visuospatial tasks. These findings suggested a male homogeneous OCD subgroup with more extensive neurological and neuropsychological deficits than all OCD patients and controls.

NR634 Thursday, May 26, 12 noon–2:00 p.m.

DSM-III-R Diagnoses in Benzodiazepine Dependent Subjects

Herminio Martinez-Cano, M.D., Psychiatry, Autonomous University, Camino De Vinateros 12 8F, Madrid 34 28030, Spain; Antonio Vela Bueno, M.D., Rolando Pomalima, M.D., Mariano Iceta, M.D.

Summary:

Although the issue of benzodiazepine dependence has drawn a lot of attention in the lay media and scientific press, there is a dearth of systematic assessment of the clinical features of benzodiazepine-dependent patients. This presentation describes the DSM-III-R-based diagnoses of a population of benzodiazepine-dependent subjects.

Patients numbered 153 (98 women and 55 men), of a mean age of 46.9 who were taking different benzodiazepines at different dose levels for an average of 4.6 years. One hundred fifty patients had at least one DSM-III-R diagnosis in Axis I other than benzodiazepine dependence; 135 patients had diagnoses in both axes I and II, while 90 patients had diagnoses on all three axes.

The most frequent Axis I diagnoses were in descending order: sleep disorders (insomnia), anxiety, affective, substance abuse, and somatoform disorders. Obsessive compulsive personality disorder and traits were the most commonly found diagnoses on Axis II, followed by histrionic and dependent personality disorder and traits. Our data indicate a very high frequency of psychopathology (predominantly insomnia, anxiety, and affective disorders) in benzodiazepine-dependent subjects and a relatively low frequency of substance abuse disorders. They point to psychopathology as the main risk factor for the development of benzodiazepine dependence.

NR635 Thursday, May 26, 12 noon–2:00 p.m.

Psychometric Characteristics of the Beck Anxiety Inventory with Adult Outpatients

John B. Jolly, Psy.D., Psychiatry, Univ of Arkansas Med Sci, 4300 W. Markham, Little Rock AR 72203; Thomas A. Kramer, M.D., Denise Gilliam, Ph.D., Janet M. Jolly, M.D., Jeffrey N. Wherry, Ph.D.

Summary:

Objective: This study examined the psychometric properties of the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988). In contrast to previous studies, the subjects were from a different geographical region, had primarily low to low-middle socioeconomic levels, and consisted of a greater percentage of minorities than previous studies.

Method: Subjects were 113 adult psychiatric outpatients who were administered a randomized packet of self-report measures that included the BAI, the Beck Depression Inventory, the Symptom Checklist 90-Revised (SCL-90R), the Positive and Negative Affect Schedule (PANAS), the Beck Self-Concept Scale (BST), and the Beck Hopelessness Scale (BHS).

Results: The BAI demonstrated excellent internal consistency, significant concurrent validity with a variety of measures assessing anxious symptoms and constructs, and, in most analyses, demonstrated significant discriminant validity with depressive symptoms and constructs. BAI scores for subjects with anxiety disorders did not differ significantly from those patients with depressive and other psychiatric disorders. Varimax-rotated principal component analyses revealed four factors; while several factors were similar to previous studies, differences in component structure (attributable to diagnostic and sociodemographic composition) were found.

Conclusions: The BAI demonstrated robust psychometric properties, with significant reliability and concurrent and discriminant validity, despite sample differences.

NR636 Thursday, May 26, 12 noon–2:00 p.m.

Comparison of Depression Measures in Veterans

Kenneth J. Hoffman, M.D., Prev. Med. CTeam, USUHS, 4301 Jones Bridge Road, Bethesda MD 20814; William F. Page, Ph.D., Robert J. Ursano, M.D.

Summary:

Objective: Two methods are used to define depression: clinical interview and psychometric scales. In follow-up interviews, 590 prisoners of war (POWs) and veterans from World War II and the Korean Conflict have been clinically evaluated for depression and responded to several depression scales (Beck, CES-D, and SCL-90). This study assesses agreement between diagnosis and depression scales using different cut points.

Methods: Using clinical diagnosis as a standard, each depression scale was plotted comparing its true positive (TP) and false positive (FP) rate for each possible score. Receiver Operator Characteristic (ROC) curves were generated and compared.

Results: Of all POWs and veterans, 34% were clinically depressed. ROC curves of all depression scales were markedly similar. A TP of 60% and FP of 20% corresponded to a Beck of 7, CES-D of 11, and an SCL-90 of 0.61.

Conclusions: There is no definitive cut-off point for any depression scale that correlated with the clinical diagnosis. The comorbidity of depression, PTSD, and substance abuse in veterans and POWs makes the development of better research measures important.

NR637 Thursday, May 26, 12 noon–2:00 p.m.

Severity of Medical Illnesses Diagnosed During Psychiatric Hospitalization

Peter Manu, M.D., Medical Services, Hillside Hospital, 75-59 263 Street, Glen Oaks NY 11004; Lynda Freedman, M.D., Joyce Fogel, M.D., Erik Nieddritis, M.D., Simcha Pollack, Ph.D., John M. Kane, M.D.

Summary:

A prospective cohort study was conducted to determine predictors of severity of the medical illnesses (SMI) diagnosed among psychiatric inpatients (pts). The sample consisted of 250 consecutive pts (mean age = 63.4 years, S.D. 20.4; 72% female) for whom a medical consultation was requested during a two-month period. Principal diagnoses were mood disorders (62%), schizophrenia (12%), and dementia (15%). Study data (16 variables) were collected at the time of consultation. SMI's were rated according to Horn's standardized scale as minor (33% of patients), moderate (50%), and major or catastrophic (17%). The raters were two internists who were provided only the chief complaint and the objective findings (interrater reliability alpha = .81). The medical history (PMHx) was scored according to the number of systems (e.g., cardiovascular, neurologic, etc) previously involved (mean = 1.54, S.D. = 1.17). The Pearson product-moment correlation matrix yielded significant associations between SMI and age ($r = .15$, $p = .015$), PMHx ($r = .19$, $p = .002$), and a diagnosis of dementia ($r = .14$, $p = .03$). However, age was strongly correlated both with PMHx ($r = .44$, $p < .0001$) and dementia ($r = .30$, $p < .0001$). PMHx and dementia were independent of each other ($r = .05$, $p = .43$) and retained their significance as predictors of SMI in a stepwise logistic regression analysis ($p < .05$). We conclude that readily available information on medical history and dementia is useful in identifying patients at risk of more severe medical illnesses during psychiatric hospitalization.

