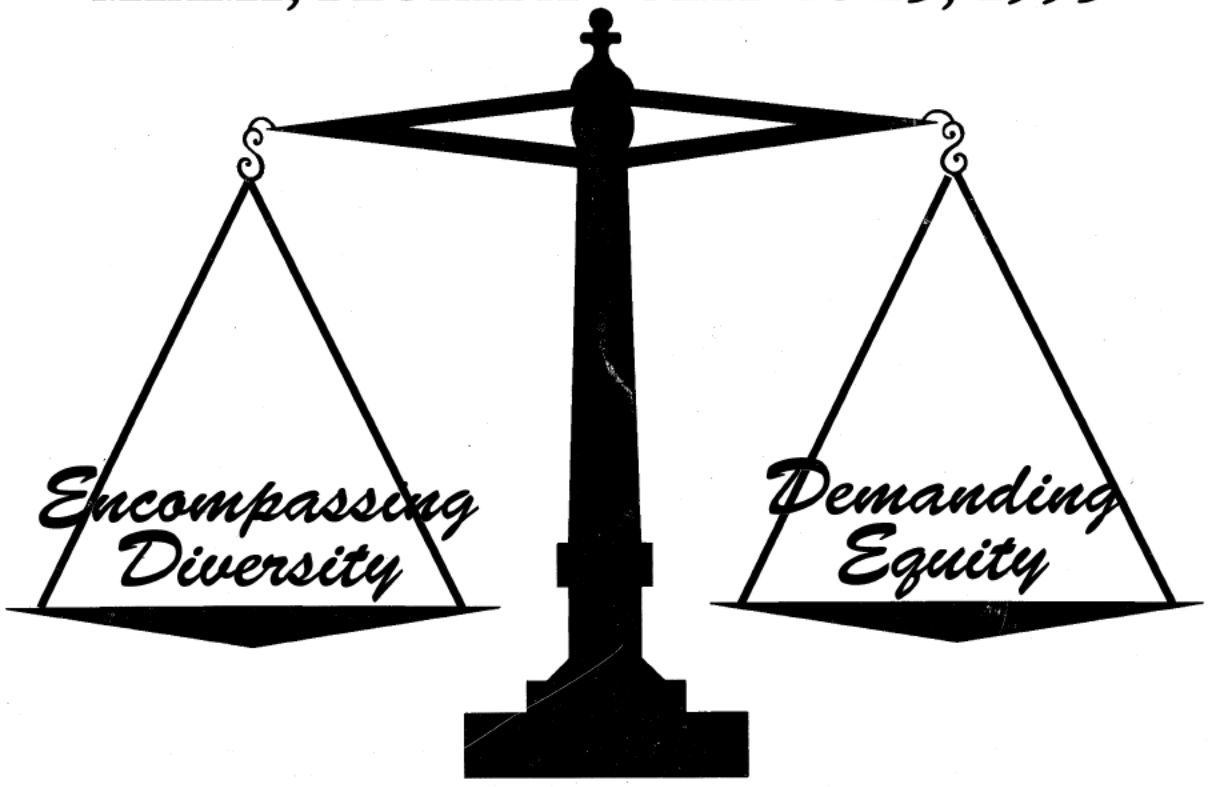
1995 Annual Meeting

New Research Program and Abstracts

AMERICAN PSYCHIATRIC ASSOCIATION

148TH ANNUAL MEETING

MIAMI, FLORIDA • MAY 20-25, 1995



PROGRAM
AND
ABSTRACTS ON NEW RESEARCH

IN SUMMARY FORM

148TH ANNUAL MEETING OF THE AMERICAN PSYCHIATRIC ASSOCIATION

MIAMI, FL
May 20-25, 1995

SUBCOMMITTEE ON NEW RESEARCH OF THE SCIENTIFIC PROGRAM COMMITTEE

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148th Annual Meeting
Miami, Florida
May 20-25, 1995

Encompassing Diversity
Demanding Equity

May 22, 1995

1400 K Street, N.W.
Washington, DC 20005
Telephone: (202) 682-6237
Fax: (202) 682-6345

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 1995 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 22, 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 suicide, brain imaging, dissociative disorders, and pharmacotherapy. 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.

Featured on Tuesday, May 23, at 9:00 a.m. is the new format "Research Advances in Medicine," with special emphasis on hemopoietic stem cell use in bone marrow transplantation, chronic fatique syndrome, epilepsy, and diabetes mellitus. The New Research Oral/Slide Sessions will be held Tuesday through Thursday, from 9:00 a.m.-10:30 a.m. Sessions will focus on neuroimaging; mood disorders and treatment techniques (Tuesday); anxiety disorders schizophrenia and other psychotic disorders (Wednesday); potpourri; mood disorders (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 stress; schizophrenia and other psychotic disorders; geriatric psychiatry; mood, premenstrual dysphoric, personality disorders; suicide; somatoform disorders; diagnostic issues; and genetics (Tuesday); anxiety; AIDS and HIV related disorders; consultation/liaison and emergency psychiatry; violence; trauma and victimization; dissociative, organic mental, sleep disorders; psychoimmunology; treatment techniques and issues; and research issues; psychopharmacology and other somatic therapies; biological psychiatry; brain imaging; neurobiology and neuropsychiatry (Wednesday); alcohol and substance abuse, eating disorders; infant, childhood, adolescent psychiatry; community psychiatry and prevention; cross-cultural and minority psychiatry; managed care and health care funding issues; forensic psychiatry; gender issues; academic psychiatry; Presidential Theme: Encompassing Diversity, Demanding Equity; Computers; Epidemiology and Other Psychiatric Disorders (Thursday).

The 47 oral/slide papers (including 11 Young Investigators) and 594 poster presentations (including 149 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 Fiester

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.
Ross J. Baldessarini, M.D.
James C. Ballenger, M.D.
Wade H. Berrettini, M.D.
Richard L. Borison, M.D.
Gabrielle A. Carlson, M.D.
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Igor Grant, M.D.
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Marvin Stein, M.D.
James J. Strain, M.D.
Kenneth J. Tardiff, M.D.
James W. Thompson, M.D.
Gary J. Tucker, M.D.
Joe P. Tupin, M.D.
Thomas W. Uhde, 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 #
Alexopoulos, George S.	Parke-Davis, Division of Warner-Lambert Company	NR247, NR556
Alpert, Jonathan E.	Eli Lilly and Company	NR301
Anton, Raymond F.	DuPont Pharma; Astra/Merck Group, Division of Merck & Co.	NR546
Aronson, Stephen M.	Janssen Pharmaceutica and Research Foundation; SmithKline Beecham Pharmaceuticals; Eli Lilly and Company; Pfizer Inc.; Parke-Davis, Division of Warner-Lambert Company	NR267
Baker, Brian	Eli Lilly and Company	NR486
Bhandary, Amar N.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR157
Bisserbe, Jean-Claude	Pfizer Inc.	NR439
Black, Donald W.	Solvay Pharmaceuticals, Inc.; The Upjohn Company	NR502
Blanco-Jerez, Carlos	Eli Lilly and Company	NR127
Boncek, Virginia M.	Burroughs Wellcome Co.	NR541
Bradford, John M.W.	Pfizer Inc.	NR441
Burke, William J.	Pfizer, Inc.; SmithKline Beecham Pharmaceuticals	NR169
Chouinard, Guy	ICN Canada	NR397
Coccaro, Emil F.	Solvay Pharmaceuticals, Inc.; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Miles Pharmaceuticals; The Upjohn Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Wyeth-Ayerst Laboratories; Ciba Geigy Corporation, Pharmaceuticals Division	NR170
Croop, Robert S.	Dupont Merck Pharmaceutical Company	NR585
Cutler, Neal R.	Sandoz Pharmaceuticals Corporation	NR254
Daniel, David G.	Janssen Pharmaceutica and Research Foundation	NR488
Denicoff, Kirk D.	Ciba Geigy Corporation, Pharmaceuticals Division	NR457
Dunbar, Geoffrey C.	SmithKline Beecham Pharmaceuticals	NR376
Eisen, Jane L.	Pfizer Inc.	NR366, NR367
Fava, Maurizio	Pfizer Inc.; Burroughs Wellcome Co.; Eli Lilly and Company; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; American Home	NR310
George, Mark S.	Medi-Physics, Inc., Amersham Healthcare	NR167, NR313
Giller, Jr., Earl L.	Pfizer Inc.	NR494
Gilmer, William S.	Eli Lilly and Company; Wyeth-Ayerst Laboratories	NR407
Glazer, William M.	Psych Resources Group	NR624
Goldberg, Terry E.	Excerpta Medica	NR473
Goldstein, Jeffrey	Zeneca Pharmaceuticals	NR461
Hamner, Mark B.	Zeneca Pharmaceuticals	NR200
Hantouche, Elie G.	Eli Lilly and Company (France)	NR328
Hays, Lon R.	Pfizer Inc.; DuPont Pharma; SmithKline Beecham Pharmaceuticals	NR334
Iqbal, Naveed	Eli Lilly and Company	NR475
Jacobsen, Frederick M.	Abbott Laboratories	NR274, NR275
Janicak, Philip G.	Abbott Laboratories; Janssen Pharmaceutica and Research Foundation	NR459
Jones, Barry D.	Janssen Pharmaceutica and Research Foundation	NR466

Presenter	Manufacturer(s)	Final Program #
Kane, John M.	Astra/Merck Group, Division of Merck & Co.; Sandoz Pharmaceuticals Corporation; Eli Lilly and Company; NOVO; Janssen Pharmaceutica and Research Foundation; McNeil Pharmaceuticals; Zeneca Pharmaceuticals; Abbott Laboratories	NR361
Katzelnick, David J.	Ciba Geigy Corporation, Pharmaceuticals Division; Solvay Pharmaceuticals, Inc.; Burroughs Wellcome Co.; Abbott Laboratories; Astra/Merck Group, Division of Merck & Co.; Eli Lilly and Company; Pfizer Inc.; CoCensys; SmithKline Beecham Pharmaceuticals	NR555
Keck, Jr., Paul E.	Janssen Pharmaceutica and Research Foundation; Abbott Laboratories; Pfizer Inc.; Zeneca Pharmaceuticals	NR484
Kline, Neal A.	Pfizer Inc.	NR390
Koran, Lorrin M.	Solvay Pharmaceuticals, Inc.	NR356
Le Melledo, Jean-Michel	Pfizer Inc.	NR118, NR119
Linden, Robert D.	Lilly Research Laboratories, a division of Eli Lilly & Company; Pfizer Inc.	NR251
Lindenmayer, Jean-Pierre	Janssen Pharmaceutica and Research Foundation	NR208
Manu, Peter	Eli Lilly and Company; Pfizer Inc.	NR415, NR623
Mauskopf, Josephine A.	Burroughs Wellcome Co.	NR289
McDougle, Christopher J.	Pfizer Inc.; Sandoz Pharmaceuticals Corporation; Solvay Pharmaceuticals, Inc.	NR531
McEntee III, William J.	Pfizer Inc.	NR264
Moscovitch, Adam	Pfizer Inc.	NR440
Nemeroff, Charles B.	Solvay Pharmaceuticals, Inc.; SmithKline Beecham Pharmaceuticals; Eli Lilly and Company; Pfizer Inc.; NIMH; NAMI; Boots; Abbott Laboratories	NR455
Nierenberg, Andrew A.	Eli Lilly and Company; Pfizer Inc.; Wyeth-Ayerst Laboratories	NR365
Pearlstein, Teri B.	Eli Lilly and Company; Burroughs Wellcome Co.	NR314
Peselow, Eric D.	Pfizer Inc.	NR433
Phillips, Katharine A.	The Upjohn Company; CoCensys Inc.; Pfizer Inc.; Eli Lilly and Company	NR374, NR375
Piergies, Antoni A.	Lorex	NR463
Rabins, Peter V.	Parke-Davis, Division of Warner-Lambert Company	NR258
Rabkin, Judith G.	The Upjohn Company	NR402
Razavi, Darius	Lilly Research Laboratories, a division of Eli Lilly & Company	NR499
Rothschild, Anthony J.	SmithKline Beecham Pharmaceuticals; Lilly Research Laboratories, a division of Eli Lilly & Company; Pfizer, Inc.	NR454
Rubin, Howard C.	The Upjohn Company	NR73
Russell, James M.	Pfizer Inc.	NR281
Satterlee, Winston G.	Eli Lilly and Company	NR235
Sheldon-Cost, Priscilla	Abbott Laboratories	NR89
Simpson, Richard J.	Solvay Pharmaceuticals, Inc.	NR357
Sramek, John J.	Sandoz Pharmaceuticals Corporation	NR401
Steiner, Martin	SmithKline Beecham Pharmaceuticals	NR354, NR355
Strain, James J.	Microcares	NR412
Thase, Michael E.	SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; Eli Lilly and Company; Burroughs Wellcome Co.; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Pfizer Inc.	NR172
Tohen, Mauricio	Eli Lilly and Company; Abbott Laboratories; Janssen Pharmaceutica and Research Foundation; Pfizer Inc.; The Upjohn Company; Otsuka	NR286
Tran, Pierre V.	Eli Lilly and Company	NR363
Van Vliet, Irene M.	Solvay Pharmaceuticals, Inc.	NR128
Von Moltke, Lisa	Pfizer Inc.	NR495
Ware, Michael R.	Solvay Pharmaceuticals, Inc.; The Upjohn Company; Abbott Laboratories; Glaxo, Inc.; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Roche Laboratories, a member of the Roche Group; Pfizer Inc.	NR353
Weiden, Peter	McNeil Pharmaceuticals	NR214
Weller, Ronald A.	Eli Lilly and Company	NR283
Wilens, Timothy E.	Burroughs Wellcome Co.	NR640, NR641
Wirshing, William C.	Janssen Pharmaceutica and Research Foundation	NR359
Wiztum, Eliezer	Ferring AB, Malmo, Sweden	NR425
Wulsin, Lawson R.	Roche Laboratories, a Division of Hoffmann-La Roche Inc.	NR391
Yonkers, Kimberly A.	SmithKline Beecham Pharmaceuticals; Pfizer Inc.; Eli Lilly and Company	NR278
Zaninelli, Rocco M.	SmithKline Beecham Pharmaceuticals	NR481
Zimmer, Ben	Wyeth-Ayerst Laboratories	NR259

NEW RESEARCH

Monday, May 22, 1995, 9:00 a.m.-10:30 a.m.

New Research 1 – Poster Session – Rooms D128/D129, Level 1, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Susan J. Fiester, M.D.

NR1 Relationship Between Frontal Lobe and Serotonergic Dysfunction in OCD
Cheryl M. Wong, M.D., Concetta Decaria, Ph.D., Lisa J. Cohen, Ph.D., Bonnie R. Aronowitz, Ph.D., Daphne Simeon, M.D., Eric Hollander, M.D.

NR2 Growth Hormone Response to Clonidine and Apomorphine in Panic Disorder
William Pitchot, M.D., Michel Hansenne, B.Sc., Antonio Gonzalez Moreno, M.D., Marc M. Ansseau, M.D.

NR3 Growth Hormone Response to Apomorphine in OCD
William Pitchot, M.D., Michel Hansenne, B.Sc., Antonio Gonzalez Moreno, M.D., Marc M. Ansseau, M.D.

NR4 ECT for Severe Tardive Dystonia
Teodor T. Postolache, M.D., Jorge H. Londono, M.D., Robert G. Halem, M.D., Mitchell D. Newmark, M.D.

NR5 Ipsapirone Challenge in Personality Disorders
Jake Falk, M.D., Robert L. Trestman, M.D., Rene Kahn, M.D., Larry J. Siever, M.D.

NR6 Risperidone in Dementia with Behavioral Disturbances
Neiza Prado, M.D., Elisse Kramer-Ginsberg, Ph.D., Neil Kremen, M.D., Patricia Hanan, R.N.C., Allan Z. Safferman, M.D.

NR7 Switching From Carbamazepine to Clozapine
Ataru Nakamura, M.D., Jose M. Benzo, M.D., Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D.

NR8 Exacerbation Risk Following Withdrawal of Oral and Depot Neuroleptic Treatment of Psychotic Patients
Adele C. Viguera, M.D., Ross J. Baldessarini, M.D., Daniel P. van Kammen, M.D., Trisha Suppes, M.D.

NR9 Risperidone Treatment of Schizophrenia in a State Hospital
Zafar Y. Ibrahim, M.D., Peter J. Buckley, M.D., Karl Donenwirth, Kenneth E. Bayer, B.S., Christine Lys, B.A., S. Charles Schulz, M.D.

NR10 Behavioral Subtypes of Alzheimer's Disease: Preliminary Data Analyses
Raymond L. Ownby, M.D.

NR11 Association of Thyroxin Level with Rate of Progression in Alzheimer's Disease
Ibrahim Abi-Rafeh, M.D., Steven Sevush, M.D., Richard S. Mallia, B.A.

NR12 Delusions of Theft and Premorbid Personality Traits in Alzheimer's Disease
Rene A. Poveda, M.D., Gloria Peruyera, B.A., Sharon Brizel, Steven Sevush, M.D.

NR13 Impact of Patient Gait Impairment on a Caregiver's Well-Being in Alzheimer's Disease
Paul A. Guzman, M.D., Miguel Alfonso, M.D., Mery Lossada, M.D., Steven Sevush, M.D.

NR14 Comparison of Mini-Mental State Exam with the Mental Alternation Test for Assessing Cognition in Geriatric Psychiatric Patients and Normal Controls
Eric Siedenburg, B.A., Stephen B. Billick, M.D., Woodward Burgert, B.A.

NR15 Platelet Serotonin Concentration Correlates with Dementia Severity in Patients with Probable Alzheimer's Disease
Richard S. Mallia, B.A., Steven Sevush, M.D., Adarsh Kumar, Ph.D., Mahendra Kumar, Ph.D., Carl Eisdorfer, M.D.

NR16 Selective Serotonin Reuptake Inhibitors for the Treatment of Depression and Psychosis in Dementia
Vijay K. Dewan, M.D., William J. Burke, M.D., William H. Roccaforte, M.D., Steven P. Wengel, M.D., Sunil R. Rangwani, M.D., David G. Folks, M.D.

NR17 Geropsychiatric Consultation in Nursing Homes: Quality, Cost Effective Care
Beverly K. Young, M.D., David M. Smith, M.D., Linda K. Ganzini, M.D.

NR18 Diagnostic Use of Brain Perfusion SPECT in Geriatric Psychiatry: A Retrospective Review
Simon Chiu, M.D., Allan Steingart, M.D., M. Ichise, M.D., H. Golan, J. Kremer, M.D., Morris Freedman, M.D.

NR19 Circadian Regulation in Abused Children
Carol A. Glod, Ph.D., Martin H. Teicher, M.D.

NR20 Neurobiology of Abuse in Personality Disorders
Bonnie J. Steinberg, M.D., Rachel Yehuda, Ph.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR21 Cholinergic Challenge in Personality Disorders
Bonnie J. Steinberg, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR22 The Role of Serotonergic Inhibitor Receptors in the Prolactin Response to Clomipramine Challenge
Joseph M. Bebchuk, M.D., Linda M. Nicholas, M.D., Amy L. Durr, M.S.N., Robert D. Ekstrom, M.P.H., George A. Mason, Ph.D., Robert N. Golden, M.D.

NR23 Binding of 3H Felbamate to Human Postmortem Brain
James K. Wamsley, Ph.D., Duane Sofia, Ph.D., Steven Hurt, Ph.D., Dusan Peckovic, M.D.

NR24 Olfactory Test Performance and CT Findings in First-Degree Relatives of Alzheimer's Disease Patients
Claudio M. Demb, M.D., M. Mehmet Haznedar, M.D., Michael J. Serby, M.D., Monte S. Buchsbaum, M.D., Marja Germans, B.A., Kenneth L. Davis, M.D.

NR25 Decreased Corpus Callosal Size in Women with Alcohol Dependence Compared to Women Controls: An MRI Study
Paul W. Ragan, M.D., Daniel W. Hommer, M.D., Reza Momenan, Ph.D., Wendol A. Williams, M.D., Daniel Rio, Ph.D., Michael J. Eckardt, Ph.D.

NR26 SPECT Brain Imaging in Normal Aging
Sonya Herrera, B.A., Hee K. Lee, M.D., Donald M. Quinlan, M.D., Erin A. Hazlett, Ph.D., Christina T. Luu, B.A., Ecaterina Rotaru, M.D., James Valence, B.A., John Herrera, Ph.D., Monte S. Buchsbaum, M.D.

NR27 SPECT Brain Imaging in Geriatric Schizophrenics
Sonya Herrera, B.A., Hee K. Lee, M.D., Donald M. Quinlan, M.D., Erin A. Hazlett, Ph.D., Christina T. Luu, B.A., Ecaterina Rotaru, M.D., James Valence, B.A., John Herrera, Ph.D., Monte S. Buchsbaum, M.D.

NR28 Gender and Cognitive Performance in Alzheimer's Disease
P. Murali Doraiswamy, M.D., Alok Krishen, M.S., Frank Stallone, Ph,D., Wendy Martin, M.D., Alan Metz, M.D., Joseph Deveaugh-Geiss, M.D.

NR29 Neuroleptic Treatment and Caudate Nuclei Volumes in Patients with Depression
P. Murali Doraiswamy, M.D., Larry A. Tupler, Ph.D., K. Ranga Rama Krishnan, M.D.

NR30 Evaluation of a Clinical Prediction Rule for Postoperative Delirium
Joseph A. Locala, M.D., David Litaker, M.D., Kathleen N. Franco, M.D., David L. Bronson, M.D.

NR31 Differences in Neuropsychiatric Profile in Alzheimer's Disease and Non-Alzheimer's Disease Dementias
Maria P. Gonzalez, Ph.D., Oscar L. Lopez, M.D., Abraham Sudilovsky, M.D., James T. Becker, Ph.D., Charles F. Reynolds III, M.D., Steven T. Dekosky, M.D.

NR32 Catatonic Disorders: Psychiatric Versus General Medical Etiology
Debra Callahan, Ph.D., Brendan T. Carroll, M.D., Harold W. Goforth

NR33 Catatonic Disorder: Treatment and Cost
John C. Kennedy, M.D., Brendan T. Carroll, M.D., Harold W. Goforth

NR34 The Harvard Telemedicine Project in Schizophrenia
Carlos A. Zarate, Jr., M.D., Lisa S. Weinstock, M.D., Peter Cukor, Ph.D., Casandra Morabito, Ph.D., Lee Baer, Ph.D., Linda Leahy, B.S.

NR35 Shifts in Diagnostic Frequencies of Bipolar Disorder Subtypes at McLean Hospital: 1981-1993
Carlos A. Zarate, Jr., M.D., Ross J. Baldessarini, M.D., Mauricio Tohen, M.D., German Baraibar, M.D., Silvina Beverina de Zarate, B.S.

NR36 Recognition of Comorbid Substance Abuse in Schizophrenia
JoAnn E. Kirchner, M.D., Richard R. Owen, Jr., M.D., Doris E. Hutchins, M.S.W, Ellen P. Fischer, Ph.D.

NR37 Suspension Therapy in Acute Schizophrenia: The Relationship of Neuroendocrine and Biochemical Parameters to Therapeutic Suspension Effects
Here W. Folkerts, M.D., Hubert Kuhs, M.D.

NR38 Remission of Substance Abuse in Mental Illness
Scot McNary, M.A., Lisa B. Dixon, M.D., Laura Rachuba, B.A., Anthony F. Lehman, M.D.

NR39 Relationship Between Schizophrenic and Obsessive Compulsive Symptoms
Amalia Merson, M.D., Barbara Viegener, Ph.D., Edward R. Allan, M.D., Laura Parker, M.A., Miklos F. Losonczy, M.D., Ileana Berman, M.D.

NR40 Schizotypal Disorder: Temporal Lobe Anomalies
Chandlee C. Dickey, M.D., Martina M. Voglmaier, Ph.D., Martha E. Shenton, Ph.D., Larry J. Seidman, Ph.D., Margaret Miznikiewicz, Ph.D., Robert W. McCarley, M.D.

NR41 Increased CD5 Plus B Lymphocytes in Schizophrenia
David J. Printz, M.D., David H. Strauss, M.D., Jack M. Gorman, M.D.

NR42 Gray Matter Heterotopias in the Psychoses
Noelle K. Gehm, B.S., Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Mary Oehler, M.D.

NR43 Schizophrenia in the Iowa 500 Series: A Re-Examination with Regard to Premorbid Personality
David R. Hunter, M.D., George Winokur, M.D.

NR44 Extrapyramidal Signs in Never Medicated First-Episode Schizophrenic Patients: Prevalence and Clinical Correlates
Anjan Chatterjee, M.D., Miranda H. Chakos, M.D., Amy R. Koreen, M.D., Stephen H. Geisler, M.D., Jose Ma. Alvir, D.P.H., Jeffrey A. Lieberman, M.D., Brian B. Sheitman, M.D.

NR45 Botulinum Toxin in the Treatment of Tardive Dystonia
Anjan Chatterjee, M.D., Mark F. Gordon, M.D.

NR46 Clinical Correlates of the Deficit Syndrome of Schizophrenia
Timothy D. Florence, M.D., Rajiv Tandon, M.D., Mona Goldman, Ph.D., John R. DeQuardo, M.D., Michael D. Jibson, M.D., Stephan F. Taylor, M.D.

NR47 Gender in Schizophrenia: Impact on Symptomatology, Outcome and Biological Markers
Mona Goldman, Ph.D., Rajiv Tandon, M.D., Robert S. Goldman, Ph.D., Irma C. Smet, Ph.D.

NR48 Biological Predictors of Suicide in Schizophrenia
Catherine F. Lewis, M.D., Rajiv Tandon, M.D., James E. Shipley, M.D., John R. DeQuardo, M.D., Michael D. Jibson, M.D., Stephan F. Taylor, M.D.

NR49 Covert Visual Attention in Deficit Schizophrenia
Juan R. Bustillo, M.D., Marianne Moran, M.A., Gunvant Thaker, M.D., Robert W. Buchanan, M.D.

NR50 Perseveration Errors on Dichotic Listening Tests: The Role of Patient Diagnosis and Fusion of Test Stimuli
Diane Gard, Amir Poreh, Ph.D., Michael J. Reinstein, M.D., Lynn Jones, R.N., Sangarapillai C. Mohan, M.D.

NR51 A Neurophysiological Study of Semantic Processing in Schizophrenia
Matthew O. Kimble, M.A., Matthew O. Kimble, M.A., Paul G. Nestor, Ph.D., Brian F. O'Donnell, Ph.D., Lloyd S. Smith, M.A., Robert W. McCarley, M.D.

NR52 Cognitive Deficits and Psychopathology in Elderly Schizophrenic and Affective Disorder Patients
Seamus F. O'Flaithbheartaigh, M.B., Peter Powchik, M.D., Philip D. Harvey, Ph.D., Michael Parella, Ph.D., Leonard White, Ph.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

NR53 Effects of Risperidone on Spatial Working Memory
Susan R. McGurk, Ph.D., Michael F. Green, Ph.D., William C. Wirshing, M.D., Donna Ames, M.D., Barringer D. Marshall Jr, M.D., Stephen R. Marder, M.D.

NR54 Concurrent Depression in First-Admission Patients with Schizophrenic Disorders
Ranganathan Ram, M.D., Lisa B. Dixon, M.D., Malathi Ram, Ph.D., Lina Jandorf, M.A., M. Tanenberg-Karant, M.D., Evelyn J. Bromet, Ph.D.

NR55 Should There Be Routine Screening of Thyroid Function in Patients Hospitalized for Major Depression or Dysthymia?
Dennis M. Ordas, M.D., Lawrence A. Labbate, M.D.

NR56 Exaggerated Platelet Reactivity in Depression
Dominique L. Musselman, M.D., Bettina T. Knight, R.N., Maryfrances R. Porter, Ulla Marzek, Aaron Tomer, M.D.

NR57 Child Depression: Cortisol, ACTH, Prolactin and Growth Hormone
Michael D. De Bellis, M.D., Ronald E. Dahl, M.D., James Perel, M.D., Boris Birmaher, M.D., Joaquim Puig-Antich, M.D., (Posthumously), Neal D. Ryan, M.D.

NR58 Combined ECT and Clozapine in Schizophrenia
Helen C. Kales, M.D., Rajiv Tandon, M.D., John R. DeQuardo, M.D., Daniel F. Maixner, M.D., Michael D. Jibson, M.D., Lisa Becks

NR59 Client Discharge From Programs of Assertive Community Treatment
Caroline Poblete, M.D., Lisa B. Dixon, M.D., Nancy Krauss, M.S.W., Eileen Hastings, M.S.W.

NR60 Parenting and Severe Mental Illness
Ann L. Hackman, M.D., Lisa B. Dixon, M.D.

NR61 Delayed-Onset Tension Pneumocephalus Presenting As Frontal Lobe Syndrome
Michael S. Jaffee, M.D.

NR62 Sexual Abuse Severity and General Psychopathology
Ernesto F. Figueroa, M.D., Kenneth R. Silk, M.D., Alissa Huth, B.A., Naomi E. Lohr, Ph.D.

NR63 Activity of Interleukins in Korean Schizophrenics
Yong-Ku Kim, M.D., Min Soo Lee, M.D., Woong Hahm, M.D., Kyu Hang Lee, M.D., Chung Kyoon Lee, M.D., Kwang-Yoon Suh, M.D.

NR64 Methylxanthines in Older Healthy Volunteers
Marc Cantillon, M.D., Douglas Johnson, Ph.D., Herbert Weingartner, Ph.D., Stanley L. Slater, M.D., Marcel Bahro, M.D., Trey Sunderland, M.D.

NR65 Risk Factors for Transfer to a Psychiatric Intensive Care Unit
Robert J. Nicolson, M.D., Anthony Feinstein, M.D.

NR66 Three Catatonia Rating Scales for Clinical and Research Use
Berta M. Guerra, M.D., Brendan T. Carroll, M.D.

NR67 Incidence of HIV Infection in Acute Psychosis
Michael E. Doyle, M.D., Lawrence A. Labbate, M.D.

NR68 Gender Differences in Body Dysmorphic Disorder
Susan F. Diaz, M.D., Katharine A. Phillips, M.D., Craig G. Gunderson, B.A.

NR69 Dreams Following Hurricane Andrew
Daniella David, M.D., Thomas A. Mellman, M.D.

Research Funding Poster Session

There will be Posters on research funding being displayed in conjunction with the Young Investigator's Poster Session. Individuals representing federal agencies and private foundations will be available to meet with new, continuing, and potential grantees and other psychiatric investigators to discuss current research grant programs. Representatives listed on page 15.

NEW RESEARCH

Monday, May 22, 1995, 1:00 p.m.-2:30 p.m.

New Research 2 – Oral/Slide Session – Room D130, Level 1, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

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

NR70	Medical Clearance of Low Risk Psychiatric Admissions James D. Hegarty, M.D., John N. Julian, M.D., Kathy M. Sanders, M.D., Theodore A. Stern, M.D.	1:00 p.m.
NR71	Ataque de Nervios and Trauma History Daniel S. Schechter, M.D., Michael R. Liebowitz, M.D., Ester Salman, B.S., Deborah Goetz, M.P.H., Sharon O. Davies, R.N., Eunice Dong	1:15 p.m.
NR72	Sertraline in Breast Milk and Nursing Infants Stephanie S. Winn, M.D., Zachary N. Stowe, M.D., Jacque C. Landry, B.A., Clinton D. Kilts, Ph.D., Timothy Ely, B.S., Charles B. Nemeroff, M.D.	1:30 p.m.
NR73	Measuring Quality-of-Life in Panic Disorder Howard C. Rubin, M.D., Tony Rabin, B.S., Julie Gladjo, Ph.D., Robert M. Kaplan, M.D., Mark H. Rapaport, M.D.	1:45 p.m.
NR74	Suicidal Behavior in Depression: Neuroendocrine Approach of the Role of Serotonin and Noradrenaline William Pitchot, M.D., Michel Hansenne, B.Sc., Antonio Gonzalez Moreno, M.D., Marc M. Ansseau, M.D.	2:00 p.m.
NR75	Serotonin and Prediction of Fluoxetine Response Time Jake Falk, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.	2:15 p.m.

NEW RESEARCH

Monday, May 22, 1995, 1:00 p.m.-2:30 p.m.

New Research 3 – Oral/Slide Session – Room D131, Level 1, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

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

NR76	Clomipramine in Adults with Pervasive Developmental Disorder Edward S. Brodkin, M.D., Christopher J. McDougle, M.D., Susan T. Naylor, M.S.N., Donald J. Cohen, M.D., Lawrence H. Price, M.D.	1:00 p.m.

NR77	Predictors of Violence in Binge Drinking Chinese-American and Korean-American College Students Henry Chung, M.D., James W. Hull, Ph.D., Edward Ma, B.S., Jeanne Mueller, Ph.D.	1:15 p.m.
NR78	Anticipation and Schizophrenia Janet E. Johnson, M.D., Charles A. Kaufmann, M.D., Jill Harkavey-Friedman, Ph.D., Dolores Malaspina, M.D., Jane Cleary, A.B., C. Robert Cloninger, M.D., Ming T. Tsuang, M.D.	1:30 p.m.
NR79	Neuroleptic-Resistant Schizophrenia: Clinical, Neuropsychological and Family History Characterization Ridha Joober, M.D., Chawki Benkelfat, M.D., Samarthja Lal, M.D., Roberta M. Palmour, Ph.D., David M. Bloom, M.D., Alain LaBelle, M.D., Harrietta Drucker, M.A., Michael Dixon, Ph.D., Guy Rouleau, M.D.	1:45 p.m.
NR80	Depression and Quality-of-Life in an Inner-City Cohort of Inpatients with Schizophrenic Disorders Ranganathan Ram, M.D., Lisa B. Dixon, M.D., Leticia Postrado, Ph.D., Laura Rachuba, B.A.	2:00 p.m.

NEW RESEARCH

Monday, May 22, 1995, 3:00 p.m.-5:00 p.m.

New Research 4 – Poster Session – Rooms D128/D129, Level 1, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Co-Moderators: Ronald O. Rieder, M.D., and Harold Alan Pincus, M.D.

NR81 Hostility, Cynicism and Suicidal Ideation in Depressed Outpatients
S. Nassir Ghaemi, M.D., Andrew A. Nierenberg, M.D., Kathy A. Clancy, M.A., Junko Kaji, B.A., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR82 Management of Bipolar Disorder with Adjunctive Risperidone: Response to Open Treatment
S. Nassir Ghaemi, M.D., Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christine J. Truman, B.A., Holly M. Hendin, B.A.

NR83 Acute and Delayed Major Depression Following Spinal Cord Injury
Yasuhiro Kishi, M.D., Robert G. Robinson, M.D.

NR84 Panic Disorder Comorbidity with Familial Bipolar Disorder
Dean F. MacKinnon, M.D., Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., J. Raymond DePaulo, Jr., M.D.

NR85 The Psychometric Properties of Hopelessness Scale in Chinese Sample
Hui-Qi Tong, M.D., Jun-Mian Xu, M.D., Yun Zhou, M.D., Bin Zhou, M.S.

NR86 Co-Occurence of Migraine with Mixed and Pure Mania
Megan M. Dwight, M.D., R. Mark Newman, M.D.

NR87 The Effect of Comorbid Depression and Anxiety on Symptom Severity
Gary S. Bruss, Ph.D., Alan M. Gruenberg, M.D., Reed D. Goldstein, Ph.D., Jacques P. Barber, Ph.D.

NR88 Dissociative Identity Disorder: Axis I and II Comorbidity
Gary S. Bruss, Ph.D., Alan M. Gruenberg, M.D., Reed D. Goldstein, Ph.D., Jacques P. Barber, Ph.D.

NR89 Characteristics of Patients Treated with Valproate
Priscilla Sheldon-Cost, Ph.D., R. Scott Cost, M.S.E., J. Raymond DePaulo, Jr., M.D.

NR90 Effects of ECT on Seizure Induction and Duration
Srinibas Mahapatra, M.D., Rajiv Tandon, M.D., John R. DeQuardo, M.D., Leon J. Grunhaus, M.D., Helen C. Kales, M.D., Lisa Becks

NR91 Timecourse of Antidepressant Effect of ECT
Daniel F. Maixner, M.D., Rajiv Tandon, M.D., John R. DeQuardo, M.D., Leon J. Grunhaus, M.D., Helen C. Kales, M.D., Lisa Becks

NR92 Organic Mood Disorders: Clinical Characteristics
Jose M. Benzo, M.D., German Baraibar, M.D., Jose M. Castillo, M.D., David Gardner, B.Sc. Phar, Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D.

NR93 Anxiety Sensitivity and Depression
Christina M. Demopoulos, M.D., Maurizio Fava, M.D., Nancy E. McLean, B.A., John D. Matthews, M.D., Michael W. Otto, Ph.D., Jerrold F. Rosenbaum, M.D.

NR94 Self-Medication and Response to Treatment in Major Depression
John J. Worthington III, M.D., Maurizio Fava, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Jerrold F. Rosenbaum, M.D.

NR95 Yohimbine Augmentation of Fluvoxamine in Refractory Depression: A Preliminary, Single-Blind Study
Angela C. Cappiello, M.D., Christopher J. McDougle, M.D., Robert T. Malison, M.D., George R. Heninger, M.D., Lawrence H. Price, M.D.

NR96 Atypical Depression in the Hospital: Clinical Features and Personality Characteristics
Celeste N. Derecho, Ph.D., Scott Wetzler, Ph.D., Lata K. McGinn, Ph.D., Gregory M. Asnis, M.D., William C. Sanderson, Ph.D.

NR97 Tryptophan Depletion and Vulnerability to Depression
Francisco A. Moreno, M.D., Sasha Panov, M.D., Louise J. Strayer, R.N., Rebecca L. Potter, M.D., Alan J. Gelenberg, M.D., Pedro L. Delgado, M.D.

NR98 Pattern of Illness and Duration of Mania in Bipolar Disorder
Christine J. Truman, B.A., Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Holly M. Hendin, B.A., S. Nassir Ghaemi, M.D.

NR99 WITHDRAWN

NR100 Neuropsychiatric Findings in Children of Early-Onset Versus Late-Onset Bipolar Illness
Claudia F. Baldassano, M.D., Gary S. Sachs, M.D., Christine J. Truman, B.A., Holly M. Hendin, B.A., S. Nassir Ghaemi, M.D.

NR101 Paroxetine for Bipolar Depression: Outcome in Patients Failing Prior Antidepressant Trials
Claudia F. Baldassano, M.D., Gary S. Sachs, M.D., Andrew L. Stoll, M.D., Beny Lafer, M.D., Christine J. Truman, B.A., Holly M. Hendin, B.A.

NR102 Dependency and Self-Criticism As Risk Factors for Major Depressive Disorder
Ari E. Zaretsky, M.D., Maurizio Fava, M.D., Katharine G. Davidson, B.A., Joel A. Pava, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D.

NR103 Differences in Thyroid Function Between Bipolar Patients with Mixed Mania and Pure Mania
Kiki D. Chang, M.D., Sean P. Stanton, B.S., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Stephen M. Strakowski, M.D.

NR104 Double-Blind Placebo-Controlled Trial of Pindolol in Depression
Robert M. Berman, M.D., Adam M. Darnell, M.D., Helen L. Miller, M.D., Dennis S. Charney, M.D.

NR105 Light Therapy: An Enhancer of Antidepressants
Khaled I. Mohamed, M.D., Gregory M. Asnis, M.D.

NR106 Maintenance ECT in Antidepressant Refractory Patients
Nirmal Sathaye, M.D., Cheng-Jen Chen, M.D.

NR107 Body Dysmorphic Disorder and Social Phobia
Joseph V. Penn, M.D., Katharine A. Phillips, M.D., Kate Dimond, B.A.

NR108 Recognition and Treatment of Depressive Disorders Among Internists
Joseph V. Penn, M.D., Robert J. Boland, M.D., James R. McCartney, M.D.

NR109 Life Events and Panic Disorder/Agoraphobia
Ghada N. Lteif, M.D., Matig R. Mavissakalian, M.D.

NR110 Childhood Trauma in Panic Disorder and Social Phobia
Randall D. Marshall, M.D., Lisa O'Donnell, B.S., Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., Franklin R. Schneier, M.D.

NR111 Headache Responses to m-CPP in OCD and Normal Controls
Cheryl M. Wong, M.D., Lisa J. Cohen, Ph.D., Concetta Decaria, Ph.D., Bonnie R. Aronowitz, Ph.D., Daphne Simeon, M.D., Eric Hollander, M.D.

NR112 OCD During Pregnancy and the Puerperium
C. Neill Epperson, M.D., Christopher J. McDougle, M.D., Rebecca M. Brown, B.A., James F. Leckman, M.D., Wayne K. Goodman, M.D., Lawrence H. Price, M.D.

NR113 Venlafaxine in Generalized Anxiety Disorder
Gerardo Villarreal, M.D., Naresh P. Emmanuel, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

NR114 Growth Hormone Deficiency and Social Phobia
Linda M. Nicholas, M.D., Manuel E. Tancer, M.D., Susan G. Silva, M.D., Louis E. Underwood, M.D., Brian Stabler, Ph.D.

NR115 A Neural Network Model of OCD: Preliminary Development
Jose M. Gonzalez, M.D., Raymond L. Ownby, M.D.

NR116 OCD and Suicide: A Systematic Investigation
Rebecca M. Brown, B.A., Christopher J. McDougle, M.D., C. Neill Epperson, M.D., Suzanne Wasylink, RN.C., Wayne K. Goodman, M.D., Lawrence H. Price, M.D.

NR117 Differential Responses t Serotonergic Challenge in OCD Clinical Subtypes
Juan J. Lopez-Ibor, Jr., M.D., Maria I. Lopez-Ibor, M.D., Jose L. Carrasco, M.D., Benedicto Crespo, M.D., Jose A. Cabranes, M.D., Jose L. Ayuso-Mateos, M.D.

NR118 Enhanced Sensitivity to CCK-4 in Women with Severe Premenstrual Symptoms
Jean-Michel Le Melledo, M.D., Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., Francois Belavance, Ph.D., Daniel Georges Bichet, M.D., Uriel Halbreich, M.D.

NR119 The Effects of CCK-4 on Plasma Arginine-Vasopressin Levels in Women
Jean-Michel Le Melledo, M.D., Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., Francois Belavance, Ph.D., S. Steinberg, M.D., Uriel Halbreich, M.D.

NR120 Seasonality of Symptoms in PMDD
Douglas D. Maskall, M.D., Raymond W. Lam, M.D., Shaila Misri, M.D., Diana Carter, M.D., Annie Kuan, B.A.

NR121 Valproate Oral Loading in the Treatment of Acute Exacerbations of Combat-Related PTSD
Shreenath V. Doctor, M.D., Gerald L. Batte, M.D.

NR122 Psychotropic Drug Use by Nonpsychiatrists
Cecelia P. Kane, M.D., Francis J. Kane Jr, M.D.

NR123 A Double Blind Study Comparing a Combined Plant Extract with Placebo in the Treatment of Anxiety
Michel S. Bourin, M.D., Thierry Bougerol, M.D., Bernard Guitton, M.D., Eric Broutin, M.D.

NR124 A Survey of Practicing Massachusetts Psychiatrists Concerning Their Experiences Prescribing Fluoxetine, Bupropion and Trazodone
Srinivasan S. Pillay, M.D., Jeffery C. Campbell, M.S., Jonathan O. Cole, M.D.

NR125 The Ictal EEG As a Marker of ECT Seizure Adequacy: The Relationship of Spike-Wave Phase EEG Features to Therapeutic Response
Here W. Folkerts, M.D.

NR126 Prescribing Practices for Bipolar Patients in a Clinical Setting
Alejandra Hallin, M.D., Eric D. Peselow, M.D., Faouzia Barouche, M.D., Lara Fieve, Gita Vaid, M.D., Ronald R. Fieve, M.D.

NR127 Fluoxetine Efficacy: A Meta-Analysis
Carlos Blanco-Jerez, M.D., Inmaculada Gilaberte-Asin, M.D., Carmen Blanco, B.S.

NR128 Psychopharmacological Treatment of Social Phobia: A Double-Blind Placebo-Controlled Study with Fluvoxamine
Irene M. Van Vliet, M.D., Johan A. Den Boer, Herman G.M. Westenberg, M.D.

NR129 Psychological Predicting Factors in Repeated Suicidal Behavior
Manuel Bousono-Garcia, M.D., Julio Bobes, M.D., Maria P. Gonzalez, Ph.D., Pilar A. Saiz, M.D., Isabel Cocana, M.D., Micaela Gonzalez-Quiros, M.D.

NR130 Profile of Medically Serious Suicide Attempts
Andy Elliot, M.D., Kenneth P. Pages, M.D., David R. Johnson, M.D., Lawrence G. Wilson, M.D., Peter P. Roy-Byrne, M.D.

NR131 Lack of Behavioral Laterality in Gilles De La Tourette's Syndrome: A Replication Study
M. Yanki Yazgan, M.D., Bruce E. Wexler, M.D., Lawrence Scahill, M.S.N., Bradley S. Peterson, M.D., Marcel Kinsbourne, M.D., James F. Leckman, M.D.

NR132 Peripheral Biological Markers and Suicide Attempt
Julio Bobes, M.D., Manuel Bousono-Garcia, M.D., Maria P. Gonzalez, Ph.D., Pilar A. Saiz, M.D., Pedro Gonzalez-Quiros, Ph.D., Jorge Diaz, Ph.D.

NR133 Atmospheric Pressure and Agitation on a Psychiatric Inpatient Unit
Teodor T. Postolache, M.D., Christian Miner, Ph.D., Richard N. Rosenthal, M.D., Patricia A. Lowrimore, M.D., Julie Reynolds, R.N.C., Igor I. Galynker, M.D.

NR134 No Relationship Found Between Mood and Occupational Stress in the Staff of an Inpatient Psychiatric Unit
Teodor T. Postolache, M.D., Patricia A. Lowrimore, M.D., Zenovi Gutkovich, M.D., Richard N. Rosenthal, M.D.

NR135 Eliminating Cultural Bias of Proverb Interpretation in Mental Status Examination Through the Use of Cross-Cultural Core Proverbs
Carlos A. Rueda, M.D., Paul A. Hriso, M.D., Emmanuel Hriso, M.D.

NR136 Children and War: Trauma and Psychosocial Services
Bradley D. Stein, M.D.

NR137 Alcoholism Treatment Research: Women and Minorities
Lauren D. Williams, M.D., Gloria Goldberg, M.S.W., Robert B. Cutler, Ph.D., Barbara J. Mason, Ph.D.

NR138 Early-Onset Male Alcoholics With and Without Antisocial Personality Disorder
Sanaa Helmi, M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Barbara J. Powell, Ph.D., H. Mikel Thomas, M.D., Barry I. Liskow, M.D.

NR139 Psychoactive Substance Use Among Inner-City Psychiatric Admissions
Abner P. Pasatiempo, M.D., Jeannette L. Johnson, Ph.D., Anthony F. Lehman, M.D.

NR140 Preliminary Data Support: An Association Between Taste Sensitivity and Alcoholism Risk
Pamela J. Moore, M.D., Henry R. Kranzler, M.D., Lance O. Bauer, Ph.D., Victor M. Hesselbrock, Ph.D.

NR141 Duration of Hospitalization Versus Improvement in First Psychosis
James D. Hegarty, M.D., Franca Centorrino, M.D., Ross J. Baldessarini, M.D., Mauricio Tohen, M.D., Jonathan W. Friedberg, M.D., Michelle Weiss, M.S.

NR142 A Longitudinal Study of Patients with Nonepileptic Seizures
Michael M. Reese, M.D., Lois E. Krahn, M.D., Teresa A. Rummans, M.D., Gerald C. Peterson, M.D., Frank W. Sharbrough, M.D., Greg D. Cascino, M.D.

NR143 Family Functioning and Depression in Medical Patients
Anna M. Boettcher, B.A., Stephen B. Billick, M.D., Woodward Burgert, B.A.

NR144 Gender Differences in Crisis Center Evaluations
Robert N. Gerstman, D.O., Kimberly R. Best, M.D., Kenneth M. Certa, M.D.

NR145 Suicide Incidence Among Prostate Cancer Patients in South Florida
Gladys R. Gregory, M.D., Maria D.D. Llorente, M.D., Michael A. Burke, M.D., Larry D. Capp, Ph.D., Yolanda B. Zarate, M.D.

NR146 Depression, Quality-of-Life, and Use of Health Services in Primary Care Patients Over 65: A Four-Year Prospective Study
Jurgen Unutzer, M.D., Wayne J. Katon, M.D., Gregory E. Simon, M.D., Edward A. Walker, M.D., David Grembowski, Ph.D., Donald Patrick, Ph.D.

NR147 Asthma and Psychopathology in Adolescent Inpatients
Ronald A. McGinnis, M.D., Wun Jung Kim, M.D., Michael P. Carey, Ph.D.

NR148 The Phenomenology and Comorbidity of Adolescents Hospitalized for the Treatment of Acute Mania
Scott A. West, M.D., Stephen M. Strakowski, M.D., Kenji Sax, M.S., Nancy J. Raute, B.A., Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D.

NR149 The Assessment of HIV Risk Factors and the Clinicians Threshold for HIV Testing in the Chronic Mentally Ill in a Low Seroprevalence Area
Amy M. O'Neill, M.D., Lesley R. Dickson, M.D., Chris Feddock, B.S.

NR150 Psychopathology, Clinical Progression and Treatment Compliance in a Sample of HIV-1 Infected Veterans
Joseph M. Mavica, D.O., Richard Douyon, M.D., Daniel Feaster, M.S., Karl Goodkin, M.D.

NR151 Beside Stuffed Animals and Borderline Personality
David M. Benedek, M.D., Lawrence A. Labbate, M.D.

NR152 Laterality of Psychogenic Somatic Symptoms
Byungook Lee, M.D., Sungkil Min, M.D., Kee Namkoong, M.D.

NR153 Major Depression and Crisis Intervention: A Cost-Effectiveness Study
Nicole Rosset, Ph.D., Antonio Andreoli, M.D., Yvonne Burnand, Ph.D., Evelyne Kolatte, M.D.

NR154 Engagement of Homeless Persons in Treatment
Laura Gaffney, B.A., Lisa B. Dixon, M.D.

NR155 Juvenile Sex Offenders: A Study of Phenomenology and Comorbidity
Viviana B. Galli, M.D., Nancy J. Raute, B.A., Danielle L. Kizer, B.S., Brian J. Mc Conville, M.D., Susan L. Mc Elroy, M.D.

NR156 Effect of Lorazepam on Cardiac Autonomic Control in Stressed Versus Unstressed State in Normal Subjects
Leslie R. Vogel, M.D., Philip R. Muskin, M.D., Eric D. Collins, M.D., Richard P. Sloan, Ph.D.

NR157 Combination Pharmacotherapy in ADHD
Amar N. Bhandary, M.D., Robert J. Gregory, M.D., Lawrence M. Carmen, M.D., John F. Tanquary, M.D.

NR158 Factors Influencing the Choice of Psychiatry As a Career
JoAnn E. Kirchner, M.D., Richard R. Owen, Jr., M.D.

NR159 Trends in Quality-of-Life Assessments in Psychiatry
Samir P. Patel, M.D., Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D.

NR160 Patient Population, Length of Stay, and Readmissions for a General Hospital Psychiatry Service: Trends Over the Past Decade
Benjamin G. Druss, M.D., Martha L. Bruce, Ph.D., Selby C. Jacobs, M.D.

NR161 Reserpine/Cocaine Interactions in Cocaine Addicts
Gregory H. Pelton, M.D., Angela C. Cappiello, M.D., Christopher J. McDougle, M.D., Robert T. Malison, M.D., Thomas R. Kosten, M.D., Lawrence H. Price, M.D.

Research Funding Poster Session

There will be Posters on research funding being displayed in conjunction with the Young Investigator's Poster Session. Individuals representing federal agencies and private foundations will be available to meet with new, continuing, and potential grantees and other psychiatric investigators to discuss current research grant programs. Representatives include:

Heddy Hibhard, R.N., M.P.H., Agency for Health Care Policy and Research; Ray Litten, Ph.D., National Institute on Alcohol Abuse and Alcoholism; Stephen Koslow, Ph.D., Division on Neuroscience and Behavioral Science, National Institute on Mental Health; David Shore, M.D., Division of Clinical and Treatment Research, National Institute of Mental Health; Ellen Stover, Ph.D., Office on AIDS, National Institute of Mental Health; Dorynne Czechowicz, M.D., National Institute on Drug Abuse; Norman Krasnegor, Ph.D., National Institute of Child Health and Human Development; Ann Brown, National Alliance for Research on Schizophrenia and Depression; Robert Post, M.D., National Alliance for the Mentally Ill

NEW RESEARCH

Tuesday, May 23, 1995, 9:00 a.m.-10:30 a.m.

New Research 5 – Oral/Slide Session – Room D130, Level 1, Convention Center

NEUROIMAGING

Chp.: Abby J. Fyrer, M.D.

NR162	Neuroimaging Correlates of a Genetic Marker for Schizophrenia Lina S. Shihabuddin, M.D., Jeremy M. Silverman, Ph.D., Monte S. Buchsbaum, M.D., Richard C. Mohs, Ph.D., Michael Metzger, B.S., Kenneth L. Davis, M.D.	9:00 a.m.
NR163	Functional Neuroanatomical Correlates of Tics in Tourette's Syndrome David A. Silbersweig, M.D., Emily Stern, M.D., Kit Chee, M.D., Michael R. Trimble, M.D., Mary Jane Robertson, M.A., Raymond J. Dolan, M.D.	9:15 a.m.
NR164	PET and Memory Across the Life Span in Normals Erin A. Hazlett, Ph.D., Monte S. Buchsbaum, M.D., Richard C. Mohs, Ph.D., Lina S. Shihabuddin, M.D., Richard Azueta, M.A., Christina T. Luu, B.A.	9:30 a.m.
NR165	Brain Glucose Metabolism in Unipolar Depression Compared with Controls Before and After Sleep Deprivation As Measured by PET FDG Eric A. Klein, B.S., Joseph C. Wu, M.D., J. Christian Gillin, M.D.	9:45 a.m.
NR166	MU and Kappa Opioid Receptor Agonists Induce Different Patterns of CBF Thomas E. Schlaepfer, M.D., Eric C. Strain, M.D., Benjamin D. Greenberg, M.D., George Bigelow, M.D., Kenzie L. Preston, Ph.D., Godfrey D. Pearlson, M.D.	10:00 a.m.
NR167	Actively Depressed Subjects Have Difficulty Inducing and Blunted Limbic rCBF During Transient Sadness Mark S. George, M.D., Timothy A. Kimbrell, M.D., Priti I. Parekh, B.A., Terence A. Ketter, M.D., Peggy J. Pazzaglia, M.D., Ann M. Callahan, M.D., Mark A. Frye, M.D., Lauren B. Marangell, M.D., Peter Herscovitch, M.D., Robert M. Post, M.D.	10:15 a.m.

NEW RESEARCH

Tuesday, May 23, 1995, 9:00 a.m.-10:30 a.m.

New Research 6 – Oral/Slide Session – Room D131, Level 1, Convention Center

MOOD DISORDERS AND TREATMENT TECHNIQUES

Chp.: James J. Strain, M.D.

NR168	Fluvoxamine Compared with Fluoxetine in Major Depression Mark H. Rapaport, M.D., Emil F. Coccaro, M.D., Yvette I. Sheline, M.D., Peter J. Holland, M.D., Teri L. Perse, M.D., Louis F. Fabre Jr, M.D.	9:00 a.m.
NR169	Weekly Fluoxetine Controls Symptoms of Depression William J. Burke, M.D., Shelton Hendricks, Ph.D., Delores McArthur, M.A., Todd W. Stull, M.D., Diane Bessette, P.A., Tracy McKillip, P.A.	9:15 a.m.
NR170	Fluoxetine and Aggression in Personality Disorder Emil F. Coccaro, M.D., Richard J. Kavoussi, M.D.	9:30 a.m.
NR171	The Ictal EEG Predicts the Efficiency of RUL ECT W. Vaughn McCall, M.D., Brian A. Farah, M.D.	9:45 a.m.
NR172	Double-Blind Crossover Antidepressant Study: Sertraline Versus Imipramine Michael E. Thase, M.D., Martin B. Keller, M.D., Alan J. Gelenberg, M.D., Robert M.A. Hirschfeld, M.D., Alan F. Schatzberg, M.D.	10:00 a.m.
NR173	Thyroid Function and Antidepressant Response Fabrice Duval, M.D., M. Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D., Jean-Paul Macher, M.D.	10:15 a.m.

NEW RESEARCH

Tuesday, May 23, 1995, 12:00 noon-2:00 p.m.

New Research 7 – Poster Session – Rooms D128/D129, Level 1, Convention Center

STRESS, SCHIZOPHRENIA, OTHER PSYCHOTIC DISORDERS, AND GERIATRIC PSYCHIATRY

Moderator: Markku I. Linnoila, M.D.

NR174 Decreased Platelet Paroxetine Binding in PTSD: Relationship to Clinical Features and Comorbidity
Christopher G. Fichtner, M.D., Hock C. Yeoh, B.S., Francine L. O'Connor, M.S., Ramesh C. Arora, Ph.D., John W. Crayton, M.D.

NR175 Stressors Affect Onset and Drug Treatment Response in Unipolar Depression
Carolyn M. Mazure, Ph.D., Martha L. Bruce, Ph.D., Selby C. Jacobs, M.D., Janet S. Cellar, M.S.N.

NR176 Natural Disasters: Stress Symptoms and Coping in Rescue Workers
Sudhakar Madakasira, M.D.

NR177 Stress, Arousal, and Deployment to Haiti
Donald P. Hall, Jr., M.D., James A. Jansen, B.S.

NR178 Neuroleptic-Induced Extrapyramidal Symptoms and Serum Iron
Ileana Berman, M.D., Amalia Merson, M.D., Julia Rachev Pavlov, M.D., Cecile E. Sison, Ph.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D.

NR179 Cognitive Deficits and Schizophrenic Symptoms
Ileana Berman, M.D., Amalia Merson, M.D., Barbara Viegener, Ph.D., Cecile E. Sison, Ph.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D.

NR180 Part/Whole Perceptual Organization in Schizophrenia
Eric L. Granholm, Ph.D., Peter A. Nelson, William B. Perry, Ph.D., Vincent Filoteo, Ph.D.

NR181 Information Processing in Late-Life Schizophrenia
Eric L. Granholm, Ph.D., R.F. Asarnow, Ph.D., Steven P. Verney, M.S., Peter A. Nelson, Dilip V. Jeste, M.D.

NR182 Mismatch Negativity During Treatment with Clozapine
Daniel S.G. Umbricht, M.D., Gerald Novak, M.D., Robert Bilder, Ph.D., Daniel Javitt, M.D., Simcha Pollack, Ph.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.

NR183 Mismatch Negativity, Neuropsychological Deficits and Psychopathology in Chronic Schizophrenia
Daniel S.G. Umbricht, M.D., Gerald Novak, M.D., Robert Bilder, Ph.D., Daniel Javitt, M.D., Simcha Pollack, Ph.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.

NR184 Premorbid Adjustment in Schizophrenia: MRI Correlates
James J. Levitt, M.D., Cynthia G. Wible, Ph.D., Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Ferenc Jolesz, M.D., Robert W. McCarley, M.D.

NR185 Spatial Working Memory in Schizophrenia: Cognitive Correlates
James J. Levitt, M.D., Paul G. Nestor, Ph.D., Maria E. Karapelou, Ed.M., Susan Law, M.A., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

NR186 Eye Tracking, Attention, and Schizotypal Symptoms in Nonpsychotic Relatives of Schizophrenic Patients
Richard S.E. Keefe, Ph.D., Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D., Philip D. Harvey, Ph.D., Lee Friedman, Ph.D., Sonia E. Lees Roitman, M.D., Rachel L. DuPre, Christopher Smith, Kenneth L. Davis, M.D., James Schmeidler, Ph.D.

NR187 Laboratory and Clinical Measures of Spatial Working Memory in Schizophrenic Patients and Controls
Richard S.E. Keefe, Ph.D., Sonia E. Lees Roitman, M.D., Rachel L. DuPre, Philip D. Harvey, Ph.D.

NR188 Negative Symptoms in Schizophrenia Are Differentially Related to Cognitive Impairment
Philip D. Harvey, Ph.D., Janel Lombardi, M.A., Martin Liebman, M.A., Peter Powchik, M.D., Michael Davidson, M.D.

NR189 Age Disorientation in Chronically Hospitalized Mood Disorder Patients
Philip D. Harvey, Ph.D., Janel Lombardi, M.A., Peter Powchik, M.D., Michael Davidson, M.D.

NR190 Event-Related Brain Potentials in Schizophrenia During Visual Information Processing
Esther F. Rabinowicz, Ph.D., Gerard Bruder, Ph.D., Craig Tenke, Ph.D., James Towey, Ph.D., Delores Malaspina, M.D., Jack M. Gorman, M.D.

NR191 Assessing the Effects of Medication on Task Performance in Schizophrenia
Esther F. Rabinowicz, Ph.D., David R. Owen, Ph.D., Raymond A. Knight, Ph.D., Xavier Amador, Ph.D., Jack M. Gorman, M.D.