NR638 Thursday, May 26, 12 noon–2:00 p.m.

Diagnostic Interview Schedule: Development and Validation of a French Computerized Version

Denis J.B. Lepage, M.D., Psychiatry, CHUS, 3001 12th Avenue North, Fleurimont Quebec J1H 5N4, Canada; Francois B. Jolicoeur, Ph.D., Ellen Moulton, B.A., F. Gheysen, M.D., E. Zarfian, M.D.

Summary:

The Diagnostic Interview Schedule (DIS) has gained wide acceptance as a structured diagnostic procedure. It has been validated in several languages and a few computerized versions have been described.

We will present a French computerized version of the DIS (3a), which we have developed and validated in a test-retest design, in a psychiatric clinical setting. Each patient (N = 81) was interviewed with the instrument once by a psychiatrist and once by a nonmedical member of the clinical staff, at intervals not longer than five days. At the end of the DIS interview, each psychiatrist determined his own diagnoses. In addition, for a majority of patients, final diagnoses were given by a senior psychiatrist who was blind to DIS results but had access to clinical information from whatever source deemed relevant.

Analysis of the data was performed by means of the kappa and Yule procedures to assess the validity and reliability of the instrument for various diagnostic categories. Results demonstrate a high degree of concordance between the various procedures, which is comparable or superior to well-known validity studies using the original paper-pencil version of the DIS in other languages. We are now applying a similar approach to other structured diagnostic instruments.

NR639 Thursday, May 26, 12 noon–2:00 p.m.

Current Toxic Status, Psychological Distress and History of Psychiatric Symptoms in Alcoholic Patients

Juana L. Vainer, M.D., Psychiatry, Allan Memorial Inst., 1025 Pine Avenue West, Montreal QC H3A 1A1, Canada; Juan C. Negrete, M.D.

Summary:

Objective: This study assessed the test-retest reliability of DSM-III lifetime diagnoses in active alcoholics as influenced by level of psychological distress at the time of the interview and current toxic status (abstinence vs. continuing drinking in the previous four weeks).

Method: One hundred alcoholics (DSM-III-R clinical diagnosis) without noticeable cognitive impairment (25 + on the Mini Mental Status Examination) underwent the examiner-assisted computerized version of the DISSI (shortened version of the NIMH-DIS). Sixty-nine of them were interviewed again a minimum of four weeks later; the stability of the lifetime symptom reports leading to the diagnosis of panic disorder, generalized anxiety, phobic disorder, depression/dysthymia, and antisocial personality disorder (was assessed.

Results: Poor agreement (Kappa below 0.5) was found for panic ($K = 0.337$) and phobic disorder ($K = 0.477$), while generalized anxiety and depression/dysthymia disorders presented only fair agreement ($K = 0.658$ and $K = 0.696$, respectively). Abstinence did not significantly influence self-reported symptoms; neither did age or gender respondents. Only current levels of psychological distress assessed by the Hopkins Symptom Checklist (HSCL-58) was found to predict the risk of inconsistent reports in alcoholics ($P < 0.05$).

Conclusion: Current levels of self-rated psychological distress, independent of current toxic status, may influence the recall of past symptom experiences among alcoholics and, thus, affect the reliability of lifetime reports in this population.

NR640 Thursday, May 26, 12 noon–2:00 p.m.

Alert for Clinicians: Somatization Symptoms and Alcoholism

Allen Y. Tien, M.D., Mental Hygiene, Johns Hopkins University, 624 N. Broadway, Baltimore MD 21205; Thomas E. Schlaepfer, M.D., Hans U. Fisch, M.D.

Summary:

Objective: An often frustrating problem for primary care providers is patients with numerous somatic complaints that do not fit established disease patterns or mechanisms. We know that a substantial proportion of people seen in primary health care settings suffer from mental conditions, and the frequent conclusion that such patients are the province of psychiatry may be correct, but probably only a small proportion actually are referred for psychiatric assessment or treatment. Another frustrating problem is that of alcohol abuse and dependence. Many people do not recognize that these are problems for them, nor do their health care providers detect such problems until they are quite severe. If it were possible to either predict which individuals are at higher risk for developing alcohol problems or detect such problems earlier in their course, this would be a significant benefit for society.

Method: We hypothesized that somatization symptoms might be associated with existing alcohol problems or with an increased chance of developing alcohol problems. Using data from the NIMH Epidemiologic Catchment Area Study, comprising over 15,000 individuals at five sites in the United States who were assessed at two points in time a year apart, simple bivariate analyses were carried out.

Results: There are associations between somatization symptoms and alcohol abuse and dependence in these community data. More complete multivariable analyses are in progress to rule out possible confounding effects and to determine if there are gender and age variations in risk.

Conclusion: Primary care physicians should consider somatization symptoms as possible indicators of risk of alcohol abuse or dependence. Psychiatrists should continue to educate their colleagues about this association.

NR641 Thursday, May 26, 12 noon–2:00 p.m.

Arthur Conan Doyle's Method of Observation and Deductive Reasoning in Psychiatric Evaluations

Paul A. Hriso, M.D., Psychiatry, St. Vincent's Med. Center, 153 W. 11 Street, New York NY 10011; Emmanuel Hriso, M.D.