NR192 WITHDRAWN

NR193 Re-Examination of Clozapine Treatment on Quality of Life in Chronic Schizophrenic Patients
Michael J. Reinstein, M.D., Amir Poreh, Ph.D., Sangarapillai C. Mohan, M.D., Lynn Jones, R.N.

NR194 Diabetes and Dementia in Schizophrenic Patients
Dharmbeer Sinha, M.D., Sukdeb Mukherjee, M.D.

NR195 The Neuropsychological Dysfunction of Frontal Lobe in Male Schizophrenic and Manic Patients
Youngnam Park, M.D., Hwag-Heui Lee, M.D.

NR196 Event-Related Potentials Indices of Language Processing in Schizotypal Personality Disorder
Margaret Niznikiewicz, Ph.D., Martha E. Shenton, Ph.D., Larry J. Seidman, Ph.D., Robert W. McCarley, M.D.

NR197 Cognitive and Symptom Correlates of Illness Management Skills in Chronic Schizophrenia
Michael B. McKee, Ph.D., Thomas E. Smith, M.D., Sally J. Mackain, Ph.D., James W. Hull, Ph.D., Maryann Yanulis, Ph.D., Donna T. Anthony, M.D., Marianne S. Goodman, M.D.

NR198 Aging on the Wrong Side of the Brain
Ede Frecska, M.D., Miklos F. Losonczy, M.D., Richard S.E. Keefe, Ph.D., Michael Davidson, M.D., Jeffrey Sparks, R.N., Kenneth L. Davis, M.D.

NR199 Quantitative Autoradiography of a Novel Cocaine Binding Site Related to the Serotonin Transporter in Schizophrenia and Suicides
Donald C. Ohuoha, M.D., F.I. Carroll, M.D., Thomas M. Hyde, M.D., Joel E. Kleinman, M.D., Richard B. Rothman, M.D.

NR200 Lack of Sustained Elevation of Plasma Prolactin in Schizophrenic Patients Treated with ICI 204,636 (Seroquel™)
Mark B. Hamner, M.D., Lisa A. Arvanitis, M.D., Barbara G. Miller, M.S., Chris G.G. Link, M.D., Walter W. Hong, M.D.

NR201 Risperidone in the Long-Term Treatment of Patients with Schizophrenia in Sweden
Eva Lindstrom, M.D., Bo Eriksson, B.Sc., Anders Hellgren, Lars Von Knorring, M.D., Goran Eberhard, Ph.D., Philippe Lemmens, Ph.D.

NR202 MRI in Familial Schizophrenia
Tonmoy Sharma, M.D., Godfrey D. Pearlson, M.D., Patrick E. Barta, M.D., Lewis Shon, Hugh Gurling, M.D., Robin M. Murray, M.D., Qiang Li, M.D.

NR203 Differential Change in Caudate Volumes with Antipsychotics
Miranda H. Chakos, M.D., Jeffrey A. Lieberman, M.D., Jose Ma. Alvir, D.P.H., Robert Bilder, Ph.D., Manzar Ashtari, Ph.D.

NR204 A Neuroendocrine Method of Antipsychotic Dose Reduction in Schizophrenia
Clayton E. Curtis, B.A., Marci Mann, M.S., Kathy Piscani, R.N., Gail Burr, R.N., Robert J. Hitzemann, Ph.D., Jack Hirschowitz, M.D.

NR205 P3 Topography in First Episode Psychosis
Dean F. Salisbury, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D.

NR206 Effects of Cholinergic Antagonism in Young Schizophrenic Patients
Zafar A. Sharif, M.D., Ahmad Raza, M.D., Fabien Tremeau, M.D., Peter A. Rao, M.D.

NR207 Schizophrenia: Thought Disorder and Context
Thomas H. Jobe, M.D., Kristin E. Rappole, B.A., Nina D. Uziel, B.S., Fransisco Lopez III, B.S., Martin Harrow, Ph.D., James R. Sands, Ph.D.

NR208 Use of Risperidone in Neuroleptic Refractory Schizophrenics in a State Psychiatric Center
Jean-Pierre Lindenmayer, M.D., Marc Vital-Herne, M.D., Franklin S. Simon, M.D., Adel Iskander, M.D., Alex Kartachov, M.D.

NR209 Validity of Family History: Method for Identifying Schizophrenia Related Disorders
Ge Li, M.D., Jeremy M. Silverman, Ph.D., Christopher Smith, Larry J. Siever, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR210 Neural Circuit Analysis in Schizophrenia From PET
Monte S. Buchsbaum, M.D., Tse-Chung Wei, Jacqueline Spiegel-Cohen, M.S., Erin A. Hazlett, Ph.D., Mehmet M. Haznedar, M.D., Christina T. Luu, B.A.

NR211 Onset, Coping and Recovery From Hallucinations in Daily Life
Philippe A.E.G. Delespaul, Ph.D., Marten W. Devries, M.D.

NR212 MRI Correlates of the Auditory P3A and P3B Event-Related Potential Components in Schizophrenia
Brian F. O'Donnell, Ph.D., Hirokazu Ohta, M.D., Robert W. McCarley, M.D., Cynthia G. Wible, Ph.D., Ron Kikinis, M.D., Martha E. Shenton, Ph.D.

NR213 FDOPA PET Study of Dopamine Function in Schizophrenia
Joseph C. Wu, M.D., Neetika Khosla, B.S., Steven G. Potkin, M.D., Ahmed Najafi, M.D., Lori LaCasse, B.S., Eric A. Klein, B.S.

NR214 Assessment and Treatment Selection for the Revolving Door Schizophrenic Inpatient
Peter Weiden, M.D., William M. Glazer, M.D., Yelena Braz, M.D., Ryan De Haas, B.A., Mona Sajous, C.S.W., Sharon Haznedar, R.N.

NR215 Neuropsychophysiologic Study of Severely Disturbed Children
Robert L. Hendren, D.O., Janet Hodde-Vargas, Ph.D., Ronald Yeo, Ph.D., Luis Vargas, Ph.D., William Brooks, Ph.D., Corey Ford, M.D.

NR216 Cerebral Ventricular Enlargement, Medication Adherence and Outcomes in Schizophrenia
Richard R. Owen, Jr., M.D., JoAnn E. Kirchner, M.D., Brian J. Cuffel, Ph.D., Ellen P. Fischer, Ph.D., Craig N. Carson, M.D.

NR217 Relationships Between Temporal Lobe Areas and Subdivisions of Prefrontal Cortex in Schizophrenia: An MRI Study
Cynthia G. Wible, Ph.D., Martha E. Shenton, Ph.D., Ronald Kikinis, M.D., Ferenc Jolesz, M.D., Robert W. McCarley, M.D.

NR218 Cognitive Vulnerability, Coping Style and Relapse in Paranoid Schizophrenics
Stefano Pallanti, Ph.D., Leonardo Quercioli, M.D., Rogerio S. Paiva, M.D., Aldo Ragazzoni, M.D., Adolfo Pazzagri, Ph.D.

NR219 Electrocardiographic Signs of Psychosis in Adults and Children
Peter M. Fink, M.D., Hector C. Sabelli, M.D., Linnea Carlson-Sabelli, Ph.D., Joseph v. Messer, M.D., Karen Walthall, B.S., Cynthia C. Tom, B.S.

NR220 Schizophrenia and the Temporal Lobe: A Replication
Erin R. Gautier, B.S., John M. Kuldau, M.D., Alexandra Weis, B.S., Christiana M. Leonard, Ph.D.

NR221 Automatic Inhibition in Schizophrenia of Auditory Processing During the Reading Aloud of Single Nouns
Jose V. Pardo, M.D., Jonathan C. Uecker, M.D., Joel T. Lee, M.S.E.

NR222 Linguistic Strategies Underlying Verbal Fluency Performance in Schizophrenia and in Controls Subjects
Philippe H. Robert, M.D., Valerie Migneco, Dominique Marmod, Cecile Reuge, Guy Darcourt, M.D.

NR223 Oxidative Injury at the Onset of Psychosis
Sridhar Gowda, M.D., Sukdeb Mukherjee, M.D., Sahebarao Mahdik, Ph.D., Elezabeth E. Correnti, M.D., Russell E. Scheffer, M.D.

NR224 Schizophrenia: Neuroleptics and Negative Symptoms
John D. O'Brien, M.D., Barbara A. Cornblatt, Ph.D., David B. Schnur, M.D., Adam Smith, Ph.D., Ilisse R. Perlmutter, M.D., Michael Obuchowski, M.A., Elizabeth A. Amiel, M.D., Douglas F. Munsey, M.D., Myrna Rasmussen, Ph.D., Gregory Osgood, B.A.

NR225 CSF Antibodies to Heat Shock Protein-60 in Schizophrenia
David H. Strauss, M.D., Yutaka Ogino, M.D., David J. Printz, M.D., Jack M. Gorman, M.D., Saudi A. Sadiq, M.D.

NR226 Corpus Callosum in Schizophrenia
Lisa A. Rowe, B.S., John M. Kuldau, M.D., Erin R. Gautier, B.S., Christiana M. Leonard, Ph.D.

NR227 Catatonia From Neuroleptics and NMS: Two Entities?
Monika A. Koch, Georgios Petrides, M.D., Andrew J. Francis Jr, M.D.

NR228 A Comparison of the Efficacy of Clozapine and Risperidone in Treatment Refractory Schizophrenia
Ahmad Raza, M.D., Tzippy Ettinger, B.A., Zafar A. Sharif, M.D., Fabian Tremeau, M.D., Peter A. Rao, M.D.

NR229 Laboratory Stressors in Schizophrenia and Mania
David B. Schnur, M.D., Rachel Yehuda, Ph.D., Scott P. Smith, M.A., Jean Franklin, M.D., Venecia M. Marte, Monica C. Dinu, M.D.

NR230 Schizophrenia, Dopamine, Transforming Growth Factors-Beta and Excitotoxins
Murray A. Cowen, M.D., Maurice R. Green, M.D., David N. Bertollo, B.A.

NR231 Do Thoughts About Abstinence Predict Future Drug Use in Cocaine Dependent Schizophrenics?
Lisa J. Roberts, M.A., Andrew L. Shaner, M.D., Thad A. Eckman, Ph.D.

NR232 Suicide Among Psychiatric Hospital Inpatients
Alec Roy, M.D., Veronika Solt, M.D., Ronald J. Draper, M.D., Matthew J. Pitera, M.D., S. Hassan, M.D., Rakesh K. Bansil, M.D.

NR233 Dopamine Receptor Structure: Psychiatric Applications
Curtiss J. DuRand, M.D., Richard C. Kaiser, M.D., Martha Teeter, Ph.D.

NR234 Glucose Metabolic Rate of the Basal Ganglia In Schizophrenia
Lina S. Shihabuddin, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Christina T. Luu, B.A., Mehmet M. Haznedar, M.D., Kenneth L. Davis, M.D.

NR235 A Clinical Update on Olanzapine: Atypical Antipsychotic
Winston G. Satterlee, M.D., Charles M. Beasley, Jr., M.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.

NR236 Five-Year Follow-Up of Outcome in a Prospective Study of First-Episode Schizophrenia at Hillside Hospital
Julia A. Becker, M.D., Amy R. Koreen, M.D., Miranda H. Chakos, M.D., Steve Geisler, M.D., Jose Ma. Alvir, D.P.H., Margaret Woerner, Ph.D., Jeffrey A. Lieberman, M.D.

NR237 Retention by Florid and Never Florid Schizophrenia Spectrum Patients
Avraham Calev, Ph.D.

NR238 A Controlled MRI Study of Tardive Dyskinesia
Christian L. Shriqui, M.D., Lawrence Annable, D.S., Gilles Bouchard, M.D., Pierre Grondin, M.D., Marie Dufour, M.D.

NR239 Neuropathological Study of 101 Elderly Schizophrenics: Preliminary Findings
Julia A. Golier, M.D., Michael Davidson, M.D., Vahroum Haroutunian, Ph.D., Peter Powchik, M.D., Dushant Purohit, M.D., Daniel Perl, M.D., Kenneth L. Davis, M.D.

NR240 The Validation of the Scale of Functioning for Schizophrenic Subjects
Mark H. Rapaport, M.D., James Bazzetta, M.A., Dilip V. Jeste, M.D., Sidney Zisook, M.D., William B. Perry, Ph.D.

NR241 Spatial Relationships of Neuroanatomic Landmarks in Schizophrenia
John R. DeQuardo, M.D., Fred L. Bookstein, Ph.D., William D.K. Green, Ph.D., James A. Brunberg, M.D., Rajiv Tandon, M.D.

NR242 Affective Reactivity and Family History in Schizophrenia
Nancy M. Docherty, Ph.D., Ellen S. Grosh, M.D., Bruce E. Wexler, M.D.

NR243 Affective Reactivity and Startle in Schizophrenia
Nancy M. Docherty, Ph.D., Christian Grillon, Ph.D.

NR244 Longitudinal Evaluation of Very Chronic Inpatients with Common Psychometric Instruments
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D.

NR245 Neuroleptics, Olfactory Sensitivity and Schizophrenia
Pinkhas Sirota, M.D., Israel Ben-David, M.D., Karen Luca-Haimovici, M.D., Joseph Zohar, M.D., Ruth Gross-Isserrof, Ph.D.

NR246 Stress Response Symptoms in Alzheimer's Disease Caregivers
Deborah B. Marin, M.D., Rachel Yehuda, Ph.D., Cynthia Green, Ph.D., Maureen Fusco, M.S.N., Bella Baruch, B.A., Kenneth L. Davis, M.D.

NR247 Caudate Size in Geriatric Depression
George S. Alexopoulos, M.D., Barnett S. Meyers, M.D., Rotimi Bajulaiye, M.D., C. Elkin, M.D., Philippe J. Khouri, M.D., T. Kakuma, Ph.D.

NR248 Differential Characteristics of Early Versus Late-Onset Panic Disorder
Javaid I. Sheikh, M.D., Pamela J. Swales, Ph.D.

NR249 Depression Predicts Mortality in Frail Elders
Steven C. Samuels, M.D., Ira R. Katz, M.D., Patricia A. Parmelee, Ph.D., Alice A. Boyce, M.A.

NR250 Salivary Cortisol and Daily Events in the Aged
Steven C. Samuels, M.D., Patricia M. Furlan, M.A., Ira R. Katz, M.D.

NR251 Sertraline and Fluoxetine in Geriatric Depression
Robert D. Linden, M.D., Paul A. Newhouse, M.D., K. Ranga Rama Krishnan, M.D., Mildred Farmer, M.D., Burton J. Goldstein, M.D., Lawrence W. Lazarus, M.D.

NR252 MRI Signal Hyperintensities in Geriatric Depression
Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., K. Ranga Rama Krishnan, M.D., Manzar Ashtari, Ph.D., Peter M. Aupperle, M.D., Mahendra C. Patel, M.D.

NR253 Survival Time Among Demented Hospice Patients
Patricia Hanrahan, Ph.D., Daniel J. Luchins, M.D.

NR254 ENA 713 in Alzheimer's Disease: Safety and Tolerance
Neal R. Cutler, M.D., John J. Sramek, Pharm.D., Jerome F. Costa, M.D., Ravi Anand, M.D.

NR255 A Longitudinal View of Late-Life Onset Depression and Dementia
Angela Pedraza, M.D., Jacqueline Valdes, Ph.D.

NR256 Side Effects of Antidepressants in Very Old Nursing Home Residents
Melinda S. Lantz, M.D., Eric N. Buchalter, D.O., Vincent Giambanco, R.P.H.

NR257 The Meaning of Global Assessment of Functioning Scores in Geropsychiatric Inpatients
Debra L. Karch, Ph.D., William S. Edell, Ph.D.

NR258 A Scale to Measure Severe Cognitive Impairment
Peter V. Rabins, M.D., Cynthia Steele, M.P.H.

NR259 Venlafaxine in Depressives Post-Cerebrovascular Aneurysm or in Hypertension
Ben Zimmer, M.D., Mary Brilmyer, R.N.

NR260 Neuropsychological Deficits and P300 Latency in Elderly Non-Demented Depressives
Balkrishna Kalayam, M.D., Gregory G. Brown, Ph.D., Robert C. Young, M.D., George S. Alexopoulos, M.D., Frank E. Musiek, Ph.D.

NR261 Elderly Attitudes on Being Told the Diagnosis of Alzheimer's Disease as Compared to Terminal Cancer
Suzanne Holroyd, M.D., Diane Snustad, M.D., Zona Chalifoux

NR262 Low-Dose Risperidone for Dementia Related Disturbed Behavior in Nursing Homes
Richard J. Goldberg, M.D., Jenna S. Goldberg

NR263 Prevalence of Psychiatric Illness in VA Nursing Home Residents
Joel E. Streim, M.D., Ira R. Katz, M.D., Steven I. Chavin, M.D., Patricia A. Parmelee, Ph.D., Andrea R. Tucker, B.A., Suzanne Difilippo, B.A.

NR264 A Double-Blind Comparison of Sertraline and Nortriptyline in the Treatment of Depressed Geriatric Outpatients
William J. McEntee III, M.D., David J. Coffey, M.D., William Bondareff, M.D., Murray Alpert, Ph.D., Ashok B. Raj, M.D.., Stephen A. Rappaport, M.D., Myron F. Weiner, M.D.

NR265 Predictors of Improvement in Cognitive Functioning in Geropsychiatric Inpatients
William S. Edell, Ph.D., Debra L. Karch, Ph.D.

NR266 Hearing Impairment and Psychiatric Illness in the Elderly
Sandhya Panguluri, M.D., Venkataramana S. Lingam, M.D., Norma C. Josef, M.D.

NR267 Risperidone in Geropsychiatry: Review of Experience in Two Teaching Public Hospitals
Stephen M. Aronson, M.D., Venkataramana S. Lingam, M.D., K.A. Hasanat, M.D.

NR268 Diagnostic Criteria For Alcohol-Induced Dementia
David M. Smith, M.D., Roland M. Atkinson, M.D.

NR269 Psychiatric Components of Failure to Thrive in the Elderly
Ira R. Katz, M.D., Patricia A. Parmelee, Ph.D., Alice A. Boyce, M.A., Andrea R. Tucker, B.A., Suzanne Difilippo, B.A.

NR270 Alzheimer's Disease Patients Support Groups
Elizabeth G. Fine, M.S.W., Deborah B. Marin, M.D., Lizette Williams, B.S., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

NR271 Use of Clozapine in Mentally Ill Elderly
Jasveen K. Dhadli, M.D., Aurelio Ortiz, M.D., Venkataramana S. Lingam, M.D., Norma C. Josef, M.D.

NR272 Personality Dysfunction and Quality of Life in Old Depressives
Robert C. Abrams, M.D., Sandra V. Horowitz, Ph.D., George S. Alexopoulos, M.D.

NR273 Personality Disorders and Social Support in Old Depressives
Robert C. Abrams, M.D., Sandra V. Horowitz, Ph.D., George S. Alexopoulos, M.D.

NEW RESEARCH

Tuesday, May 23, 1995, 3:00 p.m.-5:00 p.m.

New Research 8 – Poster Session – Rooms D128/D129, Level 1, Convention Center

MOOD, PREMENSTRUAL DYSPHORIC, AND PERSONALITY DISORDERS; SUICIDE; DIAGNOSTIC ISSUES; AND GENETICS

Moderator: Tana A. Grady, M.D.

NR274 A Prospective Long-Term Follow-Up Study of Divalproex Treatment of Bipolar Spectrum Illnesses
Frederick M. Jacobsen, M.D., Lillian Comas-Diaz, Ph.D.

NR275 Risperidone in the Treatment of Severe Affective Illness and Refractory OCD
Frederick M. Jacobsen, M.D.

NR276 T3 Suppression Test: A Better Way to Assess Hypothalamus-Pituitary-Thyroid Dysfunction in Depression?
Patricia R. Mourilhe, M.D., Peter E. Stokes, M.D., Chris Huston, Alexandra I. Barsdorf

NR277 Acute Neuroendocrine Effect of ECT on the HYPAC Axis
Patricia R. Mourilhe, M.D., Peter E. Stokes, M.D., Alexandra I. Barsdorf

NR278 Efficacy of Sertraline for Treatment of Premenstrual Dysphoric Disorder
Kimberly A. Yonkers, M.D., Uriel Halbreich, M.D., Ellen W. Freeman, M.D., C.S. Brown, M.D., Teri B. Pearlstein, M.D.

NR279 Are Post-Stroke Depressive Symptoms Frequently Non-Specific for Depression During the First Two Years After Stroke?
Tatsunobu Ohkubo, M.D., Robert G. Robinson, M.D.

NR280 Sustained Antidepressant Effect of Phenylethylamine Replacement
Hector C. Sabelli, M.D., Peter M. Fink, M.D., Jan A. Fawcett, M.D., Cynthia C. Tom, B.S.

NR281 Antidepressant Response in Depressed Patients with Anxiety
James M. Russell, M.D., Larry Koran, M.D., James P. McCullough, Ph.D., Daniel N. Klein, Ph.D., George A. Trapp, M.D.

NR282 Improvement in Winter Depression is Associated with a Phase Advance in the Dim Light Melatonin Onset
Katherine H. Thomas, M.D., Alfred J. Lewy, M.D., Robert L. Sack, M.D., Vance K. Bauer, M.A.

NR283 Prepubertal Suicidality and Parental Psychopathology
Ronald A. Weller, M.D., Parul Kapadia, M.D., Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., Sheldon H. Preskorn, M.D.

NR284 Lithium Plus Desipramine Versus Desipramine Alone in the Treatment of Major Depression: A Controlled Study
Lawrence H. Price, M.D., Angela C. Cappiello, M.D., Christopher J. McDougle, M.D., Robert T. Malison, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR285 Alpha-1-Acid Glycoprotein and Age in Major Depression
Robert C. Young, M.D., Ashok Patel, M.D., J.P. Bocksberger, M.D., Leonard Fensterheim, M.P.H.

NR286 Risperidone in the Treatment of Mania
Mauricio Tohen, M.D., Carlos A. Zarate, Jr., M.D., Franca Centorrino, M.D., James D. Hegarty, M.D., Michael Froeschl, B.S., Silvina M. Zarate, B.S.

NR287 Increased CSF Neural Cell Adhesion Molecule in Patients with Bipolar and Unipolar Mood Disorder
Maciej Poltorak, M.D., Renee Wright, B.A., Mark A. Frye, M.D., Mark S. George, M.D., Peggy J. Pazzaglia, M.D., Robert M. Post, M.D., J.J. Hemperly, Ph.D., Shari Jerrels, B.A., William Freed, Ph.D.

NR288 The Ability of Ictal EEG Ratings to Detect Changes in ECT Relative Stimulus Dose in the Clinical Setting
Andrew D. Krystal, M.D., C. Edward Coffey, M.D., Richard D. Weiner, M.D., Tracy Holsinger, M.D., Thomas E. Sibert, M.D.

NR289 Improvements in Work and Social Disability in Depressed Patients Taking Bupropion Sustained Release
Josephine A. Mauskopf, Ph.D., George P. Simeon, M.P.H., Jonathan R.T. Davidson, M.D., Ron Westlund, M.S.

NR290 Cognition and Psychosensory Features in Mood Disorders
Nutan Atre-Vaidya, M.D., Michael A. Taylor, M.D., Michael Seidenberg, Ph.D., Alicia Perrine, B.S.

NR291 Tryptophan Depletion in Bupropion or Placebo Responders
Pedro L. Delgado, M.D., Louise J. Strayer, R.N., Karen Bachar, B.A., Rebecca L. Potter, M.D., Alan J. Gelenberg, M.D., Francisco A. Moreno, M.D.

NR292 Unilateral ECT Is As Effective As Bilateral ECT in Delusional Depression
Leon J. Grunhaus, M.D., Atul C. Pande, M.D., Shmuel Hirschmann, M.D.

NR293 Attentional Disorders in Major Depressive Disorder: Result of a Comparative Study Using Computerized Tests
Jean-Georges Rohmer, M.D., Blandine Kastler, M.D., Michel Patris, M.D.

NR294 A Double-Blind, Placebo Controlled Study of Light Therapy for SAD
Virginia A. Wesson, M.D., Anthony J. Levitt, M.D., Russell T. Joffe, M.D., Eleanor F. King, R.N.

NR295 HPA Reactivity to Stress in Depressed Adolescents
Carrie M. Borchardt, M.D., Amy Perwien, B.A., Gail A. Bernstein, M.D.

NR296 Mood, Motor and Cognitive Variability of Depression
Stephen K. Brannan, M.D., Mahurin K. Rodrick, Ph.D., Janet L. Tekell, M.D., J. Arturo Silva, M.D., Helen S. Mayberg, M.D.

NR297 Relations of Personality to Depressive Subtypes
John B. Jolly, Psy.D., David C. Weisner, Ph.D., Thomas A.M. Kramer, M.D.

NR298 Seasonality of Admissions in Depressed Smokers
Dale A. D'Mello, M.D., Charles Flanagan

NR299 Dissociation and Major Depression
Alexis A. Giese, M.D., Steven L. Dubovsky, M.D., Marshall R. Thomas, M.D., Melissa Riemer, M.D.

NR300 Physical and Sexual Abuse in Psychiatric Inpatients with a Diagnosis of Dysthymia
Shobhana B. Vora, M.D., Theresa M. Miskimen, M.D.

NR301 Mini-Mental State Examination and Depression
Jonathan E. Alpert, M.D., Lisa A. Uebelacker, B.A., Nancy E. McLean, B.A., Melissa Abraham, B.A., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR302 The Scope of Family Burden in Bipolar Affective Disorder: A Preliminary Report
Deborah A. Perlick, Ph.D., John F. Clarkin, Ph.D., Joanne Sirey, Ph.D., Lawrence H. Rockland, M.D., Elizabeth Pike, M.Ed.

NR303 A New Estimate of Gi Activity in Depression
John J. Mooney, M.D., Jacqueline Samson, Ph.D., Nancy L. McHale, B.S., Jonathan E. Alpert, M.D., Martha A. Koutsos, M.D., Joseph J. Schildkraut, M.D.

NR304 Family Experience of Stigma in Bipolar Disorder
Joanne Sirey, Ph.D., Deborah A. Perlick, Ph.D., John F. Clarkin, Ph.D., Elizabeth Pike, M.Ed.

NR305 Problem Awareness and Treatment Readiness in Dual Diagnoses Patients
Ihsan M. Salloum, M.D., Howard B. Moss, M.D., Dennis Daley, M.S.W., Levent Kirisci, Ph.D., Musa Al-Maalouf, M.D.

NR306 Sinus Bradycardia at Therapeutic Lithium Levels
Mary Joseph, M.D., Victor Vieweg, M.D., Antony Joseph, M.D.

NR307 Negative Symptoms in Patients with Depression and Pseudodementia
Igor I. Galynker, M.D., Teusink Paul, M.D., Burcescu Silviu, M.D.

NR308 Risk Factors for Depression in Americans
Alec Roy, M.D., Veronika Solt, M.D., John A. Williams, M.D., S. Hassan, M.D., Matthew J. Pitera, M.D.

NR309 The Use of Depression Rating Scales in Women with Postpartum Depression
Zachary N. Stowe, M.D., Jacque C. Landry, B.A., Maryfrances R. Porter, Charles B. Nemeroff, M.D.

NR310 Efficacy of Sertraline and Imipramine in Dysthymia
Maurizio Fava, M.D., James H. Kocsis, M.D., Richard C. Shelton, M.D., Lorrin M. Koran, M.D., Marc Hertzman, M.D.

NR311 Retention for Affective Material in Depression
Avraham Calev, Ph.D.

NR312 A Survey of Prescribing Practices of Neuroleptics in the Maintenance Treatment of Bipolar Disorder
Helene Verdoux, M.D., Bruno Gonzales, M.D., Marc L. Bourgeois, M.D.

NR313 Differential Prefrontal Rapid Transcranial Magnetic Stimulation in Depression: Preliminary Observations
Mark S. George, M.D., Eric S. Wassermann, M.D., Wendol A. Williams, M.D., Timothy A. Kimbrell, M.D., Peggy J. Pazzaglia, M.D., Ann M. Callahan, M.D., Mark A. Frye, M.D., Terence A. Ketter, M.D., Michael Hallett, M.D., Robert M. Post, M.D.

NR314 A Double-Blind Comparison of Fluoxetine, Bupropion and Placebo in Premenstrual Dysphoric Disorder
Teri B. Pearlstein, M.D., Andrea B. Stone, M.D., Sally A. Lund, M.D., Harriet Scheft, M.D., Caron Zlotnick, Ph.D., Walter A. Brown, M.D.

NR315 Survey of Gynecologic and Endocrine Abnormalities Among Women with Psychosis
Cassandra Morabito, Ph.D., Mary H. Collins, M.D., Lisa S. Weinstock, M.D., Alexandra Levin, Mauricio Tohen, M.D.

NR316 Internal Consistency of DSM-III-R Personality Disorder Clusters in Middle and Late Adolescence
Daniel F. Becker, M.D., Carlos M. Grilo, Ph.D., Martha L. Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR317 Neurological and Psychological Factors in BPD
Godehard Oepen, M.D., Catherine R. Kimble, M.D., Elizabeth F. Weinberg, M.D., Amy A. Williams, B.S., Mary C. Zanarini, Ed.D.

NR318 Group Behavioral Therapy of OCD
Joseph A. Himle, M.S.W., Randolph M. Nesse, M.D., Kathleen Krone, M.S.

NR319 Relationships Between Personality and Neuropsychological Performance
Allen Y. Tien, M.D., William W. Eaton, Ph.D.

NR320 Attentional Function in Schizotypal Patients
Andrea Bergman, Ph.D., Sonia Lees-Roitman, M.A., Gregory Osgood, B.A., Barbara A. Comblatt, Ph.D., Larry J. Siever, M.D.

NR321 Patterns of Obsessive Compulsive Symptoms in Tourette Subjects Are Severity Independent: A Discriminant Analysis
Christopher M. de Groot, M.D., Robert A. Bornstein, Ph.D., Matig R. Mavissakalian, M.D., Mark David Janus, Ph.D.

NR322 Self-Injurious Behavior in Personality Disorders
Antonia S. New, M.D., Robert L. Trestman, M.D., Deana S. Benishay, M.A., Emil F. Coccaro, M.D., Larry J. Siever, M.D.

NR323 Clock Test, Depression and Alzheimer's Screening
Theodore Dreier, M.D., Becca Levy, M.A.

NR324 BPD Outcome in Outpatients: A Two-Year Follow-Up
Lynn Gaudreault, M.D., Nora Schneider, Ph.D., Antonio Andreoli, M.D.

NR325 Pain Assessment Using Signal Detection Theory
Ingrid M. Kemperman, M.D., Mark J. Russ, M.D., Tatsuyuki Kakuma, Ph.D.

NR326 Substance Use and Secondary Borderline Personality
Paul S. Links, M.D., Ronald J. Heslegrave, Ph.D.

NR327 Personality Disorders in Pathological Gamblers Seeking Treatment
Peter Berger, M.D.

NR328 Epidemiological Survey of OCD and Syndromes in a Large French Clinical Sample
Elie G. Hantouche, M.D., Marc L. Bourgeois, M.D., Myriam Bouhassira, M.D., Sylvie Lancrenon, Ph.D.

NR329 A Phenomenological Profile of OCD Patients in Bahrain
Mohmed Khalil Al-Haddad, M.B.

NR330 A Quarter Century of Suicides in a Major Urban Jail: Implications for Community Psychiatry
Curtiss J. DuRand, M.D., James A. Haycox, M.D., Edward Federman, Ph.D., Gary Burtka, M.A., John Smith, M.A.

NR331 Positive Versus Negative Symptoms and Suicide Risk
Kalman J. Kaplan, Ph.D., Martin Harrow, Ph.D., Michael J. Reinstein, M.D., James R. Sands, Ph.D.

NR332 Suicide Abuse and Dissociative Symptoms
Margaret L. Kaplan, Ph.D., Gregory M. Asnis, M.D., Deborah S. Lipschitz, M.D.

NR333 Invasiveness of Sexual Abuse Predicts Suicide Attempts
Nicholas G. Ward, M.D., David Junker, B.S., Rama Oskouian, B.S., Bryan Hartzler, B.S., Albert Carlin, Ph.D.

NR334 Suicide in Medical Students: 1989-1994
Lon R. Hays, M.D., Todd R. Cheever, M.D., Pukar Patel, M.D.

NR335 Suicidal Ideation in Urban Medical Outpatients
Mark Zimmerman, M.D., Jennifer D. Lish, Ph.D., David T. Lush, M.D., Neil J. Farber, M.D., Gary Plescia, M.A., Mary Ann Kuzma, M.D.

NR336 Female Panic Disorder Patients Manifest Greater Somatization Compared to Male Patients
Javaid I. Sheikh, M.D., Pamela J. Swales, Ph.D.

NR337 Trichotillomania and Self-Esteem: A Survey of 62 Female Hair-Pullers
Jennifer L. Soriano, Richard L. O'Sullivan, M.D., Lee Baer, Ph.D., Katharine A. Phillips, M.D., Richard J. McNally, Ph.D., Michael A. Jenike, M.D.

NR338 A Long-Term Follow-Up Study of Somatoform Disorders
Michael Bach, M.D., Doris Bach, Ph.D., Ulrike Lupke, Ph.D., Ralph Schaible, Ph.D.

NR339 Is Alexithymia Related to Somatization? A Factor Analytic Study
Michael Bach, M.D., Doris Bach, Ph.D., Martina De Zwaan, M.D.

NR340 Course of Psychological Variables in Whiplash Injury: A Two-Year Follow-Up with Age, Gender and Education Pair-Matched Patients
Bogdan P. Radanov, M.D., Matthias Sturzenegger, M.D., Stefan Begre, M.D.

NR341 Long-Term Outcome After Whiplash Injury: Follow-Up During Two Years with Patients Referred From Primary Care
Bogdan P. Radanov, M.D., Matthias Sturzenegger, M.D.

NR342 Comorbidity in Child and Adolescent Conversion Disorders
Atilla Turgay, M.D.

NR343 Are Antidepressants Effective in the Treatment of Chronic Pain?
David A. Fishbain, M.D., Brian Cutler, Renee Steele Rosomoff, M.B.A., Hubert L. Rosomoff, M.D.

NR344 Experience of Pain in Rheumatoid Arthritis: An Empirical Evaluation of the Contribution of Developmental Psychosocial Stress
Stephan Andreas Frost, M.D., Bogdan P. Radanov, M.D.

NR345 Do Normal Volunteers Know That They Are Not Psychiatrically Normal?
Clarice Gorenstein, Ph.D., Francisco Lotufo Neto, Ph.D., Marcio Melo, M.D., Valeria Lauriano, M.D., Laura Andrade, Ph.D., Valentim Gentil, M.D.

NR346 DSM-IV General Reliability Field Trials: Expert Phase
James W. Thompson, M.D., Allen J. Frances, M.D., Harold Alan Pincus, M.D., Michael B. First, M.D., Michael A. Flaum, M.D., J. Richard Hebel, Ph.D.

NR347 Differential Diagnosis of Organic Psychosis and Schizophrenia in Patients with Psychoactive Substance Use Disorders
Richard N. Rosenthal, M.D., Christian Miner, Ph.D.

NR348 Asperger's Syndrome in Later Life
Serge A. Mosovich, M.D., Lucille Horn, Ph.D., Valerie Minuchin, M.A., Bonnie R. Aronowitz, Ph.D., Eric Hollander, M.D.

NR349 Family and Genetic Studies of OCD
Margaret A. Richter, M.D., Richard P. Swinson, M.D., Russell T. Joffe, M.D., Farideh Badri, B.Sc., Elizabeth Billett, B.Sc., James L. Kennedy, M.D.

NR350 Exonic and Intronic Polymorphisms in the D3 Gene
Marc-Antoine Crocq, M.D., Fabrice Duval, M.D., Alain Buguet, M.D., Sylvie Bisser, M.D., Antonia Mayerova, Ph.D., Jean-Paul Macher, M.D.

NR351 Distribution of the TaqI Polymorphism of the Dopamine D2 Receptor in Korean Alcoholism Population
Min Soo Lee, M.D., Young Tae Kim, M.D., Dong-Il Kwak, M.D.

NR352 Psychiatric Disturbances in Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy Disease
Docteur C. Spadone, M.O. Krebs, J.M. Vanelle, M.F. Poirier, F. Guedj, H. Chabriat, H. Loo

NEW RESEARCH

Wednesday, May 24, 1995, 9:00 a.m.-10:30 a.m.

New Research 9 – Oral/Slide Session – Room D130, Level 1, Convention Center

ANXIETY DISORDERS

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

NR353 Self-Reported Sexual Dysfunctions in Social Phobic Patients — 9:00 a.m.
Michael R. Ware, M.D., Naresh P. Emmanuel, M.D., Violetta D. Czepowicz, M.D., Michael R. Johnson, M.D., Rebecca Kapp, R.N., R. Bruce Lydiard, M.D.

NR354 Long-Term Treatment and Prevention of Relapse of OCD with Paroxetine — 9:15 a.m.
Martin Steiner, Ph.D., William D. Bushnell, M.S., Ivan P. Gergel, M.D., David E. Wheadon, M.D.

NR355 A Fixed Dose Study of Paroxetine and Placebo in the Treatment of Panic Disorder — 9:30 a.m.
Martin Steiner, Ph.D., Rosemary Oakes, M.S., Ivan P. Gergel, M.D., Daniel B. Burnham, Ph.D., David E. Wheadon, M.D.

NR356 Fluvoxamine Versus Clomipramine for OCD: A Double-Blind Comparison — 9:45 a.m.
Lorrin M. Koran, M.D., Susan L. McElroy, M.D., Jonathan R.T. Davidson, M.D., Steven A. Rasmussen, M.D., Eric Hollander, M.D., Michael A. Jenike, M.D.

NR357 Cost Effectiveness of Fluvoxamine, Placebo and Cognitive Behavior Therapy Alone and in Combination in the Treatment of Panic Disorder — 10:00 a.m.
Richard J. Simpson, M.D., Donald M. Sharp, Ph.D., Kevin G. Power, Ph.D.

NR358 CSF Serotonin: Diagnostic and Seasonal Differences — 10:15 a.m.
Timothy D. Brewerton, M.D., R. Bruce Lydiard, M.D., Michael R. Johnson, M.D., James C. Ballenger, M.D., Mark D. Fossey, M.D., James E. Roberts, Ph.D.

NEW RESEARCH

Wednesday, May 24, 1995, 9:00 a.m.-10:30 a.m.

New Research 10 – Oral/Slide Session – Room D131, Level 1, Convention Center

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS

Chp.: Trey Sunderland, M.D.

NR359 Risperidone Versus Haloperidol in Treatment Refractory Schizophrenia: Preliminary Results — 9:00 a.m.
William C. Wirshing, M.D., Donna Ames, M.D., Michele Palmer Bray, B.S., Barringer D. Marshall, Jr., M.D., Michael F. Green, Ph.D., Stephen R. Marder, M.D.

NR360	Cingulate Metabolism in Schizophrenia Spectrum M. Mehmet Haznedar, M.D., Monte S. Buchsbaum, M.D., Benjamin V. Siegel, M.D., Larry J. Siever, M.D., Marja Germans, B.A.	9:15 a.m.
NR361	Efficacy of Clozapine Versus Haloperidol in a Long-Term Clinical Trial: Preliminary Results John M. Kane, M.D., Stephen R. Marder, M.D., Nina R. Schooler, Ph.D., Daniel S.G. Umbricht, M.D., Donna Ames, M.D., William C. Wirshing, M.D., Robert Baker, M.D., Rohan Ganguli, M.D., Allan Z. Safferman, M.D., Michael Borenstein, Ph.D.	9:30 a.m.
NR362	Long-Term Stability of Diagnosis and the Positive Negative Distinction in a Systematic Sample of Childhood and Adolescence Onset Schizophrenia Michel Maziade, M.D., Nathalie Gingras, M.D., Stephane Bouchard, Ph.D., Benoit Gauthier, M.D., Guy Tremblay, M.D., Serge Cote, M.D., Chantal Merette, Ph.D.	9:45 a.m.
NR363	Olanzapine in the Treatment of Schizophrenia and Other Psychotic Disorders Pierre V. Tran, M.D., Charles M. Beasley, Jr., M.D., Gary D. Tollefson, M.D., W. Satterlee, M.D., J.G. Small, M.D., G. Besancon, D. Naber, T.M. Sanger, Ph.D., J. Bailey, K.A. Graffeo, Herbert Y. Meltzer, M.D., A. Wood	10:00 a.m.
NR364	Fluid and Osmolyte Balance During Neuroleptic Malignant Syndrome Ronald J. Gurrera, M.D.	10:15 a.m.

NEW RESEARCH

Wednesday, May 24, 1995, 12:00 noon-2:00 p.m.

New Research 11 – Poster Session – Rooms D128/D129, Level 1, Convention Center

ANXIETY, AIDS AND HIV RELATED DISORDERS; CONSULTATION/LIAISON AND EMERGENCY PSYCHIATRY; VIOLENCE, TRAUMA AND VICTIMIZATION; DISSOCIATIVE, ORGANIC MENTAL, AND SLEEP DISORDERS; PSYCHOIMMUNOLOGY; TREATMENT TECHNIQUES AND ISSUES; AND RESEARCH ISSUES

Moderator: Charles B. Nemeroff, M.D.

NR365 Body Dysmorphic Disorder is Comorbid with Major Depression
Andrew A. Nierenberg, M.D., Katharine A. Phillips, M.D., Junko Kaji, B.A., Jonathan E. Alpert, M.D., John J. Worthington III, M.D., Maurizio Fava, M.D.

NR366 Does Degree of Insight in OCD Predict Improvement?
Jane L. Eisen, M.D., Steven A. Rasmussen, M.D., Katharine A. Phillips, M.D., R. Bruce Lydiard, M.D., Teresa A. Pigott, M.D.

NR367 Remission and Relapse in OCD: A Two-Year Prospective Study
Jane L. Eisen, M.D., Steven A. Rasmussen, M.D., Wayne K. Goodman, M.D., Meredith Warshaw, Ph.D.

NR368 Avoidant Personality and Social Phobia Revisited
Vladan Starcevic, M.D., Brian B. Roberts, M.D., Eberhard H. Uhlenhuth, M.D.

NR369 Decrease in Worry During Treatment of GAD
Vladan Starcevic, M.D., Stephanie K. Fallon, M.D., Eberhard H. Uhlenhuth, M.D.

NR370 The Prevalence of School Dropouts in an Anxiety Disorders Clinic Sample
Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Carol Wilson, M.Sc., Bridgette Hill

NR371 Buspirone Augmentation of Selective Serotonin Reuptake Inhibitors in Social Phobia
Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Carol Wilson, M.Sc.

NR372 Predicting Patient Dropout in Panic Disorder
Naresh P. Emmanuel, M.D., Michael R. Ware, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

NR373 Venlafaxine in Social Phobia: A Case Series
Naresh P. Emmanuel, M.D., Violetta D. Czepowicz, M.D., Gerardo Villarreal, M.D., Michael R. Johnson, M.D., Michael R. Ware, M.D., Robert N. Rubey, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

NR374 A Comparison Study of Body Dysmorphic Disorder and OCD
Katharine A. Phillips, M.D., Craig G. Gunderson, B.A., Susan L. McElroy, M.D., Gopinath K. Mallya, M.D., William P. Carter, M.D.

NR375 Diagnostic Instruments for Body Dysmorphic Disorder
Katharine A. Phillips, M.D., Katherine D. Atala, M.D., Harrison G. Pope, Jr., M.D.

NR376 A Double-Blind Placebo Controlled Study of Paroxetine and Clomipramine in the Treatment of Panic Disorder
Geoffrey C. Dunbar, M.D.

NR377 Cognitive Impulsivity Predicts Polysubstance Abuse in Hospital Inpatients
Kurt K. Hubbard, B.A., Sue Borgaro, M.A., Joel Lord, M.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D., David L. Pogge, Ph.D.

NR378 Subclinical OCD in College Students
Marcia R. Morris, M.D., Roger Blashfield, Ph.D., Babu Rankapalli, M.D., Wayne K. Goodman, M.D.

NR379 Pyridostigimine Induces Panic Attacks in Patients with Panic Disorder
Kishore M. Gadde, M.D., Thomas W. Uhde, M.D.

NR380 Early Loss and Separation in Social Phobia
Dominique Servant, M.D., Georges Gauthier, M.D., Regis Beuscart, M.D., P. Jean Parquet, M.D.

NR381 Multifamily Group Versus Group Behavioral Treatment of OCD
Michele T. Pato, M.D., Barbara Van Noppen, M.S.W., Gail Steketee, Ph.D.

NR382 Clinical Characteristics of Panic Disorder with Sleep Attacks
Hisanobu Kaiya, M.D.

NR383 New Phenomenological Dimensions for Subtyping OCD
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.

NR384 Pentagastrin Effects in Patients with GAD
Olga Brawman-Mintzer, M.D., R. Bruce Lydiard, M.D., Gerardo Villarreal, M.D., Rebecca S. Knapp, M.D., Naresh P. Emmanuel, M.D., James C. Ballenger, M.D.

NR385 Does Brief Dynamic Psychotherapy Reduce the Relapse Rate of Panic Disorder?
Ida M. Wiborg, Ph.D., Alv A. Dahl, M.D.

NR386 An Open Trial of Paroxetine in Social Phobia
Catherine L. Mancini, M.D., Michael A. Van Ameringen, M.D., Carol Wilson, M.Sc.

NR387 Quality of Life in Panic Disorder
Barbara S. Scupi, M.S., Brenda E. Benson, B.S., Una D. McCann, M.D., Thomas W. Uhde, M.D.

NR388 Is PTSD and Etiological Factor in Addictive Behavior?
Jean-Michel Darves-Bornoz, M.D., Isabelle Delmotte, M.D., Patricia Benhamou, M.D., Andree DeGiovanni, M.D., Philippe Gaillard, M.D.

NR389 PTSD, Spouse Abuse and American Indian Vietnam Veterans
Ilena M. Norton, M.D., Spero M. Manson, Ph.D.

NR390 Tricyclics, Selective Serotonin Reuptake Inhibitors and Venlafaxine: Comparative Tolerabilities in Early PTSD Treatment
Neal A. Kline, M.D.

NR391 Clonazepam Treatment of Panic Disorder in Patients with Recurrent Chest Pain and Normal Coronary Arteries
Lawson R. Wulsin, M.D., Rula Dawaher, B.A., Bernard D. Beitman, M.D., Richard J. Maddock, M.D., Victoria Wells, M.D.

NR392 P1 Mid-Latency Auditory Evoked Potential in PTSD
Gregory M. Gillette, M.D., Robert D. Skinner, Ph.D., Doyle H. Davis, M.S., Lisa Rasco, B.A., Frederick A. Boop, M.D., Edgar Garcia-Rill, Ph.D.

NR393 The Multidisciplinary Study in Patients with Chest Pain of Undetermined Etiology
Indira M. Varia, M.D., Thomas M. Bashore, M.D., Rex M. McCallum, M.D., Scott R. Brazer, M.D.

NR394 Comorbidity in Panic Disorder With and Without Agoraphobia
Alvaro Rivera, M.D., Susana Alfonso, M.D.

NR395 PTSD After Moderate Head Injury
Deborah L. Warden, M.D., Lawrence A. Labbate, M.D., Andres M. Salazar, M.D., Rachael S. Nelson, M.D.

NR396 Assessment and Treatment of OCD
Juliana Lachenmeyer, Ph.D., Kevin Handley, B.S.

NR397 Potentiation of Fluoxetine by Amunoglutethimide Steroid Suppression in OCD: A Case Report
Guy Chouinard, M.D., Marie-Claire Belanger, R.N., Sarah Sultan, M.D., Linda Beauclair, M.D., Beverley E. Pearson-Murphy

NR398 Odors and Perceptions of Room Size
Alan R. Hirsch, M.D., Jason J. Gruss

NR399 Trauma History As a Predictor of Response to Moclobemide
Diane Majcher, M.D., Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Susan A. Sabatino, B.A., John J. Worthington III, M.D., Jerrold F. Rosenbaum, M.D.

NR400 Brain Abnormalities in OCD by Morphometric MRI
Hans C. Breiter, M.D., Michael A. Jenike, M.D., Lee Baer, Ph.D., Cary R. Savage, Ph.D., Scott L. Rauch, M.D., Pauline A. Filipek, M.D.

NR401 Single Site Findings in a Safety and Efficacy Study of CI-988 in GAD
John J. Sramek, Pharm.D., Jerome F. Costa, M.D., Judith Bammert-Adams, Pharm.D., Alison E. MacPherson, B.A., Neal R. Cutler, M.D.

NR402 HIV Illness and Testosterone Replacement Therapy: Mood and Anabolic Effects
Judith G. Rabkin, Ph.D., Richard Rabkin, M.D., Glenn Wagner, M.A.

NR403 Depression and Help-Seeking of Partners in the Heterosexual HIV Transmission Study
Cheryl Ann Kennedy, M.D., Judith Abrams, Ph.D., Joan H. Skurnick, Ph.D.

NR404 Effects of Methylphenidate on HIV-Related Memory Dysfunction
Joel K. Levy, Ph.D., Francisco Fernandez, M.D.

NR405 New Pharmacological Approaches to the Treatment of HIV-1-Induced Cognitive Impairments
Benedetto Vitiello, M.D., Willo Pequegnat, Ph.D., Ellen Stover, Ph.D.

NR406 A Survey of HIV/AIDS Awareness in One District Branch
Maria L.A. Tiamson, M.D., Michael Blumenfield, M.D.

NR407 Risperidone in the Treatment of Psychiatric Symptoms in Patients with AIDS
William S. Gilmer, M.D., Stephen J. Ferrando, M.D., Jonathon D. Goldman, M.D.

NR408 Suicidal Behaviors and Outcomes in HIV-1 Infections
Richard Douyon, M.D., Joseph M. Mavica, D.O., Daniel Feaster, M.S., Karl Goodkin, M.D.

NR409 Linking Community-Based Mental Health Services to an NIMH AIDS Research Center
David G. Ostrow, M.D., Kathleen Sikkema, Ph.D., Debra Murphy, Ph.D., Jeffrey A. Kelly, Ph.D., Kenneth Multhauf

NR410 Animal Models for HIV-Induced CNS Dysfunctions
Floyd E. Bloom, M.D., Lisa Gold, Ph.D., Steven Henriksen, Ph.D., John Elder, Ph.D., Howard Fox, M.D., Tommy Phillips, Ph.D.

NR411 Psychiatric Comorbidity and General Hospital Use
Stephen M. Saravay, M.D., Eliot Goldman, Ph.D., Simcha Pollack, Ph.D., Barbara S. Weinschel, M.D., Neil Grafstein

NR412 Beside Data Collection Windows Pen Entry Notebook
James J. Strain, M.D., Jeffrey S. Hammer, M.D., Ahron Friedburg, M.D., George Fulop, M.D.

NR413 Emergency Room's Service Use by Addicts Receiving Disability
Jeffrey G. Stovall, M.D., Linda S. Grossman, Ph.D., Sandra G. McRae, Ph.D., Janet K. Willer, Ph.D., Sarz Maxwell, M.D.

NR414 Referral Trends to an Inpatient Consultation/Liaison Service
Jill S. Meyer, M.D., Frank W. Favazza, M.D., William R. Mysels, M.D., Charles Englehart, Ph.D.

NR415 Chronic Fatigue and Traumatic Life Events
Peter Manu, M.D., Rachel Yehuda, Ph.D., Earl L. Giller, Jr., M.D., Glenn Affleck, Ph.D.

NR416 Relationship Between Attention and Memory in PTSD
Julia A. Golier, M.D., Rachel Yehuda, Ph.D., Barbara A. Cornblatt, Ph.D., Richard S.E. Keefe, Ph.D., Philip D. Harvey, Ph.D., Robert A. Levengood, M.D.

NR417 An Intervention for Self-Injurious Behavior on an Inpatient Unit
Caron Zlotnick, Ph.D., Elizabeth B. Simpson, M.D., Michelle Kemp, M.A., M. Tracie Shea, Ph.D., Teri B. Pearlstein, M.D., Ann Begin, Ph.D., Ellen Costello, Ph.D.

NR418 Adverse Impact of Sexual Trauma and Battering on Veteran Women's Mental Health
Marian I. Butterfield, M.D., Cedar Koons, M.S.W., Linda Barnett, Ph.D., Lori Bastian, M.D.

NR419 PTSD and Suicide in Urban Adolescents Exposed to Violence
Jill H. Rathus, Ph.D., Gregory M. Asnis, M.D., Scott Wetzler, Ph.D.

NR420 PTSD in Cuban Refugee Children at Guantanamo Bay Naval Base, Cuba
Eugenio M. Rothe, M.D., Capt. Jerry Rose, USN, Hector Castillo-Matos, M.D., Carlos A. Gonzalez, M.D., Lourdes Garcia-Iglesias, M.D., Ruben Busquets, M.D., Capt. Douglas J. Mason, USA

NR421 Psychoendocrinology of Sexual Abuse in Women with Chronic Pelvic Pain
Christine Heim, Ulrike Ehlert, Ph.D., Juergen P. Hanker, Ph.D., Dirk H. Hellhammer, Ph.D.

NR422 Personality Change After Genocide: Disorders of Extreme Stress in Bosnians
Stevan M. Weine, M.D., Daniel F. Becker, M.D., Dolores Vojvoda, M.D., Emir Hodzic, Ph.D., Marie Sawyer, M.S., Leslie Hyman, C.I.S.W., Dori Laub, M.D., Thomas H. McGlashan, M.D.

NR423 Assessing the Characteristics of Spouse Abuse in a Military Population
Charles D. Magruder, M.D., Richard Croutharmel, M.S., Robert Mays, Ph.D., Vivian Sheliga, D.S.W., Ann E. Norwood, M.D., Alison Vawter, B.A.

NR424 Weapons Collections Among VA Patients
Thomas W. Freeman, M.D., Nichole Keesee, M.S.W., Carolyn Thornton, M.S.W.

NR425 Successful Treatment of Paraphilic Sex Offenders
Eliezer Wiztum, M.D., Ariel Rosler, M.D.

NR426 Dissociative Amnesia: Evidence For Interhemispheric Disconnection
Godehard Oepen, M.D., Edward Federman, Ph.D., Lawrence R. Herz, M.D.

NR427 The Prevalence of Dissociation in Inpatients
Virginia L. Susman, M.D., Beth Brodsky, Ph.D., Maura Lehr, M.S.W., Robert A. Grossman, M.D., Orli Avi-Yonah, Ph.D., Stephen Hurt, Ph.D.

NR428 Trauma Associated Psychopathology in Alcoholics: Screening and Diagnosis
M. Kirsten Miller, M.D., Arthur A. Alterman, Ph.D., Pam Fawcett, M.Ed., E. Holub-Beyer, M.H.R., Delinda Mercer, M.S., Karen Clay, B.A., Joseph R. Volpicelli, M.D.

NR429 Psychiatric Diagnoses and Abuse Experiences of 45 Adult Pseudoseizure Subjects
Elizabeth S. Bowman, M.D., Omkar N. Markand, M.D.

NR430 Validity of Family History Diagnosis of Alzheimer's Disease
Mohsen Aryan, Ph.D., Li Ge, M.D., Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., Vahram Haroutunian, Ph.D., Kenneth L. Davis, M.D.

NR431 Mechanisms of Programmed Cell Death in the Brain
Herbert W. Harris, M.D.

NR432 Depression and Negative Symptoms in Alzheimer's Disease
William E. Reichman, M.D., Andrew C. Coyne, Ph.D., Satish Amirneni, M.D., Bruno Molino, B.S.

NR433 Relationship Between Melancholia and Personality Disorders
Eric D. Peselow, M.D., Michael P. Sanfilipo, M.A., Faouzia Barouche, M.D., Gita Vaid, M.D., Alejandra Hallin, M.D., Ronald R. Fieve, M.D.

NR434 Effect of Cumulated Partial Sleep Deprivation on TRH Test Responses
Fabrice Duval, M.D., M. Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D., Jean-Paul Macher, M.D.

NR435 Erectile Dysfunction in Sleep Apnea and Response to Continuous Positive Airway Pressure
Ismet Karacan, M.D., Mehmet Karatas, M.D.

NR436 Academic Stress and Differential Changes in Immune Response
Sergio M. Gloger, M.D., Patricio Fischman, M.D., Isabel Caldumbide, M.S., Orietta Echavarri, M.S., Paulina Arias, B.S., Javier Puente, Ph.D.

NR437 Attributional and Defensive Styles: Do They Influence Immune Response?
Patricio Fischman, M.D., Sergio M. Gloger, M.D., Orietta Echavarri, M.S., Cristina Ramirez, M.S., Isabel Caldumbide, M.S., Cecilia Sepulveda, M.D.

NR438 Major Depression and Natural Killer Cell Activity: Relation to Severity and Past Antidepressant Medication
Antonio Andreoli, M.D., Steve Keller, Ph.D., Theresa Q. Pascual, LP, John C. Bartlett, M.D.

NR439 A Double-Blind Comparison of Sertraline and Clomipramine in Outpatients with OCD
Jean-Claude Bisserbe, M.D., Robert L. Wiseman, Ph.D., Maureen S. Goldberg, R.N., Roger M. Lane, M.D.

NR440 A Double-Blind, Placebo-Controlled Study of Sertraline in the Treatment of Outpatients with SAD
Adam Moscovitch, M.D., Robert L. Wiseman, Ph.D., Maureen S. Goldberg, R.N., Roger M. Lane, M.D.

NR441 An Open Pilot Study of Sertraline in the Treatment of Outpatients with Pedophilia
John M.W. Bradford, M.D.

NR442 Outcome of Long-Term Psychiatric Hospitalization
Carol L.M. Caton, Ph.D., Alexander Gralnick, M.D., (Posthumously)

NR443 Are Meta-Analysis Reliable? The Evidence From Three Contradictory Meta-Analyses of Treatments in Panic
Larry V. Amsel, M.D.

NR444 A New Method for Quality of Life Assessment: Tableau d'Evaluation Assisstee de la Qualite de Vie
Denis Grabot, M.A., Corinne Martin, M.D., Marc Auriacombe, M.D., Jean L. Tignol, M.D.

NR445 Are Drug Research and Clinical Patients Similar?
Phebe M. Tucker, M.D., Lisa Goulden, Ph.D., Alfretia Scarborough, M.P.H.

NR446 Published Research in Psychiatry: Who Pays?
Julio L. Jane, M.D., P. Murali Doraiswamy, M.D., Vincent Palese, PAC, Lorraine Vinci, M.S.

NEW RESEARCH

Wednesday, May 24, 1995, 3:00 p.m.-5:00 p.m.

New Research 12 – Poster Session – Rooms D128/D129, Level 1, Convention Center

PSYCHOPHARMACOLOGY AND OTHER SOMATIC THERAPIES; BIOLOGICAL PSYCHIATRY; BRAIN IMAGING; NEUROBIOLOGY; AND NEUROPSYCHIATRY

Moderator: Joel E. Kleinman, M.D.

NR447 Outcome in Schizophrenic Patients Switched From Clozapine to Risperidone
Robert Lynn Horne, M.D., Forest Miller, Ph.D.

NR448 Use of Risperidone in a Private Psychiatric Practice
Robert Lynn Horne, M.D., Forest Miller, Ph.D.

NR449 Calcium Uptake into Platelets in Depression
Michael Berk, M.D., Alphonce Nabiswa, M.D., Nicola H. Kirchmann, M.Sc.

NR450 Fluoxetine Treatment of Depression in Medical Students
Michael Berk, M.D.

NR451 Prevalence and Clinical Features of Akathisia in an Acute Inpatient Ward
Domenico Berardi, M.D., Annalisa Giannelli, M.D., Gloria Samory, M.D.

NR452 Neuroleptic-Induced Changes in Plasma Methionine-Enkephalin Degradation
Marion E. Wolf, M.D., Barbara Lesley, R.N., Carol Frenkel, R.N., John Conran, M.D., Edward D. Bukowski, M.D., Aron D. Mosnaim, Ph.D.

NR453 Listening to Antidepressants: Mood Improvement in Psychiatrically Normal Volunteers
Clarice Gorenstein, Ph.D., Valentim Gentil, Ph.D., Marcio Melo, M.D., Francisco Lotufo Neto, Ph.D., Valeria Lauriano, M.D.

NR454 Selective Serotonin Reuptake Inhibitor-Induced Sexual Dysfunction: Efficacy of a Drug (and Sex) Holiday
Anthony J. Rothschild, M.D.

NR455 Safety and Tolerance of Fluvoxamine Versus Sertraline in Depressed Outpatients
Charles B. Nemeroff, M.D., Philip T. Ninan, M.D., James C. Ballenger, M.D., John P. Feighner, M.D., John H. Greist, M.D., William Petterson, M.D.

NR456 Meta-Analysis of Studies on Carbamazepine Augmentation of Neuroleptic Treatment in Schizophrenia
Robert G. Stern, M.D., Larry V. Amsel, M.D., Michael Davidson, M.D., John D. Davis, M.D.

NR457 Carbamazepine, Lithium and the Combination: A Bipolar Maintenance Trial
Kirk D. Denicoff, M.D., Earlian Smith-Jackson, R.N., Elizabeth Disney, B.A., Ali O. Syed, B.S., Gabriele S. Leverich, M.S.W., Robert M. Post, M.D.

NR458 Negative Correlation Between Alpha-1 Acid Glycoprotein Plasma Level and Response to Haloperidol in the Acute Treatment of Schizophrenia
Ilan Levinson, M.D., Stewart B. Levine, M.D.

NR459 A Double-Blind Randomized Study of Three Haloperidol Plasma Levels for Acute Psychosis
Philip G. Janicak, M.D., Javaid I. Javaid, Ph.D., Rajiv P. Sharma, M.D., Anne M. Leach, M.D., S. Dowd, B.S., John M. Davis, M.D.

NR460 The Extrapyramidal Symptom Rating Scale: Revised Factor Structure
Lawrence Annable, D.S., Guy Chouinard, M.D., Andree Ross-Chouinard, M.D.

NR461 ICI 204,636 (Seroquel™): New Preclinical Research Data Confirm Atypical Antipsychotic Actions
Jeffrey Goldstein, Ph.D.

NR462 Sertraline and Fluoxetine in Major Depression
Claudine Mertens, M.D., F. Bartholome, P. Cosyns, M.D., H. D'Haenen, M.D., M. Van Moffaert, M.D.

NR463 Pharmacokinetic and Pharmacodynamic Interaction of Zolpidem and Fluoxetine
Antoni A. Piergies, M.D., Barbara Roth-Schechter, Ph.D., Pam Shinleber, R.N., Lisa McGarry, MT ASCP, Stephane Allard, M.D.

NR464 Cost Benefit of Clozapine Regarding Activity Level
Veronica W. Larach, M.D., Patricia T. Munoz, M.D., Gladys N. Corral, U.N., Isabel E. Hanish, Ph.D.

NR465 Risperidone in the Treatment of First Episode Psychotic Patients: A Double-Blind Multicenter Comparison with Haloperidol
R.A. Emsley, M.D., Robin McCreadie, M.D., Philippe Lemmens, Ph.D.

NR466 Risperidone Once Daily Versus Twice Daily
Barry D. Jones, M.D., Goedele deSmedt, M.D., Philippe Lemmens, Ph.D.

NR467 Are Study Dropouts Different From Completers?
Joyce R. Tedlow, M.D., Maurizio Fava, M.D., Lisa A. Uebelacker, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D.

NR468 Treatment Response in Adults with ADD and Depressive Symptoms
Mady Hornig-Rohan, M.D., Jay D. Amsterdam, M.D.

NR469 Risperidone in the Treatment of Patients with Refractory Psychosis Due to Brain Injury
Kevin M. Furmaga, Pharm.D., Ovidio A. DeLeon, M.D., Shobha B. Sinha, M.D., Thomas H. Jobe, M.D.

NR470 Effects of Pentagastrin in Patients with Social Phobia and Panic Disorder and Healthy Volunteers
Una D. McCann, M.D., Marilla Geraci, M.S.N., Shiyoko O. Slate, B.A., Diana Roscow-Terrill, M.S., Thomas W. Uhde, M.D.

NR471 Selective Serotonin Reuptake Inhibitors Alter Metabolism of Clozapine
Franca Centorrino, M.D., Judith Kando, Ph.D., Ross J. Baldessarini, M.D., Sheila A. Volpicelli, B.S., James G. Flood, Ph.D., Frances R. Frankenburg, M.D.

NR472 Symptom Changes During Drug Washout Periods in Patients with Treatment Resistant Schizophrenia
Anthony G. Kalinowski, Ph.D., Nancy J. Jaretz, R.N., Sarah K. Rosenbloom, B.A., Joseph Yin, Alan I. Green, M.D.

NR473 Differential Effects of Risperidone and Conventional Neuroleptics on Neurocognition: A Pilot Study
Terry E. Goldberg, Ph.D., David G. Daniel, M.D., David Pickar, M.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

NR474 A Clinical Study of Nimodipine and Haloperidol
Kim Hyeongseob, M.D., Whang Taeyeon, M.D., Han Ilwoo, M.D., Park Chongwon, M.D., Kim Jungun, M.D.

NR475 Olanzapine: A New Atypical Antipsychotic Medication
Naveed Iqbal, M.D., Bruce J. Schwartz, M.D., Charles M. Beasley, Jr., M.D., Susan L. Hamilton, M.S., Carol W. Weinstein, M.D., Lloyd Goldsamt, Ph.D.

NR476 Prolactin Changes with Risperidone Treatment
David N. Osser, M.D., Richard I. Shader, M.D.

NR477 Serotonin Dopamine Antagonists in Treatment of Cocaine Abuse
Faiq A. Hameedi, M.D., Conor K. Farren, M.D., Marc I. Rosen, M.D., H. Rowland Pearsall, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

NR478 Clozapine Use in Treatment Refractory Mania and Psychosis
Jayendra K. Patel, M.D., Alan I. Green, M.D., Michael D. Banov, M.D., Mauricio Tohen, M.D., Alan F. Schatzberg, M.D., Jonathan O. Cole, M.D.

NR479 A Randomized Study of Yohimbine and Anetholtrithione on Salivary Secretion in Patients Treated with Tricyclic Antidepressants
Haleh Bagheri, Pharm.D, Laurent Schmitt, M.D., Michel Berlan, Ph.D., Jean Louis Montastruc, M.D., Paul Montastruc, M.D.

NR480 Clozapine Treatment of Patients with Mental Retardation and Psychosis
Richard L. O'Sullivan, M.D., Mark L. Rubin, M.D., Jay Quintal, Psy.D., Lee Baer, Ph.D.

NR481 The Combination of Paroxetine and Neuroleptics in the Treatment of Delusional Depression
Rocco M. Zaninelli, M.D., Manfred Wolfersdorf, M.D., Frank Konig, M.D., Thomas Barg, M.S.

NR482 Evaluation of Antimutagenic Activity of Phenothiazines
Jerzy Waldemar Leszek, M.D., Kazimierz Gasiorowski, M.D., Katarzyna Szyba, Ph.D.

NR483 A Pharmacoeconomic Evaluation of Depot Versus Oral Neuroleptic Therapy
Ronald P. Landbloom, M.D., James L. Roerig, Pharm.D., Beth A. Zander, B.A.

NR484 Clinical Predictors of Acute Risperidone Response in Schizophrenia, Schizoaffective Disorder, and Psychotic Mood Disorders
Paul E. Keck, Jr., M.D., Daniel R. Wilson, M.D., Stephen M. Strakowski, M.D., Susan L. McElroy, M.D., Danielle L. Kizer, B.S., Anthony Balestreri, B.S.

NR485 A Randomized Double-Blind Trial of Risperidone Versus Clozapine for Treatment Resistant Chronic Schizophrenia
G. Bondolfi, M.D., P. Bauman, M.D., Michel Patris, M.D., J.P. May, M.D., U. Billeter, M.D., H. DuFour

NR486 Cardiac Effects of Doxepin and Fluoxetine in Patients with Major Depressive Disorder
Brian Baker, M.B., Paul Dorian, M.D., Paul Sandor, M.D., Colin Shapiro, M.B., Marilyn Jane Irvine, Ph.D.

NR487 Clinical Effects of Clozapine
Pierre-Michel Llorca, M.D., Christophe Lancon, M.D., Pascal Auquier, M.D., Thierry Boujerol, M.D.

NR488 Predictors of Differential Response to Clozapine and Risperidone
David G. Daniel, M.D., Terry E. Goldberg, Ph.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D., David Pickar, M.D., Lisa Lubick, MPP

NR489 A Comparison of Trazodone and Haloperidol for Treatment of Agitated Behaviors in Dementia
David L. Sultzer, M.D., Kevin F. Gray, M.D., Ibrahim Gunay, M.D., M. Andrew Berisford, M.A., Michael E. Mahler, M.D.

NR490 Combined Lorazepam and ECT to Treat Catatonia
Georgios Petrides, M.D., George Bush, M.D., Andrew J. Francis Jr, M.D.

NR491 Risperidone in Institutionalized Psychotic Patients Unresponsive to Conventional Antipsychotic Agents
Eugene G. Evans, Jr., M.D.

NR492 Chronic Benzodiazepine Use in a State System
Daniel J. Luchins, M.D., Mark Alexakos, MAPP

NR493 Combined Desipramine and Fluoxetine Treatment in Refractory Depression
Helen L. Miller, M.D., Pedro L. Delgado, M.D., Ronald M. Salomon, M.D., Robert M. Berman, M.D., Dennis S. Charney, M.D.

NR494 Ziprasidone: A Serotonin 2/D2 Atypical Antipsychotic?
Earl L. Giller, Jr., M.D., James Heym, Ph.D.

NR495 Predictable and Modest Inhibition of Desipramine Clearance by Sertraline at Low and High Doses
Lisa Von Moltke, M.D., David J. Greenblatt, M.D., Richard I. Shader, M.D.

NR496 Risperidone for Polydipsia and Hyponatremia in Schizophrenia
Iyad Y. Khreis, M.D., James R. Slaughter, M.D.

NR497 Carbamazepine: Associated Exfoliative Dermatitis with Severe Eosinophilia
Veronika Solt, M.D., Henry H. Kalir, M.D.

NR498 In Vivo Receptor Occupancy in Rat Brain By Novel and Reference Antipsychotic Drugs
A. Schotte, PFM Janssen, P. Bonaventure, Philippe Lemmens, Ph.D., J.E. Leysen

NR499 Anxiety and Depression Symptoms Control in Oncology: A Double-Blind Placebo Controlled Study Assessing the Effectiveness of Fluoxetine
Darius Razavi, M.D., Jean-Francois Allilaire, M.D.

NR500 Adverse Effects of Two Long-Acting Depot Antipsychotic Drugs
A. S. Shooka, M.B., M.K. Al Haddad, V. Mathur

NR501 Controlled Study of Attitude Change Towards ECT
Jagannathan Srinivasaraghavan, M.D., Pat Alfano, Ph.D., Richard Abrams, M.D.

NR502 Treatment of Compulsive Buying with Fluvoxamine
Donald W. Black, M.D., Janelle M. Gabel, R.N.

NR503 Serotonergic Responsivity in Compulsive Personality
Dan J. Stein, M.B., Robert L. Trestman, M.D., Emil F. Coccaro, M.D., Vivian Mitropoulou, M.A., Eric Hollander, M.D., Larry J. Siever, M.D.

NR504 Metabolic Rates in Brodmann Areas in Alzheimer's Disease
Dan J. Stein, M.B., Monte S. Buchsbaum, M.D., Benjamin V. Segal, M.D.

NR505 CSF Cholecystokin Dynamics in the Human
Thomas D. Geracioti, Jr., M.D., Wendell E. Nicholson, David N. Orth, M.D., Nosa N. Ekhator, M.S., Peter T. Loosen, M.D.

NR506 Sulfotransferase Activity in Different Psychiatric Disorders
Donatella Marazziti, M.D., Lionella Palego, Ph.D., Alfredo Batistini, Ph.D., Chiara Mazzanti, Ph.D., Stefano Silvestri, M.D., Giovanni B. Cassano, M.D.

NR507 Tryptophan Hydroxylase and Impulse Aggression
Yoram Yovell, M.D., Joel Gelernter, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., J. Erdos, M.D., Larry J. Siever, M.D.

NR508 Effect of Repetitive Transcranial Magnetic Stimulation on Mood, Anxiety and Obsessive Compulsive Symptoms in OCD
Benjamin D. Greenberg, M.D., Mark S. George, M.D., Juliet Dearing, B.S., Jonathan Benjamin, M.D., Margaret Altemus, M.D., Barbara Karp, M.D., Eric S. Wassermann, M.D., Mark Hallett, M.D., Dennis L. Murphy, M.D.

NR509 A Three-Year Cohort Study of Seasonal Variation in Platelet Serotonin Uptake
Stephen D. Samuelson, M.D., Jan L. Campbell, M.D., William F. Gabrielli, Jr., M.D.

NR510 Effects of Renal Factors on Plasma and Urinary HVA
Farooq Amin, M.D., Thomas Kahn, M.D., Peter Knott, Ph.D., Michael Davidson, M.D.

NR511 Personality in Temporal Lobe Disease
Gregory P. Lee, Ph.D., David W. Loring, Ph.D., Jason R. Newell, Ph.D., Susan L. Haverstock, M.D.

NR512 Effects of Light Therapy on Melatonin Production in Winter Depressives and Normal Controls
Saeeduddin Ahmed, M.D., Alfred J. Lewy, M.D., Robert L. Sack, M.D., Vance K. Bauer, M.A.

NR513 MRI Hippocampal Volumes in Chronic PTSD
Tamara V. Gurvits, M.D., Martha E. Shenton, Ph.D., Hiroto Hokama, Hirokazu Ohta, M.D., Natasha B. Lasko, Ph.D., Roger K. Pitman, M.D.

NR514 Pergolide in the Treatment of Restless Legs Syndrome
Siong-Chi Lin, M.D., Joseph Kaplan, M.D., Charles Burger, M.D., Paul A. Fredrickson, M.D.

NR515 Visual Analogue Scale for Psychopharmacological Study: Its Reliability and Validity
Yan-Ping Zheng, M.D., Keh-Ming Lin, M.D.

NR516 An Indirect Measure of Dopamine Sensitization by Serum Prolactin Levels in Humans
Matthew D. Wortman, B.S., Sean P. Stanton, B.S., Paul E. Keck, Jr., M.D., Scott A. West, M.D.

NR517 Gender Difference and The Effect of Alpha-methyl-para-tyrosine on Prolactin and Melatonin Secretion
Ralf C. Zimmermann, M.D., Lois E. Krahn, M.D., George Klee, M.D., Peter Y. Lu, M.D., Steven J. Ory, M.D., Siong-chi Lin, M.D.

NR518 Factor Analysis MRI Brain Structure in Schizophrenia
Allen Y. Tien, M.D., Thomas Schaepfer, M.D., Godfrey D. Pearlson, M.D., William W. Eaton, Ph.D., Patrick E. Barta, M.D., Elizabeth Aylward, Ph.D.

NR519 Temporal Lobe Length and Age at Illness Onset in Schizophrenia
George Bartzokis, M.D., Keith Nuechterline, Ph.D., Kevin Laack, Kenneth Dery, B.A., Marguerite Calinan, B.A., Stephen R. Marder, M.D.

NR520 Dynamic Brain Mapping Findings in Children with ADHD
Atilla Turgay, M.D., Edward Gordon, M.D., Martin Vigdor, Ph.D.

NR521 The Use of SPECT in Psychiatry
Prof. M.T. Abou-Saleh, Ph.D.

NR522 A Functional MRI Study of Transient Sadness in Healthy Adult Women: Brain Activity Due to Mood Versus the Effort of Changing Mood
Priti I. Parekh, B.A., Mark S. George, M.D., Mark Willis, Francois Lalonde, Ph.D., Terence A. Ketter, M.D., Robert M. Post, M.D.

NR523 Regional EEG Changes During Guided Recollection of Bereavement
Eric Rubin, M.D., Nina A. Sayer, M.A., James R. Moeller, Ph.D., Bruce M. Luber, Ph.D., Gary P. Katzman, B.S., Harold A. Sackeim, Ph.D.

NR524 Cortical Surface Area Increased in Schizophrenia
Patrick E. Barta, M.D.

NR525 SPECT Changes with Emotional Task in Schizophrenia
Miklos F. Losonczy, M.D., Ileana Berman, M.D., Cecile E. Sison, Ph.D., Clara Schaefer, Ph.D., Edward R. Allan, M.D., Murray Alpert, Ph.D.

NR526 Brain Glucose Metabolic Correlates of Extrapyramidal Syndrome
Benjamin V. Siegel, M.D., Monte S. Buchsbaum, M.D., Daniel Truong, M.D.

NR527 123I B-CIT SPECT Imaging Demonstrates Increased Striatal Dopamine Transporter Binding in Tourette's Syndrome
Robert T. Malison, M.D., Christopher J. McDougle, M.D., Christopher Van Dyck, M.D., Lawrence Scahill, M.S.N., Ronald M. Baldwin, Ph.D., John P. Seibyl, M.D., Lawrence H. Price, M.D., James F. Leckman, M.D., Robert B. Innis, M.D.

NR528 A PET Study of Developmental Stuttering
Glyndon D. Riley, Ph.D., Gerald A. Maguire, M.D., Joseph C. Wu, M.D., Eric A. Klein, B.S.

NR529 Catatonia in Dementia: Three SPECT Scans
Brendan T. Carroll, M.D., H. Ronald Clements, Jr., M.D., Douglas Scharre, M.D.

NR530 Effect of Comorbidity on the Cerebral Blood Flow of Obsessive Compulsive Patients
Jose L. Ayuso-Gutierrez, M.D., Maria I. Lopez-Ibor, M.D., Juan J. Lopez-Ibor, Jr., Jose A. Cabranes, M.D., Jose L. Ayuso-Mateos, M.D., Benedicto Crespo, M.D.

NR531 Acute Tryptophan Depletion in Adults with Autism
Christopher J. McDougle, M.D., Susan T. Naylor, M.S.N., Donald J. Cohen, M.D., Geo Kevork Aghajanian, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D.

NR532 Seasonal Variation of Prolactin Response to m-CPP
Robert A. Grossman, M.D., Lisa J. Cohen, Ph.D., Concetta Decaria, Ph.D., Jennifer Rosen, B.A., Eric Hollander, M.D.

NR533 Chronobiological Analysis of Prolactin in PTSD
Robert A. Grossman, M.D., Rachel Yehuda, Ph.D., Martin H. Teicher, M.D., Robert A. Levengood, M.D., Robert L. Trestman, M.D., Larry J. Siever, M.D.

NR534 Apparent Homologues of the Rat's Sexually Dimorphic Nucleus of the Preoptic Area in the Human and Rhesus Monkey
William M. Byne, M.D.

NR535 Detection of 3a-Hydroxysteroid Dehydrogenases in Human Adult and Fetal Brain
Sardana Belkin, B.S., William M. Byne, M.D., Marilyn Khanna, Ph.D., Kui-Chi Cheng, Ph.D.

NR536 Chronic Antipsychotic Treatment Induces a Long-Lasting AP-1 Complex in the Rat Striatum
Patrick J. Rogue, M.D., Guy Vincendon, M.D.

NR537 Effects of Repeated Cocaine Administration on Sensory Inhibition in Rats: Preliminary Data
Nashaat N. Boutros, M.D., Norman L. Uretsky, Ph.D., Jennifer J. Liu, Ronel Millana

NR538 Protocol for Neuroimmunologic Animal Models for Psychiatric Disease Based on Paraneoplastic Limbic Encephalopathy
John L. Black, M.D., Guy E. Griesmann, M.S., Mieko Oguro-Okano, Ph.D., Terry P. Snutch, Ph.D., Vanda A. Lennon, M.D.

NR539 Menstrual Cycle Effects on Measures of Cognitive Variables
Allan Tasman, M.D., Anita C. Maiste, Ph.D., Theresa A. Hahn, B.S., Rajani Adiga

NR540 Lithium and Neuroleptics in Combination: Is There Enhancement of Neurotoxicity Leading to Permanent Sequelae?
Stephen A. Goldman, M.D.

NR541 Comparison of the CNS Pharmacology of Two Formulations of Bupropion: Sustained Release and Immediate Release
Virginia M. Boncek, B.A., Barry R. Cooper, Ph.D., Frank E. Soroko, B.S., Bernard T. Kenney, B.S.

NR542 Catatonia, Parkinsonism, Tardive Dyskinesia and Akathisia in a Chronically Hospitalized Psychiatric Population
George Bush, M.D., Andrew Francis, M.D., Georgios Petrides, M.D.

NR543 Psychopathology Associated with Intracranial Tumors
M. Beatriz Currier, M.D., Thania V. Quesada, M.D.

NR544 Subtle Neurological Deficits and Psychopathological Findings in a Group of Homeless and Non-Homeless Veterans
Gerard Romain, M.D., Richard Douyon, M.D., Paul A. Guzman, M.D., Sue Ireland, Ph.D., Lourdes M. Mendoza, M.D., Fernando J. Milanes, M.D.

NR545 Laterality of Extrapyramidal Symptoms Related to Positive and Negative Symptoms of Schizophrenia
Dong Won Shin, M.D., Sungkil Min, M.D.

NEW RESEARCH

Thursday, May 25, 1995, 9:00 a.m.-10:30 a.m.

New Research 13 – Oral/Slide Session – Room D130, Level 1, Convention Center

POTPOURRI

Chp.: Francisco Fernandez, M.D.

NR546	Utility of the Obsessive Compulsive Drinking Scale to Measure Outcome During and Alcoholism Treatment Trial Raymond F. Anton, M.D., Darlene H. Moak, M.D., Patricia K. Latham, Ph.D.	9:00 a.m.
NR547	Drug Craving Versus Withdrawal Symptoms: Are They Different? Juris Mezinskis, Ph.D., Eugene C. Somoza, M.D., Susan Dyrenforth, Ph.D., Mark Cohen, Ph.D., R. Jeffrey Goldsmith, M.D.	9:15 a.m.
NR548	Distinguishing Eating Disorder Preoccupations and Ritual Rosalind G. Hoffman, M.D., Steven J. Romano, M.D., Suzanne Sunday, Ph.D., Katherine A. Halmi, M.D.	9:30 a.m.
NR549	Linkage Study of Chromosome 18 Marker Loci and Bipolar Disorder Peter A. Rao, M.D., James Knowles, M.D., Jean Endicott, Ph.D., Jurg Ott, Ph.D., T. Conrad Gilliam, Ph.D., Miron Baron, M.D.	9:45 a.m.
NR550	Enhanced Adrenocorticotropic Hormone Response to Metyrapone in PTSD Rachel Yehuda, Ph.D., Robert A. Levengood, M.D., Ling Song Guo, M.D., Skye A.C. Wilson, B.A.	10:00 a.m.
NR551	Severe Stress Predicts Early HIV Disease Progression John M. Petitto, M.D., Jane Leserman, Ph.D., Diane O. Perkins, M.D., Carole Murphy, M.D., David Gettes, James D. Folds, Ph.D.	10:15 a.m.

NEW RESEARCH

Thursday, May 25, 1995, 9:00 a.m.-10:30 a.m.

New Research 14 – Oral/Slide Session – Room D131, Level 1, Convention Center

MOOD DISORDERS

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

NR552	Classifying Subtypes Among Depressed Inpatients John W. Goethe, M.D., Bonnie L. Szarek, R.N.	9:00 a.m.
NR553	WITHDRAWN	
NR554	Psychopathology in the Relatives of Seasonal Winter Depressives David S. Schlager, M.D., Daniel N. Klein, Ph.D., Joseph E. Schwartz, Ph.D., Karen Kasch, M.S., Laura M. Klein, M.S.W.	9:15 a.m.
NR555	Disability and Depression Among High Utilization Primary Care Patients David J. Katzelnick, M.D., Kenneth A. Kobak, M.S.W., John H. Greist, M.D., James W. Jefferson, M.D.	9:30 a.m.
NR556	Disability in Geriatric Depression George S. Alexopoulos, M.D., Konstantina Vrontou, M.D., Barnett S. Meyers, M.D., Tatsuyuki Kakuma, Ph.D., Robert C. Young, M.D., Maria Feder, M.D.	9:45 a.m.
NR557	The Role of Pterins in Depression and the Effects of Antidepressive Therapy Prof. M.T. Abou-Saleh, Ph.D.	10:00 a.m.

NEW RESEARCH

Thursday, May 25, 1995, 12:00 noon-2:00 p.m.

New Research 15 – Poster Session – Rooms D128/D129, Level 1, Convention Center

ALCOHOL AND SUBSTANCE ABUSE; EATING DISORDERS; INFANT, CHILDHOOD AND ADOLESCENT PSYCHIATRY; COMMUNITY PSYCHIATRY AND PREVENTION; CROSS-CULTURAL AND MINORITY PSYCHIATRY; MANAGED CARE AND HEALTH CARE FUNDING ISSUES; FORENSIC PSYCHIATRY; GENDER ISSUES; ACADEMIC PSYCHIATRY; PRESIDENTIAL THEME: ENCOMPASSING DIVERSITY, DEMANDING EQUITY; COMPUTERS; EPIDEMIOLOGY; AND OTHER PSYCHIATRIC DISORDERS

Moderator: Andrew E. Skodol, M.D.

NR558 Pharmacologic Treatment for the Antisocial Personality Disordered Alcoholic: A Pilot Efficacy Study
Jan L. Campbell, M.D., Elizabeth C. Penick, Ph.D., H. Mikel Thomas, M.D., Barry I. Liskow, M.D., Barbara J. Powell, Ph.D., Elizabeth J. Nickel, M.A.

NR559 Effect of Carbamazepine and Desipramine on Treatment Retention and Urine Toxicology in Outpatient Crack Cocaine Abusers
Jan L. Campbell, M.D., H. Mikel Thomas, M.D., Barry I. Liskow, M.D., William Gabrieli, M.D., Elizabeth C. Penick, Ph.D., Louise J. Laster, B.A.

NR560 Disability Income, Cocaine Use and Repeated Hospitalization Among Schizophrenic Cocaine Abusers: A Government Sponsored Revolving Door?
Andrew L. Shaner, M.D., Thad A. Eckman, Ph.D., Lisa J. Roberts, M.A., Jeffery N. Wilkins, M.D., Douglas E. Tucker, M.D., Jim Mintz, Ph.D.

NR561 Monetary Reinforcement of Cocaine Abstinence in Cocaine Dependent Schizophrenics
Andrew L. Shaner, M.D., Thad A. Eckman, Ph.D., Lisa J. Roberts, M.A.

NR562 Family Physician's Detection of Alcohol Disorders: Survey and Chart Review
Marijo B. Tamburrino, M.D., Denis J. Lynch, Ph.D., Rollin W. Nagel, M.A., Charles B. Travis, M.D.

NR563 Depression Screening in Women: Racial Differences
Marijo B. Tamburrino, M.D., Rollin W. Nagel, M.A., Denis J. Lynch, Ph.D.

NR564 The Effect of Alcohol on Social Phobic Anxiety
Joseph A. Himle, M.S.W., George C. Curtis, M.D., Elizabeth M. Hill, Ph.D., James L. Abelson, M.D., Randolph M. Nesse, M.D., Hedieh Haghighatgou, M.S.W.

NR565 Substance Use Disorders in Schizophrenic, Schizoaffective and Bipolar Patients
Helene Verdoux, M.D., Michel Mury, M.D., Guy Besancon, M.D., Marc L. Bourgeois, M.D.

NR566 The CNS Neurochemistry of Alcoholism
Thomas D. Geracioti, Jr., M.D., Peter T. Loosen, M.D., Michael H. Ebert, M.D., Nosa N. Ekhator, M.S., Donna Burns, R.N., Wendell E. Nicholson, David N. Orth, M.D.

NR567 Crack Dancing: Are There Permanent Neurotoxic Sequelae?
George Bartzokis, M.D., Mace Beckson, M.D., Marguerite Callinan, B.A., Walter Ling, M.D., Stephen R. Marder, M.D.

NR568 Relative Contribution of Negative Emotions to the Severity of Substance Abuse Problems Experienced by Substance Abusers
Michael M. Chang, M.D.

NR569 Geriatric Trauma Patients and Alcohol Use
Mark G. Fuller, M.D., Mark Lovell, Ph.D., Daniel L. Diamond, M.D., Trevor R.P. Price, M.D., Ricard N. Townsend, M.D.

NR570 Contingency Contracting for Illicit Drug Use with Opioid Addicts in Methadone Treatment
Donald J. Tusel, M.D., Nancy A. Piotrowski, Ph.D., Patrick Reilly, Ph.D., Karen L. Sees, D.O., Peter Banys, M.D., Sharon M. Hall, Ph.D.

NR571 Nicotine Craving: A Comparison Between a New Objective Measure and Traditional Self-Report Measures
Neil Hartman, M.D., Sidney Gold, M.D., Nicholas H. Caskey, Ph.D., Bernard M. Kim, B.S., Damian C. Madsen, B.A., Murray E. Jarvik, M.D.

NR572 Validity of the Adolescent Imaginary Urine Drug Screen: Association Between Attitude When Giving Urine and Test Results
Steven L. Jaffe, M.D., Scott W. Henggeler, Ph.D., Roanne L. Jaffe, M.Ed., Susan G. Pickrel, M.D.

NR573 FDOPA Uptake Differences in Cocaine Addicts in Withdrawal and Normal Controls
Clifford B. Widmark, M.D., Joseph C. Wu, M.D., Eric A. Klein, B.S., Kate M. Bell, M.D.

NR574 High Frequency of Intense Dieting Among Abstinent Alcoholics Who Crave Sweets and Rich Foods
Michael J. Bohn, M.D., Dean D. Krahn, M.D., Jack Husted, M.S.W., Beth A. Staehler, Ph.D.

NR575 Changes in Drug Craving During Inpatient Chemical Dependence Treatment
Sue R. Dyrenforth, Juris Mezinskis, Ph.D., Mark Cohen, Ph.D., R. Jeffrey Goldsmith, M.D., Eugene C. Somoza, M.D.

NR576 Brain Metabolism of Cocaine Abusers in Middle Abstinence
Kate M. Bell, M.D., Clifford B. Widmark, M.D., Joseph C. Wu, M.D., Eric A. Klein, B.S., Lori LaCasse, B.S.

NR577 The Prevalence of Substance Use Disorders in Applicants for Thoracic Organ Transplantation
Bradley M. Pechter, M.D., Norman S. Miller, M.D., James P. Houck, M.D., Dina M. Hess, R.N.

NR578 Survey of Sexually Transmitted Diseases in Drug Addiction
Vasant Dhopesh, M.D., Carrie Lainfester, M.H.T.

NR579 Frequency of Dieting in the Sixth Grade Predicts Alcohol and Cigarette Use in the Ninth Grade
Dean D. Krahn, M.D., Douglas Piper, Ph.D., Monica King, M.S., D. Paul Moberg, Ph.D., Laura Olson, M.A., Jiyuan Wu, Ph.D.

NR580 Violence in Substance Abusers
Mace Beckson, M.D., George Bartzokis, M.D., James Herzberg, B.A., Walter Ling, M.D.

NR581 The Diagnosis and Treatment of Chronic Visual Disturbances Following LSD
Henry D. Abraham, M.D.

NR582 Yohimbine Induces Withdrawal and Anxiety Symptoms, and Increased Acoustic Startle Response in Methadone Patients
Susan M. Stine, M.D., John H. Krystal, M.D., Steven M. Southwick, M.D., Christian Grillon, Ph.D., Andrew Morgan, M.D., Dennis S. Charney, M.D.

NR583 Psychological Symptoms and Fenfluramine Treatment of Cocaine Dependence
Steven L. Batki, M.D., Mark Bradley, B.A., Mark D. Herbst, M.D., Tracey Jones, B.A., Michael Markman, B.A., Reese T. Jones, M.D.

NR584 A Double-Blind Placebo Controlled Trial of Fluoxetine for Treatment of Cocaine Abuse
Hyung K. Lee, M.D., Eliseo A. Go, M.D., John B. Osei-Tutu, M.D., Harvey Bluestone, M.D.

NR585 A Multicenter Safety Study of Naltrexone As Adjunctive Pharmacotherapy for Individuals with Alcoholism
Robert S. Croop, M.D., Dominic F. Labriola, Ph.D., Jill M. Wroblewski, M.S., Donald W. Nibbelink, M.D.

NR586 In Search of a Universal Drug Craving Scale
Eugene C. Somoza, M.D., Susan Dyrenforth, Ph.D., R. Jeffrey Goldsmith, M.D., Juris Mezinskis, Ph.D., Mark Cohen, Ph.D.

NR587 Alcoholism and Typology: Relationship to Age of Onset, Family History and Serum Cortisol
Conor K. Farren, M.D., Anthony W. Clarke, M.D., Timothy G. Dinan, M.D.

NR588 Primary Care at a Methadone Clinic
Chandresh Shah, M.D., Lena Simitian, Ph.D., Steven Chen, Ph.D.

NR589 Dual Activation of Dopamine and Serotonin Neurons As a Strategy for Substance Abuse Treatment
Michael H. Baumann, Ph.D., P. Hitzig, Richard B. Rothman, M.D.

NR590 Multivariate Analysis of Addiction Treatment
Norman S. Miller, M.D., Fred G. Ninonuevo, Ph.D., Norman G. Hoffmann, Ph.D.

NR591 Pharmacotherapy and Psychotherapy for Obese Patients with Binge Eating Disorder
Michael J. Devlin, M.D., B. Timothy Walsh, M.D.

NR592 Cholecystokinin Release and Gastric Emptying in Patients with Bulimia Nervosa
Michael J. Devlin, M.D., B. Timothy Walsh, M.D., Harry R. Kissileff, Ph.D., Rodger A. Liddle, M.D., Janet L. Guss

NR593 Tryptophan Depletion Using Revised Amino Acid Mix
Barbara E. Wolfe, M.S.N., Eran D. Metzger, M.D., David C. Jimerson, M.D.

NR594 Comparison of Impulsivity and Aggression in Women with Bulimia Nervosa and Women with Depression
Theodore E. Weltzin, M.D., Gregory G. Kolden, Ph.D., Timothy J. Strauman, Ph.D., Jerry Halverson, B.A.

NR595 Accidental Injuries and Behavioral Problems Among United States Children in Three Ethnic Groups
Regina Bussing, M.D., Edgardo J. Menvielle, M.D.

NR596 Chronic Health Conditions and Transition to Adulthood: Findings From a Cohort Study
Regina Bussing, M.D., Hillevi M. Aro

NR597 Rapidly Alternating Multiple Schedules: A Practical Method of Functional Assessment
Kathleen M. Zanolli, Julie Daggett, M.A.

NR598 Olfactory Thresholds in Boys with Tourette's Syndrome and ADHD
F. Xavier Castellanos, M.D., Nancy E. Harnett, Ph.D., William E. Klein, M.S.E.E.

NR599 Psychopharmacologic Intervention Patterns in Children and Adolescents
Ilisse R. Perlmutter, M.D., Raul R. Silva, M.D., Hollis A. Boggs, B.S.

NR600 Predictors of Firesetting Children with Disruptive Disorders
Gabriel Kaplan, M.D., Haftan Eckholdt, M.A.

NR601 Impulsive Cognitive Style and Outcome in Adolescents
David L. Pogge, Ph.D., John Stokes, Ph.D., Joel Lord, M.A., Philip D. Harvey, Ph.D., William Horan, M.A., Anne Lloyd, M.A.

NR602 Selective Mutism in Preschool Children: Anxiety As a Primary Associated Feature
Dorothy Young, M.S.W., Harry H. Wright, M.D., Tami Leonhardt, Ph.D., Michael Cuccaro, Ph.D., Laureen J. Noll, M.D.

NR603 Predictors of Level of Suicidality in Children's Psychiatric Hospitalization
Dinohra M. Munoz, M.D., Raul R. Silva, M.D., Richard I. Perry, M.D., Valerie Mnuchin, B.S.

NR604 Correlates of Antidepressant Responsive ADHD
Stephen G. Hayes, M.D.

NR605 Selective Serotonin Reuptake Inhibitors in Children: Pulse and Blood Pressure Change
Nancy B. Campbell, M.D., Marijo B. Tamburrino, M.D., Kathleen N. Franco, M.D., Cynthia L. Evans, M.D., Amy Eisaman, Royal Stacy

NR606 The Origins of Child Abuse: New Theory and Research
Max Lesnik-Oberstein, M.D., Arend J. Koers, M.D., Leo Cohen, Ph.D.

NR607 A New Measure for Assessing Trauma in Adolescents
David Bernstein, Ph.D., David L. Pogge, Ph.D., Taruna Ahluvalia, B.A., Leonard Handelsman, M.D.

NR608 A Pilot Study of Attitudes Toward Behavioral Emotional Problems, Psychopathology, and Social Desirability Among Special Education Students
Spyros J. Monopolis, M.D., John Myhill, Ph.D., Peggy Caltrider, M.S.W., Patricia Cronin, M.S.W., Patrick Crouse, M.A.

NR609 Risperidone in the Treatment of Children and Adolescents with Psychotic Illness: A Retrospective Review
Stephen Grcevich, M.D., Robert L. Findling, M.D., S. Charles Schulz, M.D., William A. Rowane II, M.D.

NR610 Families and Homelessness in Mental Illness
Lisa B. Dixon, M.D., Bette Stewart, B.A., Nancy Krauss, M.S.W., Jean Hyde, M.S., Ann L. Hackman, M.D., Anthony F. Lehman, M.D.

NR611 Medication Compliance of Programs of Assertive Community Treatment Patients
Lisa B. Dixon, M.D., Peter Weiden, M.D., Anthony F. Lehman, M.D., Michael A. Torres, M.D.

NR612 The Efficacy of Respite Care in Psychiatry
Jeffrey L. Peters, M.D., George G. Dougherty Jr, M.D., Lisa Fitzsimmons, M.S.W., Joanne Karcher, R.N., Daniel P. van Kammen, M.D.

NR613 Correlation of Family Physician Demographics with Psychiatric Referral Patterns
Gregory E. Shadid, M.D., John Gastorf, Ph.D., Joyce A. Tinsley, M.D.

NR614 Quality of Life: Exploring How Patients Change
Sharon G. Dott, M.D., David P. Walling, Ph.D.

NR615 Persons with Disabilities in Public Housing: Resident Preferences, Supports and Service Needs
Susan J. Boust, M.D., Earl H. Faulkner, M.A.

NR616 Psychiatric Care in Emilia-Romagna 1978-1994: A Soft Revolution
Angelo Fioritti, M.D., Russo Lo, M.D., Giovanni de Girolamo, M.D.

NR617 Depression in Asian-Americans
Sudhakar Madakasira, M.D.

NR618 Emotional Disorders in Adolescent Refugees From Central America and South East Asia
Cecile Rousseau, M.D., Anne Levensque, M.Sc.

NR619 An Approach to Engaging in Culturally Sensitive Research on Puerto Rican Youth
Odette Alarcon, M.D., Sumru Erkut, Ph.D., Cynthia Garcia-Coll, Ph.D.

NR620 Development of a Scale to Measure Japanese-American Values and Attitudes
Neal Anzai, M.D., Junji Takeshita, M.D., Leslie A. Matsukawa, M.D., Satoru Izutsu, Ph.D., Roger Hamada, Ph.D., Linda B. Nahulu, M.D.

NR621 Childrearing Practices in Japan and Canada
Susanne I. Steinberg, M.D., Hiromu Kohzu, M.D., Sophie Mainville, B.N., Megumi Oba, Kimiyo Hayakawa, M.A., Francine Houle, R.N.

NR622 Polypharmacy: A Problem of the Decade of the Nineties
Marion E. Wolf, M.D., Edward D. Bukowski, M.D., John Conran, M.D., Larisa Sirotovskaya, M.D., Valery Kagan, M.D., Aron D. Mosnaim, Ph.D.

NR623 Long-Term Disability Benefits for Chronic Fatigue Syndrome
Peter Manu, M.D., Thomas J. Lane, M.D.

NR624 Psychometric Properties of a Decision Support Tool
William M. Glazer, M.D., Geoffrey Gray, Ph.D.

NR625 The Behavioral Health Care Outcomes Project: Part II. The 15 Minute Psychiatric Medication Visit
Robert Raskin, Ph.D., Jill Novacek, Ph.D.

NR626 Court Ordered ECT at Veterans Affairs Hospitals in Illinois
Jagannathan Srinivasaraghavan, M.D., Atul R. Mahableshwarkar, M.D.

NR627 Appropriateness of Forensic Hospital Admissions
Toshiyuki Shibata, M.D., R. Andrew Schultz-Ross, M.D., Carole McLeod, M.A.

NR628 Patients' Attitudes Regarding Forced Medication
Lanna M. Moore-Duncan, M.D., William M. Greenberg, M.D., Rachel Herron, M.S.W.

NR629 Mental Disorders and Homicidal Behavior
Markku E.J. Eronen, M.D., Jari Tiihonen, Ph.D., Panu Hakola, Ph.D.

NR630 Biological Predictors of PTSD Following Rape
Rachel Yehuda, Ph.D., Heidi S. Resnick, Ph.D., Roger K. Pitman, M.D., David W. Foy, Ph.D.

NR631 Major Depression and Reproductive Function in Women
Joyce Meyers, M.D., Melissa Abraham, B.A., Joseph F. Borus, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

NR632 Gender and Age Differences in Hospitalization and Mortality in Patients with Epilepsy
Daniel P. Chapman, Ph.D., Russell Roegner, Ph.D., Elizabeth K. Lloyd, M.S., John R. Livengood, M.D.

NR633 The Current State of Psychiatric Care in Italy: An Overview
Giovanni de Girolamo, M.D., Angelo Fioritti, M.D.

NR634 Women Veterans in Inpatient Psychiatric Care
Sarz Maxwell, M.D., Janet K. Willer, Ph.D., Jeffrey G. Stovall, M.D., Sandra G. McRae, Ph.D., Linda S. Grossman, Ph.D., Rebecca Nelson, M.A.

NR635 Automated Patient Assessment to Improve Quality
James R. Westphal, M.D., Martin Williams, Ph.D., Enid M. Hunkeler, M.A.

NR636 Assessing Women for Mental Illness and Help Seeking Behavior in Primary Care
Marian I. Butterfield, M.D., Cedar Koons, M.S.W., Andrea Wilks, F.N.P., Lori Bastian, M.D.

NR637 Genital Reflexes Elicited By Stimulation of Autonomic and Somatic Nerves in the Investigation of Diabetic Impotence
Ismet Karacan, M.D., Yakup Sarica, M.D., Mehmet Karatas, M.D., Hacer Bozdemir, M.D., Constance A. Moore, M.D.

NR638 Obsessive-Compulsive Symptom Profile in Gilles De La Tourette Syndrome and OCD: A Phenomenological Study
Valsamma Eapen, M.B., Mary Robertson, M.D.

NR639 Genomic Imprinting in Tourette Syndrome
Valsamma Eapen, M.B., Mary Robertson, M.D., Jane O'Neil, M.B., Hugh Gurling, M.D.

NR640 Alcohol and Drug Use Disorders in Adults with ADHD: Effect of Psychiatric Comorbidity
Timothy E. Wilens, M.D., Joseph Biederman, M.D., Erik Nick, B.A., Stephen V. Faraone, Ph.D.

NR641 A Double-Blind Comparison of Desipramine and Placebo in Adults with ADHD: Preliminary Results
Timothy E. Wilens, M.D., Jefferson B Prince, M.D., Joseph Biederman, M.D., Thomas J. Spencer, M.D., Daniel A Geller, M.D., Rebecca Warburton, B.A., Phoebe Moore, B.A., Colleen E. Linehan, B.A., David R. Schleifer, B.A.

NR1 Monday, May 22, 9:00 a.m.-10:30 a.m.

Relationship Between Frontal Lobe and Serotonergic Dysfunction in OCD

Cheryl M. Wong, M.D., Psychiatry, Mt. Sinai Medical School, 1 Gustave Levy Place, New York, NY 10029; Concetta Decaria, Ph.D., Lisa J. Cohen, Ph.D., Bonnie R. Aronowitz, Ph.D., Daphne Simeon, M.D., Eric Hollander, M.D.

Summary:

Studies of obsessive compulsive disorder (OCD) have demonstrated both neuropsychological serotonergic (5-HT) dysfunction. However, none have integrated these two spheres. We report concommitant abnormalities in both areas which may impact on identification and treatment in OCD patients. On neuropsychological testing, we utilized the Trailmaking B-A (cognitive set-switching) to highlight executive function abnormalities in OCD patients (N = 50) and normal controls (N = 31). OCD patients were found to be significantly impaired on Trails B-A. Prolactin response to double-blind, single dose m-CPP and placebo served as a measure of 5-HT sensitivity. OCD patients (N = 42) had a blunted prolactin response to m-CPP in contrast to normal controls (N = 15) ($F = 2.462$, $dF = 3.62$, $p = 0.06$). Of interest, peak delta prolactin response to m-CPP significantly negatively correlated with frontal lobe set-switching impairment ($r = 0.37$, $n = 26$, $p = 0.03$). This suggested that OCD patients with greater frontal lobe impairment (perhaps associated with increased harm avoidance) had concommitantly more substantial serotonergic dysfunction. This finding may identify a subset of OCD patients who have a favorable response to serotonin reuptake inhibitors.

NR2 Monday, May 22, 9:00 a.m.-10:30 a.m.

Growth Hormone Response to Clonidine and Apomorphine in Panic Disorder

William Pitchot, M.D., Psychiatry, University of Liege, Chu Du Sart Tilman, Liege B 4000, Belgium; Michel Hansenne, B.Sc., Antonio Gonzalez Moreno, M.D., Marc M. Ansseau, M.D.

Summary:

Several lines of evidence suggest an implication of both noradrenergic and dopaminergic functions in the biology of panic disorder (PD). In particular, a blunted growth hormone (GH) response to clonidine, an α2-adrenergic agonist, has been found in five of seven studies on patients with panic disorder (Schittecatte et al. 1992). Moreover, recent reports using several different probes (yohimbine, caffeine, glucose, GHRH) failed to induce normal increase of GH in PD patients. These observations raised the possibility that PD might be a condition characterized by an intrinsic abnormality in the hypothalamic-GH-somatomedin axis (Uhde et al. 1992). The purpose of this study is to assess the pattern of GH response to injection of both clonidine and apomorphine (a dopaminergic agonist) in PD patients. Therefore, we measured the GH response to clonidine and apomorphine in 14 drug-free inpatients meeting Research Diagnostic Criteria (RDC) for panic disorder who were age- and gender-matched with 14 major depressive, and 14 minor depressive inpatients. GH was assayed at -20, 0, 20, 40, 60, and 120 min. after either clonidine (0.15 mg iv) or apomorphine (0.5 mg sc), with an interval of two days between the tests. There was no significant difference in mean, weight or drug-free period between the three groups. The three groups differed significantly in the GH peak response: after clonidine (mean $\pm$ SD), 10.5 $\pm$ 11.0 ng/ml in panics, 2.9 $\pm$ 3.2 ng/ml in major depressives, and 10.6 $\pm$ 8.7 ng/ml in minor depressives; after apomorphine, 31.1 $\pm$ 13.0, 5.8 $\pm$ 4.5, 22.3 $\pm$ 16.4, respectively. While there were significant differences between panics and major depressives, and between major and minor depressives after both clonidine and apomorphine, panics did not significantly differ from minor depressives on either tests. These results do not provide support to the catecholaminergic hypothesis of panic disorder and suggest that the hypothalamic-GH-somatomedin axis could be intact in PD.

NR3 Monday, May 22, 9:00 a.m.-10:30 a.m.

Growth Hormone Response to Apomorphine in OCD

William Pitchot, M.D., Psychiatry, University of Liege, Chu Du Sart Tilman, Liege B 4000, Belgium; Michel Hansenne, B.Sc., Antonio Gonzalez Moreno, M.D., Marc M. Ansseau, M.D.

Summary:

Several lines of evidence suggest a role for depoamine in the pathophysiology of obsessive compulsive disorder (OCD). Indeed, some trials have shown the efficacy of neuroleptic addition in the treatment of OCD patients. In this study, we assessed the growth hormone (GH) response to apomorphine (a dopaminergic agonist) 0.5 mg s.c. in eight drug-free inpatients (6M, 2F, mean age (SD) = 34.7 (12.6) meeting DSM-III-R criteria for OCD without major depression who were compared with eight male healthy volunteers (mean age (SD) = 27.1 (8.5)). The two groups did not differ in their mean GH peak response: 12.4 $\pm$ 9.7 ng/ml in OCD vs 21.1 $\pm$ 14.2 ng/ml in normal controls ($F = 0.9$, $df = 3,13$, $p = 0.37$). The results do not support the hypothesis of a dopaminergic overactivity in OCD.

NR4 Monday, May 22, 9:00 a.m.-10:30 a.m.

ECT for Severe Tardive Dystonia

Teodor T. Postolache, M.D., Psychiatry, Beth Israel Med. Ctr., First Avenue at 16th Street, New York, NY 10003; Jorge H. Londono, M.D., Robert G. Halem, M.D., Mitchell D. Newmark, M.D.

Summary:

Tardyve dystonia (TDt), a particularly refractory side effect of neuroleptics was partially and temporarily improved with ECT in two previous case reports. We describe another prominent temporary partial response of TDt to ECT.

A 34-year-old man with chronic schizophrenia who was taking haloperidol, developed severe TDt, based on the criteria by Burke et al. Patient presented with severe retrocollis, torticollis, and opisthotonos. Previous treatments for dystonia failed. Patient received 11 ECT treatments without complications. Haloperidol was continued during ECT. Clinical observations using the AIMS scale were made by an independent observer at baseline, after each treatment, and for three weeks after ECT. No improvement was noted after six ECT treatments. After the seventh, his retrocollis and torticollis began to improve, becoming minimal on final observation. The opisthotonos improved modestly. There was complete remission of athetosis. After ECT, patient was maintained on clozapine. Patient's improvement was stable for two months, with deterioration afterwards. After five months, patient's TDt was slightly better compared to baseline. This closely parallels the description by Adityanjee et al. with improvement after six treatments and maximum benefits after 11. Similarly, the results were short lasting.

NR5 Monday, May 22, 9:00 a.m.-10:30 a.m.

Ipsapirone Challenge in Personality Disorders

Jake Falk, M.D., Psychiatry, Mt. Sinai School of Med., 1 Gustave Levy Place Box 1230, New York, NY 10029; Robert L. Trestman, M.D., Rene Kahn, M.D., Larry J. Siever, M.D.

Summary:

Background: Dysregulation of the central serotonergic (5HT) system has been associated with personality disorders and with suicidality, impulsive aggression, and irritability, utilizing CSF 5-HIAA and fenfluramine challenge test, which is not selective for any serotonin receptor subtype as a serotonergic measure. A dose response study of ipsapirone (IPS), a 5HT-1A agonist, has shown that it is a useful probe of 5HT-1A function in normal subjects when temperature and cortisol are used as response variables. To preliminarily investigate the potential usefulness of IPS as a possible 5HT-subtype specific probe in personality disorder patients, we did a pilot study evaluating the response to IPS in patients and normal controls (NC).

Methods: Twenty mg of IPS was administered orally in a placebo-controlled double-blind design to 10 NC and nine patients with DSM-III-R personality disorder. Temperature, CORT, and prolactin (PRL) levels were measured prior to IPS/placebo administration and at half-hour intervals over the next three hours.

Results: IPS significantly reduced temperature in all subjects ($F[1,21] = 13.3$, $p < .01$) and increased CORT levels ($F[1,22] = 9.27$, $p < .01$). There was no diagnosis by drug interaction in either of the two measures. The temperature response to IPS correlated inversely with PRL response to fenfluramine ($r = 0.82$, $p < .01$) and positively with the Barratt Impulsiveness Scale (Risk Taking subscale; $r = 0.86$, $p < .01$).

Conclusions: Although this sample size was too small to draw any definitive conclusions, temperature and possibly CORT response to IPS and their clinical correlates may be useful measures in future studies of impulsivity in personality-disordered patients.

NR6 Monday, May 22, 9:00 a.m.-10:30 a.m.

Risperidone in Dementia with Behavioral Disturbances

Neizo Prado, M.D., Psychiatry, Hillside Hospital, 75-59 263rd St. Lowenstein Res, Glen Oaks, NY 11004; Elisse Kramer-Ginsberg, Ph.D., Neil Kremen, M.D., Patricia Hanan, R.N.C., Allan Z. Safferman, M.D.

Summary:

Behavioral disturbances frequently complicate dementia and necessitate psychopharmacological treatment. Conventional neuroleptics are regularly prescribed; however, side effects and inconsistent efficacy often limit enthusiasm. Few reports exist in elderly patients on the use of risperidone, a recently approved novel neuroleptic with efficacy in schizophrenia.

Objective: To evaluate the benefit and side effect profile of risperidone—a novel neuroleptic—in elderly, demented patients with behavioral disturbances.

Methods: DSM-III-R demented patients with agitation ($n = 18$) significant enough to warrant inpatient geropsychiatric admission were treated openly with risperidone. Dose range was individually adapted from 0.5 to 4.0 mg per day. Pre- and post-treatment symptomatology were assessed via BPRS, CGI (for agitation), BEHAVE-AD, Cohen-Mansfield Agitation Inventory (CMAI), MMSE, and Multidimensional Observational Scale for Elderly Subjects (MOSES). Extrapyramidal side effects were monitored with the AIMS and modified Simpson Dyskinesia Scale (SDS).

Results: Mean age +/- SD of patients was 81.4 +/- 5.5 years. Seven males and 11 females participated. Pre-treatment mean MMSE was 10.11 +/- 7.90. Risperidone administration resulted in significant decreases on BPRS ($p < .0001$), CGI ($p < .0001$), BEHAVE-AD ($p < .0001$), CMAI ($p < .0001$), and MOSES total ($p < .01$) and subscale (irritibility, self-care) ($p < .01$) ratings. Cognitive status (MMSE) was unaffected. Extrapyramidal ratings did not worsen during treatment. Drug was discontinued in two patients secondary to orthostatic hypotension.

Conclusions: To our knowledge, these preliminary open-label findings represent one of the only reports on risperidone use in the "old-old" elderly. Data suggest that low-dose risperidone may be an effective new alternative with an acceptable side effect profile in the psychopharmacological management of agitation/psychosis complicating dementia in the elderly. Monitoring for cardiovascular side effects is essential.

NR7 Monday, May 22, 9:00 a.m.-10:30 a.m.

Switching From Carbamazepine to Clozapine

Ataru Nakamura, M.D., Epidemiology, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Jose M. Benzo, M.D., Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D.

Summary:

Background: Limiting the overlap between carbamazepine (CBZ) and clozapine (CLZ) had been recommended because of the concern that combined use of these agents may increase the risk for granulocytopenia or agranulocytosis.

Objectives: To study the changes in the white blood cells (WBC) in patients who switched from CBZ to CLZ.

Methods: From hospital charts we collected information of all patients who received CBZ and CLZ during the same hospitalization.

Results: We identified 24 psychotic inpatients given both agents: by ≤ 5 days washout ($n = 20$), or together ($n = 4$). The mean days of washout was 3.9 ± 4.3. Four patients received both agents for 13.2 ± 15.0 days. The mean WBC during CBZ treatment was 7746.0 ± 1897.6 (neutrophils = 5007.4 ± 1636.6) and that for CLZ was 8297.8 ± 2163.0 (neutrophils: 5532.3 ± 1939.8). There was no statistically significant change in the WBC after switching from CBZ to CLZ. In addition, there was no case of granulocytopenia (neutrophils < 1500/μl) or agranulocytosis during the period of follow-up after the switch occurred 24.3 ± 13.0 days ($n = 18$) and 18 ± 6 months ($n = 6$).

Conclusion: The switch form CBZ to CLZ was safe and did not affect the WBC values at follow-up.

NR8 Monday, May 22, 9:00 a.m.-10:30 a.m.

Exacerbation Risk Following Withdrawal of Oral and Depot Neuroleptic Treatment of Psychotic Patients

Adele C. Viguera, M.D., South Belknap, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Ross J. Baldessarini, M.D., Daniel P. van Kammen, M.D., Trisha Suppes, M.D.

Summary:

Recurrences in psychotic and major mood disorders are common; while benefits of maintenance treatment are substantial, the significance of interrupting such therapies is not as clear. Our objective was to define risks-over-time of major exacerbation in chronic idiopathic psychotic disorders following abrupt discontinuation of ongoing maintenance neuroleptic treatment in comparison with previously determined risks after stopping lithium in manic-depressive disorders.

We searched for studies involving abrupt discontinuation of long-term oral maintenance treatment in schizophrenia that provide data on individual-time-to-recurrence. Survival analysis and curve-fitting were used to compute time-to-50% recurrence ($ET_{50} \pm$ SEM; median "survival" time).

Data concerning 984 subjects withdrawn from oral neuroleptics were compared with 83 subjects stopping depot neuroleptics and 101 bipolar patients withdrawn from lithium. $ET_{50} \pm$ SE was 4.0 ± 0.1 (oral), 6.7 ± 0.3 (depot), and 3.2 ± 0.2 months (lithium), and 12-month risks for "relapse" were 83%, 59%, and 78%, respectively (oral neuroleptic differed significantly from depot, but not lithium).

Risk of psychotic exacerbation is high within the first several months of discontinuing oral neuroleptics, reduced or delayed after long-acting neuroleptics, and similar to that following lithium in bipolar disorder, in which an iatrogenic-pharmacodynamic contribution is strongly suspected. The risk rates computed may be informative for research protocols and for clinical treatment.

NR9 Monday, May 22, 9:00 a.m.-10:30 a.m.

Risperidone Treatment of Schizophrenia in a State Hospital

Zafar Y. Ibrahim, M.D., Psychiatry, Case Western Reserve, 11100 Euclid Avenue, Cleveland, OH 44106; Peter J. Buckley, M.D., Karl Donenwirth, Kenneth E. Bayer, B.S., Christine Lys, B.A., S. Charles Schulz, M.D.

Summary:

Introduction: Multicenter trials of risperidone suggest that this agent possesses significant antipsychotic efficacy, in tandem with a relatively more benign side-effect profile than either conventional antipsychotics or clozapine. However, its efficacy in chronic, treatment-refractory schizophrenia is presently unclear.

Method: Symptomalogy data were prospectively collected on the use of risperidone in patients with DSM-III-R schizophrenia (mean age 36.6 years) who are long-stay patients (mean length of stay 10 years) in a state hospital.

Results: In most cases, risperidone was initiated by "overlapping" with conventional antipsychotics, and 6–8 mg risperidone was the most common maintenance dose. Available data on 21 patients show an improvement of modest extent in many patients; five patients demonstrated a reduction equal or in excess of 20% of pretreatment BPRS.

Conclusion: Risperidone can be useful in the treatment armamentarium for patients in state institutions.

NR10 Monday, May 22, 9:00 a.m.-10:30 a.m.

Behavioral Subtypes of Alzheimer's Disease: Preliminary Data Analyses

Raymond L. Ownby, M.D., Psychiatry, University of Miami, 1790 SE 23rd Ave #6B, Ft. Lauderdale, FL 33316-3657

Summary:

Objective: This study investigated whether behavioral subtypes could be defined in a group of mildly affected AD patients, based on assessment of their psychiatric symptoms. It also investigated the extent to which subtypes could be related to demographic variables, cognitive status, and duration of illness.

Method: Ratings of 112 AD patients on the Brief Psychiatric Rating Scale were factor analyzed (results presented elsewhere). Factor scores on each of the resulting factors were calculated and used in a K-means cluster analysis to detect whether discrete behavioral subtypes could be identified. Scores from the Mini-Mental State Exam and the variable estimated duration of illness were also included in the analysis. The resulting clusters were compared across demographic, neurological, and other behavioral variables to assess whether they represented definable groupings rather than randomly-generated clusters.

Results: Five subtypes were identified, including: 1) cognitively disorganized, 2) mildly depressed and paranoid, 3) agitated, 4) anxious, and 5) asymptomatic. Clusters were shown to differ significantly from each other on several demographic, medical, and behavioral measures external to those used for clustering.

Conclusions: Results are consistent with previous subtype research and have implications for assessment and treatment of psychiatric symptoms among mildly affected AD patients. Results may also be related to differential involvement of several neurotransmitter systems in each subtype.

NR11 Monday, May 22, 9:00 a.m.-10:30 a.m.

Association of Thyroxin Level with Rate of Progression in Alzheimer's Disease

Ibrahim Abi-Rafeh, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue Ste 702, Miami, FL 33136; Steven Sevush, M.D., Richard S. Mallia, B.A.

Summary:

Objectives: Recent studies have indicated a possible association between thyroid disease and Alzheimer's disease (AD). To determine whether variations in thyroid function affect the AD pathologic process, we examined the correlation between thyroid function and progression of AD.

Method: 66 subjects were drawn consecutively from patients evaluated at the University of Miami Memory Disorders Clinic who met NINCDS criteria for probable AD and who had two or more clinic visits separated by at least six months. T4 and TSH serum levels were obtained on the first visit. Folstein MMSE scores were used to calculate the rate of cognitive decline. Multiple regression analysis, controlled for patient age and MMSE score, was used to assess the relationship between thyroid measures and rate of decline.

Results: T4 levels correlated significantly with subsequent rate of decline MMSE scores ($F = 4.23$, $p = 0.04$) with higher T4 levels associated with more rapid decline. No correlation was found between TSH levels and MMSE decline.

Conclusion: The positive correlation between T4 and rate of decline suggests a possible role for thyroxine in facilitating the AD disease process. Examination of the effect of thyroid replacement therapy on the rate of AD progression may shed further light on this issue.

NR12 Monday, May 22, 9:00 a.m.-10:30 a.m.

Delusions of Theft and Premorbid Personality Traits in Alzheimer's Disease

Rene A. Poveda, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue Ste 702, Miami, FL 33136; Gloria Peruyera, B.A., Sharon Brizel, Steven Sevush, M.D.

Summary:

Objectives: Delusions of theft are variably present in patients with Alzheimer's disease (AD). To determine whether premorbid personality characteristics might predict the subsequent appearance of delusions of theft in AD patients, we examined with relationship between delusions of theft and three a priori chosen premorbid personality traits.

Method: 46 subjects meeting criteria for NINCDS probable AD were selected for study. Primary caregivers quantified the presence of each of the following three premorbid patient characteristics: aggressiveness/competitiveness, suspiciousness, and a tendency toward magical thinking. They were also asked whether delusions of theft had been present at any time during the patient's illness. Multiple regression analysis, controlled for disease severity and duration, was used to assess the relationship between the premorbid personality characteristics and the subsequent occurrence of delusions of theft.