Summary:

Arthur Conan Doyle was a physician of the late 19th and early 20th century who achieved world renown in literature through his novels of the adventures of Sherlock Holmes. The method used by the great detective and illustrated throughout the different stories written by Conan Doyle was inspired by his medical training. In fact, the method itself of observation and deductive reasoning was the basic model and tool used by the medical profession to reach diagnostic goals at a time when complementary tests were not yet available. This method of model of evaluation consists of a strict sequence of mental steps involving the observation of fine details revolving around the case. This is then followed by freely formulating deductions from observed data, much the same way physicians build a differential diagnosis. The third step consists of testing the hypothesis elaborated during the deductive process.

This truly "scientific" method of evaluation can focus and enhance the currently accepted method of neuropsychiatric evaluation, placing increased importance on observation, examination, and deductive reasoning without immediately relying on diagnostic tests. The authors describe each successive steps in Doyle's methodical investigative approach to case solving, illustrating it with clinical vignettes in psychiatric practice.

NR642 Thursday, May 26, 12 noon–2:00 p.m.

Evaluation of the Basic Sexual Knowledge of Advanced Medical Students

Errol M. Aksu, M.D., Psychiatry, Hershey Medical Center, P.O. Box 850, Hershey PA 17033; Edward O. Bixler, Ph.D.

Summary:

As HIV infection and unwanted pregnancies constitute major problems, especially among teens, public education concerning sexuality is critical. Physicians are an important resource in this educational process. Several years ago, the Kinsey Institute tested the basic sexual knowledge of a statistically representative group of 1,974 American adults in a poll conducted by the Roper Organization. The 18 questions covered a wide range of sexual topics including AIDS, contraception, erection problems, and menopause. The results indicated that the majority of those queried answered less than half of the questions correctly. In order to evaluate the same knowledge in advanced medical students, we assessed 105 third- and fourth-year students using an anonymous questionnaire with identical questions as the poll. The students performed significantly better ($p < 0.001$) than the poll sample as 96 of them answered more than half of the questions correctly. However, there were some disturbing findings. For example, only 37% of the students knew that an over-the-counter spermicide (nonoxynol-9) is available that will kill HIV. The results of this study indicate that while advanced medical students have a much better understanding of basic sexual knowledge than the average Ameri-

can, training of future physicians in sexuality is needed to equip them to educate their patients.

NR643 Thursday, May 26, 12 noon–2:00 p.m.

Psychosocial Functioning in the Ehlers-Danlos Syndrome

Ralph Rubenstein, M.D., Psychiatry, Hutzel Hospital, 4707 St. Antoine, Detroit MI 48201; Mark A. Lumley, Ph.D., Margaret Jordan, Ph.D., Petros Tsipouras, M.D., Mark Evans, M.D.

Summary:

Objective: Although the structural pathology and symptomatology of EDS are becoming increasingly clarified, the psychological and behavioral features of the syndrome have not been examined. This study examines psychosocial issues in EDS adults and children and EDS subtypes.

Method: Group interviews, questionnaires, and psychometric evaluations of 41 adults and seven children with EDS were conducted.

Results: Of the 41 adults studied, 56% had outpatient psychotherapy, 54% reported significant depression, 7% (3) had psychiatric hospitalizations, and 4% (2) had attempted suicide. Psychometric test results revealed that EDS patients scored higher on the various dimensions than healthy young adults, but slightly lower than general psychiatric outpatients. Five of the seven children were found to have clinically elevated behavioral problems and three showed significant increases in internalizing behavior. Adults expressed concerns that were grouped into three areas: difficulties in dealing with the medical system, problems in daily living and pregnancy and reproduction. Since EDS is rare and goes unrecognized, patients are often left stigmatized as malingerers or hysterics.

Conclusions: This study is a first attempt at understanding psychosocial issues of EDS. Almost one-third of adults with EDS had clinically significant psychiatric symptoms. Further studies to clarify psychopathology are suggested.

NR644 Thursday, May 26, 12 noon–2:00 p.m.

Public Attitudes to the Quality of Psychiatry

Per Hamre, DDS, Vaekeroeveien 133, 0383 Oslo; Norway; Alv A. Dahl, M.D., Ulrik F. Malt, M.D.

Summary:

Public opinion in Norway on mental disorder was investigated in September 1992 by interviewing a stratified random sample. A total of 1063 persons were interviewed by telephone, constituting a representative sample of the total Norwegian population. The hypothesis was that psychiatric treatment and psychiatric patients would be met with prejudice, and that public opinion on these questions underestimated the prevalence of mental disorders.

The quality of psychiatric treatment was considered very low compared with the treatment of heart diseases and cancer. One-third of the respondents thought there was a great difference between persons suffering from mental disorder and ordinary people. Sixty percent estimated the prevalence of mental disorder to be between 10% and 50%. The concern at some time in life to suffer from a mental disorder was expressed by 27% of the respondents. Negative attitudes to psychiatric treatment and psychiatric patients have serious consequences, both regarding outcome of individual treatment and the way society prioritizes psychiatry.

NR645 Thursday, May 26, 12 noon–2:00 p.m.

Prescription Patterns in Hospitalized Patients with Refractory Psychosis

Jean-Yves Roy, M.D., Psychiatry, L-H Lafontaine Hospital, 7401 Hochelaga Street, Montreal Quebec H1N 3M5, Canada; Guy Chouinard, M.D., Monique Tremblay, M.D., Claire L.I. Damecours, M.D.