Results: The occurrence of delusions of theft correlated significantly with aggressiveness/competitiveness ($F = 20.86$, $p = .0001$) but not with the other traits. The association was characterized by a Pearson $r = .72$, accounting for 52.2% of the observed variance.

Conclusions: Occurrence of delusions of theft correlated strongly with a premorbid history of aggressiveness/competitiveness in AD patients. This finding supports the notion that clinical heterogeneity of AD may be explained, in part, by variations in premorbid patient personality characteristics.

NR13 Monday, May 22, 9:00 a.m.-10:30 a.m.

Impact of Patient Gait Impairment on a Caregiver's Well-Being in Alzheimer's Disease

Paul A. Guzman, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue Ste 702, Miami, FL 33136; Miguel Alfonso, M.D., Mery Lossada, M.D., Steven Sevush, M.D.

Summary:

Objective: Gait impairment causes significant morbidity in patients with Alzheimer's disease (AD). Its impact on caregivers has not been systematically explored. In this study, we examined the relationship between AD patient gait impairment and a quantitative measure of caregiver depression.

Method: Ninety-eight patients (mean age = 76.4 +/- 7.78, mean Mini-Mental Status Examination (MMSE) score = 14.1 +/- 7.29) meeting NINCDS criteria for probable AD and accompanied by their primary caregiver were selected consecutively from patients being evaluated at the University of Miami Memory Disorders Clinic. Gait was assessed quantitatively by direct examination. Caregiver depression was rated according to the CES depression scale. Multiple regression analysis was used to assess the relationship between patient gait impairment and caregiver depression, controlled for patient age and dementia severity measured by MMSE.

Results: Patient gait correlated significantly with caregiver CES score ($F = 6.18$, $p = .015$).

Conclusions: Gait impairment was associated with caregiver depression. Possible causes of this association include: increased caregiver burden caused by patient immobility; increased caregiver awareness of patient's illness following appearance of physical deficits, and impact on the caregiver of comorbid disease processes (such as Parkinson's disease) associated with gait impairment. Correlation of gait with other clinical features of AD may help clarify this issue.

NR14 Monday, May 22, 9:00 a.m.-10:30 a.m.

Comparison of Mini-Mental State Exam with the Mental Alteration Test for Assessing Cognition in Geriatric Psychiatric Patients and Normal Controls

Eric Siedenburg, B.A., Psychiatry, NY Medical College, 314 East 41st #305-B, New York, NY 10017; Stephen B. Billick, M.D., Woodward Burgert, B.A.

Summary:

The Mental Alteration Test is a new assessment device for cognition in patients that requires only 60 seconds to administer. The Mini-Mental State Exam has been more widely used but requires five to 10 minutes for administration. Both tests were administered to 20 geriatric psychiatric inpatients, 15 geriatric control noninpatients, eight adult nongeriatric psychiatric inpatients, and four normal young adult controls.

There was a very significant statistical correlation between MMSE and MAT scores in all four groups. There was a very high statistical correlation between MMSE score less than 24 and MAT scores less than 16. The MAT showed both excellent specificity and good sensitivity.

The Mental Alternation Test is a quick, efficient, sensitive, and specific test for the rapid assessment of cognitive screening in geriatric psychiatric patients. This study provides further validation of the MAT.

NR15 Monday, May 22, 9:00 a.m.-10:30 a.m.

Platelet Serotonin Concentration Correlates with Dementia Severity in Patients with Probable Alzheimer's Disease

Richard S. Mallia, B.A., Psychiatry, University of Miami, 1400 NW 10th Avenue Ste 702, Miami, FL 33136; Steven Sevush, M.D., Adarsh Kumar, Ph.D., Mahendra Kumar, Ph.D., Carl Eisdorfer, M.D.

Summary:

Objective: Previous studies have suggested that platelet serotonin uptake is lower in patients with Alzheimer's disease (AD) than it is age-matched normal controls. Direct measurement of the serotonin gradient across the platelet membrane (SGPM) has corroborated the results of the earlier kinetic studies. The purpose of the present study was to extend the between-group findings by evaluating the correlation between SGPM alteration and dementia severity within a group of AD patients.

Method: Sixteen subjects meeting NINCDS criteria for probable AD were selected for study. Dementia severity was assessed using Folstein's Mini Mental Status Exam. Extracellular and intracellular platelet serotonin concentrations were measured using the method of Kumar et al. (1990). Multiple regression analysis was performed with dementia severity serving as the independent variable, SGPM as the dependent variable, and age as a covariate in the analysis.

Results: SGPM correlated significantly with dementia severity ($F = 10.04$, $p = .007$), independent of patient age.

Conclusions: The correlation of SGPM with AD dementia severity suggests that the decline in transmembrane serotonin gradient is not merely a marker that distinguishes AD patients from normal controls, but that an alteration in serotonin transport across platelet membranes may be a feature of the AD process itself.

NR16 Monday, May 22, 9:00 a.m.-10:30 a.m.

Selective Serotonin Reuptake Inhibitors for the Treatment of Depression and Psychosis in Dementia

Vijay K. Dewan, M.D., Psychiatry, University of NE Med Ctr., 600 S. 42nd Street, Omaha, NE 68198; William J. Burke, M.D., William H. Roccaforte, M.D., Steven P. Wengel, M.D., Sunil R. Rangwani, M.D., David G. Folks, M.D.

Summary:

Objective: Dementia is frequently accompanied by depression and psychosis. Recently we described a beneficial effect of SSRIs in patients with this symptom complex. This study extends these observations on the effectiveness of SSRIs for the treatment of depression and psychosis complicating dementia.

Method: All charts on an outpatient geriatric psychiatry service were reviewed to identify patients treated with SSRIs for this symptom complex. Scores on the Mini-Mental State Exam (MMSE) and the Geriatric Depression Rating Scale (GDS), which all patients completed as part of their initial evaluation, were recorded. A Clinical Global Impression (CGI) was derived from a review of the treatment history.

Results: Eighteen patients were identified who were treated with an SSRI for this indication. Their average age was 81, their mean GDS was 7.3, and their MMSE 15.3. Fifteen were treated with sertraline, two with paroxetine, and one with fluoxetine. On follow-up, 16 of 18 patients exhibited mild to moderate improvement in symptoms, with a mean CGI of 1.6. Behavioral symptoms were not aggravated by treatment in any case.

Conclusion: The results of this retrospective study suggest that SSRIs may be useful in the management of both the depression and psychosis associated with dementia. However, prospective studies are needed to strengthen this conclusion.

NR17 Monday, May 22, 9:00 a.m.-10:30 a.m.

Geropsychiatric Consultation in Nursing Homes: Quality, Cost Effective Care

Beverly K. Young, M.D., Psychiatry, Oregon Health Science, 3181 S.W. Sam Jackson Park Rd., Portland, OR 97201; David M. Smith, M.D., Linda K. Ganzini, M.D.

Summary:

As part of an initiative to improve care of veterans in nursing homes, two geropsychiatrists traveled to select nursing homes, providing consultation when acute behavioral changes occurred. Early evaluation of behavioral disturbances with on-site intervention was postulated to improve care while avoiding costly utilization of emergency and inpatient services.

Records of the first ten consultations were analyzed. Behavioral changes identified for evaluation included depression, agitation, noncompliance, and anxiety. Only one patient had received an examination by the nursing home physician in response to the behavioral change. Three cases had ER evaluations without identifying the correct diagnosis or providing a successful intervention. Nursing home staff complained of poor access to geropsychiatric care.

Four patients had a medical illness responsible for the behavioral disturbance. Interventions included treatment of vitamin B12 deficiency and hypoglycemia but medical hospitalization was necessary for two with diagnoses of peptic ulcer and urinary infection. Six patients had primarily a psychiatric diagnoses with four responding to interventions within the nursing home. Only one consult was considered unnecessary.

This on-site nursing home consultation team evaluated ten cases of behavioral disturbance which had either gone unevaluated or resulted in a fruitless ER visit. In a majority of cases, treatable medical and psychiatric disorders were diagnosed and treated on site. Nursing home staff routinely expressed a desire for easier access to geropsychiatric consultation. On-site geropsychiatric consultation of behaviorally disturbed nursing home residents deserves further study as a cost-effective way to improve quality of care.

NR18 Monday, May 22, 9:00 a.m.-10:30 a.m.

Diagnostic Use of Brain Perfusion SPECT in Geriatric Psychiatry: A Retrospective Review

Simon Chiu, M.D., Psychiatry, Baycrest Hospital, 3560 Bathurst Street, North Ontario M6A 2E1, Canada; Allan Steingart, M.D., M. Ichise, M.D., H. Golan, J. Kremer, M.D., Morris Freedman, M.D.

Summary:

Objective: The study was conducted to compare the brain perfusion SPECT in psychiatric patients ≥ 65 years who were diagnosed with: 1) dementia (DEM); 2) mood disorder (MOOD); 3) dementia-mood disorder (DEM-MOOD).

Methods: Retrospective chart review was completed on 30 patients assessed in a geriatric hospital. The clinico-demographic and SPECT scan data were examined categorically (DEM: n = 10; MOOD: n = 10; DEM-MOOD: n = 10). The scans measured uptake of 99m Tc-Hexamethylenepropyloxime (HMPAO).

Results: Mean age: 74 yrs. (range 65 to 86). In the DEM group, 9/10 had significant reduction in blood flow in the parietal-temporal region, vs. 6/10 in DEM-MOOD and 0/10 in MOOD (x^2 = 16.8, p < 0.0002; df = 2). In the MOOD and DEM-MOOD groups, 5/10 had global reduction vs. 1/10 in the DEM group (x^2 = 4.6; p = 0.1, df = 2). In the DEM-MOOD group, 4/10 of the patients had reduced frontal blood flow vs. 0/10 of MOOD and 2/10 of DEM group (x^2 = 5.0; p = 0.08; df = 2).

Conclusion: Cohort studies are warranted to establish the diagnostic utility of SPECT scan perfusion defects in elderly patients with neuropsychiatric disorders.

NR19 Monday, May 22, 9:00 a.m.-10:30 a.m.

Circadian Regulation in Abused Children

Carol A. Glod, Ph.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02178; Martin H. Teicher, M.D.

Summary:

Circadian dysregulation may be a hallmark of affective disorders (Siever & Davis, 1985). Teicher et al (1993) found prominent dysregulation of circadian activity rhythms in children that distinguished depressed subjects from controls with 94% sensitivity and 84% specificity. Yehuda et al (1994) found that cortisol rhythms were dysregulated in depressed adults, but enhanced in combat veterans with PTSD. The purpose of this study was to assess the effects of physical and sexual abuse on circadian activity levels and rhythms.

Sixteen unmedicated abused children (9.7 ± 2.1 yrs; 4F:12M), assessed via structured diagnostic interview (K-SADS-E), were compared with 15 healthy controls (8.3 ± 1.9 yrs; 6F:9M). Activity data were collected for 72 hrs. in one-minute epochs during weekdays using Motionlogger actigraphs. A trend emerged for abused children to have higher mean diurnal activity levels (p = .06). The circadian activity rhythm peaked 62 minutes later in the abused group compared with controls (p < .05). Although both were well-entrained to a 24-hour day, the abused group had a significantly longer circadian period compared with controls (24.17 vs. 23.95 hr., p < .05). No differences arose between abused and control children in the amplitude or goodness of fit of their circadian rhythm. However, abused children with PTSD had a greater relative circadian amplitude than abused children without PTSD (102% vs. 93%, p < 0.02). These observations indicate that abused children have a distinctly different circadian activity pattern than we have observed in depressed children, and that abused children with PTSD may have an enhanced circadian rhythm.

NR20 Monday, May 22, 9:00 a.m.-10:30 a.m.

Neurobiology of Abuse in Personality Disorders

Bonnie J. Steinberg, M.D., Psychiatry, Mt. Sinai School of Med., 1 Gustave Levy Place Box 1230, New York, NY 10029; Rachel Yehuda, Ph.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Summary:

There has been a growing interest in the neurobiology of early abuse, particularly as it affects neuroendocrinology, morphology and neurocognition. There is emerging evidence that early abuse has been associated not only with PTSD, but also with borderline personality disorder (BPD) [Herman et al, 1989]. BPD has also been associated with a blunted prolactin response to fenfluramine, which correlates with irritability and assault on the Buss-Durkee Hostility Inventory [Coccaro et al, 1989]. PTSD has been associated with an elevated MHPG/cortisol ratio. In order to evaluate the specificity of early trauma and borderline psychopathology, and to evaluate the relationship with biological correlates previously associated with BPD and PTSD, we evaluated 43 patients with DSM-III personality disorders. Subjects filled out the Childhood Trauma Questionnaire (CTQ). A subset had biological tests: 21 subjects underwent a fenfluramine challenge described elsewhere [Coccaro et al, 1989]. In 18 subjects baseline measures of MHPG/cortisol were determined by the average of values taken at 0930h, 0945h, and 1000h. Analyses were performed with and without controlling for irritability and assault, as they may have constituted genetic factors which might have contributed to the

likelihood of abuse. Approximately 50% of the population reported early sexual abuse, without differences between BPD and other personality disorder patients. There was no association between an elevation in any of the abuse scales (sexual abuse, physical abuse, physical neglect, emotional neglect, total score) and either BPD or avoidant personality disorder, nor was there a correlation with number of borderline traits. There was a correlation between physical and sexual abuse ($r = 0.50$, $p < 0.001$). There was a correlation between physical abuse and physical neglect ($r = 0.43$, $p < 0.01$). There tended to be a positive correlation between sexual abuse and prolactin response to fenfluramine ($r = 0.41$, $p = .06$); this finding was accounted for by the women ($r = 0.62$) and did not change when controlling for irritability or assault ($r = 0.4$). Controlling for irritability and assault, there was an inverse correlation between MHPG/cortisol and physical abuse ($r = 0.45$, $p = 0.08$), as well as with physical neglect ($r = 0.54$, $p < 0.03$). Baseline cortisol correlated positively with physical neglect in men ($r = 0.43$, $p < 0.08$) and negatively in women (–0.44, p = ns). These results suggest that the presence of early abuse may explain some of the biological heterogeneity within specific personality disorders and these patterns seem to be distinct from previous biologic correlates of BPD and PTSD.

NR21 Monday, May 22, 9:00 a.m.-10:30 a.m.

Cholinergic Challenges in Personality Disorders

Bonnie J. Steinberg, M.D., Psychiatry, Mt. Sinai School of Med., 1 Gustave Levy Place Box 1230, New York, NY 10029; Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Summary:

Objective: To examine the relationship between mood and hormonal responses to cholinergic challenge with physostigmine, reflecting cholinergic system responsiveness, in borderline personality disorder (BPD) patients, other non-BPD personality disorder patients, and normal controls.

Methods: Thirty-four personality disorder patients, of which ten meet criteria for BPD and 24 met criteria for non-borderline personality disorders, and 11 normal controls participated in a double-blind, placebo-controlled physostigmine challenge paradigm. The Profile of Mood State depression subscale (POMS-D) self-report measure was obtained at baseline and following the physostigmine or placebo infusions.

Results: In a repeated measures ANOVA of the depression subscale, under placebo and drug conditions, the increase in the POMS depression subscale was significantly greater in the total cohort of personality disorder patients overall than in normal controls ($p < 0.05$). Female subjects reported higher increases in depression than male subjects ($p < 0.02$), particularly among the BPD patients compared to the normal controls ($p < 0.05$). There was significantly greater dysphoric response to physostigmine in BPD patients ($p < 0.05$), but not in other personality disorder patients, compared to normal controls. When patients with schizotypal personality disorder were removed from the analysis, there was a significantly greater depressive response in the personality disorder patients with affective instability than in those without this trait ($p < .02$).

Conclusions: These data suggest an association between BPD and acute depressive response to physostigmine challenge, and that the cholinergic system may be involved in the regulation of affect in axis II disorders.

NR22 Monday, May 22, 9:00 a.m.-10:30 a.m.

The Role of Serotonergic Inhibitor Receptors in the Prolactin Response to Clomipramine Challenge

Joseph M. Bebchuk, M.D., Psychiatry, Unit of North Carolina, Campus Box 7160 Med School Wing B, Chapel Hill, NC 27599; Linda M. Nicholas, M.D., Amy L. Durr, M.S.N., Robert D. Ekstrom, M.P.H., George A. Mason, Ph.D., Robert N. Golden, M.D.

Summary:

The prolactin response to serotonergic (5-HT) stimulation by several pharmacological challenge agents, including the 5-HT reuptake inhibitor clomipramine (CMI), has been observed to be blunted in depressed patients. The specific serotonin receptor subtype(s) that mediate the prolactin response to 5-HT challenge have not been identified to date. We tested the hypothesis that the 5-HT1A receptor plays a role in mediating the blunted prolactin response to CMI by examining the effects of a 5-HT1A receptor antagonist, pindolol, on CMI challenge in healthy volunteers.

Under double-blind conditions, healthy volunteers received pretreatment with either the 5-HT_{1A} receptor antagonist pindolol or placebo, followed by a standard clomipramine challenge test. Plasma prolactin concentrations were measured by radioimmunoassay, and plasma concentrations of clomipramine and pindolol were measured by high-performance liquid chromatography.

Twenty subjects were studied. Pindolol did not have any effect on the prolactin response to clomipramine challenge either measured by the maximum percentage change from baseline (rank sum: $p = 0.6$) or area under the curve (rank sum: $p = 1.0$). These results suggest that the 5-HT_{1A} receptor is not involved in the prolactin response to central serotonergic challenge with clomipramine.

This work was supported in part by PHS grants MH-42145, MH-33127, MH-19111, and RR-00046.

NR23 Monday, May 22, 9:00 a.m.-10:30 a.m.

Binding of [^{3}H] Felbamate to Human Postmortem Brain

James K. Wamsley, Ph.D., Psychiatry, NY Medical College, Valhalla, NY 10595; Duane Sofia, Ph.D., Steven Hurt, Ph.D., Dusan Peckovic, M.D.

Summary:

The anticonvulsant felbamate (FBM) has been shown to compete for sites occupied by strychnine-insensitive glycine receptor (SIGR) antagonist dichlorokynurenic acid (DCKA). These SIGR sites are involved in modifying activity at NMDA-associated ion channels. Recently, FBM was shown to increase [^{3}H]glycine binding in apparent contrast to results obtained with [^{3}H]DCKA. In order to examine the association of FBM with SIGR directly, we investigated the binding of tritiated FBM ([^{3}H]FBM) to human postmortem brain.

The binding of [^{3}H]FBM to cortical (middle temporal gyrus) tissue was of high affinity, saturable, and readily reversible. Preincubation of tissue in water to osmotically burst the cells, greatly increased specific binding. Addition of glycine or D-serine to the incubation media, further increased specific binding (+35%). Addition of NMDA and glutamate also produced a slight increase (+5–10%) in specific binding. Phenobarbital was the only compound that caused a decrease in [^{3}H]FBM binding (maximal decrease of 18%). Other GABAergic drugs had no effect.

These data indicate FBM acts at an allosteric site associated with SIGR. The drug is capable of modulating activity at NMDA-associated ion channels via an action at these sites.

NR24 Monday, May 22, 9:00 a.m.-10:30 a.m.

Olfactory Test Performance and CT Findings in First-Degree Relatives of Alzheimer's Disease Patients

Claudio M. Demb, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Box 1505, New York, NY 10029; M. Mehmet

Haznedar, M.D., Michael J. Serby, M.D., Monte S. Buchsbaum, M.D., Marja Germans, B.A., Kenneth L. Davis, M.D.

Summary:

Olfactory identification deficits were reported in Alzheimer's patients even in the early stages of the disease. In our study we looked at first-degree relatives of Alzheimer's disease (AD) patients tested with the University of Pennsylvania Smell Identification Test (UPSIT), and attempted to correlate their performance with anatomical measures on brain CT scans. Eleven first-degree relatives of AD patients were CT scanned and performed the UPSIT within an average of a month apart from each other. At the time of the UPSIT the mean age was 66.9 (SD = 6.9), Mini Mental Status Exam mean total score was 28.8 (SD 1.3). UPSIT mean score was 31.5 (SD 4.5). Axial brain images were used for area analysis. A standard neuroanatomical atlas (Matsui-Hirano) was used as a reference to determine anatomical structure location. The ventricles were traced using a gradient filter which transformed images to enhance edge contour. Frontal area was assessed as the area anterior to a point 10% along the anteroposterior midline. UPSIT scores significantly correlated with frontal area measurements ($p < .05$, $r = .79$) and correlated negatively with lateral ventricular area measurements (p ns, $r = -.59$). These findings are interesting in light of known relationships between frontal lobe and olfactory identification and also because of the existence of significant olfactory deficits in Parkinson's disease.

NR25 Monday, May 22, 9:00 a.m.-10:30 a.m.

Decreased Corpus Callosal Size in Women with Alcohol Dependence Compared to Women Controls: An MRI Study

Paul W. Ragan, M.D., NIAAA/LCS, Bldg 10 Rm 3B19, 9000 Rockville Pike, Bethesda, MD 20892; Daniel W. Hommer, M.D., Reza Momenan, Ph.D., Wendol A. Williams, M.D., Daniel Rio, Ph.D., Michael J. Eckardt, Ph.D.

Summary:

Objective: To examine for gender-related differences in an area of brain white matter—the corpus callosum—in women with alcohol dependence and in women controls.

Method: MRI scans were obtained on 12 hospitalized alcoholic women (mean age ± SD = 37.5 ± 6 years) on average 19 days after their last drink and on 12 nonalcoholic women (mean age = 34.7 + 5 years). Both groups were without a history of significant head trauma or overt medical disorders, and the patients had no history of withdrawal seizures or DT's. The corpus callosum and the inner table of the skull were outlined by hand on a mid-sagittal T_1 weighted MRI image.

Results: The alcohol women had a mean CAGE score of 3.8 ± 0.6, and had been drinking an average of 19 + 13.5 kg of ethanol for an average of 117 ± 54 days over the previous six months, and had a mean lifetime ethanol consumption of 265 ± 176 kg. There was no difference in intracranial area between the controls and the alcoholics; however, the corpus callosum area was significantly smaller among the alcoholics: 710 ± 78 mm^2 versus 602 ± 98 mm^2, $t(20) = 2.81$, $p < .01$. Alcoholic males did not differ from control males in corpus callosum or intracranial area.

Conclusions: These results may indicate increased sensitivity to alcohol-induced callosal shrinkage in women.

NR26 Monday, May 22, 9:00 a.m.-10:30 a.m.

SPECT Brain Imaging in Normal Aging

Sonya Herrera, B.A., Psychiatry, Elmhurst Hospital, 79-01 Broadway, Elmhurst, NY 11373; Hee K. Lee, M.D., Donald M. Quinlan, M.D., Erin A. Hazlett, Ph.D., Christina Luu, B.A., Ecaterina Rotaru, M.D., James Valence, B.A., John Herrera, Ph.D., Monte S. Buchsbaum, M.D.

Summary:

The relationship between aging and rCBF has been repeatedly examined, yet the presence and specificity of diminished functional activity remains unresolved. In this study, single photon emission computed tomography (SPECT) brain imaging with Tc-99m-hexamethylpropylenamineoxime (Tc-99m-HMPAO) was used to examine regional cerebral blood flow (rCBF) in adult and aged normal controls. The "cortical peel" region of interest (ROI) method developed by Buchsbaum for positron emission tomography (PET) was applied to ROI analysis with SPECT. Ten aged normal controls (Na: four males/six females, mean age = 69.8, MMSE = 29.5) were recruited from a sample of individuals entered into the CERAD multicenter study and 10 adult normal controls (Nc: seven males/three females, mean age = 34.4, MMSE = 29.8) were recruited from hospital personnel and prescreened for concurrent medical, neurological, or psychiatric histories. SPECT imaging was completed under activation with a "delayed word recall" memory task adapted from the CERAD neuropsychological battery and included "no-recall" control condition. Images were acquired using the Trionix Triad three-detector head digital SPECT camera and reconstructed from 30 camera views (30 x 3), incremented through four degrees of circumference around the subject's head, at 55 seconds per view. With the cortical peal ROI SPECT adaptation, a rater blind to diagnosis chooses 10 slices for analysis based on resemblance to the Matsui and Hirano prototype atlas levels. For each slice, the outer brain contour is outlined with a boundary-finding technique developed for skull on CT scans. A strip of pixels 2 cm thick is identified and peel regions divided anatomically into lobes based on the percentage of brain perimeter accounted for by each lobe at each level in the atlas, each lobe is similarly divided into four gyri, regional rCBF values are calculated as the ratio of regional to whole-brain blood flow. The statistical model employed was a repeated-measures analysis of variance (ANOVA) with independent subject groups and repeated measures for task, lobes, gyri, and hemisphere. The results of the analysis yielded a significant three-way interaction ($p = .048$; group by lobe by gyri), examination of these findings revealed diminished activity among the aged normals in the frontal cortex at the level of the superior lobule. Comparison of the delayed word recall learning trials failed to reveal significant group differences, suggesting the presence of diminished frontal cortical activity in the absence of age-related memory impairment.

NR27 Monday, May 22, 9:00 a.m.-10:30 a.m.

SPECT Brain Imaging in Geriatric Schizophrenics

Sonya Herrera, B.A., Psychiatry, Elmhurst Hospital, 79-01 Broadway, Elmhurst, NY 11373; Hee K. Lee, M.D., Donald M. Quinlan, M.D., Erin A. Hazlett, Ph.D., Christina Luu, B.A., Ecaterina Rotaru, M.D., James Valence, B.A., John Herrera, Ph.D., Monte S. Buchsbaum, M.D.

Summary:

Single photon emission computed tomography (SPECT) brain imaging with Tc-99m-hexamethylpropylenamineoxime (TC-99m-HMPAO) was used to examine regional cerebral blood flow (rCBF) in geriatric schizophrenic patients. While the use of tracers capable of measuring rCBF has been quite extensive in schizophrenia research, to the author's knowledge this is the *first* functional imaging study to examine rCBF in a sample of more aged schizophrenics. The study was conducted at Elmhurst Hospital Center (EHC), an academic affiliate of Mount Sinai School of Medicine (MSMS). Twenty geriatric patients (four males/16 females, mean age = 64.1, mean PANSS Total = 54.57, mean MMSE = 25.7) who met DSM-III-R criteria for schizophrenia (CASH) were recruited for

clinical and neuropsychological ratings and asked to consent to SPECT scans. Ten aged normal controls (four males/six females, mean age = 69.8, MMSE = 29.5) were recruited from a sample of individuals entered into the CERAD multicenter study and 10 adult normal controls (seven males/three females, mean age = 34.4, MMSE = 29.8) were recruited from hospital personnel and prescreened for concurrent medical, neurological or psychiatric histories. SPECT Images were acquired using the Trionix Triad three-detector head digital SPECT camera and reconstructed from 30 camera views (30 x 3), incremented through four degrees of circumference around the subject's head, at 55 seconds per view. The "cortical peel" region of interest (ROI) method developed by Buchsbaum for positron emission tomography (PET) was applied to ROI analysis with SPECT. The statistical model employed was a repeated-measures analysis of variance (ANOVA) with independent subject groups and repeated measures for task, lobes, gyri, and hemispheres. The analysis yielded a highly significant two-way interaction effect (p = .0055; group by lobe) indicating diminished frontal cortical activity among the geriatric schizophrenic patients. The findings extend convergent lines of neuroimaging results that schizophrenics display "hypofrontality" to geriatric patients. The authors will present these findings in relationship to cognition and negative symptomalogy and the results of exploratory analyses of subcortical brain areas.

NR28 Monday, May 22, 9:00 a.m.-10:30 a.m.

Gender and Cognitive Performance in Alzheimer's Disease

P. Murali Doraiswamy, M.D., CNS 5 4600, Glaxo Inc., Five Moore Drive, Res. Triangle Park, NC 27709; Alok Krishen, M.S., Frank Stallone, Ph.D., Wendy Martin, M.D., Alan Metz, M.D., Joseph Deveaugh-Geiss, M.D.

Summary:

There is evidence from epidemiologic studies that female gender is an independent risk factor for Alzheimer's disease (AD). The cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-Cog) consists of 11 items designed to evaluate cognitive dysfunctions characteristic of AD. We analyzed ADAS-Cog scores from 444 AD patients selected for a clinical drug trial to evaluate gender-related differences in cognitive performance.

Females performed statistically significantly worse than males on "orientation" and "recall of test instructions" (p = 0.007). After adjusting for age, education, and dementia severity, these differences remained statistically significant. Gender differences approached statistical significance for "constructional praxis" (p = 0.054). Dementia severity and education level also had statistically significant effects on cognitive performance.

These findings will be discussed in relation to studies linking female gender with a higher risk for AD and the hypothesis that gender-related differences in some aspects of memory may arise as a consequence of neurodegeneration in AD.

NR29 Monday, May 22, 9:00 a.m.-10:30 a.m.

Neuroleptic Treatment and Caudate Nuclei Volumes in Patients with Depression

P. Murali Doraiswamy, M.D., CNS 5 4600, Glaxo Inc., Five Moore Drive, Res. Triangle Park, NC 27709; Larry A. Tupler, Ph.D., K. Ranga Rama Krishnan, M.D.

Summary:

Recent magnetic resonance (MR) studies have reported an increase in caudate nuclei volumes in schizophrenic patients taking antipsychotic drugs. Currently, it is not known whether neuroleptic-associated caudate plasticity is unique to schizophrenia or is generalizable to mood disorders.

Using MR data from 50 normal controls and age- and gender-matched depressed patients, we tested the hypothesis that exposure to neuroleptic treatment would be associated with larger caudate volumes. There were statistically significant differences in caudate nuclei volume between controls and depressed patients classified by antipsychotic treatment history. Depressed patients with prior neuroleptic treatment had larger caudate nuclei volumes, after controlling for age, gender, and cerebral volume, than the remaining depressed patients.

These results are discussed in relation to our previous studies of caudate morphometry in aging, depression, and Parkinson's disease, and the hypothesis that dopaminergic blockade by antipsychotic drugs may result in hypertrophy of striatal synaptic or somal elements.

NR30 Monday, May 22, 9:00 a.m.-10:30 a.m.

Evaluation of a Clinical Prediction Rule for Postoperative Delirium

Joseph A. Locala, M.D., Dept. of Psychiatry, P-68, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; David Litaker, M.D., Kathleen N. Franco, M.D., David L. Bronson, M.D.

Summary:

The objective of this study was to test a predictive model for the occurrence of postoperative delirium (previously reported by Marcantonio, et al.) in patients who have undergone elective, noncardiac surgery. One hundred sixty-five Cleveland Clinic patients, aged 50 years or older, were screened preoperatively with the Confusion Assessment Method (CAM) and the Telephone Interview for Cognitive Status (TICS). Complete demographic data and medical history were obtained. Patients were then assigned a Marcantonio score based on age, history of alcohol abuse, TICS score, type of surgery, Specific Activity Scale rating, and serum levels of sodium, glucose and potassium. Patients were followed prospectively and assessed for the presence of delirium on postoperative days (POD) one through four by chart review, CAM, and confirmatory TICS.

Nineteen (11.5%) patients developed delirium in the first four postoperative days. Twelve (63%) patients had onset of delirium on POD 1, five (26%) on POD 2, none on POD 3, and two (11%) on POD 4. Sixty-seven (41%) of the 165 patients were older than 70 years of age and 11 (16%) of those patients became delirious. Although an increasing trend was noted, we did not find statistically significant risk for those over age 70 compared with the 50–70-year-old-group. Patients whose Marcantonio scores were 2 or greater were much more likely to develop postoperative delirium than those with scores of 0 or 1 (RR = 4.2, [95% CI 1.9, 9.3]). Patients with initial TICS of less than 30 (indicative of baseline cognitive impairment) were at much higher risk for delirium (RR = 7.7, [95% CI 3.4, 17.2]). In conclusion, we found that TICS and Marcantonio scores have significant clinical utility in the preoperative prediction of delirium following surgery.

NR31 Monday, May 22, 9:00 a.m.-10:30 a.m.

Differences in Neuropsychiatric Profile in Alzheimer's Disease and Non-Alzheimer's Disease Dementias

Maria P. Gonzalez, Ph.D., Psiquiatria, Facultad De Medicina, Julian Claveria 6, Oviedo 33006, Spain; Oscar L. Lopez, M.D., Abraham Sudilovsky, M.D., James T. Becker, Ph.D., Charles F. Reynolds III, M.D., Steven T. Dekosky, M.D.

Summary:

Objective: To compare the neuropsychiatric profile of patients with Alzheimer's disease dementia (AD) and patients with non-Alzheimer's dementia, i.e., frontal lobe type (FLT) and subcortical

(SC): multisystem atrophy, progressive supranuclear palsy, progressive subcortical gliosis.

Patients and Methods: Included were patients enrolled in the Alzheimer Disease Research Center at the University of Pittsburgh from 1989–1994. Initial psychiatric evaluations from records of patients with FLT (n = 21), patients with SC (n = 10), and 31 patients with AD were tabulated and analyzed using the binomial distribution, the Fisher's test (one-tailed) and the paired t-test. Patients with AD were equated for each of the other two groups by severity of dementia (MMSE score).

Results: (Only psychiatric symptoms and signs significantly different are presented).

	FLT (n = 21)	AD (n = 21)	P	SC (n = 10)	AD (n = 10)	P
Lability of mood	28.6%	0.0%	.03			
Anxiety	42.9%	4.8%	.007			
Irritability	76.2%	28.6%	.006			
Social withdrawal	71.4%	33.3%	.02			
Agitation	47.6%	0.0%	.002			
Lack of energy	71.4%	33.3%	.02	90.0%	40.0%	.02
Psychomotor retardation				80.0%	30.0%	.03
Hamilton Depression	9.4 ± 5.8	3.5 ± 4.1	.000			

Conclusions: The results indicate different neuropsychiatric profiles, with FLT showing a pattern of behavior more congruent with disinhibition than that seen in AD, and SC more congruent with psychomotor retardation than in AD. Further investigation with larger samples is warranted to explore the implications of our findings for therapeutic intervention.

NR32 Monday, May 22, 9:00 a.m.-10:30 a.m.

Catatonic Disorders: Psychiatric Versus General Medical Etiology

Debra Callahan, Ph.D., Medicine, The Ohio State University, 260 Meiling, Columbus, OH 43210; Brendan T. Carroll, M.D., Harold W. Goforth

Summary:

Catatonia and catatonic signs have been classically described as occurring in schizophrenia and other psychiatric disorders. Catatonia may also be due to general medical conditions (CDGMC). We compared patients with psychiatric and general medical etiologies for discriminating features.

The clinical information comes from chart reviews, a prospective study of patients presenting with catatonic signs, and evidence from the literature. We reviewed charts of patients with catatonic signs hospitalized at OSU from 1986 to 1993. There were 47 episodes in 36 patients (psychiatric = 35; CDGMC = 12). Comparison of 15 catatonic signs revealed no significant difference in the number of signs, and the presence of all but one specific sign. Patients with CDGMC had negativism more frequently (92% vs. 51%, Yates Chi-Square ≤ 0.05).

In a prospective study of 29 episodes of catatonia admitted over one year (psychiatric = 18; CDGMC = 11) there was no significant difference in the mean total score of three catatonia rating scales between these two groups. Furthermore there was no significant difference in the frequency of the most common catatonic signs, including negativism.

While the literature on catatonia does not include comparative studies, two recent reviews suggest that psychiatric catatonia frequently (> 50%) includes: mutism, immobility, staring, posturing, negativism, and withdrawal, while CDGMC meeting DSM-IV criteria also (> 40%) includes: mutism, withdrawal, immobility, and negativism.

NR33 Monday, May 22, 9:00 a.m.-10:30 a.m.

Catatonic Disorder: Treatment and Cost

John C. Kennedy, M.D., Psychiatry, The Ohio State University, 1670 Upham Drive, Columbus, OH 43210; Brendan T. Carroll, M.D., Harold W. Goforth

Summary:

Catatonic disorders may occur in up to 9% of adult psychiatry admissions. These patients may respond favorably to treatment with lorazepam and electroconvulsive treatment.

The occurrence of catatonia may indicate a severe episode of psychosis requiring intensive treatment. Historically, episodes of catatonia required long-term treatment. We became interested in the cost of catatonic disorders after several prolonged cases and challenges by managed care companies. We found no recent studies on the costs incurred by patients with catatonic disorders.

We prospectively identified patients with catatonic features admitted to an inpatient adult (age ≥ 18 years) psychiatric unit at the Ohio State University Neuropsychiatric Facility from January 1, 1994, through December 31, 1994. Patients were identified by the: 1) Rosebush et al, 2) Bush-Francis Catatonia Rating Scale and 3) the Modified Rogers Scale.

The total number of adult admissions was 818. The average length of stay (LOS) was 10 days. The number of adult admissions with catatonic signs rated was 29 (3.54% of all admissions). There were 26 patients. The average LOS was 19.2 (SD ± 11.7) days with a median of 17 and a mode 13 (range 3 to 44 days). Episodes with psychiatric etiologies (N = 18) had a mean length of stay of 20.0 days (±13.5) with a mean cost of $11,710, while CDGMC episodes (N = 11) had an average LOS of 17.9 days (±8.41) with a mean cost of $9,459.

Several factors were associated with longer than average stays: female gender (Yates Chi-square = 3.03, df = 1, p ≤ 0.1), and treatment with ECT (Pearson Chi-square = 13.0, df = 3, p ≤ 0.005).

NR34 Monday, May 22, 9:00 a.m.-10:30 a.m.

The Harvard Telemedicine Project in Schizophrenia

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Lisa S. Weinstock, M.D., Peter Cukor, Ph.D., Casandra Morabito, Ph.D., Lee Baer, Ph.D., Linda Leahy, B.S.

Summary:

Background: Remote video psychiatric assessment holds promise for providing expert consultation to underserved areas, but has not been quantitatively studied in schizophrenia.

Methods: We assessed the reliability of the Brief Psychiatric Rating Scale (BPRS), Scale for the Assessment of Positive Symptoms (SAPS), Scale for the Assessment of Negative Symptoms (SANS) administered in person (n = 15) and by video utilizing two bandwidths 128 kbs (n = 15) and 384 kbs (n = 15). All patients met DSM-IV criteria for schizophrenia. The two Picture Tel 4000 Model 400 units were located at two Harvard-affiliated hospitals.

Results: The correlation between the two raters for the BPRS was excellent in person (.959), with video bandwidths 128 kbs (.839) and 384 kbs (.897). Similar agreement was found with the SAPS .943, .966, and .965, respectively. Reliability for SANS was good for the interview in person (.917) and with the 384 kbs (.854), but less so with 128 kbs (.669). The comfort levels for the patient during the interview ranged between "average" and "better than average."

Conclusions: Telemedicine using 384 kbs bandwidth transmission over two standard digital telephone lines resulted reliable in semistructured rating scales for psychotic symptoms. Assessment of negative symptoms in the lower bandwidth, 128 kbs, was less reliable. This has important implications when deciding on which system to use.

NR35 Monday, May 22, 9:00 a.m.-10:30 a.m.

Shifts in Diagnostic Frequencies of Bipolar Disorder Subtypes at McLean Hospital: 1981–1993

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont, MA 02178; Ross J. Baldessarini, M.D., Mauricio Tohen, M.D., German Baraibar, M.D., Silvina Beverina de Zarate, B.S.

Summary:

Objective: Evidence of increased diagnoses of major affective disorders in recent decades led us to determine if there have been diagnostic shifts among subtypes of bipolar disorder.

Method: Annual rates of psychiatric discharge diagnoses from 1981 to 1993 were reviewed, and diagnostic frequencies of bipolar disorder subtypes and schizoaffective disorder (SA) were compared.

Results: The annual total diagnostic rates for all bipolar disorders remained rather constant between 1981 and 1993, (18.3% to 15.4%), and that of SA rose five-fold from 1.4% to 8.7%. Rates of bipolar disorder not otherwise specified (NOS) increased eight-fold from 4.4% to 35%, while mania fell from 51.4% to 29.2% in the same period. Annual rates for mixed bipolar states decreased slightly from 27.4% to 18.4% while depressed subtype remained stable (16.6% to 16.1%).

Conclusions: Several factors may have influenced these trends: 1) changes between DSM-II and DSM-III-R diagnostic criteria, 2) treatment-oriented diagnostic bias associated with the increased application of alternatives to lithium and standard neuroleptics (valproate, carbamazepine, clozapine), 3) possible true increases in the incidence in SA and bipolar NOS subtype, and 4) sharply falling lengths of stay and rising readmission rates.

NR36 Monday, May 22, 9:00 a.m.-10:30 a.m.

Recognition of Comorbid Substance Abuse in Schizophrenia

JoAnn E. Kirchner, M.D., Psychiatry, Univ. Arkansas Med. School, 4301 West Markham Slot 589, Little Rock, AR 72205; Richard R. Owen, Jr., M.D., Doris E. Hutchins, M.S.W., Ellen P. Fischer Ph.D.

Summary:

Objective: To examine the recognition of comorbid substance abuse in patients with schizophrenia.

Method: Data were collected during an ongoing longitudinal study of outcomes of care for schizophrenia. Diagnoses of schizophrenia and substance abuse were made by structured interview. Substance abuse history, screening lab, alcohol withdrawal prophylaxis, and discharge diagnosis were examined in 32 VA inpatient charts (15 on acute psychiatry, 17 on detoxification ward) of patients with current substance abuse per structured interview.

Results: The most common research diagnoses were alcohol dependence (n = 28, 88%), cocaine dependence (n = 7, 22%), and polysubstance dependence (n = 6, 19%). Urine drug screens were obtained for all but two subjects. Admission breathalyzer or blood alcohol testing was obtained on 21 subjects (66%). Of acute ward subjects, four of 15 (27%) denied current use of a substance detected by screening lab, and seven of 13 (58%) with alcohol dependence research diagnosis were not provided withdrawal prophylaxis. Research and discharge diagnoses were concordant for 66% of subjects. The most frequent discordant diagnosis was alcohol dependence, which was omitted in eight of 28 subjects (29%) with a research diagnosis (6% on substance abuse ward, 58% on acute psychiatry wards; Fisher's exact test, $p < 0.05$).

Conclusions. Comorbid substance abuse in schizophrenia is often unrecognized. Alcohol dependance is particularly significant because of its prevalence, morbidity from acute witdrawal, and underdiagnosis.

NR37 Monday, May 22, 9:00 a.m.-10:30 a.m.

Suspension Therapy in Acute Schizophrenia: The Relationship of Neuroendocrine and Biochemical Parameters to Therapeutic Suspension Effects

Here W. Folkerts, M.D., Clinic Muenster, Psychiatric University, Albert-Schweitzer Str 11, Muenser 48149, Germany

Summary:

Objective: The aim of the study was to expand clinical experience with suspension therapy and to correlate clinical and neuroendocrine findings after abrupt discontinuation of neuroleptic therapy in acutely schizophrenic patients with partial remission under standard haloperidol therapy.

Method: In 22 acutely schizophrenic (DSM-IV criteria) patients with partial remission under haloperidol medication, the following parameters were measured before and after abrupt discontinuation of neuroleptics (suspension therapy): urinary excretion of epinephrine (E), norepinephrine (NE), vanillylmandelic acid (VMA), dopamine (DOP), homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA), plasma cortisol, and prolactin (PRL).

Results: There was a close relationship between low catecholamine values (E < 9 ug/24h, NE < 30 ug/24h, VMA < 3.4 ug/24h) before suspension therapy and a favorable therapeutic suspension effect. Similarly, urinary cortisol excretion was lowest in patients with a favorable effect of subsequent suspension therapy. In addition we found a trend towards lower PRL values (<52 ng/ml) before neuroleptic discontinuation being linked with a favorable effect of subsequent suspension therapy. DOP and HVA excretion before neuroleptic discontinuation did not predict the clinical suspension effect.

Conclusions: An elevated level of sympathoadrenal activity appears to be associated with an unfavorable outcome of neuroleptic treatment and with an unfavorable therapeutic suspension effect after failure of neuroleptic treatment. If neuroleptic therapy fails to induce remission, temporary suspension of neuroleptics should be considered.

NR38 Monday, May 22, 9:00 a.m.-10:30 a.m.

Remission of Substance Abuse in Mental Illness

Scot McNary, M.A., Psychiatry, University of Maryland, 4513 Romlon Street Apt 301, Beltsville, MD 20705; Lisa B. Dixon, M.D., Laura Rachuba, B.A., Anthony F. Lehman, M.D.

Summary:

Objectives: Little is known about the nature of remission from co-occurring substance use disorders (SUD) among persons with severe mental illness (SMI). We intended: (1) to evaluate the stability and characteristics of SUD remission in 70 SMI persons with a past SUD at an index psychiatric admission who were evaluated one year later, and (2) to compare SMI persons with past SUD, current SUD (N = 102), and no SUD (N = 89) on clinical and demographic characteristics.

Methods: 261 consecutively admitted inpatients with primary SMI received the SCID and Quality of Life interviews and Addiction Severity Index at admission and one-year post-discharge.

Results: Half of clients with past SUDs at baseline reported that they had no SUD symptoms within five years. These clients reported that 27 (SD 30) and 44 (SD 39) months had elapsed since they last met criteria for alcohol and nonalcohol dependence, respectively. Only 10 (14%) of the clients with past SUD at baseline relapsed by one year. Logistic regression revealed that the presence of alcohol use disorders strongly predicted membership in the remitted SUD group; gender, psychiatric diagnosis, and personality disorder weakly predicted membership. Remitted persons resembled current users in family problems, but resembled those without any lifetime SUD diagnosis in legal problems, financial adequacy, and total symptoms.

Conclusions: The majority of SMI patients with past SUDs were in stable remission. Remission of alcohol rather than other substance use disorders accounted for this. Remitted persons' current status in quality of life, functioning, and symptomatology frequently falls between that of current users and nonusers.

NR39 Monday, May 22, 9:00 a.m.-10:30 a.m.

Relationship Between Schizophrenic and Obsessive Compulsive Symptoms

Amalia Merson, M.D., Psychiatry, FDR VA Hospital, Mt. Sinai School of Medicine, Montrose, NY 10548; Barbara Viegener, Ph.D., Edward R. Allan, M.D., Laura Parker, M.A., Miklos F. Losonczy, M.D., Ileana Berman, M.D.

Summary:

Recent reports suggest that up to 25% of chronic schizophrenic patients have significant obsessive compulsive (OC) symptoms. Presence of these symptoms seems to predict a poor outcome as reflected in longer and more frequent hospitalizations and social isolation. To date, there are no published studies that systematically measured the relationship between schizophrenic and OC symptoms.

Method: The purpose of this study is to compare schizophrenic patients with OC symptoms with schizophrenic patients without OC symptoms and to assess the relationship between these symptoms and neuropsychological functioning. Thirty patients, diagnosed with schizophrenia according to DSM-III-R criteria were included in the study. All patients had to be psychiatrically stable and able to cooperate with cognitive testing. The patients were assessed using the Positive and Negative Syndrome Scale (PANSS) and the Yale Brown Obsessive Compulsive Scale (YBOCS) and had a battery of cognitive tests which included Wechsler Visual Memory Test, block design (BD), digit symbol (DSy), digit span (DS), trails, and the Wisconsin Card Sorting Test (WCST). We classified as OC patients, those who, at the time of assessment, had at least two OC symptoms for more than six months. The PANSS and YBOCS assessments were done by two experienced investigators who reached consensus rating. The cognitive tests were done by other investigators who were blind to the results of the PANSS and YBOCS.

Results: Our preliminary results in 20 patients suggest that schizophrenic patients with OC symptoms scored higher on the PANSS general symptom subscale ($t = 2.7$, $n = 20$, $p = 0.016$). We did not find a significant difference between OC and non-OC schizophrenic patients in the positive and negative symptoms measures. In addition, the patients in both groups did not differ significantly in their cognitive performance. There was, however, a significant association between severity of obsessive compulsive symptoms and poor performance in the delayed recognition task of the Wechsler Visual Memory Test ($r = 0.57$, $p = 0.03$).

Conclusions: Patients with OC symptoms appear to have higher scores in the PANSS general symptom subscale that measures such symptoms as depression, anxiety, guilt, and somatic preoccupations. Although our preliminary findings do not suggest significant differences in the overall cognitive performance between the two groups, patients with more severe OC symptoms seem to have more difficulties with the visual memory tests which were found to be impaired in patients with OC disorder.

NR40 Monday, May 22, 9:00 a.m.-10:30 a.m.

Schizotypal Disorder: Temporal Lobe Anomalies

Chandlee C. Dickey, M.D., Psychiatry, VAMC 116A, 940 Belmont Street, Brockton, MA 02401; Martina M. Voglmaier, Ph.D., Martha E. Shenton, Ph.D., Larry J. Seidman, Ph.D., Margaret Miznikiewicz, Ph.D., Robert W. McCarley, M.D.

Summary:

Schizotypal personality disorder (SPD) is genetically linked to schizophrenia and is considered part of the schizophrenia spectrum disorders. Yet individuals with SPD lack the research confounds of psychotropic usage and institutionalization and may represent a "cleaner" population to study. Abnormalities on cognitive, electrophysiologic, and neuroanatomic tests of temporal lobe structures suggest that the similarities between schizophrenics and SPD subjects also may be phenotypic. In this study 11 subjects meeting DSM-III-R criteria for schizophrenia, and 11 for SPD were compared with 11 normal controls matched for age, handedness, and parental socioeconomic status. SPD subjects showed abnormalities similar to schizophrenics but to a lesser degree. Specifically, SPD subjects compared with controls showed 1) less semantic clustering on the California Verbal Learning Test, a task considered to be subserved by the left temporal lobe ($p < .02$); 2) a higher degree of thought disorder on the Thought Disorder Index; 3) a reduced P300 amplitude at combined temporal lobe electrodes, (T3/T5, $p = .038$); and 4) reduced volume in the left amygdala-hippocampal complex in one pilot case. These data support the hypothesis of phenotypic similarities between schizophrenia and SPD in left temporal lobe structures.

NR41 Monday, May 22, 9:00 a.m.-10:30 a.m.

Increased CD5⁺ B Lymphocytes in Schizophrenia

David J. Printz, M.D., New York Psych Inst., 722 West 168th Street Unit #2, New York, NY 10032; David H. Strauss, M.D., Jack M. Gorman, M.D.

Summary:

Objective: To compare the number and percentage of circulating $CD5^+$ B lymphocytes in patients with schizophrenia and normal controls.

Background: Abnormal immune regulation in schizophrenia is suggested by the presence of autoantibodies and alterations in interleukin levels. The $CD5^+$ B lymphocyte, an antibody-producing cell found in increased numbers in autoimmune illness, has been found to be elevated in a single study of patients with schizophrenia. This finding has not been replicated.

Methods: 28 patients with schizophrenia and 19 normal controls were studied. Subjects were screened for confounding medical illness by questionnaire and laboratory assessment. Peripheral blood lymphocytes were analyzed by dual fluorescence flow cytometry. A subset of patients were tested both on and off neuroleptics.

Results: The percentage of B lymphocytes expressing the CD5 marker was elevated in patients with schizophrenia compared with controls (40.5% +/– 3.3 vs. 29.1% +/– 3.7, $p = .03$). $CD5^+$ B cell number and $CD5^+$ B cells as a percent of total lymphocytes were also significantly elevated in patients vs. controls. It was not possible to demonstrate a medication effect.

Conclusion: $CD5^+$ B lymphocytes are increased in patients with schizophrenia. This replicates the findings of an earlier study and may provide further evidence of autoimmunity in schizophrenia.

NR42 Monday, May 22, 9:00 a.m.-10:30 a.m.

Gray Matter Heterotopias in the Psychoses

Noelle K. Gehm, B.S., Psychiatry, Ohio State University, 1670 Upham Drive, Columbus, OH 43210; Henry A. Nasrallah, M.D., Stephen C. Olson, M.D., Mary Oehler, M.D.

Summary:

Heterotopic gray matter have been reported in some neurodevelopmental disorders, suggesting a disruption of neuronal migration processes during the second trimester. Schizophrenia has

been shown to be associated with impaired neurodevelopment in post-mortem as well as *in vivo* studies on brain magnetic resonance imaging (MRI) scans. We therefore hypothesized that gray matter heterotopia (GMH) is more likely to be present in the brains of schizophrenic patients than in psychiatric and healthy control groups.

Our study included 271 subjects including schizophrenia (N = 89), bipolar disorder (N = 36), obsessive compulsive disorder (N = 13), nonpsychotic siblings of schizophrenic patients (N = 27), and healthy volunteers (N – 78). All subjects underwent an MRI brain scan (GE 1.5 Tesla, TI = 800 ms, TR = 1500 ms, TE = 20 ms). A neuroradiologist who was blind to the purpose of the study or the source of the MRI scans was asked to determine if GMH were present or absent in the coronal and sagittal scans of all subjects.

No GMH were found in any of the 271 subjects. Thus, we did not find evidence for increased frequency of GMH in schizophrenia. However, it is possible that GMH may be found among the most severely ill institutionalized schizophrenic patients who are not represented in our sample of community-based patients. Finally, the neuroradiologist did identify *other* congenital brain anomalies on the MRI scans of schizophrenics (22%), schizoaffectives (29%), bipolar (23%), siblings of schizophrenics (22%), and healthy controls (13%). The possible significance of the findings is discussed.

NR43 Monday, May 22, 9:00 a.m.-10:30 a.m.

Schizophrenia in the Iowa 500 Series: A Re-Examination with Regard to Premorbid Personality

David R. Hunter, M.D., Psychiatry, University of Iowa, 1206 Mormon Trek Blvd., Iowa City, IA 52246-4415; George Winokur, M.D.

Summary:

The Iowa 500 is a well-known group of psychiatric patients which contains a substantial number of classically diagnosed schizophrenic individuals. One of the valuable characteristics of the series is the thorough charting of social histories. This allowed for careful evaluation of premorbid personality. A random sample of these patients was selected for a more detailed examination with regard to a DSM-IV diagnosis of schizophrenia. Those patients whose charts identified them as meeting criteria for a DSM-IV diagnosis of schizophrenia were then further scrutinized for a DSM-IV diagnosis of a personality disorder. There were 36 male patients and 39 female patients identified. Male patients had been ill an average of 36 months and female patients an average of 43 months prior to their first hospitalization. Five patients met criteria for a premorbid personality disorder, four women and one man. Two met criteria for schizoid personality disorder, one schizotypal, one paranoid, and one personality disorder N.O.S. Additionally, there were two other women with strong personality disorder traits that did not meet full criteria. The data from this group of 75 patients seem to support a relatively acute onset of illness, with very few patients identified with premorbid personality diagnoses.

NR44 Monday, May 22, 9:00 a.m.-10:30 a.m.

Extrapyramidal Signs in Never Medicated First-Episode Schizophrenic Patients: Prevalence and Clinical Correlates

Anjan Chatterjee, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Miranda H. Chakos, M.D., Amy R. Koreen, M.D., Stephen H. Geisler, M.D., Jose Alvir, D.P.H., Jeffrey A. Lieberman, M.D., Brian B. Sheitman, M.D.

Summary:

Objective: To assess the prevalence of extrapyramidal signs in neuroleptic-naive, first-episode schizophrenic patients and examine their clinical correlates.

Method: The patients were taken from an ongoing prospective study of the psychobiology of schizophrenia. Eighty-nine neuroleptic-naive patients were examined for the presence of extrapyramidal signs (EPS) prior to medication initiation using the Simpson Angus Extrapyramidal Sign (SAEPS) Scale. Baseline EPS was defined as a score of 1 (mild) or more on the items of bradykinesia/akinesia, rigidity, and/or cogwheeling.

Results: Fifteen (16.8%) neuroleptic-naive patients had spontaneous EPS. Patients with spontaneous EPS were less likely to be full or even partial responders to treatment than patients without baseline EPS ($x^2 = 7.85$, df = 2, p = 0.02). Survival curves differed between the EPS and non-EPS groups ($x^2 = 5.21$, df = 1, p = 0.02). The EPS group had a greater proportion of patients who had not responded after one year of treatment. The cumulative incidence of treatment response in the non-EPS group was 95% at one year (95% C.I. = 90.3, 100.0) and in the spontaneous EPS group was 60% (95% C.I. = 35.2, 84.8). The baseline mean (±SD) of global negative symptom scores (SANS) was significantly higher for the spontaneous EPS group than the non-EPS group (t = –2.59, df = 79, p = .01).

Conclusion: These findings suggest that extrapyramidal signs can be involved in the schizophrenic disease process, possibly reflecting basal ganglia pathology, and their presence may indicate a more malignant course, more negative symptoms, and a poorer level of outcome.

NR45 Monday, May 22, 9:00 a.m.-10:30 a.m.

Botulinum Toxin in the Treatment of Tardive Dystonia

Anjan Chatterjee, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks, NY 11004; Mark F. Gordon, M.D.

Summary:

Objective: To determine the safety and efficacy of botulinum toxin in the treatment of tardive dystonia.

Background: Tardive (delayed-onset neuroleptic-induced) dystonia is often more difficult to treat than idiopathic dystonia due to coexisting psychiatric disease. Various medications including clozapine, clonazepam, anticholinergics, and baclofen have been used for tardive dystonia with variable success. Botulinum toxin intramuscular injections are of demonstrated safety and efficacy in the treatment of idiopathic dystonia. It has not routinely been used to treat tardive dystonia.

Design/Methods: Eight patients (6 males) with mean age ± SD = 34.8 ± 9.3 and moderately severe focal or segmental manifestations of tardive dystonia were treated in an open fashion with Botulinum toxin in various dosages. All patients had psychiatric diagnoses (schizophrenia 3, schizoaffective disorder 2, bipolar 2, major depression 1). The dystonias were primarily in the head and neck regions and were attributed to neuroleptic exposure. Concurrent medications (at the time of injection) included benzodiazepines, neuroleptics (including clozapine), baclofen, anticholinergics, valproate and lithium. Improvement after injection was rated as no change, mild to moderate, or marked, based both on patient's report and physician's observation. All patients received multiple treatments for one or more of the following dystonias: blepharospasm, jaw dystonia and torticollis. The initial dosage was titrated in stages to minimize side effects.

Results: The mean ± SD dose of Botulinum toxin used was 452.5 ± 344.26. Overall 4 patients had mild to moderate improvement and 4 had marked improvement. Side effects included mild and transient ptosis, dysphagia, and flu-like symptoms. The average duration of benefit was 3 months.

Conclusions: Botulinum toxin is a useful primary or adjunctive therapy for focal features of tardive dystonia.

NR46 Monday, May 22, 9:00 a.m.-10:30 a.m.

Clinical Correlates of the Deficit Syndrome of Schizophrenia

Timothy D. Florence, M.D., Psychiatry, University of Michigan, 1500 Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., Mona Goldman, Ph.D., John R. DeQuardo, M.D., Michael D. Jibson, M.D., Stephan F. Taylor, M.D.

Summary:

The deficit syndrome has been proposed as a useful organizing construct in schizophrenia; schizophrenic patients are classified in two subgroups based on the presence or absence of deficit (primary enduring negative) symptoms. Despite difficulties in reliably and validly making this distinction, the deficit/nondeficit subgrouping has been found to be relatively stable on longitudinal follow-up and can explain some important aspects of the clinical and neurobiological heterogeneity of schizophrenia. In an effort to further study the utility of this construct in schizophrenia, we compared samples of deficit and nondeficit schizophrenic patients on a variety of clinical and sociodemographic measures. Both samples were derived from one extensive schizophrenia database where deficit-nondeficit subtyping was one of the variables. All patients in this database were schizophrenic inpatients (DSM-III-R and SADS/RDC) during an acute psychotic exacerbation (criterion A of DSM-III-R), were initially assessed at medication-free baseline (minimum two weeks) and again three to four weeks after clinically determined antipsychotic treatment. Positive, negative, depressive, and global symptomatology was assessed at both timepoints. Deficit (N = 24) and nondeficit (N = 78) patients were compared on a whole range of clinical characteristics (symptom severity, age of onset, premorbid function, treatment response, one-year outcome, etc.). Deficit patients were older ($p < .01$), had a longer duration of illness ($p < .001$), had higher negative symptom scores at baseline and after three to four weeks neuroleptic treatment ($p < .01$). No differences in premorbid function, age of onset, gender distribution, educational level, or race were noted between these groups. There were no differences in severity of positive or depressive symptoms between deficit and nondeficit patients. There was a trend towards greater acute improvement (change scores over three to four weeks of neuroleptic treatment) and one-year outcome in nondeficit patients when compared to deficit patients. These data suggest that deficit-nondeficit typing is a useful organizing construct in schizophrenia. Furthermore, it appears that deficit symptoms develop a *consequence* of schizophrenic illness and may be related to process deterioration in schizophrenia.

NR47 Monday, May 22, 9:00 a.m.-10:30 a.m.

Gender in Schizophrenia: Impact on Symptomatology, Outcome and Biological Markers

Mona Goldman, Ph.D., Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., Robert S. Goldman, Ph.D., Irma C. Smet, Ph.D.

Summary:

Although there has been increasing recognition of the importance of gender in explaining heterogeneity in phenomenology, neurobiology, treatment response, and course of schizophrenic illness (*Schizophrenia Bulletin* 1990;16(2)), findings across many domains of research have been inconsistent. In order to confirm or refute previous findings, and to generate new hypotheses about the role of gender in schizophrenia, we examined gender differences in 66 male and 33 female SADS/RDC and DSM-III-R diagnosed schizophrenic inpatients. All patients were medication-free (minimum two weeks) at the time of the baseline evaluation. Symptomatology was assessed when patients were medication-free and about three to four weeks after initiating clinically-determined neuroleptic treatment. Outcome was assessed at one year. Comparisons were done for 1) biological factors: ventricle-brain ratio, EEG sleep abnormalities (REM latency and reduced slow-wave sleep), and 1-mg dexamethasone suppression test; 2) a comprehensive neuropsychological test battery: Wechsler Adult Intelligence Scale—revised (full, verbal, and performance IQ), Verbal Fluency, Wisconsin Card Sort Test, Trailmaking B, Choice Reaction Time; 3) clinical variables: global symptoms (Brief Psychiatric Rating Scale—BPRS total), positive (BPRS "THOT" factor), negative (Scale for the Assessment of Negative Symptoms—global score total), and depressive symptoms (Hamilton Rating Scale for Depression), and treatment response for those symptoms as reflected in change scores and residual scores after three to four weeks of antipsychotic treatment; and 4) one-year outcome (Strauss-Carpenter scale). Males and females differed in only three comparisons: males performed better on the Trailmaking B ($p = .04$) and the Choice Reaction Time tests ($p = .07$), and females responded better than males to treatment of negative symptoms ($p = .07$). If corrections were made for multiple comparisons, even these differences would not be significant. In sum, we found little difference between males and females across a variety of dimensions of schizophrenia. However, before we accept the validity of these similarities, we need to examine alternative explanations. For example, our sample was heterogeneous with respect to age of onset and duration of illness, either of which could modify gender effects. Sampling bias (related to characteristics of male and female patients in our acute inpatient treatment setting from which this sample was recruited) could be another confounding factor. These are issues that merit attention in any study of gender differences in schizophrenia.

NR48 Monday, May 22, 9:00 a.m.-10:30 a.m.

Biological Predictors of Suicide in Schizophrenia

Catherine F. Lewis, M.D., Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., James E. Shipley, M.D., John R. DeQuardo, M.D., Michael D. Jibson, M.D., Stephan F. Taylor, M.D.

Summary:

Suicidal behavior is manifested by a large proportion of schizophrenic patients; approximately 50% of these patients seriously consider or attempt suicide and approximately 10% succeed. While some clinical predictors of suicidal behavior in schizophrenia have been described, the pathophysiological mechanisms underlying this suicidality in schizophrenia are poorly understood. Recently, hypothalamo-pituitary-adrenal axis dysfunction (as reflected by cortisol nonsuppression on the dexamethasone suppression test, DST) and REM sleep abnormalities have been related to suicidal behavior in schizophrenia. In an effort to evaluate these associations, we studied this relationship in 95 patients with schizophrenia (SADS/RDC and DSM-III-R). The lifetime history of suicidal behavior was assessed by an extensive review of the clinical chart and the SADS interview by a resident (CL), who was blind to the sleep and DST data. Patients received a 1-mg DST at medication-free baseline (N = 60) and three-four weeks after beginning neuroleptic treatment (N = 45). Patients also received a two-night polysomnographic study at medication-free baseline (N = 55) and three-four weeks after beginning neuroleptic treatment (N = 35). Preliminary analysis suggests the absence of any relationship between DST findings (assessed categorically as nonsuppression/suppression or as post-dexamethasone cortisol levels) and suicidal behavior (defined broadly or narrowly). Shortened REM latency and decreased slow-wave sleep both showed a

weak association ($p < .10$) with lifetime suicidal behavior. Stronger associations were observed between post-dexamethasone cortisol levels and negative symptoms and between shortened REM latency and both positive and negative symptoms; when these symptom measures were used as covariates in the analysis, the observed association between suicidal behavior and REM latency disappeared. Caution is indicated when relating state findings (DST and sleep data in this case) to trait aspects (lifetime suicidal behavior in this case). Common neuropharmacological mechanisms may underlie polysomnographic abnormalities and suicidal behavior in schizophrenia.

NR49 Monday, May 22, 9:00 a.m.-10:30 a.m.

Covert Visual Attention in Deficit Schizophrenia

Juan R. Bustillo, M.D., Psychiatry, MD Psych. Research, P.O. Box 21247, Baltimore, MD 21228; Marianne Moran, M.A., Gunvant Thaker, M.D., Robert W. Buchanan, M.D.

Summary:

Previous studies have suggested that visual information processing impairments are associated with schizophrenic negative symptoms. The deficit syndrome of schizophrenia is defined by the presence of primary, enduring negative symptoms, and preliminary studies have found these patients to have visual attentional impairments. Previous neurological, neuropsychological, and PET studies have found convergent evidence of a possible dysfunction of a striat-pallido-thalamo-cortical circuit that involves the posterior parietal cortex in deficit schizophrenia. POSNER et al. have found that patients with posterior parietal cortical lesions have contralaterally increased costs to invalid cues in a task of covert visual attention (CVA). Recently Strauss et al., using this same task, found increased costs in the left visual field (LVF) in inpatient schizophrenics with prominent negative symptoms. We hypothesized that, compared to nondeficit schizophrenics, deficit patients will exhibit impaired CVA with increased costs in the LVF. We are studying 40 stable outpatients with schizophrenia (20 deficit 20 nondeficit) and 20 normal volunteers with the CVA task using peripheral and central cues in a counterbalanced design. To ensure the validity of the paradigm, eye movements are monitored in all subjects with the infrared technique. Preliminary findings are consistent with the hypothesis that deficit schizophrenics have increased costs in the LVF.

NR50 Monday, May 22, 9:00 a.m.-10:30 a.m.

Perseveration Errors on Dichotic Listening Tests: The Role of Patient Diagnosis and Fusion of Test Stimuli

Diane Gard, Psychology, North Texas University, 1116 N. Kedzie, Chicago, IL 60651; Amir Poreh, Ph.D., Michael J. Reinstein, M.D., Lynn Jones, R.N., Mohan Sangrpillai, M.D.

Summary:

Poreh, Mitchell, and Green (1993) reported that schizophrenic patients often perseverate on constant vowel dichotic listening (CV-DL) tests (CV-DL) but not on dichotic digits listening (DIG-DL) tests and that these perseverations correlate with various measures of executive functions (i.e., Wisconsin Card Sorting Test; WCST). The current study set out to replicate these findings using a different CV-DL test and three groups of subjects: schizophrenics, manic-depressives, and controls. Analysis of the data confirms that schizophrenic patients perseverate on the DL-CV test. This finding was not observed in the other two groups. Additional analysis indicates that when schizophrenic patients are presented with nonfused test stimuli (stimuli with a 5_{MSEC} separation), the perseverations significantly decline $t = -2.25$, $df = 9$, $p = .051$) but are still present. Finally, the data confirm that perseveration errors on this DL-CV differentially correlate with the performance of schizophrenics on executive functions measures such as the Stroop ($r (n = 14) = .45$, $p. < 0.05$), the Trail Making Test—Part B ($r (n = 14) = .65$, $p < 0.01$), and the WCST ($r (n = 14) = .53$, $p < 0.01$). The results are discussed in light of the inconsistent performance of schizophrenics on various dichotic listening tests (Nachshon, 1988).

NR51 Monday, May 22, 9:00 a.m.-10:30 a.m.

A Neurophysiological Study of Semantic Processing in Schizophrenia

Matthew O. Kimble, M.A., Psychiatry, Brockton VAMC, 940 Belmont Street 116A, Brockton, MA 02401; Matthew O. Kimble, M.A., Paul G. Nestor, Ph.D., Brian F. O'Donnell, Ph.D., Lloyd S. Smith, M.A., Robert W. McCarley, M.D.

Summary:

Since the time of Bleuler, schizophrenia has long been thought to be characterized by a fundamental disturbance in semantic associations. To investigate possible neurophysiological abnormalities in semantic processing in schizophrenia, we utilized the N400 event-related potential (ERP) paradigm, an ERP protocol with particular sensitivity to semantic expectancy and association.

Method: 15 right-handed, medicated male schizophrenics and 15 age-matched controls read visually presented sentences off a computer screen that either had sensible final words (e.g., "Every Sunday people pray in their local **church**") or non-sensible final words ("Every Sunday people pray in their local **nest**"). ERP recording was triggered just prior to the onset of the final word and continued for 1 second.

Results: In comparison to normal controls, schizophrenic patients demonstrated prolonged N400 latency to non-sensible sentence endings. In addition, the schizophrenic group showed enhanced N400 negativity to sentence endings regardless of whether they were sensible or not.

Conclusions: Both the enhanced negativity and prolonged latency may be viewed as neurophysiological evidence of disease-related semantic overactivation that has also been demonstrated in recent behavioral priming studies. This neurophysiological abnormality may, in part, explain the disturbance in association that Bleuler considered to be fundamental to schizophrenia.

NR52 Monday, May 22, 9:00 a.m.-10:30 a.m.

Cognitive Deficits and Psychopathology in Elderly Schizophrenic and Affective Disorder Patients

Seamus F. O'Flaithbheartaigh, M.B., Psychiatry, Mt. Sinai Hospital, 1 Gustave Levy Place Box 1228, New York, NY 10029; Peter Powchik, M.D., Philip D. Harvey, Ph.D., Michael Parella, Ph.D., Leonard White, Ph.D., Michael Davidson, M.D., Kenneth L. Davis, M.D.

Summary:

Background: Cognitive dysfunction is common in schizophrenia in late life. However, it is not clear that this is specific to schizophrenia or can be seen in other psychiatric disorders. Moreover, the relationship between psychopathology and cognitive dysfunction in elderly psychiatric patients remains to be elucidated. We conducted a study of elderly chronic psychiatric patients with a DSM-III-R diagnosis of either schizophrenia or affective disorder and examined the specificity of cognitive impairment to diagnosis and its relationship to psychopathology.

Methods: 49 schizophrenic-affective pairs matched on age, sex, and cognition were examined on age of first hospitalization, highest educational level, MMSE, PANSS syndrome, and cluster scores and CGI-S. Unmatched cases from the same population,

308 schizophrenics and 50 affectives, were also examined to verify generalization of results.

Results: Not unexpectedly, PANSS "depression" cluster scores were higher in affective disorder patients compared to schizophrenics. In the unmatched series, schizophrenics were significantly more cognitively impaired than affectives. MMSE score correlated significantly with PANSS negative syndrome score ($r = -.57$, $p < .05$, matched; $r = -.67$, $p < 0.05$, unmatched) and general psychopathology score ($r=-.51, p<.05$, matched, $r=-.49, p<0.05$, unmatched). Discriminant analysis of MMSE scores using diagnosis as the grouping variable allowed for 71% and 65% correct classification of schizophrenic and affective disorder patients, respectively (Wilks $\lambda = 0.81$, $p < 0.003$). Using PANSS items, discriminant analysis correctly classified 78% of both schizophrenic and affective disorder patients (Wilks $\lambda = 0.66$, $p < 0.0003$).

Discussion: These data suggest that when matched for cognition, only PANSS negative syndrome scores were different between schizophrenics and affective patients. Nonetheless, discriminant analysis of PANSS items and MMSE scores each could significantly differentiate between diagnostic groups. This suggests that different patterns of psychopathology exist in chronic psychiatric patients with cognitive impairment despite similar overall severity of impairment and psychopathology.

NR53 Monday, May 22, 9:00 a.m.-10:30 a.m.

Effects of Risperidone on Spatial Working Memory

Susan R. McGurk, Ph.D., Camarillo Hospital, UCLA Research Center, Box 6022, Camarillo, CA 93011; Michael F. Green, Ph.D., William C. Wirshing, M.D., Donna Ames, M.D., Barringer D. Marshall, Jr., M.D., Stephen R. Marder, M.D.

Summary:

Schizophrenia patients have shown impairment on tasks of spatial working memory in which they are requested to remember the location of a stimulus. These deficits have been viewed as further evidence for prefrontal dysfunction in schizophrenia because measures of spatial working memory rely on prefrontal circuits. Based on laboratory studies, it is theoretically possible that the 5-HT2 antagonism of new antipsychotic medications such as risperidone may ameliorate prefrontal dysfunction and therefore improve spatial working memory. The current study involved 30 treatment-resistant schizophrenia patients who were participating in a double-blind comparison of risperidone vs. haloperidol. The patients were drawn from a state hospital and from a VA medical center. The subjects received a test of spatial working memory with two delay intervals (5 and 15 sec) at baseline and again after four weeks of either 6 mg of risperidone or 15 mg of haloperidol. For both delays, risperidone appeared to show a beneficial effect compared with haloperidol. Although the results were not significant, the interaction showed a trend for significance for the 5 second delay ($p < .15$, two-tailed). These results, while quite preliminary, suggest that risperidone may benefit performance on neurocognitive measures that rely upon the integrity of the prefrontal region.

NR54 Monday, May 22, 9:00 a.m.-10:30 a.m.

Concurrent Depression in First-Admission Patients with Schizophrenic Disorders

Ranganathan Ram, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore, MD 21208; Lisa B. Dixon, M.D., Malathi Ram, Ph.D., Lina Jandorf, M.A., M. Tanenberg-Karant, M.D., Evelyn J. Bromet, Ph.D.

Summary:

Objectives: Depression favorably influences the long-term outcome of schizophrenia. However, systematic short-term prospective studies have reported either no relationship or an association with negative outcomes such as relapse and re-hospitalization. This country-wide epidemiological study examines the prevalence and correlates of depression in a cohort of first-admission patients with a schizophrenic disorder.

Method: Ninety-six first admission patients from ten inpatient settings with a research diagnosis of a schizophrenic disorder were evaluated with a modified version of the SCID, multiple measures of depression, psychosocial functioning, and quality of life at index admission and six months later.

Results: Twenty-two (22%) patients had a baseline depressive syndrome concurrent with the schizophrenic syndrome. Relatively more patients with depression had made a suicide attempt prior to admission ($p < .02$) and had lower baseline functioning on the GAF ($p < .01$) than those without depression. Although baseline depression resolved when psychosis subsided, these patients had poorer role functioning at follow up ($p < .05$). Only 2 (2%) patients developed a new depressive syndrome at six months.

Conclusions: The depressive syndrome is more likely to occur during the active phase of the schizophrenic disorder than as a "post-psychotic syndrome." Identification of depression in persons with schizophrenia may be important to improve non-clinical outcomes such as role functioning.

NR55 Monday, May 22, 9:00 a.m.-10:30 a.m.

Should There Be Routine Screening of Thyroid Function in Patients Hospitalized for Major Depression or Dysthymia?

Dennis M. Ordas, M.D., 9 Tynewick Court, Silver Spring, MD 20906-2693; Lawrence A. Labbate, M.D.

Summary:

Objective: To examine the clinical practice of testing thyroid function in a mixed community and referral psychiatry inpatient unit. We wanted to evaluate: 1) the frequency of ordering screening, 2) the type of test, and 3) the incidence of thyroid function abnormality among those tested.

Methods: We reviewed thyroid function tests obtained on 279 consecutive, first-time, adult admissions to the psychiatric wards at Walter Reed Army Medical Center, from 1992 through 1993, who met the DSM-III-R diagnostic criteria for major depression or dysthymia.

Results: Of the 279 subjects, 262 (93.9%) had thyroid function tests performed that included evaluation of TSH. Eighteen patients (6.9%) had a TSH outside the normal range. Of these, there were two cases (0.8%) with results suggestive of hyperthyroidism and no overt cases of hypothyroidism.

Conclusion: Although screening thyroid tests are often routine for depressed inpatients, our data do not support this practice. Overt thyroid disease is rare among depressed inpatients.

NR56 Monday, May 22, 9:00 a.m.-10:30 a.m.

Exaggerated Platelet Reactivity in Depression

Dominique L. Musselman, M.D., Psychiatry, Emory University, 1639 Pierce Drive Ste 4000, Atlanta, GA 30322; Bettina T. Knight, R.N., Maryfrances R. Porter, Ulla Marzek, Aaron Tomer, M.D.

Summary:

There is increasing evidence that patients with major depression are at increased risk for ischemic heart disease (IHD) and that depressed patients with IHD have a less favorable prognosis than patients with IHD alone. Alterations in platelet reactivity, sympathoadrenal activity, or platelet serotonergic transporter kinetics may underlie the increased vulnerability of depressed patients to IHD.

Our study population consisted of patients diagnosed with major depression (DSM-III-R) and normal controls; all subjects were in excellent health. Two blood samples were drawn: 7:00 AM the morning following overnight bedrest and then after two minutes of standing (orthostatic challenge). Blood samples were assayed for β-thromboglobulin, platelet factor 4, epinephrine, norepinephrine, serotonin, and cortisol. Additionally, platelets were assayed for [^{3}H]-paroxetine binding site density (a measure of the 5HT transporter). Measures of platelet activation and aggregation were also obtained.

Following orthostatic challenge, depressed patients exhibited a significantly greater increase in measures of platelet activation as reflected by expression of activation-dependent surface markers and platelet release products when compared to the normal controls. These findings suggest possible pathophysiologic mechanisms by which depression acts as a significant risk factor for IHD (Supported by NIMH MH49523 and NIH DK07298 and NIH RR000039).

NR57 Monday, May 22, 9:00 a.m.-10:30 a.m.

Child Depression: Cortisol, ACTH, Prolactin and Growth Hormone

Michael D. De Bellis, M.D., Psychiatry, University of Pitts., 3811 O'Hara Street WPIC, Pittsburgh, PA 15213; Ronald E. Dahl, M.D., James Perel, M.D., Boris Birmaher, M.D., Joaquim Puig-Antich, M.D., (Posthumously), Neal D. Ryan, M.D.

Summary:

Objective: Nighttime secretion of ACTH, cortisol, prolactin, and growth hormone (GH), were examined in prepubertal major depression diagnosed by K-SADS-P (N = 38; 29 male; 10.4 ± 1.5 years) and normal children (N = 28; 13 male; 9.9 ± 1.9 years).

Methods: After "adaptation night," where an intravenous catheter and EEG electrodes were placed for blood sampling and standard all-night polysomnogram, plasma samples were obtained every 20 minutes. Hormonal concentrations were aligned by EEG-confirmed sleep onset. Areas under the curve were calculated for total secretion and compared using ANOVA.

Results: Unlike adult depressives, prepubertal depressed children had lower cortisol secretion during the first four hours after sleep onset compared with controls (26.6 ± 16.7 versus 39.4 ± 23.3 mcg/dL; $t = 2.6$; $p = .01$). ACTH, prolactin, and growth hormone secretion did not differ. Examination of clinical characteristics in depressed subjects revealed lower basal ACTH concentration in depressed inpatients versus depressed outpatients ($t = 2.87$; $p < .01$) and in depressed sexually abused versus depressed nonabused ($t = 2.1$; $p < .05$). A significant sex by diagnosis effect ($F = 4.03$, $p < .05$) revealed lower growth hormone secretion in depressed females compared with depressed males.

Conclusions: These results stress the need for provocative biological studies in prepubertal depression.

NR58 Monday, May 22, 9:00 a.m.-10:30 a.m.

Combined ECT and Clozapine in Schizophrenia

Helen C. Kales, M.D., Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109; Rajiv Tandon, M.D., John R. DeQuardo, M.D., Daniel F. Maixner, M.D., Michael D. Jibson, M.D., Lisa Becks

Summary:

Although clozapine is effective in treating about one-third to one-half of schizophrenic patients refractory to conventional antipsychotic agents, there is still a substantial number of schizophrenic patients who do not respond adequately to clozapine. Treatment options for such patients currently are limited; supplementing clozapine with a course of electroconvulsive therapy (ECT) has been suggested as one possible approach. Specifically, investigators have questioned the utility, safety, and efficacy of ECT augmentation in combination with clozapine in treatment-refractory schizophrenics. To assess the efficacy and safety of this combination, we evaluated the effects of combining clozapine and ECT in 14 schizophrenic inpatients (SADS/RDC and DSM-III-R). All these patients were being treated with clozapine at the time that ECT was considered. All these patients had significant symptomatology despite clozapine treatment; the range of symptoms included disorganization, positive symptoms, catatonia, and negative symptoms. The sample consisted of nine male and five female patients. Bilateral ECT was utilized in all patients; the number of treatments ranged from eight to 18. The dose of clozapine ranged from 200–800 mg/day. Five patients showed marked and sustained clinical improvement, five patients showed transient improvement followed by relapse, and four patients showed no response. One patient of the group that showed transient improvement followed by relapses received maintenance ECT but relapsed despite maintenance ECT. Except for one patient who experienced significant tachycardia (which continued after discontinuation of ECT), we saw no adverse effects in connection with the combination of ECT and clozapine. Supplementing clozapine with a course of bilateral ECT appears to be safe and is effective in some patients with refractory schizophrenia. More systematic trials are indicated.

NR59 Monday, May 22, 9:00 a.m.-10:30 a.m.

Client Discharge From Programs of Assertive Community Treatment

Caroline Poblete, M.D., Psychiatry, University of Maryland, 645 W. Redwood Street, Baltimore, MD 21201; Lisa B. Dixon, M.D., Nancy Krauss, M.S.W., Eileen Hastings, M.S.W.

Summary:

Objectives: Previous research has suggested that clients treated within the Program of Assertive Community Treatment (PACT) model require ongoing rather than time-limited PACT care. The study describes the characteristics of 21 individuals successfully discharged to less-intensive services from PACT model programs. The total number of patients in these programs was approximately 140.

Methods: Program directors of three PACT model programs serving severely psychiatrically disabled clients in an inner city area identified persons discharged from their programs to traditional outpatient clinics without resulting decompensation. A resident psychiatrist uninvolved in the programs conducted chart reviews and interviews of program clinicians to obtain the demographic and clinical characteristics of the discharged persons and qualitative descriptions of the discharge process.

Results: Discharged clients were a mean age of 38.9 (SD 6.9) years, 57% female, 48% minority; 78% had a schizophrenic disorder, 57% had lifetime and 24% had current substance use disorders; 48% had persistent symptoms. Though only 5% were employed, 67% lived in independent apartments and 57% had significant family supports.

Conclusions: This study suggests that it is possible for a minority of patients to benefit from PACT services and then be discharged to less-intensive services. Of note, the rate of current substance use disorders and independent living of these individuals differs from clients referred to these programs, suggesting that discharge may be more likely in individuals who have achieved stability in these domains.

NR60 Monday, May 22, 9:00 a.m.-10:30 a.m.

Parenting and Severe Mental Illness

Ann L. Hackman, M.D., University of Maryland, 645 West Redwood Street, Baltimore, MD 21201; Lisa B. Dixon, M.D.

Summary:

Objectives: There is scant literature on relationships between persons with severe mental illness (SMI) and their children and less on the influence of homelessness. This study evaluated: 1) choices these persons made about having children and the impact of their homelessness and SMI on these decisions; 2) what role those who were parents played with their children.

Methods: A semistructured interview was administered to 27 homeless adults (13 women, 14 men) with SMI receiving services from an assertive community treatment team (ACT), which is part of a research project comparing ACT to standardized services.

Results: Sixteen (59%) of the persons surveyed had children. Only one had raised any of her children beyond the age of five. Twelve of these individuals felt that their SMI, homelessness, or both had impacted on their parenting. Nine of the 11 subjects who did not have children indicated that homelessness, SMI, or both were important influences on their childlessness. Seventeen of the total study group were unhappy or had regrets about their parenting situations. Regrets about parenting situation were associated with problems of substance abuse ($p < .05$) and affective disorders ($p = .07$) regardless of parenting status.

Conclusions: This study shows that a majority of these persons had children and a majority had regrets about their experience. Further, diagnostic factors do have an influence. Clearly, these are issues that should be addressed in treating this population and that warrant further study.

NR61 Monday, May 22, 9:00 a.m.-10:30 a.m.

Delayed-Onset Tension Pneumocephalus Presenting As Frontal Lobe Syndrome

Michael S. Jaffee, M.D., Psychiatry, Wilford Hall, 2200 Bergquist Drive Ste 1, Lackland AFB, TX 78239

Summary:

An unusual case is reported involving complications after a potentially self-inflicted gunshot wound through the frontal lobes with ensuing craniotomy repair. Patient was subsequently assessed as having an abulic affect. Approximately seven weeks after the trauma, patient was found to be even less responsive to stimuli and was noted to have decreased functioning of his right arm and leg. Neurological examination revealed mild, objective, right-sided weakness not compatible with the level of decreased functioning. MRI revealed the existence of a gradually enlarging tension pneumocephalus that required another craniotomy for dura repair. The etiologies and symptomatic presentations of tension pneumocephalus are reviewed and presented. MRI scans are compared in this case, demonstrating the gradual progression of the tension pneumocephalus over one month. Several clinical variants of frontal lobe syndrome are reviewed and compared.

NR62 Monday, May 22, 9:00 a.m.-10:30 a.m.

Sexual Abuse Severity and General Psychopathology

Ernesto F. Figueroa, M.D., Psychiatry, University of Michigan, 1500 E. Med. Ctr. Dr. UH9C9150, Ann Arbor, MI 48109-0120; Kenneth R. Silk, M.D., Alissa Huth, B.A., Naomi E. Lohr, Ph.D.

Summary:

Objective: This study explores the relationship of general measures of psychopathology that correlate with dimensions of severity of childhood sexual abuse (CSXA).

Methods: All subjects (total number of subjects = 45: 37 inpatients with borderline personality disorder [BPD], five inpatients with major depression without BPD and three normal controls) were given the SCL-90-R as well as the Family Experiences Interview (FEI). The FEI is a structured interview that explores various childhood events from ages 0–18, including dimensions of severity of CSXA divided into type, duration, and perpetrator. Only subjects who reported CSXA were included. Subjects who endorsed more severe forms of CSXA were compared with subjects who experienced less severe CSXA. A series of stepwise regressions were performed. First, SCL-90 global score and subscales were dependent variables with diagnosis, gender, and dimensions of severity of CSXA as predictor variables. Second, diagnosis was the dependent variable and dimensions of CSXA as well as SCL-90-R subscales were predictors.

Results: SCL-90-R subscales that correlated with more severe dimensions of abuse were Interpersonal Sensitivity (IS), Hostility (H), Paranoia (Par), and Psychosis (Psy). These correlations were found solely in dimensions that described perpetrator, e.g. sex with a parent, with a family member, or with more than one or two different perpetrators during childhood. When diagnosis was the dependent variable, IS was the only significant predictor of the borderline diagnosis, though CSXA that was ongoing and penetrating revealed a trend towards predicting BPD.

Conclusions: CSXA may be a nonspecific factor contributing to general dimensions of psychopathology rather than a specific etiologic factor contributing to specific symptoms or symptom clusters. CSXA may contribute more specifically in BPD patients to hypersensitivity and distrust in interpersonal situations.

NR63 Monday, May 22, 9:00 a.m.-10:30 a.m.

Activity of Interleukins in Korean Schizophrenics

Yong-Ku Kim, M.D., Psychiatry, Keyo Hospital, 280-1 Wanggogdong Uiwang City, Kyunggido 437 020, South Korea; Min Soo Lee, M.D., Woong Hahm, M.D., Kyu Hang Lee, M.D., Chung Kyoon Lee, M.D., Kwang-Yoon Suh, M.D.

Summary:

Background: It has been postulated that autoimmune process may play a role in the pathogenesis of symptoms in some schizophrenic patients. Findings of altered interleukin (IL) regulation have been regarded as additional proof that schizophrenia has an autoimmunological background.

Method: Sixteen patients who fulfilled DSM-IV criteria for schizophrenia and who were drug free for at least six months, and the same number of age- and sex-matched controls were recruited. The severity of symptoms in schizophrenia was assessed by BPRS. Phytohemagglutinin (PHA)-stimulated production and serum level of IL-1β, IL-2, and IL-6 were measured by enzyme-linked immunosorbent assay (ELISA).

Results: There was a significant decrease of IL-2 production ($p < 0.001$) and a significant increase of IL-2 serum level ($p < 0.01$) in schizophrenic patients. No significant difference of IL-1β and IL-6 production was found. Some patients and controls had measurable serum level of IL-1β and IL-6. No significant correlation between production and serum level of IL-1β, -2, -6 and age, duration of illness, and BPRS score in schizophrenics was found.

Conclusion: This is the first study to describe a decrease of IL-2 production and increase of IL-2 serum level in non-Caucasian schizophrenic patients. These findings are further evidence that autoimmune process is present, regardless of ethnic origin, in some schizophrenic patients.

NR64 Monday, May 22, 9:00 a.m.-10:30 a.m.

Methylxanthines in Older Healthy Volunteers

Marc Cantillon, M.D., NIMH, Bldg 10 Rm 3D41, 10 Center Dr. MSC 1264, Bethesda, MD 20892-1264; Douglas Johnson, Ph.D., Herbert Weingartner, Ph.D., Stanley L. Slater, M.D., Marcel Bahro, M.D., Trey Sunderland, M.D.

Summary:

The effects of low- (2.5 mg/kg) and high-dose (5 mg/kg) i.v. theophylline (T) and placebo (P) were assessed in 24 healthy volunteers (mean age 70 ± 8.2 years) on three separate days. Both T doses increased pulse rate (lying, $F = 3.9$, $p < 0.05$, standing, $F = 4.41$, $p < 0.02$). Locomotor activity was increased in the T subjects in a dose-response fashion ($F = 129.4$, $p < 0.01$). On the BPRS, there were trend-level changes in the anxiety-depression subscale ($F = 2.13$, $p = 0.1$). Serum concentrations showed significant dose-related increases regarding T levels ($F = 156.52$, $p < 0.01$), lactate ($F = 16.24$, $p < 0.01$), and glucose ($F = 4.36$, $p < 0.01$). There was a clear dissociation of these physiologic/behavioral effects from cognitive data in both low- and high-dose T, i.e., no significant difference between either of the T doses and P in simple reaction time, or in performance on our cognitive test battery assessing explicit working, or long-term memory and perceptual motor functions. Thus, despite significant blood levels of T and physiological effects, we found no significant cognitive effects at the doses studied in this population.

NR65 Monday, May 22, 9:00 a.m.-10:30 a.m.

Risk Factors for Transfer to a Psychiatric Intensive Care Unit

Robert J. Nicolson, M.D., Psychiatry, University of Toronto, 50 Rosehill Avenue #710, Toronto, ON M4T 1G6, Canada; Anthony Feinstein, M.D.

Summary:

Objective: A surprisingly small literature exists on the use of psychiatric intensive care units (PICU's), given their importance in patient care. The purpose of this study was to determine variables which could predict transfer from an open ward into a PICU.

Method: Over a one-year period, 48 patients requiring transfer into a PICU were compared with a control group on demographic and illness variables. Each patient received a multi-axial DSM-IV diagnosis and was also rated using the Expanded Brief Psychiatric Rating Scale (E-BPRS).

Results: Demographically, the two groups were similar. However, patients requiring transfer had a longer duration of illness with more admissions and were more likely to have a diagnosis of schizophrenia or mania. As well, they had higher E-BPRS scores and a lower Global Assessment of Functioning Scale (GAFS) score. A discriminative function analysis was able to correctly place 96.9% of the subjects.

Conclusions: Demographic data are not helpful in predicting transfer to a PICU. However, a constellation of five variables (GAFS score and hostility, anxiety, psychosis, and total scores on the E-BPRS) was able to accurately predict patients at risk for transfer.

NR66 Monday, May 22, 9:00 a.m.-10:30 a.m.

Three Catatonia Rating Scales for Clinical and Research Use

Berta M. Guerra, M.D., Psychiatry, The Ohio State University, 1670 Upham Drive, Columbus, OH 43210; Brendan T. Carroll, M.D.

Summary:

The incidence of catatonic disorders has been reported to be as high as 9% of adult psychiatry admissions. In DSM-IV catatonia is a modifier of bipolar disorder, major depression, due to general medical conditions and a subtype of schizophrenia. It has been difficult to study to date because few rating scales were available.

We prospectively identified adult patients with catatonic signs (age ≥ 18 years) at the Ohio State University Neuropsychiatric Facility over one year with the following rating scales: 1) Rosebush et al, 2) Bush-Francis Catatonia Rating Scale and 3) the Modified Rogers Scale.

A total of 29 episodes occurred in 26 inpatients. One patient was seen by the C-L team and one as an outpatient (total = 31 episodes). The results of this study are shown in the table below.

Rating Scale	Mean (±SD)	Range
Rosebush et al	10.6 (±4.6)	3 to 22
Bush-Francis	18.2 (±8.2)	4 to 34
Modified Rogers	16.5 (±6.4)	2 to 29

We recommend the use of the Bush-Francis Rating scale for patients presenting with catatonic features based on: 1) most comprehensive allowing for diagnosis of milder cases of catatonia, 2) high reliability as compared with other catatonia rating scales, 3) high diagnostic agreement with published criteria for catatonia, and 4) availability of a standardized examination which leads to higher reliability among observers.

NR67 Monday, May 22, 9:00 a.m.-10:30 a.m.

Incidence of HIV Infection in Acute Psychosis

Michael E. Doyle, M.D., Psychiatry, Walter Reed Army Med. Center, Washington, DC 20307; Lawrence A. Labbate, M.D.

Summary:

Objective: This study was undertaken to assess the incidence of human immunodeficiency virus (HIV) infection in new-onset, acutely psychotic patients admitted to a 700-bed military referral hospital.

Methods: Hospital records were reviewed for patients admitted to any ward for an acute psychotic episode due to psychiatric or medical causes between October 1, 1991 and September 30, 1992. From this sample of 811 psychosis admissions, 518 records were excluded for known chronic psychotic illnesses, repeat admissions for recurrent affective illness with psychotic features, delirium, or known HIV infection.

Results: Of 293 patients admitted for an acute psychosis, 246 (85%) underwent testing for HIV seropositivity. Of these, 179 patients were men, 67 were women; 181 patients were military, and 65 were civilian. Of these, none tested positive for HIV.

Conclusions: For some populations, routine testing for HIV seropositivity has low yield in evaluating a medical etiology of new psychoses. Though the military population studied has lower risk factors than found in some urban centers, these data further support standards of practice wherein HIV testing is conducted only after a thorough history reveals known risk factors such as prostitution or intravenous drug use, or if physical examination arouses clinical suspicion.

NR68 Monday, May 22, 9:00 a.m.-10:30 a.m.

Gender Differences in Body Dysmorphic Disorder

Susan F. Diaz, M.D., Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Katharine A. Phillips, M.D., Craig G. Gunderson, B.A.

Summary:

Objective: Gender differences in body dismorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, have not been previously investigated. This study assessed gender differences in 130 patients with BDD.

Methods: 130 consecutive patients with BDD were assessed with a semistructured interview, the SCID, and a version of the

Y-BOCS modified for BDD. Males were compared with females with regard to demographic variables, clinical variables, and comorbidity.

Results: 61 (47%) of the subjects were female and 69 (53%) were male. Men and women did not significantly differ in terms of many variables examined, including rates of major depression and anorexia nervosa. However, females were more likely to have lifetime bulimia (f = 8 [13%] v. m = 1 [1%], p = .009), while males were more likely to have lifetime alcohol abuse or dependence (f = 11 [18%] v. m = 28 [41%], p = .005). There was a trend toward an earlier age of onset in men (15.4 ± 5.8 yrs v. 17.5 ± 7.8 yrs., p = .09). The genders did not significantly differ in terms of number of body parts or which body parts they were concerned with, with the exception of men being significantly more preoccupied with body build (f = 1 [2%] v. m = 17 [25%], p < .001). Men were also more likely to report a history of frequent teasing about appearance and use a hat for camouflage, while women were more likely to use cosmetics for camouflage. Although males were as likely as females to seek nonpsychiatric treatment (e.g., dermatololgic, surgical) of BDD (m = 51 [74%] v. f = 49 [80%]), women were more likely to receive such care (f = 43 [70%] v. m = 35 [51%], p = .02).

Conclusion: Although similar in many demographic and clinical variables, men and women with BDD had some noticeable differences, including body parts of concern, comorbidity, and nonpsychiatric treatment obtained.

NR69 Monday, May 22, 9:00 a.m.-10:30 a.m.

Dreams Following Hurricane Andrew

Daniella David, M.D., Psychiatry, University of Miami, 1400 N.W. 10th Ave. #304A D-79, Miami, FL 33136; Thomas A. Mellman, M.D.

Summary:

Background: The re-experiencing nightmare is considered to be an integral feature of post-traumatic stress disorder (PTSD). Supporting data have come from combat veterans. Little is known about nightmares in other trauma-exposed populations. We, therefore, studied dream reports of subjects exposed to a natural disaster.

Methods: Subjects were recruited who had high impact from Hurricane Andrew and who were free of a psychiatric disorder in the six months prior to the hurricane (n = 59). Structured evaluations of psychiatric morbidity were performed at 6–12 months following the hurricane, and subjects completed self-report questionnaires regarding sleep patterns, dream frequency, and dream content in the previous month. Dreams were categorized according to general content and analyzed for associations to PTSD and overall morbidity.

Results: Of the 59 subjects, 32 described dreams. Forty seven percent (n = 15) of the reports involved threatening/negative themes and 53% (n = 17) were pleasant, supportive, or indifferent. Frequencies of dream categories did not differ significantly between subjects with and without active PTSD. Only four of the dream reports featured content directly related to the hurricane (two of which were the re-experiencing of a threat) and all of these were reported by subjects with PTSD).

Conclusion: Our preliminary data suggest that event-related nightmares following a natural disaster are specifically associated with PTSD, but do not occur at a high frequency.

NR70 Monday, May 22, 1:00 p.m.-2:30 p.m.

Medical Clearance of Low Risk Psychiatric Admissions

James D. Hegarty, M.D., Epidemiology, McLean Hospital, 115 Mill Street, Belmont MA 02178; John N. Julian, M.D, Kathy M. Sanders, M.D., Theodore A. Stern, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate screening laboratory studies in LMR psychiatric admissions are low yield, delay dispostion, contribute to emergency room overcrowding, and represent a major indirect cost to the ER.

Summary:

Objective: The MGH Medical Clearance Project was established to analyze the cost-effectiveness of routine medical clearance in psychiatric admissions. This initial study defines a low medical risk (LMR) group of psychiatric admissions for whom minimal medical screening may be appropriate.

Method: A retrospective review of all emergency room (ER) psychiatric evaluations and consultations at the MGH from July 1, 1994 to December 1, 1994 (N = 1284). LMR was defined as: age ≤55, normal vital signs systolic blood pressure (BP 90–180 mm Hg, diastolic BP 50–180 mm Hg, heart rate 60–110 beats per minute and temperature <99°F); orientation to person and place; absence of new-onset psychiatric symptoms and no active substance abuse.

Results: Fifty-six percent (N = 723) of patients were hospitalized. Forty-seven percent (N = 344) of hospitalized patients met LMR criteria. LMR admissions receiving laboratory studies experienced a 32% increase in ER length-of-stay (LOS) compared with LMR patients who did not. Laboratory studies did not affect management of any LMR admission. These findings are consistent with a 95% confidence interval for risk of acute medical morbidity in LMR admissions of zero to five per thousand. While direct costs of screening laboratories averaged only $53 per LMR admission, the 32% increase in LOS represents a potentially enormous indirect cost to the ER.

Conclusion: Screening laboratory studies in LMR psychiatric admissions are low yield, delay disposition, contribute to emergency room overcrowding, and represent a major indirect cost to the ER.

References:

1. Henneman P, Mendoza R, Lewis R: Prespective evaluation of emergency medicine department's medical clearance. *Annal Emer Med,* Vol 24, pp 672-677, Oct. 1994.

NR71 Monday, May 22, 1:00 p.m.-2:30 p.m.

Ataque de Nervios and Trauma History

Daniel S. Schechter, M.D., Post Graduate Education, NY State Psych Inst, 722 W 168th Street Box 83, New York NY 10032; Michael R. Liebowitz, M.D., Ester Salman, B.S., Deborah Goetz, M.P.H., Sharon O. Davies, R.N., Eunice Dong

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the association between childhood trauma and the Hispanic culture-bound syndrome "ataque de nervios."

Summary:

Objective: This study examines the association between childhood trauma and the Hispanic culture-bound syndrome "ataque de nervios." A relationship between "ataque" and history of childhood trauma is suggested by the hysterical and dissociative features of many "ataque" episodes. Given that recent studies suggest that "ataque" symptomatology is influenced by specific psychiatric diagnoses, comorbidity is also examined.

Methods: Hispanic subjects seeking treatment at an anxiety disorders clinic (goal for study is N = 156) were assessed for "ataque de nervios" and history of childhood physical and/or sexual abuse and/or traumatic separation, with specially designed

self-report instruments. Axis I psychiatric diagnoses were assessed with structured interviews and clinical narratives.

Preliminary Results: Of the 50 subjects studied thus far, 72% were female and 70% rated positive for "ataque de nervios." Trauma history was positive in 71% of "ataque-positive" individuals versus 33% of "ataque-negative" individuals. Of "ataque-positive" subjects, comorbid depression was associated with the highest rate of trauma.

Conclusions: The results suggest that "ataque" is likely a marker for trauma. Early trauma may be etiologic for "ataque de nervios," especially in conjunction with affective disorder.

References:

1. Lewis-Fernandez R: "Culture and Dissociation: A Comparison of Ataque de Nervios among Puerto Ricans and Possession Syndrome in India." From *Dissociation: Culture, Mind, and Body.* American Psychiatric Press, Inc., Wash. D.C., 1994.

2. Liebowitz MR: Ester S. Carlos MJ, et al: "Ataque de Nervios and Panic Disorder." *Amer J Psych,* 151:6, pp. 871–75. June, 1994.

NR72 Monday, May 22, 1:00 p.m.-2:30 p.m.

Sertraline in Breast Milk and Nursing Infants

Stephanie S. Winn, M.D., Psych c/o Dr. Z. Stowe, Emory University, P.O. Drawer AF, Atlanta GA 30322; Zachary N. Stowe, M.D., Jacque C. Landry, B.A., Clinton D. Kilts, Ph.D., Timothy Ely, B.S., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate some of the effects of drugs in human milk.

Summary:

Approximately 10% of postpartum women will experience a depressive episode during the first postpartum year, and many of these women may choose to nurse. There remains little definitive information about the potential hazards of antidepressants during lactation. We measured the quantity of sertraline and desmethylsertraline in human breast milk and assessed the effects on nursing infants.

Nine postpartum women with major depression who presented to the Pregnancy and Postpartum Mood Program for treatment chose to continue nursing while being treated with sertraline (25–200 mg/d). These nursing women and nine matched non-nursing depressed postpartum women consented to participate in the breast milk assay and infant follow-up study. A total of 119 breast milk, 23 maternal serum, and two infant samples were collected. The infants' total dose of sertraline was estimated from these samples. Primary infant outcome measures included: 1) growth charts, 2) number of illnesses, and 3) maternal report of developmental milestones.

All assays had standard curves extracted from control serum and breast milk using the internal standard CP-53-630-1, sertraline, and desmethylsertraline. The concentrations of both sertraline (19.0–173.1 ng/ml) and desmethylsertraline (28.4–293.7 ng/ml) varied considerably and did not correlate with maternal dose or serum concentration. The infant serum concentrations of sertraline (2.7 and <1.0 ng/ml) and desmethylsertraline (4.1 and 3.4 ng/ml), were considerably less than maternal serum. Mothers reported no adverse effects. Presently, pediatric records and maternal reports were available for one control and five nursing mother/infant pairs.

These data confirm that sertraline and desmethylsertraline are excreted into human breast milk. While the infant is exposed, the limited data do not suggest any adverse effects. Further study in this area is warranted as women with PPD treated with antidepressants may desire to continue nursing.

References:

1. Atkinson HC, Begg EJ, Darlow BA: Drugs in Human Milk: Clinical Pharmacokinetic Considerations. *Clin Pharmacokinet* 14:217–240, 1988.

2. Wisner KL, Perel JM: Serum Nortriptyline Levels in Nursing Mothers and Their Infants. *Am J Psych* 148:1234–1236, 1991.

NR73 Monday, May 22, 1:00 p.m.-2:30 p.m.

Measuring Quality-of-Life in Panic Disorder

Howard C. Rubin, M.D., Psychiatry VA 116A, Univ CA San Diego, 3350 La Jolla Village Drive, San Diego CA 92161; Tony Rabin, B.S., Julie Gladjo, Ph.D., Robert M. Kaplan, M.D., Mark H. Rapaport, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the effect upon health related quality of life and panic disorder.

Summary:

Panic disorder is characterized by debilitating psychological and physiological symptoms of anxiety. Few studies have examined its effect upon health related quality of life (HRQOL).

This study quantifies the effects of panic disorder on HRQOL in a group of 35 subjects and age- and gender-matched controls. HRQOL was assessed with the Quality of Well Being Scale (QWB), an instrument validated with non-psychiatric illnesses. Using information on current functioning and duration, we can express health outcomes in terms of equivalents of well years of life—Quality-Adjusted Well Years (QALYs).

Compared to age- and gender-matched controls, our subjects at a baseline evaluation had significantly lower QWB scores (.826 vs. .720, $t = 5.28$ $p < .001$). This finding indicates that patients suffering from active panic disorder lose .126 QALYs per year of life or that the equivalent of one year of life is lost for each eight patients with panic disorder. Such a decrease in QALYs is comparable to losses in non-insulin dependent diabetes mellitus, suggesting that untreated panic disorder is associated with significant functional disability.

We will present preliminary longitudinal data on the effects of treatment on QWB scores. We will discuss the strengths and weaknesses of the QALYs approach and review its potential for policy analysis in mental health care.

References:

1. Kaplan RM, Anderson JP: The quality of well being scale: rationale for a single quality of life index, in Quality of life: assessment and application. Edited by Rosser R and Walker SR. London, MTP Press, 51–77, 1988.

2. Massion AO, Warshaw MG, Keller MB: Quality of life and psychiatric morbidity in panic disorder and generalized anxiety disorder. *Am J Psychiatry* 150:600–607, 1993.

NR74 Monday, May 22, 1:00 p.m.-2:30 p.m.

Suicidal Behavior in Depression: Neuroendocrine Approach of the Role of Serotonin and Noradrenaline

William Pitchot, M.D., Psychiatry, University of Liege, Chu Du Sart Tilman, Liege B 4000, Belgium; Michel Hansenne, B.Sc., Antonio Gonzalez Moreno, M.D., Marc M. Ansseau, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe data about the biological correlates of suicidal behavior focuses on the serotonergic system.

Summary:

The prevailing neurochemical theory about biological correlates of suicidal behavior focuses on the serotonergic system (Asberg et al. 1987). Few data are available about the possible implication of the noradrenergic function (Pitchot et al. 1994). In this study, we assessed the growth hormone (GH) response to clonidine, an α2-adrenergic agonist, and the cortisol, ACTH, GH, prolactin, and temperature responses to flesinoxan, a 5-HT1A agonist, in 30 DSM-III-R major depressed inpatients subgrouped into suicide attempters (n = 15) and nonattempters (n = 15). The patients were assessed after a drug-free period of at least three weeks. Mean delta cortisol responses to flesinoxan were significantly lower in the group of depressed patients with a history of suicide attempts than in the group without history of suicidal behavior: for the delta cortisol values 14.5 ± 16.3 μg/l vs 101 ± 94 μg/l ($F = 8.9$, df = 5,25, $p = 0.006$). There was also a very significant difference between suicide attempters and nonattempters for the temperature (delta T°) responses to flesinoxan: 0.20 ± 0.24°C vs 0.60 ± 0.24°C ($F = 18,1$, df = 5,25, $p = 0.0003$). GH responses to clonidine were not significantly different between attempters and nonattempters. The results of the present study support the implication of the serotonergic system, particularly 5-HT1A receptors, in the control of self-directed aggressive behavior. In contrast, noradrenergic disturbances, particularly at the level of α2-adrenergic receptors, seem to play a more minor role.

References:

1. Asberg M, Schalling D, Träskman-Bendz L, Wagner A: Psychobiology of suicide, impulsivity, and related phenomena. In: Meltzer HY (Ed), Psychopharmacology: Third Generation of Progress, Raven Press, New York, pp 655–668, 1987.

2. Pitchot W, Ansseau M, Gonzalez Moreno A, Wauthy J, Hansenne M, von Frenckell R: Relationship between alpha2-adrenergic function and suicidal behavior in depressed patients. *Psychiat Res* 52:115–123, 1994.

NR75 Monday, May 22, 1:00 p.m.-2:30 p.m.

Serotonin and Prediction of Fluoxetine Response Time

Jake Falk, M.D., Psychiatry, Mt. Sinai School of Med., 1 Gustave Levy Place Box 1230, New York NY 10029; Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the possibility that pretreatment PRL response to fenfluramine as an indicator of central serotonin activity may serve as a predictor of response time of MDD to fluoxetine.

Summary:

Objective: Serotonin [5-HT] dysregulation has clearly been demonstrated to be associated with major depressive disorder [MDD]. Fluoxetine [FLU], a selective 5-HT reuptake inhibitor, has been shown to be effective in the treatment of depression. However, the relationship between pretreatment 5-HT activity and the response to FLU is not well understood. The fenfluramine [FEN] challenge test assesses the "net" functioning of the central 5-HT system. Increase in the serum prolactin [PRL] level represents an index of the FEN-induced activation of the 5-HT system. Increase in PRL of <6 is considered a "blunted" response.

Methods: In this study, 13 patients fulfilling DSM-III-R criteria for MDD were given a FEN challenge. All patients were free of major medical illness, substance abuse, and psychotic disorders. After two weeks free of all medications, 60 mg FEN PO was administered at 10:00 am. PRL levels were measured 50 minutes and one hour after placement of I.V. (just prior to administration of FEN), i.e., at baseline, and hourly thereafter until 3 pm. Following this protocol, all patients were assigned randomly and in a double-blind manner to either FLU 20 mg QD or placebo [PLA] for 11 weeks. All patients were assessed weekly with the Hamilton Depression Rating Scale [HDRS]. A decrease of >6 points in the HDRS relative to baseline score was considered to constitute a treatment response.

Results: Two of the 13 patients had blunted PRL responses to FEN. Both were randomly assigned to the FLU arm of the study. No relationship was found between blunting status or peak PRL level and response rate. Of the six patients in the PLA group, one "responded." All seven in the FLU group responded. Among these seven responders, there was a pronounced negative correlation between the peak PRL response to FEN and the time it took to first show a response to FLU ($r = 0.93$, $p < 0.001$, $n = 7$), i.e., decrease in HDRS of >6.

Conclusions: Although this evidence is very preliminary and will be updated prior to presentation, it raises the possibility that pretreatment PRL response to FEN as an indicator of central 5-HT activity may serve as a predictor of the response time of MDD to FLU.

References:

1. Coccaro E, et al: Serotonergic studies in patients with affective and personality disorders. *Arch J Psych,* vol 46, pp. 587-599, 1989.

2. Siever LJ, et al: The growth hormone response to clonidine in acute and remitted depressed male patients. *Neuropsychopharm,* vol 6, No. 3, pp. 165-177, 1992.

NR76 Monday, May 22, 1:00 p.m.-2:30 p.m.

Clomipramine in Adults with Pervasive Developmental Disorder

Edward S. Brodkin, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Christopher J. McDougle, M.D., Susan T. Naylor, M.S.N., Donald J. Cohen, M.D., Lawrence H. Price, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe how clomipramine is effective in reducing interfering behaviors in many adults with PDD.

Summary:

The purpose of this study was to determine the efficacy of the potent serotonin (5-HT) uptake inhibitor clomipramine for reducing repetitive thoughts and behaviors and aggression, and for improving the social relatedness of adults with pervasive developmental disorder (PDD).

Methods: Thirty-five subjects, 24 men and 11 women, who met DSM-III-R criteria for PDD, were entered into a 12-week open-label trial of clomipramine. The mean ± SD age of the group was 30.2 ± 7.0 years, with a range of 18–44 years. Clomipramine was begun at 50 mg/day and dosage was increased by 50 mg/week to a maximum dose of 250 mg/day, based on clinical response and side effects. Behavioral measures of global improvement, repetitive thoughts and behaviors, aggression, and social relatedness were obtained at baseline and then every four weeks throughout the trial.

Results: Of the 33 patients who completed the 12-week trial, 18/33 (55%) were responders based on CGI scores of "much" or "very much improved." Improvement was seen in repetitive thoughts and behaviors, aggression, and social relatedness. The mean dose of clomipramine for the group was 139.4 ± 50.4 mg/day.

Conclusions: These preliminary data suggest that clomipramine is effective in reducing interfering behaviors in many adults with PDD.

References:

1. Brasic JR, Barnett JY, Kaplan D, Sheitman BB, Aisemberg P, Lafargue RT, Kowalik S, Clark A, Tsaltas MO, Young JG: Clomipramine ameliorates adventitious movements and compulsions in prepubertal boys with autistic disorder and severe mental retardation. *Neurology* 44:1309–1312, 1984.

2. McDougle CJ, Price LH, Volkmar ER, Goodman WK, Ward-O'Brien D, Nielsen J, Bregman J, Cohen DJ: Clomipramine in autism: Preliminary evidence of efficacy. *J Am Acad Child Adolesc Psychiatry* 31(4):746–750, 1992.

NR77 Monday, May 22, 1:00 p.m.-2:30 p.m.

Predictors of Violence in Binge Drinking Chinese-American and Korean-American College Students

Henry Chung, M.D., Psychiatry, Cornell Medical College, 525 East 68th Street Box 200, New York NY 10021; James Hull, Ph.D., Edward Ma, B.S., Jeanne Mueller, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that binge drinking and the behavioral sequelae of violence is an underrecognized problem in Asian American college students. Future studies on binge drinking should include adequate Asian samples to further explore the extent of drinking related violence.

Summary:

Objective: To identify risk factors associated with violence in binge drinking Chinese American and Korean American college students.

Methods: The study was presented as an investigation of patterns of alcohol use in Asian American college students including risk factors associated with heavy drinking. Subjects completed an 83-item survey that covered factors such as: demographic, peer and social reference, physiological, family history, attitudinal, acculturation, and physical and behavioral consequences related to drinking patterns. Previous logistic regression analyses had identified several predictors that were significantly associated with binge drinking: having a best friend who is a heavy drinker, believing that drinking is an integral part of social life, having permissive attitudes toward intoxication, lack of religious involvement, being Korean, or born in the U.S. Three items related to violence (fighting, property damage, physical injury) were collapsed into a dichotomous variable for logistic regression analyses with the predictors of binge drinking as independent variables.

Results: Of the six binge drinking predictors, having a best friend who was a heavy drinker ($p < .0000$), believing that drinking is an itegral part of social life ($p < .0053$), and being born in the U.S. ($p < .0162$) were significantly associated with violence in this study. Ethnicity, lack of religious involvement, and permissive attitudes toward intoxication were not associated with violence.

Conclusion: This study lends further support to the importance of social and cultural influences on drinking and its behavioral consequences, notably violence, in Asian American college students. This study also underscores the need to include Asian American samples in future larger sample studies in the study of the relationship between alcohol and violence.

References:

1. Akutsu PD, Sues, Zane N WS, Nakamura CY: Ethnic differences in alcohol consumption in the United States: an investigation of cultural and physiological factors. *J Stud Alcohol* 50:261–267, 1994.

2. Wechsler H, Davenport A, Dowdall G, Moeykens B, Castillo S: Health and behavioral consequences of binge drinking in college: a national survey of students at 140 campuses. *JAMA* 272:1672–1677, 1994.

NR78 Monday, May 22, 1:00 p.m.-2:30 p.m.

Anticipation and Schizophrenia

Janet E. Johnson, M.D., Psychiatry, NY State Psych Inst., 722 West 168th Street, New York NY 10032; Charles A. Kaufmann, M.D., Jill Harkavey-Friedman, Ph.D., Dolores Malaspina, M.D., Jane Cleary, A.B., C. Robert Cloninger, M.D., Ming T. Tsuang, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize and explain the phenomenon of genetic anticipation, particularly in regards to schizophrenia, and have an appreciation of the difficulties and biases that are inherent in this type of analysis.

Summary:

Anticipation is a genetic phenomenon wherein age of disease onset decreases and severity increases in successive generations. Anticipation is described for seven neuropsychiatric disorders. Expanding trinucleotide repeats are the underlying molecular mechanism. We report results of an analysis of anticipation performed with multiplex families segregating schizophrenia.

Thirty-three families were identified through the NIMH Genetics Initiative meeting the following criteria: at least two affected members in successive generations and no evidence of bilineality. Affectation diagnoses included schizophrenia, schizoaffective-depressed, and psychosis NOS. Additional analysis included the Cluster A personality disorders.

Three indices of age of onset were used: first psychotic symptoms, first psychiatric treatment, and first psychiatric hospitalization. Disease severity was measured by number of hospitalizations, past month GAS, and global SAPS and SANS ratings.

Four sampling schemes (McInnis, 1993) were tested: random pairs, random transmitting pairs, all possible pairs, and all possible transmitting pairs. Additional analyses used only pairs ascertained through the parental generation.

Anticipation was demonstrated for age of onset, regardless of the index or sampling scheme used ($p < 0.005$). Anticipation was not supported for disease severity.

The results are discussed in light of potential biases that affect the analysis of anticipation.

References:

1. McInnis M, et al: Anticipation in Bipolar Affective Disorder. *Am J Hum Genet* 53:385–390, 1993.

2. Ross C, et al: Genes with triplet repeats: candidate mediators of neuropsychiatric disorders. Trends in Neurosciences, Vol. 16, No. 7:254–260, 1993.

NR79 Monday, May 22, 1:00 p.m.-2:30 p.m.

Neuroleptic-Resistant Schizophrenia: Clinical, Neuropsychological and Family History Characterization

Ridha Joober, M.D., Psychiatry, McGill University, 1033 Pine Avenue West, Montreal Quebec H3A 1A1, Canada; Chawki Benkelfat, M.D., Samarthja Lal, M.D., Roberta M. Palmour, Ph.D., David M. Bloom, M.D., Alain LaBelle, M.D., Harrietta Drucker, M.A., Michael Dixon, Ph.D., Guy Rouleau, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the preliminary results in 12 families of resistant and five of responsive probands indicating an increased familial

aggregation in first-degree relatives of resistant schizophrenic patients.

Summary:

Phenotype heterogeneity may account for a significant part of the failure to determine specific genetic susceptibility factors in schizophrenia. We hypothesized that schizophrenic patients resistant to typical neuroleptics might represent a more suitable subgroup for studying the genetics of schizophrenia. The aim of the present study was to characterize and contrast neuroleptic-resistant and neuroleptic-responsive patients, with respect to clinical and neuropsychological variables, and with respect to the prevalence of schizophrenia spectrum disorders in families, for the ultimate purpose of conducting molecular genetic studies.

As of now, 44 patients (23 resistant and 21 responders) have been selected on the basis of rigorous criteria of lifetime response to neuroleptics. All patients underwent a comprehensive assessment, including a structured psychiatric interview for genetic studies (DIGS), behavioral scoring of positive and negative symptoms, CPT, frontal lobe executive functions and memory testing. The prevalence of schizophrenia in first-degree relatives was estimated by family interview for genetic studies (FIGS).

In addition to the expected differences in overall level of psychopathology, the two subgroups (Resistant vs Responders; mean $\pm$ SD) differed markedly with respect to age of onset (18.57 $\pm$ 5.73 vs 25.38 $\pm$ 3.61, $p < .0001$), number of hospitalizations (7.11 $\pm$ 4.6 vs 4.8 $\pm$ 4.2, $p = .11$), verbal IQ (84.6 $\pm$ 20.4 vs 106.3 $\pm$ 18.3, $p < .0001$), frontal bone executive function as per WCST (number of achieved categories: 1.39 $\pm$ 1.26 vs 2.61 $\pm$ .86, $p = .0005$; percentage of perseveration errors: .47 $\pm$ .26 vs .19 $\pm$ .13, $p < .0001$) and memory performance (logical memory, immediate: 4.0 $\pm$ 1.7 vs 7.9 $\pm$ 2.63, $p < .0001$; delayed: 2.41 $\pm$ 2.17 vs 6.23 $\pm$ 2.69, $p < .0001$; % retention: 52.97 $\pm$ 35.69 vs 78.81 $\pm$ 26.07, $p = .0094$). Preliminary results in 12 families of resistant and five of responsive probands indicate an increased familial aggregation in first-degree relatives of resistant schizophrenic patients (11/61 vs 1/36, Fisher exact test, two tailed = .029).

References:

1. Brenner, H.D., Dencker, S.J., Goldstein, M.J. et al. Defining treatment refractoriness in schizophrenia. *Schizophr. Bull.* 16:551-564, 1990.

2. Keefe, S.E., Mohs, R.C., Losonczy, M.F. et al. Characteristics of very poor outcome schizophrenia. *Am. J. Psychiatry.* 144:889-895, 1988.

3. Sautter, F., McDermott, B., Garver, D. Familial differences between rapid neuroleptic response psychosis and delayed neuroleptic response psychosis. *Biol. Psychiatry. 33:15-21, 1993.*

NR80 Monday, May 22, 1:00 p.m.-2:30 p.m.

Depression and Quality-of-Life in an Inner-City Cohort of Inpatients with Schizophrenic Disorders

Ranganathan Ram, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21208; Lisa B. Dixon, M.D., Leticia Postrado, Ph.D., Laura Rachuba, B.A.

Educational Objectives:

At the conclusion of this presentation the participant will be a) aware of the importance of identifying depressive syndromes in inner city inpatients with a schizophrenic disorder; b) understand its negative influence on the quality of life of the patient; and c) appreciate ethnic differences in the rates of depression.