Summary:

Once home to more than 6500 patients (1961), Louis-H. Lafontaine Hospital has undergone a downsizing to 1100 patients over the last 30 years. In view of these circumstances, we decided to investigate the prescription patterns prevailing within its long-term facility. On June 17, 1993, we did a cross-sectional survey of every medical prescription within this population (594 patients) and then converted the neuroleptic doses to haloperidol antipsychotic equivalent daily dosages (haloperidol equivalents). Among the 569 patients receiving antipsychotic agents (95.8%), haloperidol equivalents ranged from 2 to 126 mg/day. Haloperidol equivalents were equal to or greater than 40 in 137 patients (24.07%). The current study focuses of 52 of these patients (21 women, 31 men; 9% of our sample) who received 60 or more haloperidol equivalents/day. While our figures seem comparable to the very little data published on this subject, we investigated the various circumstances, both clinical and institutional, leading to the prescription of high neuroleptic doses. An adequate staff/patient ratio decidedly favours lower doses. Within the adequately staffed sector of our facility, the haloperidol equivalents per ward ranged from 16.03 to 22.61 (mean: 19.74), whereas in the more densely populated sector, they ranged from 21.22 to 37.04 (mean: 29.7). However, single rooms do not necessarily lead to lower doses than dorms. Tradition plays a role here: some of the single-room wards are, in effect, located in a section of the hospital traditionally devoted to agitated and difficult patients where we still tend to refer severe cases of psychosis. As a consequence, the haloperidol equivalents in this traditionally custodial single-room sector of the hospital averaged 32.92 per ward as opposed to 25.14 in the dorm section and 19.39 in the recently redecorated sector. Across all types of wards, finally, (dorm, small dorm, single room or modern ward, traditionally custodial or liberal wards), the use of newer drugs, risperidone or clozapine for instance, lead to more favourable prescription patterns: 19.36 haloperidol equivalents/day for a population of 50 patients as opposed to a general average of 26.71 for our entire sample.

NR646 Thursday, May 26, 12 noon–2:00 p.m.

Socioeconomic Drift Among Patients with Schizophrenia and Severe Affective Disorder

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Summary:

We studied downward drift in socioeconomic status (SES) among patients with schizophrenia and severe affective disorder in relation to the general population. This data-linkage study was a retrospective, 17-year follow up of patients aged 30–59 years, who had schizophrenia (ICD 295, n = 17,796)) or severe affective disorder (ICD 296, n = 6,521) as the primary diagnosis at hospital discharge in 1987–88 in Finland. The observed SES of these patients in 1970, 1975, 1980, and 1987 from the censuses was compared with the expected distribution, using general population data from the same censuses as the reference. The SES categories were: employer and self-employed; upper white-collar; lower white collar; blue-collar; farmer; and nonemployed.

The observed social drift among psychiatric patients during 17 years preceding the hospital discharge was mainly from employed

to nonemployed. A substantial social drift was seen among schizophrenic patients, and their risk of being nonemployed was four to 10 times higher than expected, depending on age, gender, and year. Marked differences in socioeconomic distribution were already present in 1970. Among patients with severe affective disorder much less social drift had taken place over time, and their SES distribution in 1970 was very close to that of the general population. In 1987 their risk of being nonemployed was two to three times higher than expected.

NR647 Thursday, May 26, 12 noon–2:00 p.m.

Faculty Attitudes About Abuse of Medical Students

Francis Kane, M.D., Psychiatry, Emory University, 490 Peachtree Street, #561-C, Atlanta GA 30308; Thomas A. Kramer, M.D.

Summary:

This report documents the first study of medical faculty opinion about medical student perceptions of abuse, which currently stands at 54% of seniors reporting abuse in the last AAMC questionnaire.

Methods: An anonymous questionnaire was sent to 550 medical school faculty—213 replied (38.7%).

Results: Overall, 50% of this faculty sample agreed that students complaints were well founded. Two clusters emerged (A = Surg, Ob/Gyn, Rad, Basic Sci.) (B = Int. Med., Ped. Psych). Cluster A was significantly (1) less likely to agree students were abused, (2) reported less medical school abuse themselves, (3) were more likely to be satisfied with the school's program for correcting these problems, (4) saw women as oversensitive to faculty sexual humor. Overall 20% agreed and only ⅓ of men disagreed, (5) saw racial minority students as more sensitive to criticism. Fifty percent overall saw racial minorities different in sensitivity to criticism. In addition, 44% had themselves been abused in school; 15% agreed they took out their frustrations on students; and nearly 50% agreed they didn't know enough about resident treatment of students. Few faculty were aware of any discipline of offenders.

Results will be discussed in terms of implications for change in school programs that deal with abuse, and relevance of prior studies of personality factors in medical students such as tolerance of ambiguity and authoritarianism to the clustering of our sample.

NR648 Thursday, May 26, 12 noon–2:00 p.m.

Female Psychiatric Residents: A Research Future?

Kaye L. McGinty, M.D., Psychiatry, University of Kentucky, 820 South Limestone Annex 4, Lexington KY 40536; Catherine A. Martin, M.D., Karen L. DeMoss, Ph.D., Kelly S. Kearfott Hill, M.D.

Summary:

Objective: The objective of this study was to investigate factors influencing career choice by female psychiatry residents, with particular focus in the research track.

Method: A questionnaire investigating developmental and training influences on career tracks in women residents in child and adult psychiatry was distributed to 68 women in three residency programs, with a response rate of 56%.

Results: Involvement in research occurred in college and medical school but reached its lowest frequency in residency (32%). Residents involved in research were more likely to attend scientific meetings ($p < 0.05$) and to have publications, presentations, ($p < 0.05$) and mentors ($p < 0.05$). Residents' first priorities for a residency were a broad-based, supported training environment, while availability of research activity or prominent mentor was last. The most valued characteristic of a mentor was nurturance, with national recognition least. Choice of an academic career was associated with performing research in residency ($p < 0.05$), having a mentor in medical school ($p < 0.05$), and identifying oneself as a self starter and as independent ($p < 0.05$). A public health career was associated with having a systems, political perspective ($p < 0.05$), and private track with being less likely to describe oneself as a self starter and independent ($p < 0.05$).

Conclusion: Recruiting women residents into research involves providing a nurturing and challenging academic mentor and environment.

NR649 Thursday, May 26, 12 noon–2:00 p.m.