Summary:

Objectives: Patients with schizophrenic disorders experience significant depression which may negatively impact on their quality of life. The objective of this study is to determine the prevalence of depression in a sample of inner-city based, newly admitted patients with a schizophrenic disorder and to examine the association of depression with systematically collected measures of quality of life.

Method: 435 consenting persons who were consecutively admitted to two inner-city psychiatric hospitals were interviewed. They received a modified version of the Structured Clinical Interview for DSM-III-R and the Lehman Quality of Life interview. Of 123 patients diagnosed with a schizophrenic disorder, 75% were African American.

Results: 35% of persons diagnosed with a schizophrenic disorder also met criteria for a comorbid (lifetime) depressive syndrome. Relatively more Caucasians were diagnosed with depression than African Americans (72% versus 24.7%, $p < .0$). The depressed subgroup of patients also had significantly lower scores on quality of life measures such as general life satisfaction ($p < 0.001$), satisfaction with living situation ($p < 0.05$), job satisfaction ($p < 0.05$), and satisfaction with leisure activities ($p < 0.02$).

Conclusions: The rates of depression seems to be influenced strongly by ethnicity. Depressive comorbidity is associated with lower quality of life scores in patients with a schizophrenic disorder. Identification and treatment of these syndromes is important to improve the quality of life. Further attention needs to be paid to the diagnosis of depression in African Americans.

References:

1. Siris SG: Diagnosis of Secondary Depression in Schizophrenia: Implications for DSM IV. *Schizophrenia Bulletin* 17:1, 75–97, 1991.

2. Lehman AF, Myers CP, Thompson J: Implications of mental and substance use disorders—A comparison of single and dual diagnosis patients. *J Nerv Mental disorders* 181:6, 365–370, 1993.

NR81 Monday, May 22, 3:00 p.m.-5:00 p.m.

Hostility, Cynicism and Suicidal Ideation in Depressed Outpatients

S. Nassir Ghaemi, M.D., Massachusetts General Hos, WAC-815, 15 Parkman Street, Boston MA 02114; Andrew A. Nierenberg, M.D., Kathy A. Clancy, M.A., Junko Kaji, B.A., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Objective: Suicidal ideation has been thought to be related to suppressed hostility or anger turned inwards, but this hypothesis has not been tested adequately. Also, those who have suicidal ideation alone have been less studied than those who attempt or complete suicide. Our objective was to examine differences between depressed patients with and without suicidal ideation, focusing on anger, aggression, and hostility.

Methods: 42 outpatients with major depression were compared on the Adult Suicide Ideation Questionnaire (ASIQ) and measures of anger (Anger Attacks Questionnaire, Symptom Questionnaire), aggression and hostility (Cook-Medley Hostility Inventory, CMHI) cynicism (CMHI), life events (Positive and Negative Life Events Scale), and depression (Hamilton Depression Rating Scale, Beck Depression Inventory).

Results: There were no differences between those who possessed significant suicidal ideation (ASIQ score >23) and those who had no suicidal ideation (ASIQ score ≤23) on any measures, except for the cynicism measure where the suicidal group demonstrated more evidence of cynicism (6.6 $\pm$ 3.2 vs. 4.5 $\pm$ 2.7, $F = 4.4$, $p = 0.04$).

Conclusions: Suicidal ideation is associated with cynicism but unrelated to measures of hostility, anger, or aggression, or to severity of depression in outpatients.

NR82 Monday, May 22, 3:00 p.m.-5:00 p.m.

Management of Bipolar Disorder with Adjunctive Risperidone: Response to Open Treatment

S. Nassir Ghaemi, M.D., Massachusetts General Hospital, WAC-815, 15 Parkman Street, Boston MA 02114; Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christine J. Truman, B.A., Holly M. Hendin, B.A.

Summary:

Objective: Patients with bipolar disorder often present acute symptoms which prove refractory to standard neuroleptic medications. Risperidone, an atypical antipsychotic agent, may offer an attractive alternative. We reviewed the outcome of all outpatients with bipolar disorder who received adjunctive risperidone for affective symptoms in our clinic (n = 14).

Methods: Data were harvested from the treating psychiatrists' prospective assessment of response using the Clinical Global Improvement (CGI) scale and the Global Assessment of Functioning (GAF) scale.

Results: Nine patients (64%) were much improved (CGI ≥ 2), and none worsened. Mean GAF scores rose from 48.2 ± 4.9 during the month before risperidone treatment to 58.8 ± 7.3 during the month after risperidone treatment (t = 4.49, p = 0.0006, paired t-test). Mean duration of treatment was 6.4 ± 2.7 weeks, and the mean maintenance dose was 2.75 ± 1.8 mg/daily. Three patients stopped treatment due to side effects (ataxia/dizziness or weight gain). Nine patients had either failed prior neuroleptic treatment or had been unable to tolerate neuroleptic medications.

Conclusion: This report suggests that risperidone is a useful treatment for bipolar disorder, including symptoms refractory to standard neuroleptic medications. Confirmation awaits prospective controlled studies.

NR83 Monday, May 22, 3:00 p.m.-5:00 p.m.

Acute and Delayed Major Depression Following Spinal Cord Injury

Yasuhiro Kishi, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive #2887 JPP, Iowa City IA 52242; Robert G. Robinson, M.D.

Summary:

Objective: Patients with major depressions that began during the acute period following spinal cord injury (SCI) were compared with patients with major depression that began during the chronic period following SCI. We hypothesized that these two types of depressions might have different etiologies and clinical correlates.

Methods: A group of 60 patients of SCI were examined using a semistructured psychiatric interview during the hospital admission and at three and six months follow-up.

Results: Thirteen patients had major depression during the initial in-hospital evaluation (acute onset) and eight had major depression first diagnosed at either three or six months follow-up (delayed onset). Patients with acute onset depressions had greater severity of physical impairment and a higher frequency of premorbid history of psychiatric disorder than nondepressed patients. Delayed onset depressions, in contrast, had more rostral spinal level of injury than nondepressed controls. At the onset of depression, acute onset depressions were characterized by higher number of vegetative and anxious symptoms and were more severe as measured by the Ham-D than delayed onset depressions.

Conclusion: Finding that the phenomenology and clinical correlates of acute and delayed onset depressions are different suggests that there may be differences in the underlying etiology and pathophysiology of these disorders.

NR84 Monday, May 22, 3:00 p.m.-5:00 p.m.

Panic Disorder Comorbidity with Familial Bipolar Disorder

Dean F. MacKinnon, 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 DePaulo, Jr., M.D.

Summary:

Objective: We have evaluated a sample of 57 bipolar families, identified for a genetic linkage study, to investigate bipolar and panic disorder comorbidity rates across families.

Method: The bipolar probands (n = 57) and their affected first-degree relatives (n = 121) were assessed by trained psychiatrists using the SADS-L interview and diagnosed by RDC. The relatives were divided into two groups based on the presence or absence of panic disorder in the proband of their family. The rate of panic disorder in the two groups was compared using chi-square analysis. As a control, rates of other comorbid diagnoses also were compared.

Results: 18% of the relatives had panic disorder. Panic disorder was more common in the group of relatives of the probands with comorbid panic disorder (36% vs. 13%, p = 0.02). Alcoholism was less common in this group (7% vs. 35%, p = 0.005). Alcoholism was equally common among probands with and without panic disorder.

Conclusions: Panic disorder in bipolar probands predicts a higher rate of panic disorder among affected relatives and a decreased rate of comorbid alcoholism. These findings may help define genetic subtypes of familial bipolar disorder.

NR85 Monday, May 22, 3:00 p.m.-5:00 p.m.

The Psychometric Properties of Hopelessness Scale in Chinese Sample

Hui-Qi Tong, M.D., Psychiatry, Shanghai Medical Univ., No. 96 Xinle Road, Shanghai 200031, P.R. China; Jun-Mian Xu, M.D., Yun Zhou, M.D., Bin Zhou, M.S.

Summary:

To evaluate the psychometric properties of the Hopelessness Scale, we administered the Beck's Depression Inventory, the Hamilton Depression Scale, the Hopelessness Scale (we modified it by rating 0–4), and the clinical rating of suicidal behavior to 76 depressed patients and two control groups: 46 nondepressed schizophrenic subjects and 107 normal subjects. The results showed that the modified HS had a high degree of internal consistency (Cronbach alpha = 0.93). High item-total correlations and high test-retest reliability over a two-week period with nomal subjects were also found. Principal components analyses revealed two factors with the depressed group: The sample of depressed patients showed highly significant correlation between the total HS score and the total BDI, total HAMD score. The result also indicated that all items of the HS can discriminate the depressive group from the two control groups. They can also discriminate the suicidal group (suicide ideator or attempter) from the nonsuicidal group in the depressed patients, while BDI and HAMD failed to do so. We conclude from the study that the Hopelessness Scale has high reliability and validity in this sample of Chinese subjects.

NR86 Monday, May 22, 3:00 p.m-5:00 p.m.

Co-Occurence of Migraine with Mixed and Pure Mania

Megan M. Dwight, M.D., Psychiatry, University of Cincinnati, P.O. Box 670559, Cincinnati OH 45267; R. Mark Newman, M.D.

Summary:

Objective: Migraine headache commonly co-occurs with bipolar disorder. To investigate whether migraine is more common in bipolar patients with depressive symptoms, we compared the rate of migraine headache in patients with mixed and pure mania.

Methods: Patients age 12 years or older presenting with psychosis were recruited from inpatient and outpatient sites. Patients were excluded if they had been previously hospitalized or if symptoms resulted entirely from substance abuse or medical illness. All diagnoses were made using the Structured Clinical Interview for DSM-III-R.

Results: Of 124 patients with bipolar disorder, 77 were diagnosed with pure mania and 47 with mixed mania. Migraine occurred in 19.5% of patients with pure mania and in 14.9% of patients with mixed mania. This difference was not significant. There was a trend for increased rate of migraine in patients with lower socioeconomic status.

Conclusions: Migraine headache is common in bipolar disorder, but does not occur more frequently in mixed states than in pure manic states. The trend toward increased incidence of migraine in patients in lower socioeconomic groups may represent a pattern of increased somatic symptoms in affective illness in this group of patients.

NR87 Monday, May 22, 3:00 p.m.-5:00 p.m.

The Effect of Comorbid Depression and Anxiety on Symptom Severity

Gary S. Bruss, Ph.D., Garroway Lab., Inst. Penna. Hospital, 111 N. 49th Street, Philadelphia PA 19139; Alan M. Gruenberg, M.D., Reed D. Goldstein, Ph.D., Jacques P. Barber, Ph.D

Summary:

Many patients in the midst of an acute major depressive episode simultaneously report symptoms consistent with a co-occurring diagnosable anxiety disorder. This study focused upon the extent to which the comorbidity of these disorders affects the severity of symptoms in each condition. We hypothesized that patients with comorbid conditions would report a greater severity of depressive and anxious symptoms compared with patients with major depression and no anxiety disorder.

DSM-III-R Axis I diagnoses were derived using the modified Schedule for Affective Disorders and Schizophrenia (modSADS). Clinician-rated (i.e., structured versions of the HAM-D and HAM-A) and self-report measures (i.e., BDI and BAI) were used to assess the severity of depressive and anxious symptoms in both groups of patients. Sixty-six inpatients participated in the study (i.e., 40 and 26 patients in each group, respectively). The results varied depending upon the type of measures used. There were no statistically significant differences in symptom severity between the two groups on the basis of the HAM-D and HAM-A assessments ($p = .17$ and $p = .07$, respectively). Alternatively, both self-administered instruments yielded statistically significant differences in symptom severity scores between the two groups as predicted (BDI: $p = .05$; BAI: $p = .01$). The implications of the findings are discussed, with recommendations for future research, particularly the role of multivariate and multimodal assessment.

NR88 Monday, May 22, 3:00 p.m.-5:00 p.m.

Dissociative Identity Disorder: Axis I and II Comorbidity

Gary S. Bruss, Ph.D., Garroway Lab., Inst. Penna. Hospital, 111 N. 49th Street, Philadelphia PA 19139; Alan M. Gruenberg, M.D., Reed D. Goldstein, Ph.D., Jacques P. Barber, Ph.D.

Summary:

While several studies have documented the polysymptomatic presentation of patients with Dissociative Identity Disorder (DID), a lack of uniformity in diagnostic definitions and in the methodologies of these studies makes it difficult to draw conclusions regarding the actual comorbidity of DID and other Axis I and Axis II conditions. To our knowledge, no studies exist examining comorbidity utilizing empirically based structured diagnostic interviews for DSM-III-R or DSM-IV.

This report reflects the preliminary findings on eight inpatients diagnosed with DID who represent the initial group of subjects in a larger study evaluating the comorbidity of 40 DID inpatients.

Diagnoses were derived using: the modified SADS for Axis I; the PDE for Axis II, and the DDIS for DID. All patients met criteria for at least one other Axis I disorder. The mean number of other comorbid Axis I disorders was 5.6. Eighty-eight percent of patients met criteria for a major mood disorder (57% for major depression, chronic; 14% for major depression, recurrent, 29% for bipolar disorder). A notable trend in 83% of patients with major depression was the deteriorating course of depressive illness over time (i.e., progression from early-onset dysthymia to double depression to chronic major depression). Seventy-five percent of patients met criteria for an anxiety disorder; 75% for an eating disorder; 38% for substance abuse; 13% for schizoaffective disorder. All patients met criteria for at least one Axis II disorder. The mean number of Axis II disorder was 3.3. Eighty-eight percent of patients met criteria for borderline personality disorder. The distribution of Axis II disorders spanned all three clusters. The treatment implications of the clinical heterogeneity of patients with DID will be discussed.

NR89 Monday, May 22, 3:00 p.m.-5:00 p.m.

Characteristics of Patients Treated with Valproate

Priscilla Sheldon-Cost, Ph.D., Psychiatry, Johns Hopkins, Meyer 3-181 600 N Wolfe Street, Baltimore MD 21287; R. Scott Cost, M.S.E., J. Raymond DePaulo, Jr., M.D.

Summary:

Valproic acid has been shown to be an effective antimanic drug and may be particularly effective in the treatment of mixed states. We undertook a chart review to examine the characteristics of inpatients treated with valproic acid at The Johns Hopkins Hospital. Two overlapping samples were used: data set 1 contained inpatient records from 1988–1994 with ICD-9 diagnostic codes 296.40–296.7 ($N = 2098$) and electronic pharmacy data; data set 2, contained only records from 1994 of patients who had received valproate ($N = 45$) or patients who had received lithium but not valproate ($N = 25$). These data (set 2) were derived from direct chart review. Data set 1 was divided into three groups; patients given valproate, patients given tegretol but not valproate, and patients given lithium but neither valproate nor tegretol.

There was a significantly higher percentage of patients in the valproate group in data set 1 with a diagnosis of mixed bipolar disorder ($p < .01$) and a significantly smaller percentage of patients with bipolar NOS in both the valproate and tegretol groups ($p < .001$ and .05, respectively). In data set 2, there was a similar trend (i.e. more mixed and fewer NOS in the valproate group), which did not reach significance.

Patients given valproate had been given more psychotropic medications ($p < .05$); had longer lengths of stay in hospital ($p < .001$); and had a trend toward more years of illness ($p < .06$). The most common rationale for treatment with valproate was treatment failure with lithium (74%). The commonest rationale for treatment with lithium was the first diagnosis of bipolar illness (76%). Valproate was judged (at discharge) to be fully effective or partly effective in 46% and 41% of patients, respectively. Lithium was judged effective in 52% and partly effective in 40% of the lithium group.

More patients in the valproate group had a family history of affective disorder, whereas the lithium group had more family history of substance abuse ($p < .05$). There was a trend in the valproate group toward being more likely to have attempted suicide ($p < .06$), while there was no difference in the occurence of psychotic symptoms. The two groups did not vary significantly with respect to age, sex, marital status, employment, or living situation. However, there were more whites ($p < .01$) and a trend toward more history of substance and alcohol abuse ($p < .06$) in the valproate group.

These data suggest that inpatients currently selected for valproate therapy tend to have more severe and treatment-resistant bipolar illness compared with those given lithium therapy.

NR90 Monday, May 22, 3:00 p.m.-5:00 p.m.

Effects of Prior ECT on Seizure Induction and Duration

Srinibas Mahapatra, M.D., Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor MI 48109; Rajiv Tandon, M.D., John R. DeQuardo, M.D., Leon J. Grunhaus, M.D., Helen C. Kales, M.D., Lisa Becks

Summary:

During a course of electroconvulsive therapy (ECT), resistance to seizure induction (seizure threshold) increases, and seizure duration decreases; in fact, this "anticonvulsant" effect of ECT has been related by some experts to the antidepressant effects of ECT. How long these effects persist is unclear and a topic of controversy (*Eur Arch Psychiatry Clin Neurosci,* 1994, 243:293–295). In general, ECT has not been associated with many long-term effects. To further study this question, we compared seizure characteristics and ECT stimulus parameters across different courses of ECT in patients with recurrent major depressive disorder (MDD) who received two or more courses of electroconvulsive therapy over a 10-year period. Forty patients with 117 courses of ECT over this period were studied. Patients were not receiving any benzodiazepines, anticonvulsants, or psychotropic medications during any of these courses of ECT. Controlling for the stimulus parameters, seizure duration was significantly affected by course ($p < .02$); seizure duration decreased with increasing course number. When analyzed separately, this effect was observed for treatments 1, 2, 3, and 4 of each course. Sequential significant decreases in seizure duration were observed until course 4, when reduced sample size and a possible floor effect may have limited our ability to detect such a relationship. Higher energy levels were utilized in later courses of ECT, suggesting the possibility of higher seizure threshold in later courses of ECT; however, seizure threshold was not directly assessed in this study. These data suggest that ECT may have relatively long-lasting effects on seizure induction and maintenance. The precise duration of this effect is, however, unclear. Teasing out this relationship from effects of long-term depressive illness and other factors on seizure induction and maintenance is also difficult. The precise mechanisms underlying this long-term anticonvulsant effect of ECT is unclear; the relevance of this effect to antidepressant efficacy of ECT and process of relapse in depression merits further study.

NR91 Monday, May 22, 3:00 p.m.-5:00 p.m.

Timecourse of Antidepressant Effect of ECT

Daniel F. Maixner, M.D., Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor MI 48109; Rajiv Tandon, M.D., John R. DeQuardo, M.D., Leon J. Grunhaus, M.D., Helen C. Kales, M.D., Lisa Becks

Summary:

Although electroconvulsive therapy (ECT) is an extremely effective modality for treating depression, the specific timecourse and pattern of its antidepressant effect is not clearly delineated. A better understanding of the temporal profile of ECT's antidepressant effect would be clinically useful and could potentially elucidate underlying neurobiological mechanisms. In an effort to address this question, we studied the course of depressive symptomatology during 150 courses of electroconvulsive therapy. Ninety patients with recurrent major depressive disorder (MDD), who received these 150 courses of ECT, constituted the sample for this study. ECT dosage parameters were not strictly controlled but were determined by the ECT consultant administering the treatments. The severity of depression was assessed by the 17-item Hamilton Rating Scale for Depression (HRSD) and the Global Depression Rating (GDR), which were administered on a weekly basis. Mean HRSD scores improved by 18 points over the course of ECT. Approximately 40% of this improvement occurred over the first week, as reflected by reduction in total HRSD scores from week 0 to week 1. The extent of clinical improvement progressively decreased with increasing number of weeks; while this effect was most pronounced when the entire sample was considered, it was also noted in the subgroup of patients receiving more than nine ECT treatments. Vegetative symptoms (sleep, appetite) improved first, closely followed by psychomotor activity (retardation/agitation), followed by mood and depressive cognition. Although the greatest degree of improvement occurred during the initial phases of the ECT course, there was a distinct group of patients who responded late in the course; this suggests that minimal/no response early in the course of ECT treatment does not necessarily predict nonresponse over the entire course. Although the antidepressant effect of ECT is more rapid than that observed with antidepressant medications, the overall profile of response of various components of depression is similar. This suggests a commonality in the neurobiological mechanisms underlying the antidepressant effects of ECT and antidepressant medications.

NR92 Monday, May 22, 3:00 p.m.-5:00 p.m.

Organic Mood Disorders: Clinical Characteristics

Jose M. Benzo, M.D., Epidemiology, McLean Hospital, 115 Mill Street, Belmont MA 02178; German Baraibar, M.D., Jose M. Castillo, M.D., David Gardner, B.Sc. Phar, Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D.

Summary:

Objectives: To study the causes and treatment of organic mood disorder (OMD).

Methods: We collected from hospital charts the causes of OMD; type, dose, adverse effects and response to treatment assessed using the clinical global impression for improvement scale (CGI-I).

Results: 76 patients were identified: 39 (51%) of 76 patients had secondary depression; 20 (26%) were manic, and 17 (22%) had a mixed presentation. The most common causes of OMD were: head injury 16 (21%), cerebrovascular accident 15 (19.7%), and temporal lobe epilepsy 10 (13.1%). The most commonly associated etiology in the depressed nine (45%) and mixed five (29%) subgroups was head injury, and for the manic subgroup was CVA 7 (35%). There were not difference in response to treatment between the three drugs. Only three patients developed significant side effects, all taking CBZ: one developed sedation, one blurred vision and ataxia, and the other one transient elevation of hepatic transaminase levels; only in this third one was the discontinuation of CBZ needed.

Conclusions: The most common causes of OMD are neurological diseases. Mood stabilizers are safe and effective to treat OMD.

NR93 Monday, May 22, 3:00 p.m.-5:00 p.m.

Anxiety Sensitivity and Depression

Christina M. Demopoulos, M.D., Psychiatry, Mass General Hospital, WAC 815 Parkman Street, Boston MA 02114; Maurizio Fava, M.D., Nancy E. McLean, B.A., John D. Matthews, M.D., Michael W. Otto, Ph.D., Jerrold F. Rosenbaum, M.D.

Summary:

Background: Anxiety sensitivity is defined as the tendency to fear anxiety symptoms due to the belief that these symptoms have catastrophic consequences. In a previous study (Otto et al., in press), depressed patients with and without anxiety disorders were found to have elevated scores of the Anxiety Sensitivity Index compared to normal controls.

Objective: We wanted to assess the relationships between anxiety sensitivity and depression, anxiety, somatic symptoms, and hypochondriacal concerns.

Method: We studied 116 depressed outpatients participating in a study involving open treatment with fluoxetine 20 mg/day for eight weeks. Diagnosis of major depressive disorder was made with the use of the SCID-P and patients were required to have a 17-item Hamilton Rating Scale for Depression (HAM-D-17) score ≥16 at entry. All subjects were administered for Anxiety Sensitivity Index (ASI), the Illness Attitude Scale, and the Symptom Questionnaire (assessing anxiety and somatic symptoms).

Results: We found that ASI scores were significantly positively related to severity of depression ($r = .23$; $p = .02$), anxiety ($r = .36$; $p < .0001$), hypochondriacal concerns ($r = .49$; $p < .0001$), and somatic symptoms ($r = .18$: $p = .05$). ASI scores decreased significantly following antidepressant treatment ($t = 5.5$; $p < .0001$) and their change was significantly correlated with changes in levels of anxiety, depression, and hypochondriacal concerns.

Conclusion: Our results suggest that anxiety sensitivity is correlated with depression and responds to antidepressant treatment with fluoxetine 20 mg/day.

NR94 Monday, May 22, 3:00 p.m.-5:00 p.m.

Self-Medication and Response to Treatment in Major Depression

John J. Worthington III, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street, Ste 815, Boston MA 02114; Maurizio Fava, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Jerrold F. Rosenbaum, M.D.

Summary:

Background: A common phenomenon observed among depressed individuals is that of self-medication, using legal or illegal drugs of various kinds.

Objective: We undertook the first ever prospective investigation on the use of alcohol, nicotine, and caffeine in depressed outpatients and the effects of acute treatment with fluoxetine on the consumption of these drugs.

Method: 94 outpatients meeting DSM-III-R criteria for major depressive disorder were administered a questionnaire pre- and post-treatment to quantify the daily intake of alcohol, nicotine, and caffeine. None of these patients met criteria for current alcohol or substance abuse. Patients were then treated openly for eight weeks with 20 mg/day of fluoxetine.

Results: We found at baseline that there was a significant relationship between severity of depression and degree of consumption of nicotine. The degree of alcohol consumption at baseline was a significant predictor of poorer outcome, with this relationship remaining significant even after adjusting for severity of depression at baseline. We observed small, nonsignificant reductions in the consumption of alcohol, nicotine, and caffeine after treatment.

Conclusions: It appears that those patients with greater alcohol consumption at baseline are less likely to respond to pharmacological treatment than those who consume less or no alcohol, consistent with the hypothesis of a depressogenic effect of this substance.

NR95 Monday, May 22, 3:00 p.m.-5:00 p.m.

Yohimbine Augmentation of Fluvoxamine in Refractory Depression: A Preliminary, Single-Blind Study

Angela C. Cappiello, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Christopher J. McDougle, M.D., Robert T. Malison, M.D., George R. Heninger, M.D., Lawrence H. Price, M.D.

Summary:

Preclinical studies have shown that monoaminergic adaptive changes, such as enhanced serotonin and decreased β-adrenergic receptor function, are implicated in antidepressant efficacy. Evidence suggests that intact serotonin function is necessary for antidepressant-induced down-regulation of β-adrenergic receptors. We hypothesized that activation of the noradrenergic system by an α_2-adrenergic receptor antagonist would interact with the enhancement of serotonin function resulting from long-term selective serotonin uptake inhibitor (SSUI) treatment, resulting in potentiation of the clinical efficacy of the SSUI.

Methods: Six inpatients with major depression refractory to at least two antidepressant trials participated in a single-blind trial with yohimbine added to ongoing fluvoxamine treatment for three weeks. Weekly assessments, including the Hamilton Depression Rating Scale (HDRS) and the Short Clinical Rating Scale (SCRS), were obtained.

Results: ANOVA demonstrated significant improvement in HDRS scores ($F = 5.77$; $DF = 3, 15$; $P < .008$) and in the depression scores on the SCRS ($F = 9.32$; $DF = 3, 15$; $P < .001$).

Conclusions: These preliminary data suggest some efficacy of yohimbine addition to fluvoxamine in severely depressed patients refractory to other treatments. Further studies using more selective α_2-antagonists will be needed to clarify the clinical significance of this effect.

NR96 Monday, May 22, 3:00 p.m.-5:00 p.m.

Atypical Depression in the Hospital: Clinical Features and Personality Characteristics

Celeste N. Derecho, Ph.D., Psychiatry, Einstein Medical Co., 3055 Lakewood Drive, Fort Lauderdale FL 33332; Scott Wetzler, Ph.D., Lata K. McGinn, Ph.D., Gregory M. Asnis, M.D., William C. Sanderson, Ph.D.

Summary:

Objective: This study investigates the prevalence and characteristics of *atypical depression* (AD) among depressed inpatients.

Method: Twenty-one depressed inpatients were diagnosed using the SCID, rated on the Hamilton Depression Rating Scale (HAMD), and assessed for AD using the Atypical Depressive Disorder Scale (ADDS). AD was defined as the presence of mood reactivity and two of four associated features: hyperphagia, hypersomnia, leaden paralysis, rejection sensitivity. All subjects completed the SCL-90, the MCM-II, and a suicide survey.

Results: Seven patients (33%) met criteria for AD. AD and nonAD patients did not differ in terms of severity of depression, history of suicide attempts, level of clinical symptomatology, age of onset of depression, prior hospitalizations, and most personality characteristics. However, AD patients scored significantly higher than nonAD patients on the SCL-90 Interpersonal Sensitivity and MCMI-II Avoidant scales, and were more likely to be single.

Conclusion: AD is fairly prevalent on an inpatient service, comparable to the frequency found in outpatient settings. AD is not a milder form of depression. The only differences between AD and nonAD patients reflect the personality trait of rejection sensitivity which is a defining feature of AD.

NR97 Monday, May 22, 3:00 p.m.-5:00 p.m.

Tryptophan Depletion and Vulnerability to Depression

Francisco A. Moreno, M.D., Psychiatry, University of Arizona, 1501 N. Campbell Avenue, Tucson AZ 85724; Sasha Panov, M.D., Louise J. Strayer, R.N., Rebecca L. Potter, M.D., Alan J. Gelenberg, M.D., Pedro L. Delgado, M.D.

Summary:

Brain serotonin (5-HT) content is dependent on plasma levels of tryptophan (TRP). Rapid and transient depletion of TRP causes a brief depressive relapse in most patients successfully treated with and taking SSRIs, but little change in drug-free, symptomatic depressed patients. This study investigates the effects of TRP depletion in drug-free subjects in clinical remission from a prior major depressive episode (MDE).

Method: In an ongoing pilot study, 10 subjects with a prior MDE (DSM-IV), currently in clinical remission (mean time well 60 months, range 6 to 231 months) and drug-free for ≥3 months, and five age- and gender-matched healthy subjects (without personal or family history of AXIS I Disorder), received TRP depletion (final N = 13/group). Testing involves two 2-day tests one week apart in a double-blind, controlled (full strength and quarter strength drink) crossover fashion. Each test includes a TRP-free, 15 amino acid drink day and a follow-up day. Hamilton Depression Scale (HAM-D) ratings and plasma TRP levels are obtained prior to, during and after testing.

Results: 7/10 subjects with history of MDE had an ≥5 pt. increase in HAM-D (mean 6 ± 5 prior and 14 ± 9 after the drink). None of the healthy controls had clinically significant mood changes (mean HAM-D scores 1 ± 1 prior and 3 ± 1 after the drink).

Implications: In the context of prior TRP depletion studies with antidepressant-treated and drug-free, symptomatic depressed patients, these results suggest that depression may not be caused by an abnormality of 5-HT function, but rather by dysfunction of other systems or brain regions modulated by 5-HT. TRP depletion may be useful for identifying individuals at high risk for depression, with or without previous history.

NR98 Monday, May 22, 3:00 p.m.-5:00 p.m.

Pattern of Illness and Duration of Mania in Bipolar Disorder

Christine J. Truman, B.A., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114; Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Holly M. Hendin, B.A., S. Nassir Ghaemi, M.D.

Summary:

DSM-IV recognizes depression, mania, hypomania, and mixed episodes, noting that episodes are demarcated by periods of full or partial remission. Bipolar patients, however, may present with episodes with only one mood state or complex (multiphasic) episodes. Several researchers suggest bipolar patients typed by sequence of affective phases respond differently to prophylactic medication. This study seeks to determine if the duration of mood elevation differs for a monophasic, biphasic, or polyphasic episode.

All patients seen at our bipolar clinic receive a standardized assessment of mood symptoms and are assigned a clinical status based on DSM-IV definitions. A systematic mood charting technique was applied to these prospective ratings over a two-year period to determine the length of each phase and pattern of episode. Under naturalistic open treatment conditions, the duration of manic episodes was compared for four episode types: monophasic, biphasic with initial mood elevation (MDI), biphasic with initial depression (DMI), and polyphasic.

Mood charts were constructed for 25 patients. Thirty-three episodes of mood elevation were identified (monophasic 42%, MDI 15%, DMI 6%, and polyphasic 12%). Episode duration and time until recovery varied between groups. Pattern of illness may be a useful indicator of prognosis in bipolar patients.

NR99 Monday, May 22, 3:00 p.m.-5:00 p.m.

WITHDRAWN

NR100 Monday, May 22, 3:00 p.m.-5:00 p.m.

Neuropsychiatric Findings in Children of Early-Onset Versus Late-Onset Bipolar Illness

Claudia F. Baldassano, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114; Gary S. Sachs, M.D., Christine J. Truman, B.A., Holly M. Hendin, B.A., S. Nassir Ghaemi, M.D.

Summary:

Background: Neuropsychiatric impairment has been reported in bipolar probands and their offspring. Prior data from our sample indicate children of bipolar probands with early onset have significantly higher incidence of childhood psychopathology compared to children of late onset probands. Several investigators have shown an association between neuropsychiatric deficits and psychopathology. We examined children of early and late onset probands and compared the prevalance of neuropsychiatric deficits.

Methods: Eight children of late onset probands (onset > 18) were age- and sex-matched to eight children of early onset probands (onset ≤ 18). Blind raters tested dominant hemispheric functioning using the WISC-R Vocabulary subtest, Sentence Memory Test, and Verbal Fluency test. Non-dominant functioning was evaluated using the Block Design of the WISC-R, the Judgement of Line Orientation, the Benton Visual Retention Test, the Developmental Test of Visual and Motor Integration, the Wisconsin Card Sort, and the Rey Osterrieth Complex Figure.

Conclusion: We present findings in neuropsychologic testing, examination for soft signs, and obstetrical history, and compare the children of early onset to late onset bipolar probands. Our findings suggest a greater discrepancy between verbal and performance IQ and lower mean performance IQ in the children of early onset probands.

NR101 Monday, May 22, 3:00 p.m.-5:00 p.m.

Paroxetine for Bipolar Depression: Outcome in Patients Failing Prior Antidepressant Trials

Claudia F. Baldassano, M.D., Psychiatry, Mass General Hospital, WACC 815 15 Parkman Street, Boston MA 02114; Gary S. Sachs, M.D., Andrew L. Stoll, M.D., Beny Lafer, M.D., Christine J. Truman, B.A., Holly M. Hendin, B.A.

Summary:

Background: Major depression is common and often debilitating for the bipolar patient. Of particular concern, are those acutely depressed bipolar patients who have not responded to previous trials of antidepressants. This investigation uses an open design to explore the efficacy and affective switch rate of paroxetine for the treatment of bipolar depression in this population.

Method: The charts of 20 depressed outpatients who received paroxetine, and who met DSM-III-R criteria for bipolar disorder, were systematically, reviewed using a semi-structured format. All patients included had previously failed treatment with at least one standard antidepressant agent. Treatment efficacy and treatment emergent mania/hypomania were assessed.

Results: A high rate of efficacy (65%) and low rate of treatment-emergent mania (10%) were found.

Conclusion: These results suggest that paroxetine should be considered as first-line treatment for bipolar depression, especially in patients with a history of prior unsuccessful antidepressant treatment or a history of treatment-induced mania.

NR102 Monday, May 22, 3:00 p.m.-5:00 p.m.

Dependency and Self-Criticism As Risk Factors for Major Depressive Disorder

Ari E. Zaretsky, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street, Ste 815, Boston MA 02114; Maurizio Fava, M.D., Katharine G. Davidson, B.A., Joel A. Pava, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Background: Beck (1983) has proposed that two personality traits, sociotropy and autonomy, are important in predicting the type of life events triggering depression and its symptom profile. Whereas sociotropic individuals derive most of their self-esteem from interpersonal interactions and are very sensitive to disapproval and rejection (dependent), autonomous individuals derive most of their self-esteem from attaining their personal goals and are often discontented with themselves (self-critical).

Objective: To determine whether dependent and self-critical personality traits are associated with a) specific types of life events that occur during index episodes of major depression and b) certain subtypes of depression.

Method: Eligible subjects were depressed outpatients with a SCID-P-determined diagnosis of major depressive disorder who completed a) the Dysfunctional Attitude Scale (DAS), a 40-item questionnaire which contains dependent and self-critical subscales and measures self-worth contingencies, and b) the Life Experiences Survey (LES), an inventory of 57 life events. The items of the LES were classified as congruent with dependency, self-criticism or neither. Simple linear regressions were performed to determine the relationship between self-criticism and dependency and life events as well as depression subtypes. Depression severity was measured before and after eight weeks of fluoxetine treatment with the HAM-D-17.

Results: The DAS dependency subscale showed significant correlations with life events regardless of congruency, whereas the DAS self-criticism subscale was not associated with any type of life events. Dependency and self-criticism were not associated with either melancholia or atypical depression. The baseline HAM-D scores were positively correlated with both DAS subscales and the total DAS score.

Conclusions: These results confirm a growing body of research that has found an association between sociotropic/dependent personality traits and life events. Our results also supported earlier studies reporting a correlation between depression severity and dysfunctional cognitive style.

NR103 Monday, May 22, 3:00 p.m.-5:00 p.m.

Differences in Thyroid Function Between Bipolar Patients with Mixed Mania and Pure Mania

Kiki D. Chang, M.D., Univ of Cincinnati, 231 Bethesda ML 559, Cincinnati OH 45267; Sean Stanton, B.S., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Stephen M. Strakowski, M.D.

Summary:

Background: Subclinical hypothyroidism has been reported in a large percentage of rapid-cycling bipolar patients in most relevant studies (Bauer, et al., 1990). Studies have also revealed inconsistent data regarding thyroid abnormalities in bipolar patients during manic episodes. However, thyroid function has not been adequately studied in bipolar populations diagnosed with mixed mania. These patients represent a distinct clinical state separate from pure mania and may have separate biological markers, a predominance of women, poorer outcome, and differing response to pharmacological treatment (McElroy, et. al., 1992). In this study, we have investigated differences in thyroid function between bipolar patients with mixed mania and patients with pure mania.

Method: The sample (N = 53) included bipolar patients admitted to the psychiatric wards at University of Cincinnati Hospital. Patients were separated by those with mixed mania (n = 21) versus those with pure mania (n = 32) by the Structured Clinical Interview for the DSM-III-R. Plasma concentrations of TSH, T3, and T4 were evaluated in each group by immunoassay (Immunol, Technicon).

Results: The majority of these patients had thyroid hormone levels within the normal range, with Grade II hypothyroidism in 19% of mixed manic patients and 3% of pure manic patients. However, patients with mixed mania demonstrated a significantly higher level of TSH (mean $\pm$ SD = 2.98 $\pm$ 2.76 vs. 1.62 $\pm$ 1.29, p = .02) and a lower level of T4 (mean $\pm$ SD = 7.03 $\pm$ 1.58 vs. 8.17 $\pm$ 2.26, p = .05) than patients with pure mania. No significant differences in T3 were found.

Conclusions: These results suggest that subtle thyroid abnormalities may exist in bipolar patients with mixed mania. Regardless of a state of absolute subclinical hypothyroidism, patients with mixed mania may be relatively hypothyroid to those with pure mania. These results support the validation of mixed mania as a distinct clinical syndrome separate from pure mania.

NR104 Monday, May 22, 3:00 p.m.-5:00 p.m.

Double-Blind Placebo-Controlled Trial of Pindolol in Depression

Robert M. Berman, M.D., Psychiatry, West Haven VAMC, 950 Campbell Avenue 116A, West Haven CT 06516; Adam M. Darnell, M.D., Helen L. Miller, M.D., Dennis S. Charney, M.D.

Summary:

Two groups have recently reported on the use of pindolol, a 5-HT_{1A} antagonist and non-specific beta blocker, in depression. These studies have reported that 1) concurrent administration of pindolol with most antidepressant medications hastens clinical response when given to treatment naive patients; and 2) pindolol addition to most previously inadequate treatment regimens effects a clinical response. Validity of these pilot studies is limited by use of an open-label, unblinded study design. We wish to report our preliminary findings from two randomized, controlled trials examining the use of pindolol in treatment naive (Study A) and treatment refractory (Study B) depressed patients.

Methods: In Study A, treatment naive patients are concurrently started on fluoxetine and either active pindolol (2.5 mg p.o. t.i.d.) or placebo. At the end of six weeks, all patients are placed on placebo pindolol. In Study B, fluoxetine-refractory patients are maintained on fluoxetine with the addition of either active pindolol (2.5 mg p.o. t.i.d.) or placebo. At the end of three weeks, all patients are placed on active pindolol.

Results: To date, 17 patients have finished Study A, completing at least two weeks on protocol. After two weeks of medication, two of eight patients on active pindolol demonstrated at least 50% decreases in Hamilton Depression Rating Scores (HDRS), specifically decreasing from 21 to 6 and 30 to 9. Two other patients demonstrated a robust response, with HDRS's decreasing from 29 to 15 and 31 to 17. At the same time point, 0 of 9 patients on

placebo demonstrated at least a 50% decrease in HDRS. In one patient the HDRS decreased from 33 to 17. Expanded results of Study A and analysis of results from Study B will be presented.

NR105 Monday, May 22, 3:00 p.m.-5:00 p.m.

Light Therapy: An Enhancer of Antidepressants

Khaled I. Mohamed, M.D., Psychiatry, Montefiore Medical, 111 E 210th Street, Bronx NY 10467; Gregory M. Asnis, M.D.

Summary:

Light therapy is a well-known antidepressant treatment for seasonal affective disorder (SAD). A unique quality is that it is a nonpharmacological approach, safe and most importantly for this presentation, has a rapid onset of action (2–5 days). We wanted to investigate whether the combination of light therapy with a selective serotonin reuptake inhibitor, fluoxetine, would induce a rapid response in non-seasonal affective disorder. The latter routinely takes a minimum of four to six weeks to respond to antidepressants alone.

We evaluated in a pilot study four patients who were diagnosed by DSM-IV criteria as having a major depressive disorder, nonpsychotic subtype, all were females with an age range of 24–43 years old. Patients were drug free for a minimum of one month and were medically healthy. Treatment consisted of fluoxetine (20 mg/day) and light therapy 10,000 Lux for one hour in the morning (between 0800–1100 hrs) for eight weeks. Severity of depression was assessed at baseline and weekly using the Beck Depression Inventory and Hamilton Depression Scale.

The four subjects had a mean symptomatic improvement at the end of one week of treatment of 46%, case1 66%, case2 22%, case3 58%, and case4 39%. Although these are preliminary findings in an open study, they are indeed encouraging. For this presentation, we will present data from weeks 2–8 as well as expand our sample size.

NR106 Monday, May 22, 3:00 p.m.-5:00 p.m.

Maintenance ECT in Antidepressant Refractory Patients

Nirmal Sathaye, M.D., Psychiatry, East Orange East VAMC, Tremont Avenue, East Orange NJ 07019; Cheng-Jen Chen, M.D.

Summary:

Pharmacotherapy and ECT are two effective modalities of treatment for major depression. Long-term pharmacotherapy is recommended to prevent relapse of symptoms. Estimates that about 80% of those who responded initially to ECT did not relapse when maintenance ECT was used (Stephens et al., 1993). However, data on the rate of success in preventing relapse of maintenance ECT in patients refractory to antidepressants is minimal (to our knowledge). In addition, the treatment options for antidepressant resistant cases in the event that maintenance ECT fails are also limited. We report data on four pharmacotherapy resistant cases of major depression, who were initially treated with index ECT and then maintained on maintenance ECT for almost 1.5 years.

Two of our cases are currently free of depressive symptoms and receive maintenance ECT once every three months. The other two patients responded to the maintenance ECT treatments initially but then became refractory to them. One of the patients was given ECT as frequently as once every week for a period od six months but he failed to sustain the effects of the treatment. Interestingly, both these patients responded to Tegretol either alone or in combination with an antidepressant and are currently free of depressive symptoms.

Detailed information on our cases will be presented.

NR107 Monday, May 22, 3:00 p.m.-5:00 p.m.

Body Dysmorphic Disorder and Social Phobia

Joseph V. Penn, M.D., Residency Training Office, 345 Blackstone Blvd, Providence RI 02906; Katharine A. Phillips, M.D., Kate Dimond, B.A.

Summary:

Background: Body dysmorphic disorder (BDD), a preoccupation with an imagined defect in appearance, has been hypothesized to be related to social phobia (SP). Although most BDD patients develop social phobia secondary to BDD, the relationship between BDD and primary social phobia is unclear.

Methods: 134 consecutive subjects with DSM-IV BDD were assessed with a semistructured interview, the SCID, the YBOCS modified for BDD, the Rathus assertiveness scale. BDD subjects without primary social phobia were compared with BDD subjects with comorbid primary social phobia (i.e., social phobia not due to BDD).

Results: 47 of 134 BDD subjects (35%) met criteria for primary social phobia. The two groups, BDD vs. BDD + SP, did not differ in terms of most variables examined, including demographics, clinical features, or comorbidity. Both groups had similarly high degrees of introversion and impairment, with mean GAF scores of 48 $\pm$ 12 in the BDD group and 42 $\pm$ 13 in BDD + SP group. The two groups were equally likely to respond to open treatment with an SRI; contrary to our prediction, BDD symptoms in the BDD + SP group did not respond better to MAOI's than in the BDD group ($^3/_{16}$ [19%] vs. $^7/_8$ [50%], respectively). However, the BDD + SP group had lower assertiveness scores and, as predicted, higher rates of alcohol abuse/dependence (24 [51%] vs. 17 [20%], $p < 0.001$) and other substance use disorders (17 [36%] vs. 17[20%], $p < 0.05$).

Conclusions: Although most BDD subjects had social phobia secondary to BDD, a large percentage also had primary social phobia. Our preliminary findings suggest that BDD patients with and without comorbid primary social phobia have many similarities, perhaps due to the presence of secondary social phobia in most of the patients without primary social phobia. However, those with comorbid social phobia were less assertive and more likely to abuse alcohol and other drugs.

NR108 Monday, May 22, 3:00 p.m.-5:00 p.m.

Recognition and Treatment of Depressive Disorders Among Internists

Joseph V. Penn, M.D., Residency Training Office, 345 Blackstone Blvd, Providence RI 02906; Robert J. Boland, M.D., James R. McCartney, M.D.

Summary:

Objectives: Depression is underdiagnosed and undertreated by nonpsychiatric practitioners. Research suggests needed improvement in recognition and treatment of depressive disorders by primary care practitioners, however limited information is available on internists. This pilot study was undertaken to better understand internists' ability to recognize depression, choice of appropriate medications, dosage, and treatment patterns.

Methods: Questionnaires were distributed to 45 internal medicine housestaff, 45 internal medicine attendings, and 42 adult psychiatry residents. Each questionnaire contained 4 vignettes: 1) Major depression (MDD) 2) MDD with melancholic features 3) Atypical MDD 4) MDD with psychotic features. Eleven questions per case covered diagnoses, management, and treatment.

Results: Preliminary findings on 42 psychiatry residents, 20 medicine attendings, and 24 medicine housestaff suggested that many medicine attendings and housestaff: 1) had difficulty in recognizing major depression and subtypes, 2) had indicated they would initiate pharmacologic treatment 3) often made incorrect or

questionable pharmacological choices, and 4) had a low threshold for psychiatric consultation or referral. Formal statistical analyses are pending.

Conclusions: Our preliminary findings among internists are consistent with research on primary care physicians suggesting the depression is underdiagnosed and undertreated. Complete data analysis of the full sample will be presented with intragroup comparisons.

NR109 Monday, May 22, 3:00 p.m.-5:00 p.m.

Life Events and Panic Disorder/Agoraphobia

Ghada N. Lteif, M.D., Dept of Psychiatry, Ohio State University, 1670 Upham Drive, Columbus OH 43210; Matig R. Mavissakalian, M.D.

Summary:

A patient-rated checklist adapted from the Psychiatric Epidemiology Research Interview was used to assess the frequency and desirability of life events of the 12 months prior to an index evaluation of a large sample of patients with DSM-III diagnosis of panic disorder or agoraphobia with panic, on the average 12 years after the onset of their illness.

A total of 1360 events were reported; 25% of these events were considered to be most undesirable, whereas 22% were estimated to be most desirable. Negative life events were predominantly health-related issues and interpersonal conflicts. Making new friends, having significant success at work, and taking up a new activity were examples of positive events. Correlations of life events with clinical and demographic variables as well as with symptom-rating scales were also analyzed. Negative life events were associated with greater psychopathology and neuroticism scores. Positive life events were associated with greater extraversion scores, greater years of education, employment status, and less functional impairment due to symptoms.

This exploratory study does not allow interpretation from an etiologic perspective. It begins to shed light on the possible role of life events in the course of the disorder.

NR110 Monday, May 22, 3:00 p.m.-5:00 p.m.

Childhood Trauma in Panic Disorder and Social Phobia

Randall D. Marshall, M.D., NY State Psych Inst., 722 West 168th Street Unit 13, New York NY 10032; Lisa O'Donnell, B.S., Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., Franklin R. Schneier, M.D.

Summary:

Several reports document high rates of childhood trauma in psychiatric outpatients. Whether specific types of trauma are associated with particular disorders in adulthood other than PTSD remains unclear. A history of patients' childhood traumatic events was systematically assessed at an anxiety disorders research clinic (N = 371). Rates of childhood trauma were: sexual abuse (15%); early separation (32%); alcoholic family member (31%); punishment by hitting (27%); physical injury through punishment (16%); and witnessed violence between parents (22%). A chi square analysis was then conducted for each set of traumatic events in patients with panic disorder (PD) (N = 112) and patients with social phobia (SP) (N = 73). No significant differences were found. Within diagnostic groups, women with PD and agoraphobia were more likely to have been raped as adults (2/64 = 3%) than were women with PD but no agoraphobic avoidance (9/44 = 20%, p = .003). The association of childhood trauma and symptom severity will also be reported (data entry in progress).

Theoretically linked trauma such as childhood separation or humiliating punishment experiences, however, were not specifically associated with PD or PDA. Childhood trauma may represent a nonspecific vulnerability to these disorders. Trauma may be more relevant to symptom severity and functional impairment than to etiology.

NR111 Monday, May 22, 3:00 p.m.-5:00 p.m.

Headache Responses to m-CPP in OCD and Normal Controls

Cheryl M. Wong, M.D., Psychiatry, Mt. Sinai Medical School, 1 Gustave Levy Place, New York NY 10029; Lisa J. Cohen, Ph.D., Concetta Decaria, Ph.D., Bonnie R. Aronowitz, Ph.D., Daphne Simeon, M.D., Eric Hollander, M.D.

Summary:

The serotonin (5-HT) agonist m-CPP has been found to induce migraine-like headaches in both patients with eating disorders and normal controls, with bulimics being especially susceptible to headache induction. However, no studies of headache response in patients with obsessive compulsive disorder (OCD), a group having 5-HT dysfunction as evidenced by blunted prolactin response to m-CPP, have been conducted. In this report, we studied headache response in 41 OCD patients and 21 normal controls who received m-CPP (0.5 mg/kg po) and placebo. We found that both OCD patients ($p < 0.03$) and normal controls ($p < 0.07$) had more headaches following m-CPP than placebo. Of interest, induction of headaches was increased only in female subjects ($p < 0.07$). Female OCD patients had a 1.5-fold increase in headache response. These findings suggest that post-synaptic 5-HT mechanisms may be involved in both migraine-like headache production and OCD, especially in female patients with OCD.

NR112 Monday, May 22, 3:00 p.m.-5:00 p.m.

OCD During Pregnancy and the Puerperium

C. Neill Epperson, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Christopher J. McDougle, M.D., Rebecca M. Brown, B.A., James F. Leckman, M.D., Wayne K. Goodman, M.D., Lawrence H. Price, M.D.

Summary:

Significantly elevated cerebrospinal fluid (CSF) levels of the neurohormone oxytocin (OT) have been found in adults with obsessive compulsive disorder (OCD) (non-tic-related). Oxytocin levels increase in the third trimester of pregnancy and the puerperium. The purpose of this study was to determine if pregnancy and/or the puerperium are associated with the onset of exacerbation of OCD.

Methods: Subjects were outpatients or inpatients of the Yale OCD clinic with a primary diagnosis of OCD (DSM-III-R/IV). All women admitted to the clinic from its inception (9/11/85) to the present were assessed. Retrospective data from discharged patients were collected from medical records and confirmed by direct telephone interview. Prospective data from current patients were gathered via clinical interview. Comorbid psychiatric diagnoses were determined using a semi-structured interview modeled after the SADS. A detailed history of pregnancy and its effects on obsessive compulsive (OC) symptoms was obtained.

Results: Thus far, we have assessed 32 women aged 19–69 years (mean $\pm$ SD = 40.7 $\pm$ 14.3 years). The mean age of onset of OCD for the group was 28.8 $\pm$ 12.4 years. Twenty-one of the 32 women have been pregnant. In two cases (10%), the onset of OCD occurred with pregnancy. Eight of 19 women (42%) who had OCD prior to becoming pregnant reported an exacerbation of OC symptoms during pregnancy and another two (11%) during the puerperium. OC symptoms improved in two women during pregnancy and in one following delivery. Some women reported no change in symptoms.

Conclusions: Preliminary findings from this ongoing study indicate that pregnancy and the puerperium are associated with the induction or exacerbation of OC symptoms in a subset of women. Detailed results including comorbid diagnosis, severity of OCD, and types of OC symptoms will be presented.

NR113 Monday, May 22, 3:00 p.m.-5:00 p.m.

Venlafaxine in Generalized Anxiety Disorder

Gerardo Villarreal, M.D., Dept of Psych, Med Univ of South Carolina, 171 Ashley Ave, Charleston SC 29425-0742; Naresh P. Emmanuel, M.D., R. Bruce Lydiard, Ph.D., James C. Ballenger, M.D.

Summary:

Objective: Benzodiazepines have been the treatment of choice for generalized anxiety disorder (GAD), but concerns have been raised about possible dependence and withdrawal symptoms. Other alternatives include buspirone that has a delayed onset of action, and tricyclic antidepressants that have significant side effects. This is a pilot study to investigate the efficacy and safety of venlafaxine in patients with GAD.

Method: These are preliminary data of an ongoing, open-label, pilot study of venlafaxine in GAD. We studied seven GAD patients (four females and three males) for eight weeks. All patients were evaluated using the structured Clinical Interview for DSM-III-R. The Hamilton Anxiety Rating Scale (HAM-A) and clinical global impression (CGI) were the primary outcome measures. Doses of venlafaxine ranged from 56.25 mg to 187.5 mg.

Results: Of the five patients that completed at least two weeks of treatment, four were considered responders (much or very much improved on CGI), and one was minimally improved. HAM-A scores changed from 18.7 ± 6 to 6.2 ± 4.6.

Conclusion: Our results indicate that venlafaxine might be useful in the treatment of GAD. Data from an enriched sample will be presented. Further studies are warranted.

NR114 Monday, May 22, 3:00 p.m.-5:00 p.m.

Growth Hormone Deficiency and Social Phobia

Linda M. Nicholas, M.D., Psychiatry, University North Carolina, CB #7160, Chapel Hill NC 27599-7160; Manuel E. Tancer, M.D., Susan G. Silva, M.D., Louis E. Underwood, M.D., Brian Stabler, Ph.D.

Summary:

Objective: We previously found high rates of social phobia (SP) in growth hormone-deficient (GHD) adult subjects treated with growth hormone (GH) during childhood. To determine if SP is related to GHD, 21 GHD subjects (14 males, 7 females) were compared with 13 non-GHD short-statured (SS) controls (7 males < 163 cm, 6 females < 155 cm).

Methods: Structured interviews (SCID-NP) were conducted and subjects completed the following self-report scales: Fear of Negative Evaluation (FNE), Fear Questionnaire (FQ), Social Avoidance and Distress Scale (SADS), Beck Depression Inventory (BDI), and Tridimensional Personality Questionnaire (TPQ). Two-way ANOVAs were performed for each self-report measure.

Results: 48% (10/21) of GHD and 15% (2/13) of SS subjects met DSM-III-R criteria for SP. Compared to SS subjects, GHD subjects scored significantly higher on the FNE (p = 0.05), FQ (p = 0.009), BDI (p = 0.02), and TPQ-harm avoidance (TPQ-HA) subscale (p = 0.008) and significantly lower on the TPQ-novelty seeking (TPQ-NS) subscale (p = 0.05). Additionally, a significant group-by-gender interaction effect was demonstrated on the TPQ-HA subscale (p = 0.04); multiple comparison analyses indicated GHD females scored significantly higher relative to SS females (p = 0.002) and SS makes (p = 0.05).

Conclusion: These results support a role for disordered GH secretion independent of short-stature in the pathogenesis of SP. Interestingly, the data also suggest that harm avoidance is particularly evident in GHD females.

NR115 Monday, May 22, 3:00 p.m.-5:00 p.m.

A Neural Network Model of OCD: Preliminary Development

Jose M. Gonzalez, M.D., Psychiatry, University of Miami, 118 Madeira Avenue #2, Coral Gables FL 33134; Raymond L. Ownby, M.D.

Summary:

Objective: To decide whether a neural network model of obsessive compulsive disorder (OCD) could be developed and to test the extent to which its behavior might be related to the behavior of patients with OCD.

Method: Research on the functional neuroanatomy of OCD was used in designing a neural network model of the disorder. The network was constructed and trained with a back-propagation algorithm, and its behavior was then assessed under various conditions.

Results: Results show that a) the network behaved both normally and abnormally, depending on what combinations of perceptual, motivational, and neurochemical inputs were presented to it, and b) several simulated etiologic mechanisms for OCD produced changes in the networks' behavior similar to patients' report of OCD symptoms.

Conclusion: It is possible to develop a neural model of OCD whose behavior appears to model that of OCD patients. Further development may make the model useful in understanding the complex etiology of OCD and in testing therapeutic methods for it.

NR116 Monday, May 22, 3:00 p.m.-5:00 p.m.

OCD and Suicide: A Systematic Investigation

Rebecca M. Brown, B.A., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Christopher J. McDougle, M.D., C. Neill Epperson, M.D., Suzanne Wasylink, RN.C., Wayne K. Goodman, M.D., Lawrence H. Price, M.D.

Summary:

No comprehensive assessment of suicidal behavior has been conducted in DSM-III-R/IV OCD patients. Many OCD patients have comorbid major depression and panic disorder where the incidence of suicide attempts in these disorders is 15% and 12%, respectively. The purpose of this study was to systematically examine suicidality in adult OCD patients.

Methods: Subjects had a principal diagnosis of OCD (DSM-III-R/IV) as patients of the Yale OCD Clinic. Retrospective data (since 9/11/85) were collected from medical records and confirmed by telephone interview. Prospective data were gathered via clinical interview. Comorbid psychiatric diagnoses were determined by semistructured interview modeled after the SADS. Detailed histories of suicidal behavior were obtained.

Results: Thus far, we have assessed 60 patients, 32 women and 28 men, aged 19 to 69 years (mean ± SD = 38.3 ± 13.7 years). Nine subjects (15%) had made suicidal gestures or attempts rating in severity from 2 to 4 (mean, 2.4 ± 1.2) using the SADS criteria for lethality. All nine had comorbid personality, affective, or panic disorders. No OCD patients without comorbid diagnoses (N = 27) made suicidal gestures or attempts.

Conclusions: Preliminary findings indicate that OCD patients with vs. without comorbidity are at significant greater risk for suicidal behavior. Further results will be presented.

NR117 Monday, May 22, 3:00 p.m-5:00 p.m.

Differential Responses to Serotonergic Challenge in OCD Clinical Subtypes

Juan J. Lopez-Ibor, Jr., M.D., Psychiatry, Hospital San Carlos, Plaza Cristo Rey SN, Madrid 28040, Spain; Maria I. Lopez-Ibor, M.D., Jose L. Carrasco, M.D., Benedicto Crespo, M.D., Jose A. Cabranes, M.D., Jose L. Ayuso-Mateos, M.D.

Summary:

Serotonergic challenges in obsessive compulsive disorder (OCD) have provided controversial results in different studies and both blunted and increased hormonal responses to serotonin agonists have been reported. OCD is often associated with tic disorder and depression, both reported to be related to serotonergic abnormalities. Such comorbidity could possibly account for this disparity.

Twenty-two patients with OCD and seven healthy controls were studied. Eight patients had comorbid depression and six had comorbid tic disorder. 12.5 mg of intravenous clomipramine were administered and response of cortisol, prolactin and ACTH were evaluated at 15, 30, 60, and 90 minutes after the infusion.

Cortisol response was significantly reduced ($p < 0.05$) in the group of OCD patients compared with the control group.

The presence of comorbid depression was associated with a significantly blunted ACTH response compared with OCD alone ($p < 0.05$) at 15 and 30 minutes post infusion and with a significantly reduced maximum peak of ACTH ($p < 0.05$).

Patients with comorbid tics and OCD had greater hormonal responses than patients with OCD alone. Cortisol concentrations were significantly increased at 60 ($p < 0.05$) and 90 ($p < 0.01$) minutes post infusion and ACTH response was increased at 15 ($p < 0.05$), 30 ($p < 0.05$) and 60 ($p < 0.01$) minutes. The AUC for ACTH was significantly larger ($p < 0.01$) in OCD patients with comorbid tics.

These findings support the idea of different clinical subtypes of OCD. Associated depressive and motoric symptoms might account for differential responses to serotonergic challenges.

NR118 Monday, May 22, 3:00 p.m.-5:00 p.m.

Enhanced Sensitivity to CCK-4 in Women with Severe Premenstrual Symptoms

Jean-Michel Le Melledo, M.D., Psychopharm., St. Mary's Hospital, Lacombe 3830, Montreal H3T 1M5, Canada; Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., Francois Belavance, Ph.D., Daniel Georges Bichet, M.D., Uriel Halbreich, M.D.

Summary:

An overlooked area in biological studies of panic is the influence of menstrual cycle (MC) and the MC-related disorder, premenstrual dysphoric disorder (PDD), on behavioral sensitivity to panicogenic agents. In this regard, we have studied the behavioral effects of systemic administration of cholecystokinin-tetrapeptide (CCK-4) in normal women with and without PDD. CCK-4 is a neurotransmitter which is also a well validated panicogenic agent. A randomized placebo-controlled, three-period design was used. Placebo was administered in the first study period which coincided with the luteal phase of the MC. CCK-4 (35 μg) was administered in periods two and three under two conditions: during the luteal phase and follicular phase of the MC. Subjects were blind to the order in which placebo and CCK-4 were administered. Behavioral response to CCK-4 was evaluated with an 18-item DSM-III-R derived panic syndrome scale. Preliminary analysis (12 women with PDD, 13 controls) of sum intensity scores (i.e., the sum of the intensity ratings) revealed that women with PDD were behaviorally hypersensitive to CCK-4 ($F(1,21) = 10.49$, $p < 0.004$). The mean ($\pm$SEM) sum intensity score during the follicular and luteal phase of the MC cycle was 20.4 $\pm$ 2.8 and 22.9 $\pm$ 4.0, respectively, for women with PDD, and 14.1 $\pm$ 2.2 and 15.4 $\pm$ 2.0, respectively, for women without PDD. These preliminary data suggest that the enhanced behavioral responsivity to CCK-4 evident in women with PDD is attributable, at least in part, to hypersensitivity of the CCK_B receptor system and/or alterations in neurotransmitter systems which interface with CCK.