Psychiatry Training in Internal Medicine Residencies

Mark D. Sullivan, M.D. Psychiatry, University of Washington, Mail Stop RP-10, Seattle WA 98195; Steven A. Cohen-Cole, M.D., Roger G. Kathol, M.D., Geoff Gordon, M.D., Steven R. Hahn, M.D.

Summary:

Most outpatient care for psychiatric disorders is done by primary care physicians, yet the psychiatric training received by primary care residents is often minimal. A survey about psychiatric training was sent to all training directors of internal medicine residencies in the U.S. A total of 238 replies were obtained from traditional programs (58% response) and 110 replies from primary care programs (62% response). Three-fourths of traditional and two-thirds of primary care training directors thought that their program should spend more time on psychiatric disorders. For all categories of psychiatric disorder, psychiatric training intensity and the director's satisfaction with the training was greater in the primary care programs. For example, 33% of traditional vs. 47% of primary care directors were satisfied with their residents' depression training ($t = 2.3$, $p < .02$). For each category of psychiatric disorder less than half of the training directors were satisfied. Training in somatoform disorders, psychotropic drugs, and office psychotherapy were identified as most deficient. Inadequate time and funding were identified as the primary barriers to implementing a curriculum in psychiatry. Most favored additions to the curriculum were psychiatric consultants in medical clinics and on medical wards. Innovative collaborations between psychiatry and medicine departments are necessary if treatment of psychiatric disorders in primary care is to be improved.

NR650 Thursday, May 26, 12 noon–2:00 p.m.

Psychosocial Predictors of Postpartum Depressive Symptomatology

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Summary:

Objective: This paper describes the results of a prospective study to identify psychosocial predictors of postpartum depressive symptomatology. A vulnerability-stress model was developed and tested.

Method: Data was gathered from 246 pregnant women at the fourth month of pregnancy and the sixth month after birth. Methods of recruitment and the initial attrition rate (40%) will be discussed. Characteristics of the women who have not participated in the research have been studied and show no statistical difference from those of participants (t-tests; chi-square). Participants were assessed according to a number of psychosocial variables including social, cognitive, and life-stress variables. Levels of postpartum depressive symptoms were measured by the widely used Edinburgh Postnatal Depression Scale.

Results: A path analysis indicated our vulnerability-stress model accounted for 26% of the variance in postpartum depression level.

Depression level during pregnancy showed the strongest association with postpartum depressive symptomatology ($R2 = 0.15$; $p < .01$). However, three other predictor variables were also significant in the path analysis: low socioeconomic status ($R2 = 0.04$; $p < .05$), negative life events ($R2 = 0.05$; $p < .01$), and previous episodes of emotional disorders ($R2 = 0.02$; $p < .01$).

Conclusions: These results support a vulnerability-stress model of postpartum depressive symptomatology. Implications for the counseling of pregnant women and their families will be discussed.

NR651 Thursday, May 26, 12 noon–2:00 p.m.

Gender Differences in Axis I Comorbidity in Major Depressive Disorder

Maurizio Fava, M.D., Psychiatry, Mass. General Hospital, 15 Parkman St. ACC 815, Boston MA 02114; Melissa Abraham, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: The aim of our study was to assess gender differences in Axis I comorbidity in patients with a primary diagnosis of major depressive disorder (MDD), as well as gender differences in age of onset of MDD.

Methods: Age of onset of MDD and Axis I disorders was assessed in 117 men (mean age: 39.1 ± 9.1) and 227 women (mean age: 38.2 ± 11.2) with the Structured Clinical Interview for DSM-III-R–Patient Edition (SCID-P) (Spitzer et al, 1989).

Results: The mean HAM-D-17 score was 19.0 ± 3.7 in men and 19.7 ± 6.8 in women. The age of onset of MDD was significantly lower in women (mean age: 22.0 ± 11.9) than in men (mean age: 25.0 ± 12.3). On the SCID-P, women were significantly more likely than men to meet criteria for comorbid bulimia nervosa (17% vs. 3%), while men were significantly more likely to meet criteria for lifetime history of alcohol abuse/dependence (40% vs. 25%). No other significant gender differences in comorbid Axis I disorders were observed.

Conclusions: Our findings are consistent with those of previous studies showing a greater prevalence of alcohol abuse in men and of eating disorders in women. However, in contrast with other investigations, depressed women were not more likely to suffer from anxiety disorders than depressed men.

NR652 Thursday, May 26, 12 noon–2:00 p.m.

Factors Associated with Sexuality Among Women with Metastatic Breast Cancer

Leslie Smithline, B.A., Psychology, University of Pitts., 4015 O'Hara Street Room 604, Pittsburgh PA 15260; Julia L. Zarcone, M.A., Cheryl Koopman, Ph.D., David Spiegel, M.D.

Summary:

Objective: This study examines demographic variables and mood states in women with metastatic breast cancer and their spouses that related to interest in and ability to enjoy sexuality.

Methods: Forty-seven women with metastatic breast cancer and 22 spouses were recruited through their oncologists. Women and their spouses were administered the Positive States of Mind Questionnaire (Horowitz, 1990) and the Profile of Mood States (McNair, 1973) at study entry.

Results: Eighty-eight percent of the women and 100% of their spouses indicated that sexual pleasure was something they had wanted to experience; however, only 23% of the women and 26% of their spouses reported that it was easy to experience. For patients, living with a spouse was significantly related to less difficulty in being able to experience sexual pleasure ($t = 2.59$, $p = < .05$). Ability to experience sexual pleasure was significantly correlated between patients and their spouses ($r = .07$, $p < .02$). Among patients, feeling less anxious was significantly related to interest in experiencing sexual pleasure ($r = -.28$, $p = .05$), but not to ability to experience it.

Conclusions: Sexuality is an important aspect of quality of life for metastatic breast cancer patients and their spouses. Further research needs to examine psychosocial factors that affect sexuality for this population.