NR119 Monday, May 22, 3:00 p.m.-5:00 p.m.

The Effects of CCK-4 on Plasma Arginine-Vasopressin Levels in Women

Jean-Michel Le Melledo, M.D., Psychopharm., St. Mary's Hospital, Lacombe 3830, Montreal, Que H3T 1M5, Canada; Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., Francois Belavance, Ph.D., S. Steinberg, M.D., Uriel Halbreich, M.D.

Summary:

Evidence of interactions between the cholecystokinin (CCK), oxytocin (OT), and arginine-vasopressin (AVP) systems exists and alterations of OT and AVP during the menstrual cycle (MC) have been suggested. However, involvement of CCK, AVP, OT and their interactions have been shown to be species specific. Consequently, application of animal findings to human is difficult. Therefore, we decided to use challenges with CCK-4 (cholecystokinin-tetrapeptide, a neurotransmitter which is also a panicogenic agent) to study better how the CCK system and OT and AVP interact during the MC of both women without premenstrual dysphoric disorder (PDD) and with PDD. A randomized placebo-controlled three-period design was used. Placebo was administered in the first study period which coincided with the luteal phase of the MC. CCK-4 (35 μg) was administered in periods two and three under two conditions: during the luteal phase and follicular phase of the MC. AVP and OT were measured by RIA in plasma before and after the injections of placebo and CCK4. CCK-4 induced an increase of AVP during both the first and the second CCK-4 administration (first administration: $p = 0.007$, second administration: $p = 0.0029$) which coincided with physical and behavioral effects of CCK-4. These results suggest that in humans, CCK-4 and endogenous CCK_B agonist, can stimulate AVP release and that this peptide might play a role in the pathophysiology of panic attack.

NR120 Monday, May 22, 3:00 p.m.-5:00 p.m.

Seasonality of Symptoms in PMDD

Douglas D. Maskall, M.D., Psychiatry, University of BC, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Raymond W. Lam, M.D., Shaila Misri, M.D., Diana Carter, M.D., Annie Kuan, B.A.

Summary:

Objective: Late luteal phase dysphoric disorder (LLPDD) and seasonal affective disorder (SAD) are cyclical disorders often manifested by "atypical" features of depression. In addition, light therapy has been shown to benefit women with non-seasonal LLPDD. We designed the following study to determine whether patients with LLPDD demonstrate significant seasonal variation in symptoms.

Method: 154 consecutive female patients attending a teaching hospital PMS clinic were assessed according to DSM-III-R criteria. All subjects completed the Seasonal Pattern Assessment Questionnaire (SPAQ), modified to include items on the seasonality of premenstrual symptoms. The Global Seasonality Score (GSS), and index of seasonality of mood and vegetative symptoms often used to identify patients with SAD, was generated from the SPAQ. Results were compared with those of a nonclinical group (N = 50).

Results: 100 subjects met DSM-III-R criteria for LLPDD. Compared to the nonclinical group, the LLPDD subjects had a signifi-

cantly higher mean GSS score (10.9 vs. 7.0; $t_{2,148} = 4.86$, $p < 0.001$). 38% of the LLPDD group met SPAQ criteria for SAD, compared to 8% in the nonclinical group ($p < 0.001$). 27% of the LLPDD group rated their seasonal variation in premenstrual symptoms as marked or severe, while 30% considered overall seasonal changes to be a marked or severe problem.

Conclusions: These results suggest that patients with LLPDD have significant seasonal patterns in mood and premenstrual symptoms. These seasonal patterns may have implications for the clinical assessment and treatment of LLPDD. For example, light therapy may be beneficial for patients with seasonal worsening of LLPDD.

NR121 Monday, May 22, 3:00 p.m.-5:00 p.m.

Valproate Oral Loading in the Treatment of Acute Exacerbations of Combat-Related PTSD

Shreenath V. Doctor, M.D., Psychiatry, Baylor College of Med., One Baylor Plaza, Houston TX 77030; Gerald L. Batte, M.D.

Summary:

Post-traumatic stress disorder (PTSD) among combat veterans is often characterized by worsening episodes where there is a progressively shorter well interval between successive episodes. During acute exacerbations of PTSD, patients may exhibit hypervigilance, extreme irritability, angry outbursts, and violent behavior. Severe sleep disturbances characterized by inability to initiate and maintain sleep, nightmares, and nocturnal limb movements may also occur. Intrusive memories, thoughts and flashbacks with corresponding affective states from the original trauma may be reported. Patients may develop severe avoidance with emotional numbing and social alienation. A possible pathophysiological process underlying this disorder may be kindling.

Acute exacerbations of PTSD where intensive initial pharmacotherapy is necessary for stabilization require rapidly achieving therapeutic concentrations. Use of lithium and carbamezapine in higher doses similar to oral loading strategies have resulted in nonacceptance due to dose related side effects.

In bipolar disorder, valproate has been found to be safe in administration by oral loading achieving therapeutic serum concentrations within 24 hours with minimal side effects. We therefore tried an oral loading strategy with valproate, a drug known to interfere with kindling, to treat the acute exacerbation of combat-related PTSD and present a small clinical trial.

Four male veterans prior to and two weeks following loading with valproate at dosages ranging from 15–25 mg/kg. for acute exacerbation for PTSD were evaluated using a modified 17-item PTSD symptom scale (MPSS-SR) which assessed for both frequency and severity of symptoms over a two-week period. Loading doses ranged from 1000 mg–2000 mg with 24-hour serum valproic acid levels ranging from 58–107 mg/ml (mean 78.8 mg/ml). The immediate benefit noted by all four patients was improved initiation and maintenance of sleep. All four veterans reported significant improvement in hyperarousal/hyperreactivity symptoms. Three veterans reported significant improvement in avoidant/withdrawal symptoms. All four patients noted significant improvement in reexperiencing symptoms. All four patients showed significant improvement in observed signs of PTSD. All CBC, platelet, and liver function test values remained within normal limits and no serious adverse effects were noted. None of the patients in the study reported symptoms worsening.

NR122 Monday, May 22, 3:00 p.m.-5:00 p.m.

Psychotropic Drug Use by Nonpsychiatrists

Cecelia P. Kane, M.D., Psychiatry, Emory School Medicine, 1701 Uppergate, Atlanta GA 30322; Francis J. Kane, Jr., M.D.

Summary:

This study examines psychotropic drug use by nonpsychiatrists on general hospital medical, surgical, and ob-gyn services.

Methodology: Pharmacy records for a three-month period from a 550-bed medical school-affiliated general hospital were reviewed for use of tranquilizers, antidepressants, and neuroleptics (hypnotics were excluded). A review of tranquilizer use was performed several months later at a VA hospital.

Results: 538 of 4508 patients (11.9%) received regular daily prescription; 60.4% were women and 58.2% were over 60. A total of 367 (66.3%) received antidepressants, while 384 (71.2%) received BZD's; long-acting BZD's were used for 135 (25%); 54% received both BZD and antidepressants; 57% of non-SSRI use was in small doses at hs. A total of 136 consecutive charts were reviewed (64% F, 36% M). Only 13% had psychiatric diagnoses and psychiatric consults were present in 6%. Consults were seen as desirable for 32 more (24%). Undermedication (8%), inappropriate medication (27%), major polypharmacy (5%), and prescription of habit-forming drugs for outpatient use occurred in 27 (19.8%). Neuroleptics and SSRI's were prescribed in appropriate dosage, while TCA's were generally given in inadequate dosage. Excessive use of LA BZD was also found in the VA sample (52% of 572 prescriptions).

Conclusions: Antidepressant use is much increased, though almost half seem prescribed as a substitute for hypnotics. Underdosage with TCS's was common. There seemed excessive LA BZD use in both hospitals. Polypharmacy in hospital was common. Few patients had psychiatric diagnoses, and clinical comment about drug effect was virtually absent. The data indicate the need for more intensive education in psychotropic drug use in primary care providers.

NR123 Monday, May 22, 3:00 p.m.-5:00 p.m.

A Double Blind Study Comparing a Combined Plant Extract with Placebo in the Treatment of Anxiety

Michel S. Bourin, M.D., Psychopharmacology, University Hospital, 1 Rue Gaston Veil, Nantes 44035, France; Thierry Bougerol, M.D., Bernard Guitton, M.D., Eric Broutin, M.D.

Summary:

Euphytose (EUP) is a combination of six dry extracts: Crataegus, Ballota, Passiflora and Valeriana, which have mainly sedative effects, and Cola and Paullinia, which mainly act on debility. This multicenter, double-blind, placebo-controlled general practice study was carried out in outpatients suffering from general anxiety (DSM-III-R criteria). The study was coordinated by psychiatrists. Ninety-five patients were included in the EUP group and 96 patients in the placebo group. They all received two tablets three times a day over 28 days. Evaluation using the HAM-A Rating Scale were carried out on D_0, D_7, D_{14}, and on D_{28}. Comparing the two groups on an intention-to-treat basis, 42.1% of patients (EUP group) had a HAM-A score of less than 10 at D_{28} versus 27.1% in the placebo group) $p = 0.029$). Changes in the HAM-A score between D_0 and D_{28} were as follows: D_0 (EUP 26.12 ± 4.0, placebo 26.27 ± 4,5), D_7 (EUP 19.65 ± 5.7, placebo 21.37 ± 5.6) D_{14} (EUP 15.36 ± 5.7, placebo 17.48 ± 6.7), D_{28} (EUP 12.63 ± 7.3, placebo 15.2 ± 8.1). From D_7 to D_{28} there was a statistically significant difference ($p = 0.042$) between the two treatments, indicating that EUP is better than placebo in the treatment of mild anxiety. A further trial in healthy volunteers studied the psychometric effects of this drug (Bourin, in press) showing that EUP had no sedative effects and could be an alternative treatment of BZD in mild anxiety.

NR124 Monday, May 22, 3:00 p.m.-5:00 p.m.

A Survey of Practicing Massachusetts Psychiatrists Concerning Their Experiences Prescribing Fluoxetine, Bupropion and Trazodone

Srinivasan S. Pillay, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Jeffery C. Campbell, M.S., Jonathan O. Cole, M.D.

Summary:

Objective: The purpose of this study was to investigate the effects of the potential for suicidality on fluoxetine, seizures on bupropion, and priapism on trazodone, on the prescribing practices of psychiatrists.

Method: A sample of 368 psychiatrists who listed Psychopharmacology or Affective Disorders among their specialties, was randomly selected from the 1992 membership directory of The Massachusetts Psychiatric Society. The survey was conducted using standardized questionnaires administered via a computer-aided telephone interviewing system.

Results: There were statistically significant associations between psychiatrists having observed suicidality in patients on fluoxetine and worrying about suicidality, monitoring patients more carefully, warning patients and relatives, and avoiding the use of fluoxetine. For trazodone, there were statistically significant associations between observed full priapism and warning patients and relatives, as well as using trazodone less. There were no statistically significant associations between observed seizures on bupropion and the prescribing practices of psychiatrists.

Conclusions: The prescribing practices of psychiatrists was more strongly associated with observed suicidality on fluoxetine, than with observed priapism on trazodone or seizures on bupropion. It appears that greater consistency needs to be achieved with regard to monitoring these side effects. Implications of these findings are discussed.

NR125 Monday, May 22, 3:00 p.m.-5:00 p.m.

The Ictal EEG As a Marker of ECT Seizure Adequacy: The Relationship of Spike-Wave Phase EEG Features to Therapeutic Response

Here W. Folkerts, M.D., Clinic Muenster, Psychiatric University, Albert-Schweitzer Str 11, Muenser 48149, Germany

Summary:

Objective: Until now we could not separate therapeutically adequate from inadequate seizures; the seizure duration appears to be not a sensitive predictor or therapeutic response of electroconvulsive therapy (ECT).

Method: In light of recent studies reporting ictal electroencephalogram (EEG) differences between weak and potent forms of ECT, we performed a 40-subject (27 patients with major depressive disorder, 13 schizophrenic patients; [according to DSM-IV-criteria]) open clinical trial to evaluate electrophysiological differences between responders and nonresponders of right unilateral ECT using a new developed EEG-rating scale.

Results: There were no differences between the two groups concerning the distribution of age, gender, diagnosis, and doses of methohexital. A number of EEG variables separated responders (n = 29, 72.5%) from nonresponders to ECT; we found statistical significant evidence of more "organized" stereotype spike-wave-pattern (chi 5.87, $p < 0.01$), more pronounced slowing ($p < 0.0001$, two tailed t-test), and earlier onset of slowing ($p < 0.05$, two tailed t-test) during spike-wave phase for the responder representing earlier and more intense activation of subcortical (e.g. thalamus) structures.

Conclusions: The findings of this study suggest that some EEG features may be associated with therapeutic outcome, but further work is needed to elaborate a reliable ictal EEG algorithm for seizure adequacy.

NR126 Monday, May 22, 3:00 p.m.-5:00 p.m.

Prescribing Practices for Bipolar Patients in a Clinical Setting

Alejandra Hallin, M.D., Psychiatry, NYU School of Medicine, 630 First Avenue Apt 9F, New York NY 10016; Eric D. Peselow, M.D., Faouzia Barouche, M.D., Lara Fieve, Gita Vaid, M.D., Ronald R. Fieve, M.D.

Summary:

Though much clinical research into the prophylaxis of bipolar affective disorder involves trials of single agents (lithium, depakote, carbamazepine), many clinicians have noted that monotherapy is usually not sufficient for many bipolar patients in clinical care settings. The objective of this paper is to evaluate treatment regimens for stable bipolar patients treated in a clinical setting.

We examined the records of all patients who were active at the Foundation for Depression/Manic Depression on July 1, 1989 and August 1, 1994. Overall, all patients who met criteria for bipolar illness and had a stable mood for six months were included in our analysis. This involved approximately 240 patients from the 1989 evaluation and 190 from the 1994 evaluation.

With respect to the 1989 sample, approximately 57% of the stable bipolar patients were maintained on single agents (48% lithium alone). With respect to the 1989 sample, 37% of patients were maintained on monotherapy (26% lithium).

Despite an absence of controlled studies validating this approach, it seems clear that in clinical settings, polypharmacy (lithium plus neuroleptic/antidepressant) is both common and probably appropriate.

NR127 Monday, May 22, 3:00 p.m.-5:00 p.m.

Fluoxetine Efficacy: A Meta-Analysis

Carlos Blanco-Jerez, M.D., Psychiatry, St. Vincent's Hospital, 144 W. 12th Street, New York NY 10011; Inmaculada Gilaberte-Asin, M.D., Carmen Blanco, B.S.

Summary:

The role of serotonin in different psychiatric disorders has been shown in multiple studies. The extensive involvement of serotonin in the pathogenesis of psychiatric disorders is probably explained by the diversity of its receptors and the interrelationships with other cerebral neurotransmitter systems.

Fluoxetine, a selective serotonin reuptake inhibitor, has been reported useful in the treatment of several serotonin-related disorders. In order to assess the validity of this, we reviewed all the double-blind trials (N = 83) between 1985–1994 that included fluoxetine as part of the design. The efficacy of fluoxetine was assessed for the treatment of depression, obsessive compulsive disorder, bulimia, obesity, premenstrual syndrome, alcoholism, pain, trichotillomania, and Gilles de la Tourette syndrome. Fluoxetine showed its highest efficacy in the treatment of premenstrual syndrome (75%–94%) and depression (46%–67%), while its lowest efficacy was in trichotillomania (no differences from the control group). Fluoxetine showed moderate efficacy in the treatment of obsessive compulsive disorder, pain, and obesity.

Our analyses are consistent with the involvement of serotonin in a broad range of psychiatric disorders. The different efficacy of fluoxetine in the spectrum of clinical syndromes suggests that the role of serotonin in the pathogenesis of psychiatric disorders is not uniform and is influenced by complex interactions with other neurotransmitters.

NR128 Monday, May 22, 3:00 p.m.-5:00 p.m.

Psychopharmacological Treatment of Social Phobia: A Double-Blind Placebo-Controlled Study with Fluvoxamine

Irene M. Van Vliet, M.D., Psychiatry, Academic Hospital, P.O. Box 85500, Utrecht 3508 GA, Netherlands; Johan A. Den Boer, Herman G.M. Westenberg, M.D.

Summary:

Previous studies have shown selective and non-selective monoamine oxidase inhibitors (MAOIs) to be effective in the treatment of social phobia. In this study we investigated the efficacy of selective serotonin reuptake inhibitors (SSRIs) in social phobia. Thirty patients with social phobia (DSM-III-R) were treated with the SSRI fluvoxamine (150 mg daily) using a 12-week, double-blind, placebo-controlled design. A substantial improvement was observed in seven (46%) patients on fluvoxamine and in one (7%) on placebo. Statistically significant effects were seen on measures of social anxiety and general (or anticipatory) anxiety in patients treated with fluvoxamine compared with placebo. The level of phobic avoidance decreased also but the difference at endpoint between fluvoxamine and placebo failed to reach statistical significance. It is concluded that treatment with the SSRI fluvoxamine has beneficial effects in patients suffering from social phobia, suggesting that serotonergic mechanisms might be implicated in social anxiety.

NR129 Monday, May 22, 3:00 p.m.-5:00 p.m.

Psychological Predicting Factors in Repeated Suicidal Behavior

Manuel Bousono-Garcia, M.D., Psiquitria, Facultad Medicina, Julian Claveria 6, Oviedo 33006, Spain; Julio Bobes, M.D., Maria P. Gonzalez, Ph.D., Pilar A. Saiz, M.D., Isabel Cocana, M.D., Micaela Gonzalez-Quiros, M.D.

Summary:

Objectives: The aim of this epidemiological study was to differentiate between the clinical and psychological profile of repeaters and non-repeaters of parasuicide behavior in order to identify factors of high or low risks in new attempts and also to predict the risk of such behavior.

Patients and Methods: Attempted suicide patients (n = 118) who received care at the University General Hospital of Oviedo (Spain) from 1/1/1992 to 6/30/1994 were included in the study. Assessment of psychological profile (Eysenck Personality Questionnaire-Adult, General Health Questionnaire-28 items -GHQ-28-, General Well Being Index -GWBI-, Hamilton Anxiety Scale, Hamilton Depression Rating Scale) was carried out at least three months after the index behavior.

The Chi-square test and logistic regression analysis were carried out in order to compare the profiles of repeaters and non-repeaters.

Results: (Only stastistically significant correlations are presented)

	REPEATERS (n = 45)	NON-REPEATERS (n = 73)	p
Age (<25 years)	24.1%	75.9%	.0074
GHQ-28 (<7)	23.1%	76.9%	.0050
GWBI (<61)	25.0%	75.0%	.0142
Hamilton Depression (>15)	70.6%	29.4%	.0000
Hamilton Anxiety (>15)	62.2%	37.8%	.0000
Previous Absence Psychiatric Disorder	9.1%	90.9%	.0005
Previous Absence Psychiatric Treatment	17.9%	82.1%	.0091

*Chi-square

Conclusions: Our data suggest a high risk profile that consists of adults over 25 years with a different neuropsychological profile (more psychological distress, higher scores of anxiety and depression, and the presence of previous psychiatric diagnosis and treatment).

NR130 Monday, May 22, 3:00 p.m.-5:00 p.m.

Profile of Medically Serious Suicide Attempts

Andy Elliot, M.D., Psychiatry, Harborview Medical Center, 325 Ninth Avenue ZA-15, Seattle WA 98104; Kenneth P. Pages, M.D., David R. Johnson, M.D., Lawrence G. Wilson, M.D., Peter P. Roy-Byrne, M.D.

Summary:

Because important demographic and clinical differences have been found between suicide attempters and completers, we explored whether similar differences might be found between groups of suicide attempters with different levels of attempt severity. Such differences could enhance both prevention efforts and the management of these patients post-attempt. This study compared the demographic, diagnostic, clinical, and attempt characteristics, as well as the psychiatric diposition, of 65 patients medically hospitalized for a suicide attempt with 28 patients seen in the ER for attempts but not medically hospitalized. Although those with medically serious attempts had a higher rate of substance-induced mood disorder (but not substance abuse) patients seen in the ER had more prior psychiatric hospitalization, more prior attempts, a higher rate of prior sexual and physical abuse, and a higher rate of borderline personality. Despite the greater psychiatric morbidity of ER patients, medically hospitalized patients were more likely to be psychiatrically hospitalized or referred for outpatient treatment. These findings suggest that more persistent mood effects of substance use may lead to serious suicide attempts despite less extensive psychiatric morbidity and that psychiatrists consider medical severity of attempt more than overall psychiatric morbidity in the decision to hospitalize or refer for outpatient treatment.

NR131 Monday, May 22, 3:00 p.m.-5:00 p.m.

Lack of Behavioral Laterality in Gilles De La Tourette's Syndrome: A Replication Study

M. Yanki Yazgan, M.D., Child Psychiatry, Yale School of Medicine, 230 South Frontage Road, New Haven CT 06520; Bruce E. Wexler, M.D., Lawrence Scahill, M.S.N, Bradley S. Peterson, M.D., Marcel Kinsbourne, M.D., James F. Leckman, M.D.

Summary:

Objective: We previously reported lack of asymmetry on a battery of lateralizing neurobehavioral measures in adults with Gilles de la Tourette's syndrome (GTS) and basal ganglia alterations, and in children with GTS. In this study we aimed to replicate those findings in a larger, independent sample of adult patients, and explore the associations between neurobehavioral alterations and clinical features.

Methods: Twenty-one adult GTS patients (33 +/- 5.5 years) and 26 normal controls (35 +/- 4.3 years) were administered a battery of lateralizing neurobehavioral measures including line bisection (perceptual and pre-motor versions), verbal-manual interference-VMI (verbal memory and "verbal-motor" versions), and whole body turning bias tests.

Results: Patients lacked normal asymmetries on line bisection (both versions) ($p = .03$), turning bias ($p = .004$), and VMI ($p = .045$). Perceptual-attentional and pre-motor left biases on line bisection inversely correlated with motor and global tic severity ($r = -.62$, $p = .02$). VMI asymmetry also correlated with motor tic severity ($r = -.57$, $p = .04$).

Conclusions: 1) In adults with GTS, lack of asymmetry on lateralized neurobehavioral tests related to the basal ganglia was shown, replicating our previous findings. 2) Correlations between the line bisection and VMI, and clinical ratings of tic severity suggested that right hemisphere hypoactivation and decreased right hemisphere efficiency were associated with greater tic severity.

NR132 Monday, May 22, 3:00 p.m.-5:00 p.m.

Peripheral Biological Markers and Suicide Attempt

Julio Bobes, M.D., Psiquiatria, Facultad Medicina, Julian Claveria 6, Oviedo 33006, Spain; Manuel Bousono-Garcia, M.D., Maria P. Gonzalez, Ph.D., Pilar A. Saiz, M.D., Pedro Gonzalez-Quiros, Ph.D., Jorge Diaz, Ph.D.

Summary:

Objectives: A case control study was made to discover whether it was possible to establish a profile on the basis of peripheral biological markers in suicide attempters (especially serum lipids and hormonal levels).

Case Group: Patients (n = 102) who received care at the University General Hospital of Oviedo (Spain) for attempted suicide between 1/1/92 and 6/30/94 were included in this epidemiological study. Biological parameters (cholesterol, triglycerides, HDL-C, VLDL-C, LDL-C, cortisol a.m., TSH, and GH) were determined for at least three months after the index behavior.

Control Group: Identical biological parameters from blood donor subjects matched by age and sex were obtained.

Results: (Only statistically significant correlations between case and control groups are presented).

	GLOBAL		
	CASE (n = 102)	CONTROL (n = 102)	p
Trygl.	117.12 ± 70.82	91.64 ± 68.88	.013
VLDL-C	23.46 ± 14.13	18.07 ± 12.27	.006

	MALE			FEMALE		
	CASE (n = 28)	CONTROL (n = 28)	p	CASE (n= 74)	CONTROL (n = 74)	p
Trygl.	–	–		113.3 ± 74.3	88.1 ± 69.7	.035
VLDL-C	–	–		22.7 ± 14.8	17.3 ± 11.9	.017
LDL-C	116.0 ± 41.0	139.2 ± 43.0	.015	–	–	
Cort.	21.5 ± 4.9	16.1 ± 5.8	.001	–	–	

*Paired T-Test

Conclusions: Our data indicate the possible existence of peripheral biological markers (lipids and cortisol) in parasuicidal behavior. Nevertheless, further in-depth studies need to be carried out to confirm these findings.

NR133 Monday, May 22, 3:00 p.m.-5:00 p.m.

Atmospheric Pressure and Agitation on a Psychiatric Inpatient Unit

Teodor T. Postolache, M.D., Psychiatry, Beth Israel Med. Ctr., First Avenue at 16th Street, New York NY 10003; Christian Miner, Ph.D., Richard N. Rosenthal, M.D., Patricia A. Lowrimore, M.D., Julie Reynolds, R.N.C., Igor I. Galynker, M.D.

Summary:

As a part of a more comprehensive study, we analyzed prospectively over a three-month period the relationship between the atmospheric pressure and the number of prn medication for agitation on a locked, general, psychiatric inpatient unit located in New York City.

We computed bivariate cross correlation functions between the number of prn medication for agitation divided by the daily census (PRN/Patient/24hours) and the average daily atmospheric pressure.

A positive correlation between the PRN/Patient/24Hours and the atmospheric pressure of the prior day (time lagged −1 day) was found ($r = 0.41$, $n = 88$, $p < 0.001$). The result was robust to the multiple regression adjustment for other meteorological variables (maximum and minimum temperature, wind speed, maximum relative humidity, total daily sunshine), chronological (photoperiod, day of the week, lunar cycle), and social factors (daily mood and stress levels of staff, salary cycle).

Our result connects a previous report of a negative correlation between CSF 5-HIAA and the atmospheric pressure with the substantial volume of data supporting the inverse relationship between serotonergic activity and aggressive, disruptive, and impulsive behavior.

NR134 Monday, May 22, 3:00 p.m.-5:00 p.m.

No Relationship Found Between Mood and Occupational Stress in the Staff of an Inpatient Psychiatric Unit

Teodor T. Postolache, M.D., Psychiatry, Beth Israel Med. Ctr., First Avenue at 16th Street, New York NY 10003; Patricia A. Lowrimore, M.D., Zenovi Gutkovich, M.D., Richard N. Rosenthal, M.D.

Summary:

A higher workload was found to be negatively associated with mood in air traffic controllers. Mood appears to be sensitive to changes in levels of stress in the general population.

The main purpose of our study was to assess if there is any relationship between the average work-related stress (SL) and average mood (ML) in the staff of a psychiatric inpatient service. Out of 29 staff members who volunteered, six (20%) dropped out. Over three months, during the morning report, staff members completed visual scales for current mood and work-related stress levels. Daily averages of z scores were used. A simple correlation was performed for same-day ML and SL. Bivariate cross correlations were computed between time lagged SL and ML. No significant relationship was found.

In a second analysis, selected chronological and social events (photoperiod, day of the week, time since payday) did not contribute significantly to the variance in the same-day SL or ML.

We have found significant relationships in individual staff members between stress and mood and chronological or social factors; however, prominent differences in regard to the quality, direction, and time lags of the individual associations were noted. These findings, supporting previously described striking differences among individuals in regard to the interrelation between stress and mood, may represent an important stabilizing factor of the average mood and perceived occupational stress on a psychiatric service with probable benefits for patient care.

NR135 Monday, May 22, 3:00 p.m.-5:00 p.m.

Eliminating Cultural Bias of Proverb Interpretation in Mental Status Examination Through the Use of Cross-Cultural Core Proverbs

Carlos A. Rueda, M.D., Psychiatry, St. Vincent's Med. Ctr., 153 West 11 Street, New York NY 10011; Paul A. Hriso, M.D., Emmanuel Hriso, M.D.

Summary:

Objective: To enhance the validity of abstraction testing in mental status examination by using a very specific type of proverb (Core Proverb).

Method: The authors conducted an extensive review of the literature on the subject of proverbs and their use in psychiatry. The authors developed the concept of "core proverb" as well as a list of such proverbs applicable to different languages.

Results: Classic proverbs are forms of non-literal language containing meaning drawn from experience that reflect both cultural

and cognitive components. Proverb familiarity decreases the probability of abstract interpretation. In such cases, learned response and memory are tested rather than true abstraction. Bias is thus created by using culturally specific proverbs. Core proverbs are simple proverbs which contain universal themes and analogic symbols allowing conceptual understanding independent of cultural background. A list of such proverbs would objectively target a wider variety of patients.

Conclusion: The "Core proverb" is an essential concept eliminating cultural bias in proverb interpretation. The knowledge and use of such proverbs would allow clinicians to truly focus on abstraction skills as well as the idiosyncratic thinking of patients.

NR136 Monday, May 22, 3:00 p.m.-5:00 p.m.

Children and War: Trauma and Psychosocial Services

Bradley D. Stein, M.D., Psychiatry, WPIC, 3811 O'Hara Street, Pittsburgh PA 15217

Summary:

Objective: To describe the differences in traumatic exposure between Bosnian and Croatian refugee children and to consider the implications for planning psychosocial services.

Methodology: Groups of children were assessed in Bosnia (n = 357) and Croatia (n = 156) using adapted versions of the Childhood War Trauma Questionnaire and the Questionnaire for Children about Traumatic Experiences of War.

Results: All of the children had been displaced for their homes. One percent of the Bosnian children had been separated from their mother, while 28% of the Croatian refugees had been separated from their mother. Ten percent of the Bosnian children had been detained, while only 0.6% of the Croatian children had this experience. Also, 2.6% of the Croatian children reported being shot at, while 97% of the Bosnian children reported being exposed to combat.

Conclusions: Findings demonstrate that both groups have suffered severe trauma, but significant differences, including life threat and separation from parents, exist between the groups. The implications are that Bosnian refugees would be expected to have a higher level of PTSD, and that programs that work with the mother are more likely to be successful with the Bosnian children than the Croatian children. Programs cannot simply be transplanted from Croatia to Bosnia, but must account for these significant differences.

NR137 Monday, May 22, 3:00 p.m.-5:00 p.m.

Alcoholism Treatment Research: Women and Minorities

Lauren D. Williams, M.D., Psychiatry, Univ of Miami Med School, 1400 NW 10th Avenue RM314; Miami FL 33136; Gloria Goldberg, M.S.W., Robert B. Cutler, Ph.D., Barbara J. Mason, Ph.D.

Summary:

Generalizability of clinical research findings require data about variations in rate of study enrollment among various subpopulations, particularly women and minorities. Furthermore, implementation of alcoholism treatment research findings in clinical settings requires information about potential barriers to treatment participation for these subpopulations. Demographic information and referral outcome was systematically collected from the 347 alcoholics who telephoned to inquire about treatment on alcoholism clinical research protocols over a one-year period. The ratio of male to female callers was 7:3, with 2:1 scheduling appointments, 3:2 keeping appointments, and 3:2 actually enrolling in a treatment study. These data suggest that although a smaller ratio of female alcoholics may initially call for treatment, those who do call may be more likely to actually enter treatment than are males. A ratio of 2:1 white to nonwhite alcoholics called the clinic, with 7:3 scheduling appointments, 8:1.6 keeping appointments, and 8:1 actually entering the study. These data suggest that minority alcoholics appear less likely than white alcoholics to enter treatment protocols. However, discriminant function analysis found income to be a better predictor of entry into treatment than race, age, or sex, and analysis of covariance found whites and nonwhites did not differ in rate of entry into treatment when income is used as the covariate. The primary reasons for minority nonparticipation were the inability to speak English and the failure to keep appointments.

NR138 Monday, May 22, 3:00 p.m.-5:00 p.m.

Early-Onset Male Alcoholics With and Without Antisocial Personality Disorder

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

Summary:

For many clinicians, early-onset alcoholism is virtually synonymous with antisocial personality disorder (ASP). Indeed, we reported a much higher prevalence of ASP among early-onset (≤24 years) than late onset (≥ 25 years) inpatient male alcoholics. (Helmi et al., 1994). Nevertheless, a substantial number of early-onset alcoholics are not, and will never satisfy diagnostic criteria for ASP. Do early-onset male ASPs differ from early-onset non ASPs along clinically relevant dimensions? We utilized a large group (N = 197) of male alcoholics hospitalized on a VAMC alcoholism treatment unit who were extensively evaluated at intake: 89 of these (45%) satisfied criteria for ASP while 108 (55%) did not. One year later, 169 (86%) were re-evaluated. Early-onset ASPs were younger, less well educated, and employed for a shorter time in the previous year than early-onset non ASPs. Early-onset ASPs reported more psychiatric disorder among first-degree relatives (i.e., drug abuse, somatization disorder, and ASP), but a positive family history of alcoholism *did not* distinguish the ASP from non ASP groups. Age first drank, age alcoholism first became a problem, and age first treatment for drinking were significantly lower in the early-onset ASP groups. Multiple measures of alcoholism severity were higher in the ASP group; however, the two groups *did not* differ on current and lifetime measures of general psychopathology. More alcohol-related firings, arrests, jailings, and separations were found for the ASP subgroup at intake. One year later, despite the marked clinical improvement in the sample as a whole, early-onset ASPs continued to demonstrate greater alcoholism severity, more serious antisocial acts, and poorer psychosocial functioning. Our findings indicate that early-onset male alcoholics do not represent a clinically homogeneous group: Early onset alcoholism combined with ASP appears to represent an especially malignant form of the disease.

This was supported by the NIAAA (Grant #R01AA07386 & #R21AA07539) and the Medical Research Service of the Department of Veterans Affairs (Grant #589-103-341-26-1291)

NR139 Monday, May 22, 3:00 p.m.-5:00 p.m.

Psychoactive Substance Use Among Inner-City Psychiatric Admissions

Abner P. Pasatiempo, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Jeannette L. Johnson, Ph.D., Anthony F. Lehman, M.D.

Summary:

Substance use disorder comorbid with psychiatric illness is encountered frequently in many psychiatric admissions and recognized as complex and difficult to manage clinically. To explore the frequency of this occurrence, we studied psychoactive substance use in patients admitted to two inner-city psychiatric hospitals serving an urban catchment area. The Structured Clinical Interview for DSM-III-R (SCID) and Addiction Severity Index were used to assess all participants.

Results were analyzed from 468 admissions in which major psychiatric illness such as schizophrenia (14.7%), bipolar disorder (11.3%), depression (16%), and anxiety disorder (1.3%) were diagnosed. Psychoactive substances most commonly used (past 30 days) were stimulants (95.7%), hypnotic/anxiolytics (94.7%), hallucinogens (93.4%), polydrug (89.1%), cannabis (27.1%) across all diagnoses. Alcohol was widely used among major psychiatric diagnoses except anxiety disorder patients. Schizophrenia patients used cannabis (27.1%), hallucinogens (7.1%), cocaine (5.7%), and opiates (1.7%). Depressed patients used cocaine (7.5%), hallucinogens (7.1%), cannabis (6.3%), and opiates (4.6%). Bipolar patients used stimulants (100%), cannabis (12.8%), hallucinogens (7.1%), and cocaine (3.8). Anxiety disorder patients only used cocaine (0.9%).

These findings suggest varied use of psychoactive substances among inner-city psychiatric admission. Treatment implications for specific substances among specific psychiatric diagnoses should be explored and will be discussed.

NR140 Monday, May 22, 3:00 p.m.-5:00 p.m.

Preliminary Data Support: An Association Between Taste Sensitivity and Alcoholism Risk

Pamela J. Moore, M.D., Psychiatry, University of CT, 263 Farmington Avenue MC2103, Farmington CT 06030; Henry R. Kranzler, M.D., Lance O. Bauer, Ph.D., Victor M. Hesselbrock, Ph.D.

Summary:

The ability to taste phenylthiocarbamide (PTC), thought to be a Mendelian trait, is found in 70% of Caucasians. PROP(6-n-propylthiouracil), which is structurally similar, odorless, and less toxic than PTC, has come to substitute for it. Pelchat and Danowski (1992) found an association between the inability to taste PROP and parental alcoholism, with a higher proportion of PROP non-tasters among children of alcoholics (47.8%), than among children of nonalcoholics (15.6%). Bartoshuk (1993) suggested that tasters may be less inclined to drink, due to greater sensitivity to the unpleasant stimulus effects of alcohol. We evaluated PROP tasting in 25 males and females who, along with their parents, were evaluated with structured interviews and in whom taste thresholds were determined by forced choice (modified Harris/Kalmus method). Mean age of the subjects was 17.0 ($\pm$1.3) yr.; they typically drank 2.7 ($\pm$4.8) alcoholic drinks per week. Fifty-two percent of subjects had a negative paternal history (NPH) and 48% had a positive paternal history (PPH) of alcohol dependence. Mean taste threshold in NPH subjects was 5.5 ($\pm$2.0) compared to 3.8 ($\pm$2.2) in PPH subjects [$F(1,23) = 3.97$, $p = 0.06$]. Fifty percent of PPH subjects and 23% of NPH subjects were non-tasters [Fisher's exact test, $p = 0.16$]. Preliminary results suggest a replication of the reported association between PROP taste insensitivity and parental history of alcoholism.

NR141 Monday, May 22, 3:00 p.m.-5:00 p.m.

Duration of Hospitalization Versus Improvement in First Psychosis

James D. Hegarty, M.D., Psychiatry, Mass General Hospital, Acute Psychiatry Service, Boston MA 02114; Franca Centorrino, M.D., Ross J. Baldessarini, M.D., Mauricio Tohen, M.D., Jonathan W. Friedberg, M.D., Michelle Weiss, M.S.

Summary:

Objective: To pursue a rare opportunity to evaluate the impact of administratively determined shortening length of psychiatric hospitalization on clinical improvement and discharge status in psychiatric patients in a first episode of psychotic illness to avoid effects of chronic disability.

Method: Patients hospitalized in a first episode of SCID-based DSM-III-R psychotic illness (68% major affective) were assessed repeatedly between admission and discharge by a 27-item Brief Psychiatric Rating Scale (BPRS) and global clinical impression (CGI) scores from 1989–94.

Results: Among 269 patients (aged 34 $\pm$ 15 yrs., 59% men), yearly cohorts did not differ significantly by age, gender, type of illness, or initial severity (initial BPRS, overall, averaged 62 $\pm$ 15). Length of hospital stay (LOS) fell consistently (2.8-fold), from 45 to 16 days. Mean improvement (BPRS) during hospitalization decreased from 39% in 1989 to 16% in 1994. Patients with nonaffective psychotic disorders showed somewhat lesser improvement than those with affective diagnoses (27% vs. 18%). Between 1989–90 and 1993–94, variance (CV) in individual status at discharge rose from 46% to 93%, and the corresponding proportion of patients showing minimal improvement (BPRS fell by <0.1%/day) rose from 3.7% to 18.4%. Rates of change in BPRS were much slower over days 11–30 (0.96%/day) than 0–10 (2.8%/day) among those hospitalized ≥30days. Neither the annual crude rate of change (overall BPRS decrease/LOS = 1.4%/day), nor the initial rate for the first two weeks in hospital (2.7%/day) rose significantly with decreasing LOS. Readmissions within 30 days rose as LOS fell.

Conclusions: As hospitalization of first-episode psychotic patients decreased from 6.4 to 2.3 weeks between 1989 and 1994, inpatient clinical improvement decreased substantially, its variance increased markedly, while the *rate of change* per day did not increase significantly, and more patients were soon rehospitalized. These results encourage flexible, individualized allocation of health care resources for the care of psychotic patients to adjust to diminishing support for prolonged hospitalization.

NR142 Monday, May 22, 3:00 p.m.-5:00 p.m.

A Longitudinal Study of Patients with Nonepileptic Seizures

Michael M. Reese, M.D., Psychiatry, Mayo Clinic, 200 First Street SW, Rochester MN 55905; Lois E. Krahn, M.D., Teresa A. Rummans, M.D., Gerald C. Peterson, M.D., Frank W. Sharbrough, M.D., Greg D. Cascino, M.D.

Summary:

Introduction: Nonepileptic seizures (pseudoseizures) are defined as episodic changes in behavior which resemble epileptic seizures except EEG monitoring reveals no abnormal electrical activity. Although there are many causes of nonepileptic seizures (i.e. syncope, migraine), psychiatric disorders are the most common etiology. Little is known about whether these patients accept a psychiatric explanation for their symptoms and subsequently receive psychiatric treatment or if they continue to seek neurologic care. This project aims to examine the health care utilization and quality of life over time of patients with nonepileptic seizures.

Methodology: During a 31-month period, we reviewed the medical records of 94 consecutive inpatients monitored on a neuroepilepsy unit diagnosed with nonepileptic seizures attributed to a psychiatric cause. To assess the level of functioning and quality of life patients were subsequently sent a 122-item questionnaire developed by the authors.

Results: Of the 86 patients who agreed to participate in this follow-up study, 71 (76%) completed the questionnaire. Mean duration of follow-up was 578 ± 280 days. Responders were more likely to have had past psychiatric treatment (NS, p = 0.17) than nonresponders, but otherwise the two groups did not differ. The plurality of subjects reported fewer seizures (32%), their general health as "good" (37%), and quality of life as "much better" (33%). At follow-up many patients had either discontinued (50%) or reduced (17%) use of anticonvulsant medications. Furthermore, 47 patients were taking at least one psychotropic medication, most frequently fluoxetine (15), sertraline (9), and lorazepam (8). Nonpharmacologic treatments included psychotherapy (28), cognitive/behavioral therapy (14), family counseling (8), and marital counseling (7).

Conclusion: The psychiatric literature includes few follow-up studies of patients with nonepileptic seizures. Overall a majority of patients in this study reduced usage of anticonvulsant medications suggesting less intensive neurologic treatment of their symptoms. Moreover, it appeared that many subjects subsequently had received some form of psychiatric care.

NR143 Monday, May 22, 3:00 p.m.-5:00 p.m.

Family Functioning and Depression in Medical Patients

Anna M. Boettcher, B.A., Psychiatry, NY Medical College, 206 E 95th Street #2C, New York NY 10128; Stephen B. Billick, M.D., Woodward Burgert, B.A.

Summary:

Objective: To evaluate the prevalence and severity of depression, family functioning, and psychiatric symptomatology in medically ill patients. It was hypothesized that increasing severity of medical illness and depressive symptoms would be correlated. Second, it was proposed that as medical illness increased so would family dysfunction.

Methods: Subjects were a random sample of medical, surgical, and ob/gyn adult patients at an urban university hospital. The Beck's Depression Inventory (BDI), Hamilton Depression Scale (HRS), the Family Assessment Device (FAD), and the Brief Psychiatric Rating Scale (BPRS) were administered to each patient during their hospitalization. Demographic data and medical and psychiatric history were collected.

Results: 30% and 11% of the subjects had BDI scores consistent with mild and moderate-to-severe depressive symptoms, respectively. The BDI was directly correlated with severity of medical illness and family dysfunction in problem solving and communication. Family dysfunction was not directly correlated with increasing medical illness, but it was strongly correlated with the BPRS and any psychiatric history.

Conclusion: There is a significant amount of psychiatric pathology on nonpsychiatric services. A simple inquiry into psychiatric history would identify most of the patients at risk.

NR144 Monday, May 22, 3:00 p.m.-5:00 p.m.

Gender Differences in Crisis Center Evaluations

Robert N. Gerstman, D.O., Psychiatry, Abbotts Square Apts, 530 South 2nd Street Unit 614, Philadelphia PA 19147; Kimberly R. Best, M.D., Kenneth M. Certa, M.D.

Summary:

Objective: A major difficulty in staffing emergency services relates to the variability of patient presentations over time. Staffing must be able to handle peak loads, and yet down time has to be kept to a minimum. The present study sought to determine if there were any factors which might help predict utilization of services.

Method: Logged records of consecutive presentations to an urban university hospital psychiatric emergency service were reviewed for a two-year period 1/93–12/94. Presentations were divided by time of day (in four-hour blocks), day of week, and eighth of month, as well as by gender and diagnosis. Over 5,000 visits were examined.

Results: The most marked finding was a significantly greater number of males than females in the study population. The difference was accounted for, predominantly, by a greater incidence of substance abuse in men. Hourly and daily variations were not consistent over time.

Conclusions: Hoped–for patterns to assist staffing assignment were not supported by this study. Hypotheses related to increased utilization at certain periods of the month were also unsupported. Psychiatric emergency service utilization by men with primary substance abuse problems accounts for a significant amount of staff time and effort.

NR145 Monday, May 22, 3:00 p.m.-5:00 p.m.

Suicide Incidence Among Prostate Cancer Patients in South Florida

Gladys R. Gregory, M.D., 20622 NW 33rd Court, Miami FL 33056; Maria D.D. Llorente, M.D., Michael A. Burke, M.D., Larry D. Capp, Ph.D., Yolanda B. Zarate, M.D.

Summary:

Objective: To compare the incidence of suicide deaths among prostate cancer patients with incidents in patients with all other cancers. Also, to isolate the biopsychosocial factors that may contribute to increased suicide deaths among prostate cancer patients in South Florida.

Method: We reviewed 847 autopsy records for men age 65 and older in Dade County, Florida who had committed suicide between January 1982 and October 1994. Medical illnesses included in autopsy charts were reviewed to determine diagnoses prior to suicide. We also examined narratives written by police investigators, physician's comments, suicide notes, and personal diaries of suicide victims to ascertain biopsychosocial stressors that may have contributed to the patient committing suicide. Factors such as concomitant medical illnesses, living arrangements, support systems, race, age, religion, history of psychiatric illness, medications, education, employment classification, and method of suicide were included.

Results: Of the 847 cases, 146 had clinically diagnosed cancer. Thirty-eight cases had clinical prostate cancer—4% of total cases and 26% of cancer patients. Of the 38 prostate cancer cases, uncontrolled pain was the most frequently cited reason for suicide, followed by multiple medical problems and depression. Fifty percent of the patients had recent medical care and five cases had physician contact within 24 hours of suicide.

Conclusion: These data suggest there are specific psychosocial issues related to prostate cancer that may have precipitated suicide in these cases (pain, depression, medical problems). Identification of these factors will allow medical practitioners who have proximate contact to recognize patients who may be at risk for suicide.

NR146 Monday, May 22, 3:00 p.m.-5:00 p.m.

Depression, Quality-of-Life, and Use of Health Services in Primary Care Patients Over 65: A Four-Year Prospective Study

Jurgen Unutzer, M.D., Psychiatry, University of Washington, Mail Stop RP-10, Seattle WA 98195; Wayne J. Katon, M.D., Gregory E. Simon, M.D., Edward A. Walker, M.D., David Grembowski, Ph.D., Donald Patrick, Ph.D.

Summary:

To shed further light on the epidemiology and impact of depression in elderly primary care patients, we will report results from a study of 2,558 elderly primary care patients who were prospectively followed over a four-year period in a large staff model HMO. During this four-year period, annual interviews were conducted with all patients which evaluated depressive symptoms, quality of life, health status, chronic medical illnesses, health risk behaviors, utilization, and cost of health services.

At baseline, the mean score on the CES-D (Center for Epidemiological Studies Depression Scale) was 8.05. 672 patients (26% of the sample) had CES-D scores of 12 or higher, indicating mild to moderate depressive symptoms. 207 (14%) scored 16 or higher, meeting previously established criteria fro depression. 100 patients (4%) were severely depressed with CES-D scores of 22 or above. At 48-month follow-up, the average CES-D score increased slightly to 9.32, and 18% of those interviewed had CES-D scores of 16 or greater.

In this poster, we will describe the relationship of depression to demographic characteristics, quality of life, stressful life events, medical illness, functional status, and the use and cost of health services over the four-year study period.

NR147 Monday, May 22, 3:00 p.m.-5:00 p.m.

Asthma and Psychopathology in Adolescent Inpatients

Ronald A. McGinnis, M.D., Psychiatry, Medical College, 3000 Arlington Avenue, Toledo OH 43699; Wun Jung Kim, M.D., Michael P. Carey, Ph.D.

Summary:

Objective: The purpose of this study was to determine the prevalence of asthma in an inpatient hospital population and to compare characteristics of asthmatic and nonasthmatic patients.

Method: Two-hundred fourteen consecutive adolescent admissions, aged 13–17, were screened for asthma by obtaining a history of a medical diagnosis of asthma and the use of bronchodilator medication within two years of admission. The asthmatics and nonasthmatics were then compared using measurements of psychological inventories (MAPI, RADS, FES, LEC) T4 cortisol levels, and demographic variables (age, gender, race, socioeconomic status) using chi square and t-tests as statistical test for significance.

Results: The incidence of asthma was found to be over-represented in the adolescent inpatient population when compared with the rate of asthma for this age group in the community (12.6% vs. 6%, chi square 19.64 $p < 0.001$). Individual differences were not found to be significant between groups, with the exception of serum cortisol levels, certain life experiences, and some personality features.

Conclusions: Asthmatics are over-represented in inpatient adolescent psychiatric populations; however, the asthmatics do not present with unique psychopathology. The implications of a few exceptional findings will be discussed at the presentation.

NR148 Monday, May 22, 3:00 p.m.-5:00 p.m.

The Phenomenology and Comorbidity of Adolescents Hospitalized for the Treatment of Acute Mania

Scott A. West, M.D., Department of Psychiatry, Univ of Cincinnati Med Ct, 231 Bethesda Avenue ML 559, Cincinnati OH 45267-0559; Stephen M. Strakowski, M.D., Kenji Sax, M.S., Nancy J. Raute, B.A., Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D.

Summary:

The purpose of this study was to examine the phenomenology and comorbidity of adolescents hospitalized for the treatment of acute mania. We hypothesized that mixed bipolar disorder would be more common than the manic subtype, and that the two groups would significantly differ on ratings of depression and frequency of comorbid psychiatric diagnoses.

Thirty-six patients 12–18 years of age admitted consecutively for the treatment of acute mania were assessed using the Structured Clinical Interview for DSM-III-R (SCID-P), the Schedule of Affected Disorders and Schizophrenia for School-Age Children (K-SADS-III-R), and symptom rating instruments to assess the presence and severity of manic and depressive symptoms.

Twenty-four (66%) patients were diagnosed with DSM-III-R bipolar disorder, mixed type. Overall ratings of depression, but not mania, were significantly higher in patients with mixed bipolar disorder. Overall, 31 (86%) patients had at least one comorbid psychiatric diagnosis, the most common being attention-deficit hyperactivity disorder in both mixed (70.8%) and manic (66.7%) groups.

These findings suggest that mixed bipolar disorder is the predominant subtype in adolescents hospitalized for acute mania, and that there is a high frequency of psychiatric comorbidity, most notably ADHD, in both mixed and manic subtypes.

NR149 Monday, May 22, 3:00 p.m.-5:00 p.m.

The Assessment of HIV Risk Factors and the Clinicians Threshold for HIV Testing in the Chronic Mentally Ill in a Low Seroprevalence Area

Amy M. O'Neill, M.D., Dept of Psych, U of KY Med Ctr Annex II, 800 Rose Street, Lexington KY 40536-0080; Lesley R. Dickson, M.D., Chris Feddock, B.S.

Summary:

Objective: This study evaluates the clinician's assessment of HIV risk factors and threshold for HIV testing of the chronic mentally ill (CMI) in a southeastern, low-seroprevalence area.

Method: The charts of 387 patients between 18 and 59 years old admitted to a state psychiatric hospital during four months in 1993 were reviewed. Demographics, psychiatric and medical diagnoses, the clinician's assessment of nine HIV risk factors, and the frequency and results of HIV testing were obtained.

Results: 361 (93%) subjects had three or fewer risk factors assessed. No patient had all nine risk factors assessed. Nine (2.3%) patients had no risk factors assessed. Of the 19 (5%) patients tested for HIV, seven (37%) had no known positive risk factors, eight (42%) had one known positive risk factor, four (21%) had two positive risk factors. Of those not tested, 62 (17%) had at least one positive risk factor and five (1%) had at least two positive risk factors.

Conclusion: Despite evidence of increased risk factors and seroprevalence among the CMI, clinicians may be unaware of the need to screen and test for HIV in areas not regarded as "epicenters of the AIDS epidemic." Other findings are discussed.

NR150 Monday, May 22, 3:00 p.m.-5:00 p.m.

Psychopathology, Clinical Progression and Treatment Compliance in a Sample of HIV-1 Infected Veterans

Joseph M. Mavica, D.O., Psychiatry, Univ. of Miami VAMC, 1201 NW 16th Street, Miami FL 33125; Richard Douyon, M.D., Daniel Feaster, M.S., Karl Goodkin, M.D.

Summary:

Aids is a multifaceted disease with both neuropsychiatric and medical presentations. Most epidemiological studies show that

the highest rate of noncompliance and suicide occur in patients afflicted with psychiatric and chronic medical conditions. With the advent of the AIDS epidemic we predict an even higher rate of noncompliance. Patients affected with this disease are often noncompliant with their medical treatment. The effects of treatment noncompliance on the general clinical progression of AIDS is unknown and underestimated.

Objective: 1) Concurrent psychopathology and clinical progression of HIV-1 infection may be associated with treatment noncompliance, 2) Depressed mood and suicidal ideations may impact negatively on patient compliance with treatment.

Methods: seventy-eight male patients from the Special Immunology Services at the Miami Veterans Affairs Medical Center were screened on consecutive visits using the following measures: the Beck Depression Inventory, the Spielberger Anxiety Scale, the Mini-Mental Status Exam, as well as the most recent CDC staging (using both 1986 & 1993 criteria) within six months of screening date. Treatment noncompliance was measured by pill counts and the number of cancellations and noshows versus the number of appointments made. Compliance was assessed 6 months before and after the screening date. Data were summarized by means of ANOVA and Pearson's Product Moment Correlations.

Results: Noncompliance has a significant negative effect on the clinical progression. Use of psychotropics is associated with increased compliance. There is a negative relationship between compliance and suicidal ideations.

Conclusions: Psychopathology affects AIDS outcomes and treatment compliance. Treatment noncompliance may be an expression of covert suicidal ideations. The implications of treatment noncompliance in the management of AIDS patients will be discussed.

NR151 Monday, May 22, 3:00 p.m.-5:00 p.m.

Beside Stuffed Animals and Borderline Personality

David M. Benedek, M.D., Psychiatry, Walter Reed AMC, 6825 16th Street NW, Washington DC 20307; Lawrence A. Labbate, M.D.

Summary:

Objective: To explore the relationship between psychiatric diagnosis and the presence of stuffed animals at the bedside in a population of adult female psychiatric inpatients.

Method: An observer made random periodic surveys of the wardrooms of adult psychiatric inpatients over 12 months. The observer was blind to the diagnoses of these patients and recorded the names of all patients whose living space displayed one or more stuffed animal. The discharge diagnoses of these patients were later independently determined and compared with those of the ward population in general.

Results: 36 female patients were identified who displayed stuffed animals in their rooms. Borderline personality disorder was among the discharge diagnoses in 22 (61%) of these patients. Of 98 adult female patients admitted to the same unit over four months, seven (7%) were noted to have borderline personality disorder among their discharge diagnoses.

Conclusion: Borderline personality disorder is significantly more prevalent in adult female psychiatric inpatients who display bedside stuffed animals than in the adult female inpatient population in general.

NR152 Monday, May 22, 3:00 p.m.-5:00 p.m.

Laterality of Psychogenic Somatic Symptoms

Byungook Lee, M.D., Psychiatry, Severance Hospital, 134 Shinchon-Dong, Seodaemun-ku, Seoul 120752, Republic of Korea; Sungkil Min, M.D., Kee Namkoong, M.D.

Summary:

Objective: The purpose of this study is to examine the types of chief somatic complaints, their laterality in the body, their diagnosis, and the severity of anxiety and depression.

Method: The 50 neurotic patients who had complained of unilateral somatic symptoms were examined by interview. The diagnostic criterion used was DSM-III-R. The severity of depression and anxiety was assessed with Hamilton's depression scale and Hamilton's anxiety scale, respectively. We also collected demographic data from patients.

Results: The chief psychogenic somatic symptoms complained of by patients were significantly more on the left side of the body than on the right side (left: right = 76%:24%). Headache was the most common symptom. The left predominance of the headaches was not statistically significant. When we divided the patients into two groups according to the site of the chief complaint, demographic data, diagnosis, and the score on the anxiety or depression scale, there was no difference between the left- and right-sided group.

Conclusions: These results confirmed the previous report that psychogenic somatic symptoms were more common on the left side of the body. We interpreted these results as indicating that the right hemisphere is more related to emotional disorder.

NR153 Monday, May 22, 3:00 p.m.-5:00 p.m.

Major Depression and Crisis Intervention: A Cost-Effectiveness Study

Nicole Rosset, Ph.D., Psychiatry, University of Geneva, 47 Rue Du 31 Decembre, Geneve 1207, Switzerland; Antonio Andreoli, M.D., Yvonne Burnand, Ph.D., Evelyne Kolatte, M.D.

Summary:

Significance: Major depression (MD) frequently presents with acute symptoms requiring intensive treatment and inpatient care. Further research should determine whether assignment to specialized outpatient crisis intervention is associated with increased efficacy and decreased treatment costs in these subjects.

Methods: Consecutive MDE patients referred with an HDRS score (17 items) >20 were randomly assigned to combined clomipramine protocol/intensive crisis intervention (ICI) ($n = 20$) and clomipramine protocol/supportive day treatment (SCI) ($n = 21$). Psychotic disorder, bipolar disorder, and severe substance abuse were exclusion criteria. A comparison group ($n = 15$) had standard hospitalization. Subjects had standardized assessments at intake and discharge. Extensive questionnaires were filled out to tape treatment costs.

Results: Crisis intervention assignment resulted in reduced hospitalization days ($p < 0.05$), increased compliance with antidepressant medication (p ranging from <0.05 to <0.01), as well as decreased hospitalization costs and loss of days of work compared with SCI assignment. Both ICI and SCI had lower treatment costs compared with standard hospitalization ($p < 0.001$).

Comment: These results suggest that the implementation of well-structured crisis intervention programs may result in better treatment and reduced costs for psychiatric subjects referred for intensive treatment.

NR154 Monday, May 22, 3:00 p.m.-5:00 p.m.

Engagement of Homeless Persons in Treatment

Laura Gaffney, B.A., Psychiatry, University of Maryland, 645 Portland Street, Baltimore MD 21230; Lisa B. Dixon, M.D.

Summary:

Objectives: Little is known about the process of engaging homeless persons with severe mental illness (SMI) in services. This

study surveyed the reasons why 34 homeless persons with SMI who were actively participating in a Program for Assertive Community Treatment (PACT) model program as part of a research project agreed to receive comprehensive outreach services.

Methods: A medical student volunteer who was not a part of the treatment team interviewed 34 individuals receiving services from the team to determine their reasons for initially signing up and then continuing with the program, their expectations, and satisfaction with their current services.

Results: Clients reported most frequently that housing, not psychiatric help, was a reason for enrolling (71%) and continuing (66%) in the program. A desire for psychiatric help was cited by 50% of individuals at referral. Interestingly, only 20% of individuals cited help with addiction as a reason for enrollment at referral, but 65% felt addiction help was a reason for program continuation. Maintaining housing was cited as the most important goal of services, and clients reported experiencing the most help in this area.

Conclusions: This study illustrates that the most important engagement tool for homeless persons with SMI is to provide housing. The provision of psychiatric services alone may be unsuccessful in engaging these persons in treatment. Further, persons with SMI and comorbid addictions may be motivated to pursue treatment after being engaged in services through housing.

NR155 Monday, May 22, 3:00 p.m.-5:00 p.m.

Juvenile Sex Offenders: A Study of Phenomenology and Comorbidity

Viviana B. Galli, M.D., College of Medicine, University of Cincinnati, 231 Bethesda Avenue, Cincinnati OH 45267; Nancy J. Raute, B.A., Danielle L. Kizer, B.S., Brian J. Mc Conville, M.D., Susan L. Mc Elroy, M.D.

Summary:

Published studies on adolescent sex offenders show a low prevalence of mood disorders (1,2) This is the only study that used the Structural Clinical Interview for DSM-III-R (SCID I), Diagnostic Interview for Children and Adolescents (DICA-A), Hamilton Depression Scale, Yale-Brown Obsessive Compulsive Scale (YBOC), an impulse control disorder scale, and a questionnaire targeting paraphilic and non-paraphilic diagnoses. We studied 14 adolescents 12–18 years of age referred by the juvenile court or a rehabilitation center, and one from psychiatric inpatient hospitalization. Twelve (80%) had two or more paraphilias, 13 (86%) had mood disorders, eight (53%) had impulse control disorder, six (40%) had anxiety disorder, six (40%) had substance abuse. Twelve (80%) subjects had recurrent and intrusive paraphilic and non-paraphilic thoughts. Most spent minimal time in direct or indirect activities related to their sexual offense; they were more impulsive and more likely to act upon thoughts or urges. This showed that most of the adolescent sex offenders belong to similar phenomenology to impulse control disorder. Only a minority belonged to the obsessive compulsive disorder, which contrasts with results obtained from adult pedophiles (submitted). This study demonstrates 1) the high prevalence and multiplicity of comorbid diagnoses, 2) treatment should target comorbidity as well as the primary diagnosis.