NR653 Thursday, May 26, 12 noon–2:00 p.m.

Historical Analysis of the Evolution of American Biological Psychiatry in the 20th Century

Ross J. Baldessarini, M.D., MRC-316, McLean Hospital, 115 Mill Street, Belmont MA 02178.

Summary:

Objective: To evaluate activity levels and topics of interest in biological research and therapeutics in American psychiatry from 1944–1994, relative to competing approaches.

Method: Monthly contents and annual subject index samples of reports in *Am J Psychiatry* were categorized as: general, administrative, psychosocial, general clinical, forensic, substance abuse, neurobiomedical, or biologically therapeutic; samples (≥2) obtained for each year and scored independently ($r = 0.8$, $p < 0.01$) were pooled in five-year epochs to demonstrate the annual proportion of the last two categories; subject indices of *Arch Gen Psychiatry* were similarly analyzed.

Results: Steady interest in "biomedical" topics was found throughout the period analyzed (mean ± SD = 43.7 ± 12.9%), with inexplicable decreases in the 1960s–1970s in both journals. While the *quantity* of effort was sustained, topics and techniques of interest obviously have evolved. There was evidence of strikingly similar strategies in some areas—notably, formulation of biological hypotheses of pathophysiology—etiology from knowledge of actions of new treatments, whether older shock therapies or newer pharmacotherapies.

Conclusions: American biological psychiatry evidently evolved in a more steady and continuous way than is sometimes appreciated, with remarkable formal and logical similarities of older and current approaches.

NR654 Thursday, May 26, 12 noon–2:00 p.m.

Influence of Family Approach in Halfway House Residence on the Rehospitalization of Schizophrenic Patients

Francis L. Ritz, M.D., Psychiatrie, Institutions University, 67 Rue Lausanne, Geneva 1201, Switzerland; Jacqueline Lalive Aubert, M.D.

Summary:

Minuchin's structural family therapy model (MFA) was used with a group of schizophrenic patients living in a halfway house who were followed over a period of five years.

Methods: 41 patients aged 19 to 53 (mean/29 years) with the diagnosis of schizophrenia according to DSM-III-R were studied over this period; all patients included in the study were required to be living with at least two family members. Twenty patients, three females and 17 males accepted to be followed once a month with the MFA approach; the further 21 patients, nine females and 12 males, received supportive therapy without family intervention. The two groups were on regular neuroleptic treatment.

Results: 50% of patients treated by MFA approach were hospitalized, compared with 62% without a family approach. The total length of stay in the halfway house for the first group was 9841 days; for the second group it was 8543 days. The length of inpatient treatment for the first group was 171 days (1.7% of the total), as compared with 751 days for the second group (8.8% of the

total). Total hospitalizations for the MFA group were 14, while 30 were noted in the second group.

Discussion: The use of Minuchin's family approach appears to help the reorganization of the family structure along less stressful lines.

NR655 Thursday, May 26, 12 noon–2:00 p.m.

Enhancement of Learning with a Floral Odor

Alan R. Hirsch, M.D., Smell & Taste FND., 845 North Michigan Avenue, Chicago IL 60611; Lisa H. Johnston, M.D.

Summary:

Various studies have evaluated the effects of odor on behavior, but none has systematically assessed the effect of odor specifically on learning. In order to do so, we evaluated the learning ability of 22 subjects both in the presence and in the absence of a specific floral odor, using the paradigm of the trail-making subtest of the Halsted-Reitan Test Battery. Subjects with normal olfactory ability who considered the odorant hedonically positive demonstrated that on subsequent trial they learned to complete the tasks 17% faster on average in the presence of the floral odor than in the nonodorized condition. These findings imply that future studies may validate the use of odors as adjuvants to education as well as to rehabilitation and psychotherapy.

NR656 Thursday, May 26, 12 noon–2:00 p.m.

A Controlled Study of Cognitive-Behavior Therapy with Buspirone or Placebo in Panic Disorder with Agoraphobia: A One-Year Follow-Up

Jean A. Cottraux, M.D., Psychiatry, Hopital Neurologique, 59 Goulevard Pinel, Lyon 69394, France; Ivan D. Note, M.D., Charly Cungi, M.D., Patrick Legeron, M.D., Francois Heim, M.D., Laurent Chneiweiss, M.D.

Summary:

Objective: This multicenter study compared buspirone with placebo in patients receiving cognitive-behavior therapy (CBT) for panic disorder with agoraphobia (DSM-III-R criteria).

Method: Buspirone was given double blindly (20–60 mg per day) for 16 weeks, followed by a one-week taper. CBT was administered in 16 weekly individual sessions.

Results: Ninety-one patients entered the study; 14 placebo-responders were excluded during the 15-day wash-out period; 77 patients were randomized into two groups: CBT with buspirone and CBT with placebo; 48 patients reached week 16 and 41 week 68. Clinical status, rate of drop-outs, and baseline sociodemographic or psychometric variables were comparable in the two groups. A significant within-group improvement of depression agoraphobia, panic frequency, generalized anxiety, HSCL-90, and quality of life, was found at week 16 and retained at week 68 in the two groups. The general criterion of improvement (50% reduction of the main target agoraphobic behavior) showed no between-group difference at weeks 16 and 68. At week 16, between-group comparison of changes from baseline showed that CBT + bupirone was significantly better on a generalized anxiety scale ($p = 0.033$), the agoraphobia score of the Fear Questionnaire ($p = 0.008$), and tended to be so on the Quality of Life scale ($p = 0.076$). At week 68, no between-group difference was found on any measure.

Conclusions: Buspirone can be effectively combined with CBT for panic disorder with agoraphobia and enhances its effects on generalized anxiety and agoraphobia.

NR657 Thursday, May 26, 12 noon–2:00 p.m.

Sertraline in Social Phobia: A Double-Blind, Placebo-Controlled Crossover Pilot Study

David J. Katzelnick, M.D., Dean Foundation, 8000 Excelsior Drive, Suite 302, Madison, WI 53717; John Greist, M.D., James W. Jefferson, M.D., Kenneth A. Kobak, M.S.

Summary:

Introduction: Recently recognized as a prevalent, chronic and often severe disorder,[1] social phobia has become the focus of increased investigation.[2] While no currently available medication has an FDA approved indication for social phobia, recent investigations have suggested treatment efficacy of several classes of drugs, including beta-blockers,[3] monoamine oxidase inhibitors (MAOIs),[2] and benzodiazepines.[4,5] Each of these treatment approaches has potential complications, such as abuse and dependence (benzodiazepines), hypertensive crisis (MAOIs) and depression (B-blockers).[6] While several case reports and open trials suggest treatment efficacy of SSRIs for social phobia,[6–10] no double-blind, placebo-controlled studies have been reported to date.

Method: The study utilized a randomized, double-blind, crossover design. Subjects were 12 patients (8 males, 4 females, mean age 42.62 (SD = 7.54)) with a DSM-III-R diagnosis of Social Phobia (300.23). Subjects were randomized to either sertraline (50–200 mg/d flexible dosing) or placebo for 12 weeks, followed by taper and no treatment for two weeks and were then crossed over to the other condition for 12 weeks. The primary outcome measure was the Liebowitz Social Anxiety Scale (LSAS).[1] Mean baseline LSAS score was 63.4, indicating a sample with clinically severe social phobia. Subjects were administered both a clinician and computer-administered versions of the primary outcome measure. Data were analyzed using an intent to treat analysis.

Results: Results of within-groups analysis with the collapsed data set found a statistically significant improvement with sertraline, $t(11) = 4.41$, $p = .001$, but not with placebo $t(11) = 1.21$, $p = .252$. The mean change score on the LSAS for patients receiving sertraline was 22.0 (SD = 17.3), compared to 5.5 (SD = 15.8) for patients receiving placebo $t(11) = 2.05$, $p = .065$. Forty-two percent of patients were rated as moderately or markedly improved while on sertraline, compared to 17% while on placebo, $X^2(1) = 1.82$, $p = .178$. No significant difference was found between computer- and clinician-administered versions of the LSAS, $t(11) = 1.26$, $p = .223$, and the correlation between the forms was .89, $p = .0001$.

Conclusions: Based on the results of this small sample study, sertraline seems an effective treatment for social phobia. As a class, SSRIs are well tolerated and free of potentially dangerous side effects that have limited the use of MAOIs, which are also effective in social phobia. Controlled studies of sertraline, placebo and MAOIs, which are also effective in social phobia. Controlled studies of sertraline, placebo and MAOIs with larger populations and parallel design are warranted.

Results also suggest that computer administration may be a preferable mode of assessment in patients with this disorder.

NR658 Thursday, May 26, 12 noon–2:00 p.m.

The Profile of Persons Hospitalized by Court Remand and the Outcome

Chitra M. Shenoy, M.D., 3303 Shore Road, Oceanside NY 11572.

Summary:

Objective: To study the profile of persons court remanded for hospitalization.

Method: Physician-prepared reports of 73 consecutive admissions involving 66 persons over a three-year period were studied for age, gender, ethnicity, reason for commitment, principal psychiatric diagnosis, disposition, and recidivism.

Results: There were 66 one-time admissions and seven readmissions. The average age of this group, consisting of 48 males and 18 females, was 36 years (range 18–67). There were 47 (71%) Caucasians, 12 (18%) African-Americans, five (8%) Hispanics, and two (3%) Asians. Reasons for commitment were violation of order of protection (51/73 instances or 70%), child neglect (8/73 or 11%), aggressive behavior in the court (3/73 or 4%), and other (15%). Psychiatric diagnoses were: schizophrenia (18/66 persons or 27%), substance abuse (15/66 or 23%), adjustment disorder (6/66 or 9%), bipolar disorder (5/66 or 8%), depressive disorder NOS (5/66 or 8%), schizoaffective disorder, delusional disorder, marital problem (3/66 or 5% each), intermittent explosive disorder (1/66 or 2% each). Disposition: One person was discharged to a state hospital, one to a private hospital, and all others to mental health clinics.

Conclusions: The court-remanded persons in this study were predominantly male Caucasians, suffering from either schizophrenia or substance abuse, committed for violating the order of protection. The small number of repeat offenders (9.5%) indicates that court-ordered hospitalization was an effective behavioral deterrent in this population.

NR659 Thursday, May 26, 12 noon–2:00 p.m.

Housing Choice and Supported Housing for Homeless Persons Served by Assertive Community Treatment

Lisa Dixon, M.D., Psychiatry, University of Maryland, 645 W. Redwood Street, Baltimore MD 21201; Nancy Krauss, M.S.W., Patrick Myers, M.A., Anthony Lehman, M.D.

Summary:

Objective: The purpose of this study was to assess the use of a limited number of Section 8 housing certificates and client performance by homeless persons with severe mental illness (HPSMI) served by an experimental assertive community treatment team (ACT).

Methods: Differences between receivers and nonreceivers of certificates and months to complete Section 8 applications were analyzed. Reasons HPSMI did not receive certificates and housing outcomes were summarized with regard to patient preference.

Results: The 34 (44%) of HPSMI who wanted and received certificates had significantly less psychopathology after three months than nonreceivers ($p < .05$) and tended to have more affective disorders than schizophrenia ($p = .07$). Of the 43 nonreceivers, 19 (44%) patients actively did not want a certificate, six patients did not engage with the program long enough to complete the process, four patients were not eligible due to HUD criteria, and four did not get apartments for miscellaneous reasons. Only 10 patients (23%) who wanted a Section 8 were not supported because of staff safety concerns. The majority of the 43 patients not getting a Section 8 did obtain independent or minimally supervised housing. Patients receiving a Section 8 took 5.7 (SD 5.8) months to apply. Longer time to apply was associated with schizophrenia ($p < .05$), and increased baseline ($p < .05$) and three-month psychotic symptoms ($p < .01$).

Conclusions: This study suggests that it is possible to honor patient preference for the majority of HPSMI if adequate resources are provided. Most of these HSPMI received and succeeded at their housing choice, which was frequently independent living. Staff may view persons with schizophrenic disorders and more symptoms as needing more supervision. These HPSMI may also take longer to pursue independent living via a Section 8 certificates were they made available.

NR660 Thursday, May 26, 12 noon–2:00 p.m.

Predicting Homeless Status in a Population of Chemically Dependent Veterans

Juris P. Mezinskis, Ph.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Eugene C. Somoza, M.D., Sue R. Dyrenforth, Ph.D., Mark W. Cohen, Ph.D.

Summary:

The purpose of this study was to develop an intake instrument for identifying people at risk for becoming homeless. A sample of 458 veterans applying for chemical dependence treatment at an urban VA medical center, was given a structured intake interview (Addiction Severity Index). Current homeless status (defined as not having a stable living arrangement) was reported by 142 patients or 31%. A discriminant function analysis of 244 intake data items identified 18 variables that were predictive of current homeless status (Wilks' Lambda: .67, $p < .001$). The predictive items were as follows: 1) chemical dependence factors (years of cocaine use, recent use of alcohol), 2) legal factors (more drug arrests, more arrests for disorderly conduct, but fewer arrests for assault, fewer driving violations, not being court referred for treatment, not being on probation) 3) family/social factors (living with a drug abuser, recent problems with their mother, poor relationship with a sex partner, siblings with drug problems), 4) financial factors (recent employment problems, not receiving physical or psychiatric disability income, fewer years of steady employment), and 5) a psychiatric factor (recent depression). The discriminant function correctly predicted 91% of the stable housing cases, 52% of the homeless cases, and 79% of the total cases. Stable cases can be predicted with great accuracy. Current homeless status may be more difficult to predict because patients may be positive for the predictive variables, but not homeless at that particular point in time. Therefore, nonhomeless patients identified by this formula might be the focus of specific interventions to stabilize, reduce, or eliminate the risk factors.

NR661 Thursday, May 26, 12 noon–2:00 p.m.

Housing the Homeless: Results of a Random Controlled Trial

Stephen M. Goldfinger, M.D., Psychiatry, HMS Mass General Hospital, 74 Fenwood Road, Boston MA 02115; George Tolomiczenko, Ph.D., Winston Turner, Ph.D., Russell Schutt, Ph.D., Olinda Gonzalez, Ph.D., Sondra Hellman, R.N.C.S., Norma Ware, Ph.D.

Summary:

One hundred eighteen (118) seriously and persistently mentally ill homeless individuals were randomly assigned to either independent apartments (IL) or Evolving Consumer Households (ECH). ECHs initially were staffed much like traditional group homes. However, tenants at these residents were assisted in developing skills to increasingly take over management functions: deciding on activities and house budget, determining staffing patterns, and establishing virtually all rules for the household. Intensive case managers followed subjects in both conditions.

Findings at 12 months: Of 63 subjects initially placed in ECH residences, 47 (74.6%) were still in their original placement after 12 months. Of 55 IL subjects, 30 (57.6%) were still in those placements (excluding three who have died). Overall, only 13 individuals (16%) had returned to shelters or were living on the street. Detailed 12 month follow-up housing data are currently available for 113 subjects. ECH subjects ($n = 63$) averaged 15.0 days homeless (streets or shelters); those in ILs ($n = 50$) averaged 38.2 days homeless ($t = 2.03$, $p \leq 0.04$). The groups also differed significantly in terms of the fraction of subjects who had *any* episodes of homelessness during the first 12 months: 21 IL subjects (42%) had spent at least one day homeless, while only 13 of the 63 ECH

subjects (21%) had an episode of homelessness in that period ($x^2 = 6.05$, $p \leq 0.014$). The groups did not differ in the average number of days spent institutionalized (about 24 days for both).

Conclusion: At 12-month follow-up, group residences that provide homeless individuals with the opportunities to develop community living skills appear to be significantly more effective than independent apartments in reducing total days homeless, and in decreasing residential instability. Eighteen-month follow-up data for the sample will be available soon.

NR662 Thursday, May 26, 12 noon–2:00 p.m.

Mental Alternation Test Performance and Functional Status at Discharge in the Chronically Mentally Ill

Beverly N. Jones, M.D., Psychiatry, Bowman Gray, Medical Center Blvd, Winston-Salem NC 27157; Geetha Jayaram, M.D., Jack F. Samuels, Ph.D., Hilary Robinson, ROT.

Summary:

Objective: This study examined the relationship between the Mental Alternation Test and discharge functional status. We hypothesized that patients who failed this brief test of attention and concentration, would also have problems in daily functioning at discharge.

Method: The project was a prospective study of inpatients from an inner-city population of chronically mentally ill. Informed consent was obtained from all participants. Forty-three patients agreed to participate; 65 other patients admitted during this period were not tested. Patients were administered the Mental Alternation Test (MAT), the Milwaukee Evaluation of Daily Living Skills (MEDLAS), and the Occupational Therapy Task Observation Scale (OTTOS).

Results: The MAT correlated significantly with the MEDLS ($r = 0.505$, $p < .001$). A cutting score of $^{9}/_{10}$ on the MAT identified patients impaired on the MEDLS with good sensitivity (69.2%) and specificity (77.3%). The MAT cutting score of $^{9}/_{10}$ distinguished abnormal MEDLS performance (Chi-square 7.480, $p < .01$). The MAT did not correlate well with the OTTOS ($r = 0.047$) with moderate sensitivity (50%) and specificity (66%).

Conclusions: The Mental Alternation Test can help identify individuals at risk for impaired functioning at discharge.

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