NR156 Monday, May 22, 3:00 p.m.-5:00 p.m.

Effect of Lorazepam on Cardiac Autonomic Control in Stressed Versus Unstressed State in Normal Subjects

Leslie R. Vogel, M.D., Psychiatry, Columbia University, 622 W. 168th Street Box 427, New York NY 10032; Philip R. Muskin, M.D., Eric D. Collins, M.D., Richard P. Sloan, Ph.D.

Summary:

To determine cardiac autonomic effects of lorazepam (LZ), a modified double-blind, randomized, placebo-controlled study was conducted. Seven normal subjects received LZ (3 mg qd) or placebo for one week, a week taper, then crossed over. Following each drug, 24-hour Holters and mental/physiological stressors were administered. Heart rate variability (HRV) was measured over 24 hours, and during laboratory stressors. For the 24-hour **unstressed** period, two-tailed t-tests revealed LZ-induced *increases* in heart rate (HR), $p < 0.002$; *decreases* in: standard deviation R-R, $p < 0.05$; high frequency power [0.15–0.40 Hz], $p < 0.03$; percent differences between adjacent R-R intervals >50 msec, $p < 0.002$; root mean square successive differences, $p < 0.02$. However, during the **stressed** state on LZ, these HRV changes lost statistical significance. Only HR remained significantly increased ($p < 0.02$). These results demonstrate **vagolytic** effects of LZ in the **unstressed** state which, except for preserved HR increases, are attenuated under **stress.** Since vagal activity appears cardioprotective against arrhythmias, then LZ may be deleterious post-m.i. by decreasing vagal modulation. However, these differential responses to LZ suggest that autonomic effects of benzodiazepines may be state dependent.

NR157 Monday, May 22, 3:00 p.m.-5:00 p.m.

Combination Pharmacotherapy in ADHD

Amar N. Bhandary, M.D., Psychiatry, Baylor College of Med., 11411 Pepperdine Ln, Houston TX 77071; Robert J. Gregory, M.D., Lawrence M. Carmen, M.D., John F. Tanquary, M.D.

Summary:

Objective: Attention deficit hyperactivity disorder (ADHD/ADD) is the commonest congenital neuropsychiatric syndrome, affecting 3%–5% of children and commonly persists into adulthood. Traditionally, ADHD treatment exclusively focuses on centrally mediated symptoms. Psychostimulants retain a mainstay role in targeting such symptoms, but often weakly control, or sometimes aggravate, peripherally mediated symptoms, impulsivity and sleep disturbances, and stimulants' adverse effects.

Method: Based on our inference of therapeutic superiority, we attempted a novel and previously unreported strategy of combining dextroamphetamine (psychostimulant) and nadolol (long-acting beta blocker), underutilized agents of these two classes. We reviewed the literature on psychostimulants, beta blockers, and their germane neurochemistry. Three previously undiagnosed ADHD adults were reassessed employing subjective (descriptive interviews with patient and family) and objective measures (Wender Utah Rating Scale-Revised, Symptoms Check List 90, Massachusetts ADD Rating Scale, Physical Symptoms Check List, Yale-Brown Obsessive Compulsive Scale, spouse and parents' rating scales). A medical workup preceded final diagnosis. Treatment was initiated on dextroamphetamine with regular clinical assessment that included rating scales. Later, nadolol was added.

Results: Dextroamphetamine improved central symptoms while causing sympathetic arousal aggravating peripheral symptoms. Nadolol ameliorated these symptoms, improved sleep, had stimulant benefits, and reduced headaches. On stabilization, no noteworthy adverse effects or medication abuse were noted.

Conclusion: Psychostimulant-beta blocker combination treatment employing dextroamphetamine and nadolol is safe and acts synergistically in ADHD treatment, significantly benefiting most symptoms while reducing adverse medication effects.

NR158 Monday, May 22, 3:00 p.m.-5:00 p.m.

Factors Influencing the Choice of Psychiatry As a Career

JoAnn E. Kirchner, M.D., Psychiatry, Univ Arkansas Med School, 4301 West Markham Slot 589, Little Rock AR 72205; Richard R. Owen, Jr., M.D.

Summary:

Objectives: To determine factors that influence a career choice in psychiatry and the educational level at which that choice is made.

Method: Thirty-eight psychiatry residents (19 females, 19 males) from five consecutive class years at the University of Arkansas for Medical Sciences (UAMS) were asked to 1) rank the three factors influencing their decision to specialize in psychiatry from a list of 16 choices, and 2) the educational level at which they considered and decided to specialize in psychiatry.

Results: The third-year medical student clerkship was the most frequently chosen influence for choosing psychiatry (58% of both males and females). Amount of patient interaction was one of the influences for 58% of women, compared with 11% of men (Chi-square = 9.47, df = 1, $p < 0.005$). Lifestyle was one of the influences for 58% of men, compared with 32% of females. The decision to specialize in psychiatry was made in the third or fourth year of medical school by 82% of the subjects.

Conclusions: Our survey demonstrates the importance of the clinical experiences of medical students in their decision to specialize in psychiatry. Our results suggest that psychiatry residency training programs should focus on the quality of educational experiences during the clinical years of medical school to enhance recruitment into psychiatry.

NR159 Monday, May 22, 3:00 p.m.-5:00 p.m.

Trends in Quality-of-Life Assessments in Psychiatry

Samir P. Patel, M.D., Psychiatry, Boston University Hosp., 720 Harrison Avenue Ste 905, Boston MA 02118; Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D.

Summary:

Objectives: Quality of life (QOL) in psychiatric disorders is conceptually diverse and assessed in different ways. The objective of this study was to determine trends in the use of rating scales, and the types of patient populations and clinical settings studied.

Methods: Medline literature and associated reference lists were searched to yield the largest number of articles that purport to assess QOL of psychiatric disorders.

Results: Between 1966 and 1994, 55 studies were found, 43 (78%) of these having been published since 1989 and representing a 3.6-fold increase compared with 1966–88. Seventy-one percent were cross-sectional evaluations, and 58% were reported to be in community clinical settings. Twenty-one different QOL rating scales were utilized, of which 16 (76%) were utilized once; 11 studies (19%) utilized no specific scale; 32 (58%) studies reported having assessed a generic or mixed patient population; schizophrenia is the most commonly assessed specific diagnosis (27%).

Conclusions: Interest in the assessment of quality of life has clearly increased since 1989. There is much variability in the use of rating scales, the majority of which are used only once. A consensus among researchers regarding the use of specific QOL rating scales would promote valid and reliable comparisons. Future studies need to focus on longitudinal assessments of specific diagnoses and treatments.

NR160 Monday, May 22, 3:00 p.m.-5:00 p.m.

Patient Population, Length of Stay, and Readmissions for a General Hospital Psychiatry Service: Trends Over the Past Decade

Benjamin G. Druss, M.D., Psychiatry, Yale University, 158 Sperry Road, Bethany CT 06524; Martha L. Bruce, Ph.D., Selby C. Jacobs, M.D.

Summary:

Objective: To examine trends in patient demographics, lengths of stay, and readmission rates for an academic, general hospital psychiatry service.

Methods: A hospital database recorded clinical, insurance, and demographic data for all admissions to a psychiatric inpatient service since October 1, 1984 (n = 4482). Logistic regression analyses were performed to assess the association of these variables with length of stay and likelihood of readmission within one year.

Results: Between 1985 and 1993, there was a 64% decline in length of stay ($T = -9.62$, $p < 0.0001$) and a 56% increase in likelihood of readmission (Chi Square = 3.87, $p = 0.047$). There was a 68% drop in privately insured admissions, and an increase in severity of diagnoses. Over time, clinical and demographic variables became progressively less predictive of length of stay, and having Medicaid or a psychotic diagnosis became increasingly associated with likelihood of readmission.

Conclusion: This hospital is increasingly treating poorer, sicker, and more chronic patients with shorter admissions and more readmissions. This is the first study to document changes in length of stay and readmissions while systematically controlling for confounding variables. Patients with Medicaid and with psychotic disorders showed a relative rise in readmissions, which could be consistent with inadequate lengths of stay.

NR161 Monday, May 22, 3:00 p.m.-5:00 p.m.

Reserpine/Cocaine Interactions in Cocaine Addicts

Gregory H. Pelton, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Angela C. Cappiello, M.D., Christopher J. McDougle, M.D., Robert T. Malison, M.D., Thomas R. Kosten, M.D., Lawrence H. Price, M.D.

Summary:

Both clinical and preclinical research has implicated the monoaminergic systems in the neurobiological, psychological, and physiological effects of cocaine. To further characterize monoaminergic/cocaine interactions, reserpine, a lipophillic alkaloid that readily penetrates the brain and causes a marked depletion of 5-HT, DA, and NE stores, was administered to cocaine dependent subjects and their response to intranasal cocaine assessed.

Method: Eleven hospital subjects with a DSM-III-R diagnosis of cocaine dependence (5 females, 6 males) received two intranasal cocaine challenges (2.0 mg/kg), one immediately before and the other after five to seven days of treatment with either reserpine (0.5 mg/day) or placebo, administered in double-blind fashion. Psychological/behavioral effects (including level of euphoria and craving), biochemical effects (including plasma HVA, MHPG), and physiological effects (including BP and HR) were assessed.

Results: Reserpine 0.5 mg/day attenuated the euphoric "high" of cocaine by approximately 20%, with no clear effect on craving, while there was essentially no change on either of these psychological/behavioral indicies after placebo. The other behavioral measures, physiological changes, and biochemical effects are still being analyzed and will be reported.

Conclusion: Depletion of the monoaminergic system by reserpine may attenuate the euphorigenic effects of cocaine. Other behavioral and biochemical effects will be further discussed and implications for further research presented.

NR162 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Neuroimaging Correlates of a Genetic Marker for Schizophrenia

Lina S. Shihabuddin, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Jeremy M. Silverman, Ph.D., Monte S. Buchsbaum, M.D., Richard C. Mohs, Ph.D., Michael Metzger, B.S., Kenneth L. Davis, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand findings which show a correlation between enlarged ventricles on CT scans and a susceptibility to schizophrenia related disorders.

Summary:

Evidence for a genetic linkage marker for schizophrenia and related disorders on the short arm of chromosome 5 (5p14.1-13.1) in one large pedigree (family #17) was found. We examined ventricle/brain ratio (VBR) and brain atrophy by computer tomography scans in the proband and 10 of the proband's 12 first-degree relatives. Of the 11 family members scanned, six (three schizophrenics, two schizotypal personality disorders, and one unaffected) carried the marker allele that co-segregated with schizophrenia related disorders, five (all unaffected) did not. The family members with the schizophrenia-related marker allele had significantly ($p < 0.005$) larger VBRs (controlling for age) than the family members lacking the schizophrenia-related marker allele. These findings suggest the possibility that, in family #17, a relatively enlarged VBR on neuroimaging may be associated with a schizophrenia-related gene and present susceptibility to schizophrenia-related disorders. In addition to a replication of these findings in other similarly linked families yet to be identified, further studies will be required using higher resolution structural as well as functional neuroimaging.

References:

1. Cannon TD, Medrick SA and Parnas: Genetic and perinatal determinants of structural brain deficits in schizophrenia. *Arch Gen Psychiatry* 46:883-889, 1989.

2. Farmer A, Jackson R, McGuffin P, Storey P: Cerebral ventricular enlargement in chronic schizophrenia: Consistencies and contradictions. *Br J Psychiatry* 150:324-330, 1987.

NR163 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Functional Neuroanatomical Correlates of Tics in Tourette's Syndrome

David A. Silbersweig, M.D., Psychiatry, New York Hospital, 525 East 68th St Box 171, New York NY 10021; Emily Stern, M.D., Kit Chee, M.D., Michael R. Trimble, M.D., Mary Jane Robertson, M.A., Raymond J. Dolan, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1) understand the use of new PET brain imaging techniques to identify the neural correlates of neuropsychiatric symptoms; 2) consider a proposed neuropathophysiology of tics in Tourette's syndrome, based upon the results of this study.

Summary:

Objective: Tics, the prominent symptom of Tourette's syndrome (TS), are incapacitating, involuntary behaviors. Their pathophysiology is not well understood and they have not been imaged selectively. The objective of this positron emission tomography (PET) study was to identify the neural correlates of tics in TS.

Methods: Five RH male outpatients with a DSM-IV diagnosis of TS, and frequent motor and vocal tics on neuroleptic medication, were scanned (12 times each) with a 3-D $H_2{}^{15}O$ PET slow bolus technique. The exact timing of the tics was recorded on video and audio tape. An event-related countrate correlational analysis (which considers radiotracer delivery during regional cerebral blood flow changes associated with target symptom occurrence) was then performed, and a statistical parametric map ($p < 0.01$, omnibus) was generated.

Results: Activations were detected bilaterally in the striatum, primary motor/sensory cortices, and auditory/language association cortices. Broca's area, and right anterior cingulate cortex, thalamus, and cerebellum were also activated.

Conclusions: New PET methods have allowed the detection of a brain state associated specifically with tics in TS. Aberrant activity in these distributed cortical-subcortical circuits may explain the spontaneous initiation of, or failure to suppress, specific motor and vocal behavioral repertoires.

References:

1. Silbersweig D, Stern E, Frith CD, Cahill C, Schnorr L, Grootoonk S, Spinks T, Clark J, Frackowiak R, Jones T: Detection of thirty-second cognitive activations in single subjects with positron emission tomography: A new low dose $H_2{}^{15}O$ regional cerebral blood flow three-dimensional imaging technique. *J Cereb Blood Flow Metab* 13:617-629, 1993.

2. Silbersweig D, Stern E, Schnorr L, Frith CD, Ashburner J, Cahill C, Frackowiak R, Jones T: Imaging transient, randomly-occurring neuropsychological events in single subjects with positron emission tomography: An event-related countrate correlational analysis. *J Cereb Blood Flow Metab* 14:771-782, 1994.

NR164 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

PET and Memory Across the Life Span in Normals

Erin A. Hazlett, Ph.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Richard C. Mohs, Ph.D., Lina S. Shihabuddin, M.D., Richard Azueta, M.A., Christina T. Luu, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should understand 1) which brain areas are especially relevant to age-related memory change and 2) how positron emission tomography imaging can be used to assess changes in regional brain activity during memory performance throughout the human lifespan.

Summary:

The present study examined glucose metabolism using PET with ^{18}F-2-deoxyglucose in a group of 62 healthy adults (ages 21 to 87). During the uptake period, all subjects performed a modified version of the California Verbal Learning Test (CVLT). All subjects were screened by history, psychiatric interview, physical exam, and laboratory testing and scanned with our new high resolution (4.5 mm FWHM) scanner. Brain function was measured using our stereotaxic atlas method and expressed in mean relative glucose metabolic rate (GMR). Results indicate that performance on the CVLT declines significantly with age ($r = -.40$, $p < .01$). In addition, with age relative GMR declines markedly in the medial frontal ($r = -.40$, $p < .01$) and temporal lobe ($r = -.50$, $p < .01$), yet increases in the occipital lobe ($r = .26$, $p < .05$). Better memory performance is associated with higher relative GMR in the left medial temporal lobe ($r = .41$, $p < .01$) and this correlation remains statistically significant when the age effect is controlled (partial $r = .28$, $p < .05$). In order to better understand successful preservation of memory function with age, post-hoc t-tests contrasting good and poor memory performers (age 50 and over) were conducted. The good performance group showed significantly higher relative GMR in the temporal lobe compared to the poor performance group ($t = 2.13$, $p = .04$). Conversely, relative GMR is significantly lower in the occipital lobe of the good performers compared to the poor

performers (t = –2.36, p = .03). Taken together, this pattern of findings: 1) demonstrates the expected age-related decline in performance, 2) indicates that good performance on the CVLT is highly related to relative GMR in left medial temporal lobe, an important area for verbal memory processing, and (3) suggests that age-related changes are subserved by a shift in the deployment of cognitive effort away from categorizing in the frontal lobe and long-term preservation of memory items in the temporal lobe to visual system-related processing in the occipital lobe.

References:

1. Buchsbaum MS, Siegel B: Neuroimaging and the aging process in psychiatry. *Int Rev Psychiatry* 6:109-118, 1994.

2. Siegel BV, Buchsbaum MS, Starr A, Mohs RC, Neto DC: Glucose metabolic rate and progression of illness in Alzheimer's disease. *Int J Geriatric Psychiatry,* in press.

NR165 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Brain Glucose Metabolism in Unipolar Depression Compared with Controls Before and After Sleep Deprivation As Measured by PET FDG

Eric A. Klein, B.S., Psychiatry, University of CA Irvine, c/o Joseph C. Wu, M.D., Rm 163 Irvine Hall, Irvine CA 92715; Joseph C. Wu, M.D., J. Christian Gillin, M.D.

Educational Objectives:

The participant should be able to recognize the key role limbic and basal ganglia structures play in different subtypes of depression which respond to sleep deprivation.

Summary:

Objective: Based on previous findings, two hypotheses were tested in this study: 1) Do depressed patients who respond to sleep deprivation have higher cingulate metabolic rates? 2) Do depressed patients irrespective of response to sleep deprivation have decreased basal ganglia metabolic rates?

Method: Forty-three depressed outpatients and 26 normal controls (NC) participated in a positron emission tomography scanning with 18-Fluorodeoxyglucose. Subjects underwent total sleep deprivation for one night and were rescanned and reassessed using the Hamilton-D inventory. There were 12 depressed responders (DR) with a 40% or greater decrease in Hamilton score compared with 31 depressed non-responders (DNR). Each subject's baseline scan was subtracted from each post-sleep deprivation scan. Statistical parametric maps (SPMs) which yielded a p-valued image were used to analyze results.

Results: The DR were significantly higher than the NR and the NC in the left anterior cingulate metabolism ($p < .05$). DR and the DNR were bilaterally lower in putamen metabolic activity compared to NC ($p < .05$).

Conclusion: This largest study of its type to date not only demonstrates the key role played by limbic metabolism in modulating affective state, but also suggests different subtypes of depression and possibly different clinical treatment regimes based on differing responses to sleep deprivation.

References:

1. Wu JC, Gillin C, Buchsbaum M, Hershey T, Johnson C, Bunney WE: Effects of sleep deprivation on brain metabolism of depressed patients. *Am J psychiatry* 149:538-543, 1992.

2. Volk S, Kaendler SH, Weber R, Georgi K, Mail F, Hertel A, Pflug B, Hor G: Evaluations of the effects of total sleep deprivation on cerebral blood flow using single photon emission computerized tomography. *Acta Psychiatry Scandinavia* 86:478-483, 1992.

NR166 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

MU and Kappa Opioid Receptor Agonists Induce Different Patterns of CBF

Thomas E. Schlaepfer, M.D., Psych Meyer 3-166, The Johns Hopkins Hosp, 600 N Wolfe St, Baltimore MD 21287; Eric C. Strain, M.D., Benjamin D. Greenberg, M.D., George Bigelow, M.D., Kenzie L. Preston, Ph.D., Godfrey D. Pearlson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to realize the importance of functional neuroimaging in substance abuse research.

Summary:

Among the various postulated opioid receptors in the brain, the mu and the kappa type have received particular attention. Humans experience the subjective effects of mu versus kappa opioid agonists differently: mu agonists seem to produce euphoria while kappa agonists lead to sedation.

The purpose of this study was to test the hypothesis that opioids with mu versus kappa effects would produce anatomically distinct patterns of cerebral perfusion as assessed with single photon emission computed tomography (SPECT). Non-dependent opioid abusers (n = 9) received intramuscular injections of 4 mg/70 kg hydromorphone (a prototypic mu agonist), 6 mg/70 kg butorphanol (a mixed agonist-antagonist with kappa opioid effects), and saline placebo in a double-blind, random order design. Sixty minutes after drug administration the SPECT tracer [^{99m}Tc]-HMPAO was given intravenously. SPECT scans were performed using a triple head camera. Analyses were done by averaging subjects' images for each respective condition after correcting for the injected dose of radioactivity, and then calculating significant cerebral blood flow (CBF) changes in the averaged brains between the placebo and hydromorphone, and the placebo and butorphanol conditions.

Hydromorphone led to a distinctive increase in CBF in the mediofrontal area, while butorphanol caused a mixed picture of increases and decreases in CBF mainly in the area of the cingulate gyrus. These results suggest opioids known to have different patterns of subjective and behavioral effects also produce anatomically-distinct patterns of change in cerebral blood flow. In addition, this study demonstrates the application of SPECT functional neuroimaging in the study of medications with potential abuse liability.

References:

1. Jaffe JH, Martin WR: Opioid analgesics and antagonists. In *Goodman and Gilman's The Pharmacological Basis of Therapeutics.* (Gilman, A.G., Goodman, L.S., Rall, T.W., Murad, F., eds.) MacMillan Pub. Co., New York, pp. 493-495, 1985.

2. Preston KL, Bigelow GE, Bickel WK, Liebson IA: Drug discrimination in human postaddicts: Agonist-antagonist opioids. *J Pharmacol Exp Ther,* 250:184-196, 1989.

NR167 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Actively Depressed Subjects Have Difficulty Inducing and Blunted Limbic rCBF During Transient Sadness

Mark S. George, M.D., Bldg 10 Room 3N212, NIMH, 10 Center Drive, Bethesda MD 20892-0001; Timothy A. Kimbrell, M.D., Priti I. Parekh, B.A., Terence A. Ketter, M.D., Peggy J. Pazzaglia, M.D., Ann M. Callahan, M.D., Mark A. Frye, M.D., Lauren B. Marangell, M.D., Peter Herscovitch, M.D., Robert M. Post, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate that abnormal brain activity may persisit even after phenomelogical recovery from clinical depression.

Summary:

Background: Transient sadness is complexly related to clinical depression. Many episodes of clinical depression begin after periods of prolonged sadness and unresolved grief. Conversely, some actively depressed patients complain of emotional blunting or being unable to experience sadness. PET studies have shown that healthy adults activate their anterior cingulate and prefrontal cortex during transient sadness.

Methods: We imaged seven actively depressed subjects, seven healthy controls, and seven formerly depressed subjects in remission, all medication-free and matched for age and sex. 015 water PET images were obtained during self-induced neutral, sad, and happy states.

Results: During the neutral state, depressed and remitted subjects showed decreased activity in the prefrontal cortex and anterior limbic system compared to controls. During transient sadness, both the depressed and remitted subjects showed blunted limbic activation. Actively depressed subjects found the emotion induction tasks more difficult and could not induce transient sadness to the same degree as controls or remitted depressed subjects. When they could induce the transient emotional state, they were often unable to switch back to neutral.

Conclusions: Actively depressed subjects have difficulty switching out of their pathological mood state and becoming transiently sad. Both active and remitted depressed subjects show blunted limbic activation when trying to induce transient sadness. These results demonstrate that abnormal brain activity may persist even after phenomenological recovery from clinical depression.

References:

1. George MS, Ketter TA, Parekh PI, et al.: Regional brain activity during transient self-induced sadness or happiness in healthy women. *Am J Psychiatry* 1995 (In Press).

2. Post RM: Transduction of psychosocial stress into the neurobiology of recurrent affective disorders. *Am J Psychiatry,* 149:999-1010, 1992.

NR168 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Fluvoxamine Compared with Fluoxetine in Major Depression

Mark H. Rapaport, M.D., Psychiatry, UCSD UN Cal San Diego, 8950 Villa Jolla Drive Ste2243, La Jolla CA 92037; Emil F. Coccaro, M.D., Yvette I. Sheline, M.D., Peter J. Holland, M.D., Teri L. Perse, M.D., Louis F. Fabre Jr, M.D.

Educational Objectives:

To recognize efficacy and safety distinctions between SSRIs during treatment of patients with major depression.

Summary:

The effectiveness and safety of fluvoxamine maleate, 50 to 150 mg daily in comparison with fluoxetine HCl 20 to 80 mg daily were studied in outpatients with DSM-III-R-defined major depressive disorder, in a randomized, double-blind, parallel-group, multicenter study. After a one- to two-week placebo run-in, patients underwent double-blind treatment for seven weeks. The Hamilton Depression Rating Scale (HAM-D) was used as the primary efficacy measure. Secondary efficacy measures included HAM-D factor scores, the Clinical Global Impression Scale (CGI), the Hamilton Psychiatric Rating Scale for Anxiety (HAM-A), the Raskin-Covi Scale, and the SCL-56. Vital signs, clinical laboratory tests (hematology and biochemistry), adverse events, concomitant medication, and scales for suicidal ideation and akathisia comprised the safety evaluations.

One hundred fifteen patients were screened for the study. One hundred patients were randomized: 51 to fluvoxamine maleate and 49 to fluoxetine. The mean change in HAM-D 21-item total score from baseline to week 7 was −15.52 for fluvoxamine (25.15 to 9.63) and −15.85 for fluoxetine (25.57 to 9.72) ($p = 0.641$). No statistically significant differences were seen between groups at any visit. Sixteen patients did not complete the study (eight in each group). There were no statistically significant differences between groups at any visit, including end-point, for the primary efficacy variable (HAM-D 21-item total score). Secondary and supportive measures confirmed the results obtained with the HAM-D. In spite of a rather high incidence of treatment emergent adverse events, treatments were well-tolerated, with few dropouts. fluoxetine HCl was associated with more adverse events overall, especially nausea ($p = 0.03$).

References:

1. Lapierre J, et al.: Treatment of major affective disorder with fluvoxamine. *J Clin Psychiatry.* 48:65-68, 1987.

2. Cohn JB, Wilcox C: A comparison of fluoxetine, imipramine, and placebo in patients with major depressive disorder. *J Clin Psychiatry.* 45:26-31, 1985.

NR169 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Weekly Fluoxetine Controls Symptoms of Depression

William J. Burke, M.D., Psychiatry, 600 South 42nd Street, PO Box 985575, Omaha NE 68198-5575; Shelton Hendricks, Ph.D., Delores McArthur, M.A., Todd W. Stull, M.D., Diane Bessette, P.A., Tracy McKillip, P.A.

Educational Objectives:

This presentation characterizes the effects of alternate dosing strategies for individuals after they have completed the acute phase of treatment for depression. The unique pharmacokinetic properties of fluoxetine will be discussed along with speculation as to how they might influence the continuation and maintenance phases of treatment for depression.

Summary:

Objective: Fluoxetine (FLX) has a unique pharmacokinetic profile. Its major metabolite, norfluoxetine, possesses FLX's antidepressant efficacy and a half-life of seven to 15 days, suggesting the possibility of nonstandard dosing strategies. This study examined the efficacy of a weekly dose of FLX for the continuation phase of treatment for major depressive disorder (MDD).

Methods: Forty subjects initially received open-label treatment with 20mg of FLX daily for eight weeks. Subsequently, 34 subjects with a Hamilton Depression Rating Scale (HDRS) of 12 or less were randomized in a double-blind design to one of three treatment groups (placebo, 20mg FLX daily, or 60mg FLX weekly) and followed for three months. Additional outcome measures included the Hopkins Symptom Check List (SCL) and the Montgomery-Asberg Depression Scale.

Results: Significant group effects were obtained for all measures. The 20mg and 60mg groups had significantly better scores than the placebo group. There were no significant differences between the drug groups except for the SCL where the 60mg group exhibited better scores.

Conclusions: A weekly dose of FLX may be as efficacious as daily doses in controlling the symptoms of MDD after the acute phase of treatment.

References:

1. Kupfer DJ: Long-term treatment of depression. *J Clin Psychiatry* 52:5(suppl):28-34, 1991.

2. Montgomery SA, Baldwin D, Shah A, Green M, Fineberg N, Montgomery D: Plasma-level response relationships with fluoxetine and zimelidine. *Clin Neuropharmacology* 13:S71-S75, 1990.

NR170 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Fluoxetine and Aggression in Personality Disorder

Emil F. Coccaro, M.D., Dept of Psych, Med College of PA EPPI, 3200 Henry Ave, Philadelphia PA 19129-1137; Richard J. Kavoussi, M.D.

Educational Objectives:

To identify the extent and nature of treatment efficacy of fluoxetine, a potent and selective 5-HT uptake inhibitor, on overt impulsive aggressive behavior and irritability in DSM-III-R personality disordered subjects.

Summary:

An inverse relationship between indices of central serotonin (5-HT) system function and of trait measures of impulsive aggressive behavior has been demonstrated repeatedly in humans over the past 15 years. To date, however, there has been no specific experimental test of the serotonin hypothesis of impulsive aggression in humans. Herein, we report on the interim data analysis from a double-blind, placebo-controlled, 12-week clinical trial of fluoxetine in the treatment of impulsive aggressive behavior in non-major depressed (mean HAM-D: 6.3 ± 5.2) DSM-III-R personality disordered individuals (M = 28; F = 12). All subjects met DSM-III-R criteria for personality disorder (borderline PD = 11; non-borderline PD = 29) and all had demonstrated signs of consistent impulsive aggressive behavior during a two-week placebo lead-in phase. Twenty-seven were randomized to fluoxetine and 13 to placebo. Primary outcome variables were overt aggression and irritability as assessed by (Overt Aggression Scale-Modified: Coccaro et al., 1990). Over time, fluoxetine significantly decreased: a) overt aggressive behaviors (weeks 10-12: ANOVA $p < 0.05$) and, b) irritability (weeks 4-12: ANOVA $p < 0.05$); endpoint analysis revealed the same findings. There were no interactions noted between drug condition and gender, specific PD diagnosis (e.g., BPD vs. Non-BPD) or HAM-D depression scores. These data suggest that fluoxetine has significant antiaggressive effects, independent of any antidepressant effects, in personality disordered individuals with substantial histories of overt impulsive aggressive behavior and irritability.

References:

1. Coccaro EF, Siever LJ, Klar HM, Maurer G, Cochrane K, Mohs RC, Davis KL: Serotonergic studies in affective and personality disorder: Correlates with suicidal and impulsive aggressive behavior. *Arch Gen Psychiatry* 46:587-599, 1989.

2. Coccaro EF, Harvey PD, Kupsaw-Lawrence E, Herbert JL, Bernstein DP: Development of neuropharmacologically based behavioral assessments of impulsive aggressive behavior. *J Neuropsychiatry* 3:S44-S51, 1991.

NR171 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

The Ictal EEG Predicts the Efficiency of RUL ECT

W. Vaughn McCall, M.D., Psychiatry, Bowman Gray School Med., Medical Center Blvd, Winston-Salem NC 27157; Brian A. Farah, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the ictal EEG differences between titrated, moderate dose, and fixed, high dose RUL ECT.

Summary:

Objective: At the present time ECT practitioners lack proven physiologic markers of treatment outcome to guide selection of stimulus dose. This study examined the utility of the ictal EEG in predicting treatment outcome.

Method: Seventeen depressed patients (mean age 73 years; three male, 14 female) randomly received either titrated moderately suprathreshold RUL ECT or high fixed dose (403 mC) RUL ECT. Depression severity was blindly assessed with the Hamilton Depression Scale. The ictal EEG (Fp1-A1) was blindly rated on a seven-point scale for regularity of morphology and a three-point scale for post-ictal suppression.

Results: The fixed, high dose (FHD) had a more rapid antidepressant effect and required fewer treatments than the titrated, moderate dose (TMD) group. The FHD group had greater mean regularity ratings (3.5 ± 1.2) than the TMD group (2.9 ± 1.3) ($F = 5.8$; $df = 1, 115$; $p < 0.02$). Both convulsive and EEG seizure durations were shorter in the FHD group. Post-ictal suppression ratings were not different for the two groups.

Conclusions: FHD is a more efficient form of RUL ECT than TMD. FHD produces greater EEG seizure regularity scores than TMD. Hence, regularity ratings may be a marker for RUL ECT treatment efficiency. This is one of the first reports of improved treatment efficiency associated with shorter seizures.

References:

1. Weiner RD, Krystal AD: The EEG monitoring of ECT seizures. In Coffey CE (ed.), The Clinical Science of Electroconvulsive Therapy. pp 93-109. Washington, DC: APA Press, 1993.

2. Nobler MS, Sackeim HA, Solomon M, et al.: EEG manifestations during ECT: Effects of electrode placement and stimulus intensity. *Biol Psychiatry* 34:321-330, 1993.

NR172 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Double-Blind Crossover Antidepressant Study: Sertraline Versus Imipramine

Michael E. Thase, M.D., Department of Psychiatry, Western Psychiatric, 3811 O'Hara Street, Pittsburgh PA 15146; Martin B. Keller, M.D., Alan J. Gelenberg, M.D., Robert M.A. Hirschfeld, M.D., Alan F. Schatzberg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1) state the effectiveness of tricyclics when used following an SSRI; and 2) state the effectiveness of SSRIs when used following a tricyclic.

Summary:

The selective serotonin reuptake inhibitors (SSRIs) have now surpassed the tricyclics (TCAs) as antidepressant of first choice in the United States. Some patients treated with either of those agents fail to respond to their physician's treatment of first choice, however, and the effectiveness of sequential treatment with these classes has not been widely studied. This is particularly true for treatment of chronic depression, for which research has lagged behind that of uncomplicated episodic depression. Results of a double-blind crossover study of 165 chronically depressed outpatients who failed initial 12-week trials of imipramine (in doses titrated to 300 mg) or sertraline (in doses titrated to 200 mg) will be reported. Patients were initially randomized in a ratio of 2 sertraline: 1 imipramine. Following a one- to two-week wash-out, nonresponders were crossed over to the opposite medication for a 12-week trial. Results of a preliminary analysis of the first 77 patients (of which 50 crossed to imipramine and 27 crossed to sertraline) are as follows: 89% of the patients completed crossover treatment with sertraline compared to 76% of patients completing crossover treatment with imipramine. Sixty-three percent of the imipramine nonresponders responded to sertraline and 47% of the sertraline nonresponders responded to imipramine. These results suggest that chronically depressed patients failing an adequate trial of one class of antidepressant medication should receive a sequential trial of an alternate class of medication.

References:

1. McGrath PJ, Stewart JW, Nunes EV, et al.: A double-blind crossover trial of imipramine and phenelzine for outpatients with treatment-refractory depression. *Am J Psychiatry,* 250:118-123, 1993.

2. Thase ME, Rush AJ: Treatment resistant depression. In: *Psychopharmacology: The Fourth Generation of Progress,* edited by Bloom FE, Kupfer DJ. Raven Press, New York, pp 1081-1097, 1995.

NR173 Tuesday, May 23, 9:00 a.m.-10:30 a.m.

Thyroid Function and Antidepressant Response

Fabrice Duval, M.D., Psychiatry, Centre Hospitalier, 27 rue du 4eme RSM, 68250 Rouffach 00110, France; M. Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D., Jean-Paul Macher, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that response to antidepressant treatment is associated with changes in thyroid function resulting in lower levels of circulating thyroid hormones.

Summary:

Objective: Several studies suggest that antidepressant treatment leads to changes in thyroid function tests: either decreased peripheral thyroid hormone levels or increased thyrotropin (TSH) levels (basal or post-TRH stimulation). This study sought to determine if these changes in thyroid function are related to a direct effect of the antidepressant on the thyroid axis or rather to a change in clinical state.

Method: Thyroid function was evaluated in 30 euthyroid inpatients meeting DSM-IV criteria for major depressive episode (MDE) through the determination of free triiodothyronine (FT_3), free thyroxine (FT_4) and TSH before and after 8 AM and 11 PM TRH challenges (200 μg I.V.), on the same day. Results at baseline (treatment free) were compared with those after one month of antidepressant treatment with either amitryptiline (n = 14), fluoxetine (n = 8), or toloxatone (n = 8).

Results: Clinical efficacy and effects on thyroid function did not differ across the three antidepressant drugs. Compared with pretreatment values, significant reductions in basal serum 8 AM FT_4 ($p < 0.025$), 11 PM FT_4 ($p < .025$), and 8 AM FT_3 levels ($p < 0.02$), increases in 11 PM TRH-stimulated TSH (ΔTSH) ($p < 0.01$) and ΔΔTSH values (difference between 11 PM-ΔTSH and 8 AM-ΔTSH) ($p < 0.025$) were observed in responders (n = 11) but not in partial- (n = 6) and non-responders (n = 12). Moreover, non-responders exhibited lower pretreatment 11 PM-TSH values than responders (basal: $p < 0.01$; ΔTSH: $p < 0.02$).

Conclusions: These data suggest that: 1) changes in thyroid function are related to clinical recovery rather than to a direct effect of the antidepressant drug; 2) patients with the lowest nocturnal TSH secretion have the worst antidepressant response and this may be a factor contributing to treatment resistance.

References:

1. Joffe RT, Levitt AJ: The thyroid and depression, in the thyroid axis and psychiatric illness. Edited by Joffe RT, Levitt AJ. Washington, American Psychiatric Press, 1993.

2. Duval F, Mokrani MC, Crocq MA, et al: Influence of thyroid hormones on morning and evening TSH response to TRH in major depression. *Biol Psychiatry* 35:926-934, 1994.

NR174 Tuesday, May 23, 12 noon-2:00 p.m.

Decreased Platelet Paroxetine Binding in PTSD: Relationship to Clinical Features and Comorbidity

Christopher G. Fichtner, M.D., Chief Psych Service 116A, VA Medical Center, 3001 Green Bay Road, North Chicago IL 60064; Hock C. Yeoh, B.S., Francine L. O'Connor, M.S., Ramesh C. Arora, Ph.D., John W. Crayton, M.D.

Summary:

Objective: While PTSD appears to involve disturbed catecholamine systems, a possible role for serotonin (5-HT) systems in the expression of PTSD symptoms has also become a focus of recent interest. We previously reported an association between decreased binding (B_{max}) of ^{3}H-paroxetine to blood platelet 5-HT uptake sites and anxiety in PTSD patients. In the current study we assessed possible relationships between B_{max} of ^{3}H-paroxetine binding and comorbid psychiatric diagnoses in PTSD patients.

Method: We studied platelet ^{3}H-paroxetine binding in 41 SCID-diagnosed male Vietnam combat veterans with PTSD, who also completed the Mississippi Scale (MS), the Spielberger State-Trait Anxiety Inventory (STAI), and the Beck Depression Inventory (BDI).

Results: For the binding of ^{3}H-paroxetine to blood platelets, mean (±S.D.) K_D and B_{max} values were 0.046 ± 0.016 nM and 990.0 ± 279.2 fmols/mg protein, respectively. There was a significant positive correlation between K_D and B_{max} ($r = 0.38$, $p < .02$). B_{max} correlated inversely with STAI Form Y1 ($r = -0.59$, $p < .001$), STAI Form Y2 ($r = -.054$, $p < .001$), the BDI ($r = -0.49$, $p < .001$), and the MS ($r = -0.52$, $p < .001$). However, there were no significant differences between PTSD patients with and without the following diagnoses: major depression ($t[37] = -0.43$, $p > .65$), panic disorder ($t[39] = -0.22$, $p > .65$), all comorbid anxiety disorders combined ($t[39] = -0.94$, $p > .35$), alcohol abuse or dependence ($t[39] = 0.23$, $p > .65$), and all substance abuse disorders combined ($t[39] = .91$, $p > .35$).

Conclusions: A decrease in platelet 5-HT uptake sites in PTSD is associated with symptoms of anxiety and depression, but may not be explained by the presence of other categorical diagnoses. PTSD symptoms may relate to underlying psychobiological factors not well captured by other comorbid diagnostic entities.

NR175 Tuesday, May 23, 12 noon-2:00 p.m.

Stressors Affect Onset and Drug Treatment Response in Unipolar Depression

Carolyn M. Mazure, Ph.D., Psychiatry, Yale University Med Sch, Yale New Haven Hosp MU10-5 EP, Martha L. Bruce, Ph.D., Selby C. Jacobs, M.D., Janet S. Cellar, M.S.N.

Summary:

Both recent neurobiological and long-held psychosocial formulations suggest that stressful life events a) are risk factors for depressive onset, particularly in first episode patients, and b) may affect drug response. However, few studies have compared stressor occurrence in patients to controls; even fewer have examined chronic stressors; and only two studies investigating stressors and treatment course have standardized treatment. Methodological deficits in assessment of stressors also have made it difficult to determine the magnitude of purported relationships.

Method: An ongoing case-control study and a treatment-outcome study, in first vs recurrent episode cases, are presented. DSM-III-R major (unipolar) depressives (17-item HAM-D ≥ 18; N = 16) were matched to nondepressed community controls; drug response after a six-week standardized antidepressant trial equalled HAM-D < 10 + HAM-D decrease ≥50%. The Structured Event Probe & Narrative Rating Interview (Dohrenwend et al 1993) was used to assess acute stressful events and chronic stressors.

Data show high reliability for interview administration and ratings of stressor characteristics.

Case-Control Results: Antecedent stressful events were more likely in unipolar patients vs nondepressed community controls (63% vs 0%; Fisher Exact Test p = .004). First-episode cases did not have higher event rates than recurrent patients (66% vs 60%); but chronic stressors were more likely in cases than controls, and in first episode than recurrent cases.

Treatment-Outcome Results: Antecedent events did not predict response (42% vs 66%). However, patients with chronic stressors responded to pharmacotherapy more favorably (83% vs 22%; FET p = .03).

Data from these studies suggest that stressors may influence onset and drug response, and indicate the importance of evaluating both acute and chronic stressors.

NR176 Tuesday, May 23, 12 noon-2:00 p.m.

Natural Disasters: Stress Symptoms and Coping in Rescue Workers

Sudhakar Madakasira, M.D., Dept. of Psychiatry, Univ. of MS Medical Cente, 2500 North State Street, Jackson MS 39216-4505

Summary:

The psychological impact of disasters on the victims is well established but the impact on rescue workers has been only recently recognized. Approximately one third of the workers report symptoms of post-traumatic stress disorder (PTSD). Post-disaster debriefing has been reported to be helpful in dealing with the disaster experience but the coping strategies that are useful on the disaster scene have not been well studied. The purpose of our study was to survey symptoms of PTSD and their coping strategies in rescue workers six months after the tornadoes in 1992 that devastated 20 counties in Mississippi, killing 15 people and injuring more than 200. PTSD symptoms were assessed by the Frederick reaction index and coping strategies by an 11-item inventory adapted from a study by Dyregrov and Mitchell. Of the 799 rescue workers who were mailed the survey questionnaire, 139 (17%) responded, including 28 (22.6%) who were not on the disaster scene. Although none was injured, 29 (21%) reported being personally affected by the tornadoes. A total of 36 (28%) met the criteria for mild PTSD, 10 (8%) for moderate PTSD, and one (1%) for severe PTSD. Age, number of years of experience, or number of previous disaster events did not differentiate those with PTSD from those without. The mean score of the PTSD symptoms did not differ between those on the scene and those away ($t = 1.72$, $p < .09$) but was significantly higher in females ($t = 2.67$, $p < .01$). Those who were personally affected by the tornadoes also had higher mean of PTSD symptoms ($t = 3.48$, $p < .001$) and utilized more coping ($t = 2.23$, $p < .03$). The mean PTSD symptom score also correlated with the mean coping score ($r = .21$, $p < .02$). Those with PTSD also utilized more of cognitive restructuring strategies such as blocking feelings, derealization, focusing on tasks, shielding thoughts, and consideration of other workers. These results suggest that the prevalence of stress symptoms is high in rescue workers even when they do not assist; women workers and those who are personally affected by the disaster have higher levels of stress; cognitive restructuring strategies are frequently utilized to deal with disaster stress.

NR177 Tuesday, May 23, 12 noon-2:00 p.m.

Stress, Arousal, and Deployment to Haiti

Donald P. Hall, Jr., M.D., Combat Stress, Fort Bragg, NC, 3410 Regiment Drive, Fayetteville NC 28303; James A. Jansen, B.S.

Summary:

Objective: To study the relationship between demographic variables and past experience on self-reported stress and arousal symptoms of soldiers preparing for combat.

Method: 239 members of the U.S. Army's 28TH Combat Support Hospital were surveyed for stress and arousal indicators, using the Stress Arousal Checklist (SACL), during preparation for deployment to Haiti. Demographic and coping factors such as time spent in sleep, exercise, socialization, and meditation were assessed by questionnaire.

Results: Advanced age, higher rank, and greater sleep time groups had significantly higher arousal scores ($p < 0.05$). Sex, race, time on prior deployment, and other coping factors were not associated with significant change in arousal scores. There was no significant difference between groups in stress scores.

Conclusions: Remarkably, none of the coping factors studied had a significant effect on level of psychological stress. However, based on significantly lower arousal scores, lower ranking, younger, and sleep-deprived soldiers may be at higher risk for accidents. These findings may also apply to other emergency service organizations.

NR178 Tuesday, May 23, 12 noon-2:00 p.m.

Neuroleptic-Induced Extrapyramidal Symptoms and Serum Iron

Ileana Berman, M.D., Psychiatry, FDR VA Hospital, Mt. Sinai School of Medicine, Montrose NY 10548; Amalia Merson, M.D., Julia Rachev Pavlov, M.D., Cecile E. Sison, Ph.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D.

Summary:

Introduction: Several studies have reported inverse correlation between serum iron levels and neuroleptic induced akathisia, acute dystonic reactions, and neuroleptic malignant syndrome. The data reflecting the relationship between serum iron levels and neuroleptic induced extrapyramidal symptoms (EPS), however, are sparse and nonconclusive. Animal studies suggest that low serum iron could mimic D2 blockade which is implicated in EPS. On the bases of the above mentioned findings, we hypothesize that low serum iron may be associated with neuroleptic induced EPS. In this study we examined the relationship between EPS and serum iron in chronic schizophrenic patients.

Method: Forty male patients were recruited for the study. The patients were diagnosed with chronic schizophrenia according to DSM III-R criteria. Patients had to have hematocrit of at least 35 mm, to be medically stable and on the same dose of neuroleptic for at least two weeks prior to the assessment. Patients on antiparkinsonian agents at the time of the assessment as well as patients with akathisia were not included. The patients were rated with Simpson Angus scale. Abnormal Involuntary Movement Scale (AIMS), and Barnes Akathisia Scale. Patients' venous blood samples for estimation of serum iron level, total iron binding capacity (TIBC), transferrin, and ferritine were analyzed in the same laboratory. We divided the patients into two groups: one group without significant EPS who had a total Simpson Angus score of 4 or less ($n = 23$), and another group with significant EPS who scored higher than 4 ($n = 16$).

Results: The mean ages were 64 in the group with EPS and 54 in the group without significant EPS. We found significant negative correlations between severity of EPS and serum iron ($r = 0.43$, $p = 0.004$, $n = 36$) and TIBC ($r = 0.37$, $p = 0.02$, $n = 31$) but not significant correlation between EPS scores and ferritine and transferrin. Two-tailed t-test analyses showed significant differences between patients with and without EPS in the serum iron level ($t = 2.1$, $p = 0.05$) and TIBC ($t = 2.9$, $p = 0.007$).

Conclusions: Our results suggest that iron may be implicated in the neuroleptic induced EPS. This finding may have impact on treatment strategies of EPS.

NR179 Tuesday, May 23, 12 noon-2:00 p.m.

Cognitive Deficits and Schizophrenic Symptoms

Ileana Berman, M.D., Psychiatry, FDR VA Hospital, Mt. Sinai School of Medicine, Montrose NY 10548; Amalia Merson, M.D., Barbara Viegener, Ph.D., Cecile E. Sison, Ph.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D.

Summary:

There is an increased awareness in the field that cognitive deficits represent an important aspect of schizophrenic pathology. Various studies have reported that schizophrenic patients have difficulties performing cognitive tasks that measure attention, learning, memory, and executive functions. There is evidence that cognitive impairments may be correlated with both positive and negative symptoms of schizophrenia.

Method: The purpose of this study is to assess the relationship between schizophrenic symptoms and neuropsychological performance in a group of 30 patients diagnosed with schizophrenia according to DSM-III-R criteria. All patients had to be psychiatrically stable (i.e., same dose of medication for at least two weeks prior to the assessment, no acute exacerbation for one month prior to the assessment), have Minimental Status score of at least 25, and be able to cooperate with cognitive testing. The patients were assessed using the Positive and Negative Syndrome Scale (PANSS) and had a battery of cognitive tests which included Minimental Status Examination (MME), Wechsler Visual Memory Test, block design (BD), digit symbol (DSy), digit span (DS), trails, verbal fluency, similarities and the Wisconsin Card Sorting Test (WCST). The PANSS assessments were done by two experienced investigators who achieved an interater reliability of 0.8 or higher. The cognitive tests were done by raters who were blind to the PANSS scores.

Results: Our preliminary results suggest that negative symptoms are directly correlated with poor performance on WCST. Patients with higher negative scores seemed to have higher number of perseverative responses and errors ($r = 0.43$, $p = 0.05$, and respectively $r = 0.39$, $p = 0.07$, $n = 16$). Poor performance on trails was also correlated with negative symptoms ($r = 0.48$, $p = 0.02$, $n = 20$). On the other hand, we found that severity of the positive symptoms was correlated with poor performance in the DS ($r = -0.62$, $p = 0.006$, $n = 16$) and low MME scores ($r = -0.52$, $p = 0.01$, $n = 18$).

Conclusions: Positive and negative symptoms appear to be correlated with different cognitive deficits. Our findings support the previous reports that negative symptoms may be associated with poor performance on the WCST suggesting possible link with frontal dysfunction. Positive symptoms, on the other hand, seem to be associated with poor performance on tasks that are more global measures of the cognitive functioning such as MME and DS. These findings should be cautiously interpreted since they represent only preliminary results of a more extensive study currently in progress.

NR180 Tuesday, May 23, 12 noon-2:00 p.m.

Part/Whole Perceptual Organization in Schizophrenia

Eric L. Granholm, Ph.D., Psychology, VA Medical Center, 3350 La Jolla Village Drive, San Diego CA 92161; Peter A. Nelson, William B. Perry, Ph.D., Vincent Filoteo, Ph.D.

Summary:

Perception of hierarchical patterns on a global/local task was examined in 17 schizophrenic patients and 21 normal controls in a paradigm similar to that used by Robertson & Lamb (1989). Subjects detected an H or S target which appeared at either the global (whole) or local (part) level of a composite stimulus (e.g., a global E constructed with local H's) presented in 3°, 6°, and 9° of visual angle. Consistent with previous studies of normal individuals, a global advantage in reaction time was found for patterns subtending less than 6° and a local advantage was found for larger patterns in the controls. In contrast, the schizophrenics' performance changed little as a function of visual angle. The groups differed most in the 9° condition, where the normal local advantage was absent in schizophrenics who actually showed a global advantage. This finding suggests either impairment in processing local parts of hierarchical stimuli (consistent with left posterior superior temporal-parietal dysfunction) or impairment in the distribution of attentional resources to this system (consistent with lateral parietal or frontal-parietal dysfunction).

NR181 Tuesday, May 23, 12 noon-2:00 p.m.

Information Processing in Late-Life Schizophrenia

Eric L. Granholm, Ph.D., Psychology, VA Medical Center, 3350 La Jolla Village Drive, San Diego CA 92161; R.F. Asarnow, Ph.D., Steven P. Verney, M.S., Peter A. Nelson, Dilip V. Jeste, M.D.

Summary:

Introduction: Performance on a well-studied information processing task in schizophrenia research, the span of apprehension task (SOA), was examined in older schizophrenics and normal controls. Previous research suggests that the SOA task may tap a subtle "core" deficit in schizophrenia that may mark a genetic vulnerability, and possibly pathophysiology, of the disease. Although cognitive tasks like the SOA tasks have been extensively studied in younger adults and children with schizophrenia, performance on these tasks has not been examined in older schizophrenics.

Methods: Eleven late-life schizophrenic (LLS) patients and 11 elderly controls, all over age 45, detected 'T' and 'F' targets in briefly flashed arrays of 1, 6, or 12 letters on the SOA task.

Results: Consistent with the findings in younger schizophrenics, the LLS patients detected significantly fewer target stimuli in larger letter arrays (6 and 12 letter arrays), but not with smaller arrays (1 letter array). Neither age of onset or duration of illness was correlated with the SOA performance of the schizophrenics.

Conclusion: The characteristic SOA task impairment in the LLS patients suggests that LLS shares a common cognitive impairment with childhood and adult schizophrenia, and provides evidence for a core deficit, and possibly pathophysiology, in schizophrenia that is independent of age or age of onset.

NR182 Tuesday, May 23, 12 noon-2:00 p.m.

Mismatch Negativity During Treatment with Clozapine

Daniel S.G. Umbricht, M.D., Research Department, Hillside Hospital, 75-59 263 Street, Glen Oaks NY 11004; Gerald Novak, M.D., Robert Bilder, Ph.D., Daniel Javitt, M.D., Simcha Pollack, Ph.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.

Summary:

MMN is an auditory event-related potential (ERP), indexing preattentive information processing, and mediated, in animals, by NMDA-receptors. Reduced MMN in schizophrenia implicated impaired NMDA-mediated neurotransmission. These NMDA-receptors appear to be regulated via 5-HT-2 and 5-HT-1c receptors. Clozapine might indirectly enhance NMDA-mediated neurotransmission through its antagonism of these serotonin receptors, thus

ameliorate MMN deficits and thereby affect symptomatology in schizophrenia.

We are currently obtaining MMN (standards 1000 Hz; deviants 1200 Hz, 14% sequential probability), psychopathological, and neuropsychological assessments in a double-blind study of clozapine versus haloperidol at baseline and after four months of treatment or at study termination. A brain MRI is obtained at baseline.

Preliminary analyses (N = 9) show that clozapine, but not haloperidol, increases MMN in the mastoid leads, but decreases MMN in the frontocentral (Fz) lead (significant treatment by session interaction). Change of MMN at Fz is significantly correlated with symptomatology. These preliminary findings indicate that clozapine's effects on the neuronal generator of MMN are related to its effects on symptomatology. We will present detailed analyses of imaging, neuropsychological, and ERP data from a larger sample of patients and discuss our findings in the light of our original hypothesis.

NR183 Tuesday, May 23, 12 noon-2:00 p.m.

Mismatch Negativity, Neuropsychological Deficits and Psychopathology in Chronic Schizophrenia

Daniel S.G. Umbricht, M.D., Research Department, Hillside Hospital, 75-59 263 Street, Glen Oaks NY 11004; Gerald Novak, M.D., Robert Bilder, Ph.D., Daniel Javitt, M.D., Simcha Pollack, Ph.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.

Summary:

Mismatch negativity (MMN) is an early auditory event-related potential indexing preattentive information processing and reflecting the functioning of an automatic mismatch detector and of an acoustic working memory. Reduced MMN has been demonstrated in schizophrenia. In animals MMN is mediated through NMDA receptors. NMDA receptors are also believed to be involved in working memory, learning, and neuronal plasticity. Their dysfunction may be involved in specific cognitive abnormalities in schizophrenia.

We are currently investigating whether and how decreased MMN correlates with specific neuropsychological deficits of measures of working memory and associative learning and with psychopathological features in medicated, chronic schizophrenic patients. ERPs are obtained in an auditory oddball paradigm (standards 1000 Hz; deviants 1200 hz, 14% sequential probability) in an 'ignore' condition. Patients undergo extensive neuropsychological testing and are assessed with the BPRS and the SANS.

Results of preliminary analyses of data from 16 patients do not support the hypothesis that reduced MMN correlates with specific impairments of measures of working memory, associative learning, and recall. In regard to psychopathology, smaller MMN is only associated with **lower** negative symptom score and **lower** score on the BPRS hostility factor. Data on a larger cohort of patients will be presented in detail.

NR184 Tuesday, May 23, 12 noon-2:00 p.m.

Premorbid Adjustment in Schizophrenia: MRI Correlates

James J. Levitt, M.D., Psychiatry Brockton VAMC, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Cynthia G. Wible, Ph.D., Martha E. Shenton, Ph.D., Ron Kikinis, M.D., Ferenc Jolesz, M.D., Robert W. McCarley, M.D.

Summary:

Objective: Premorbid adjustment in schizophrenia (SZ) is a significant predictor of subsequent psychosocial pathology (Levitt et al., 1994), and may predict subsequent neuropsychological and neurophysiological abnormalities in SZ (Levitt et al., 1994). Here we examined the relationship between premorbid adjustment and magnetic resonance (MR) frontal and temporal neuroanatomical structures in SZ.

Method: We interviewed 10 chronic male SZ veterans, and first-degree relatives, using the Cannon-Spoor et al. Premorbid Adjustment Scale (PAS) and also obtained objective data from school records. 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 mm and data were stored as 124 1.5-mm coronal slices.

Results: Worse premorbid adjustment in SZs was associated with reduced tissue volume in both right and left frontal grey and white matter (grey matter: $r = -.69$, $p = .02$; $r = -.58$, $p = .05$; white matter: $r = -.96$, $p < .001$; $r = -.74$, $p = .01$). Subdividing frontal structures, worse premorbid adjustment in SZs was associated with reduced grey matter tissue volume in 1) right superior frontal gyri but not left ($r = -.57$, $p = .055$; $r = -.33$, $p = .2$); 2) right and left middle frontal gyri ($r = -.61$, $p = .04$; $r = -.62$, $p < .04$); 3) right and left orbital frontal gyri ($r = -.66$, $p = .028$: $r = -.71$, $p = .02$); and 4) with a trend for right and left inferior frontal gyri ($r = -.51$, $p = .08$; $r = -.43$, $p = .12$). Worse premorbid adjustment in SZs was also associated, but less strongly, with tissue loss in temporal grey matter structures including 1) right posterior temporal grey matter ($r = -.75$, $p = .01$) and a trend for right hippocampus (hippocampus weighted) grey matter ($r = -.75$, $p = .10$) and a trend for right hippocampus (hippocampus weighted) grey matter ($r = -.55$, $p = .10$).

Conclusions: Worse premorbid adjustment in SZ may be associated with frontal tissue loss in both grey and white matter and, to a lesser extent, may be associated with temporal grey matter tissue loss, specifically, in the right posterior temporal lobe and right hippocampus.

NR185 Tuesday, May 23, 12 noon-2:00 p.m.

Spatial Working Memory in Schizophrenia: Cognitive Correlates

James J. Levitt, M.D., Psychiatry Brockton VAMC, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Paul G. Nestor, Ph.D., Maria E. Karapelou, Ed.M., Susan Law, M.A., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: Spatial working memory has attracted considerable interest in schizophrenia (SZ) research as representing an impairment that may reflect dorsolateral prefrontal cortex pathology. In nonhuman primates, spatial working memory is assessed by an oculomotor delayed-response task; neurons near the principal sulcus appear to code directionality of the intended movement during the delay phase.

Method: Thirteen chronic right-handed male SZ veterans and 10 right-handed normal controls, matched on age and PSES, were administered the Dot Test (Keefe et al., 1994), a human analogue to the oculomotor delayed-response task. Subjects were presented a stimulus, a dot, on a white piece of paper, and were then tested on the location of the test stimulus in both delayed and non-delay conditions.

Results: The non-delay mean error distance for SZs was significantly longer than for NCLs (1.3 vs. 1.0 cm; $t(21) = -2.87$, $p < .01$); the delay mean error distance for SZs was also significantly longer than for NCLs (3.3 vs. 1.6 cm; $t(21) = -3.62$, $p = .002$). Moreover, an ANOVA revealed a significant group by task interaction with SZs' performance deteriorating more than NCLs with the delay condition ($F = 6.93$, $df = 1,21$, $p < .02$). In addition, mean error distance and mean error distance difference (delay minus nondelay) both correlated significantly with Trails B ($r = .61$, $p = .03$; $r = .53$, $p = .059$), the WMS Digit span forward task ($r = -.65$ $p = .02$; $r = -.67$ $p = < .02$), the WCST number of categories

achieved ($r = -.75$, $p = < .02$; $r = -.66$, $p < .04$), and number of perseverative errors ($r = .8$, $p < .02$; $r = .79$, $p < .02$), and the WMS visual memory span test ($r = -.65$, $p = .057$; $r = -.62$, $p = .067$).

Conclusions: Our findings help support a deficit in spatial working memory in SZs vs. in NCLs. Moreover, the Dot test yields significant correlations with other standard neuropsychological measures thought to be sensitive to schizophrenic pathology.

NR186 Tuesday, May 23, 12 noon-2:00 p.m.

Eye Tracking, Attention, and Schizotypal Symptoms in Nonpsychotic Relatives of Schizophrenic Patients

Richard S.E. Keefe, Ph.D., Psychiatry, Bronx VAMC, 130 West Kingsbridge Road, Bronx NY 10468; Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., Larry J. Siever, M.D., Philip D. Harvey, Ph.D., Lee Friedman, Ph.D., Sonia E. Lees Roitman, M.D., Rachel L. DuPre, Christopher Smith, Kenneth L. Davis, M.D., James Schmeidler, Ph.D.

Summary:

Background: Biological relatives of schizophrenic patients demonstrate increases in schizotypal personality disorder symptoms, eye tracking deficits, and attentional disturbances. It remains to be determined if these hypothesized components of a schizophrenia-related phenotype are associated with one another, or independent. The present study investigated the relationship of schizotypal personality disorder symptoms and neurocognitive abnormalities in nonpsychotic relatives of patients with schizophrenia.

Methods: Eighty-three nonpsychotic first-degree relatives of 38 schizophrenic patients and 45 comparison subjects were evaluated clinically and administered tests of eye tracking and the continuous performance test (CPT) of visual attention.

Results: Eye tracking qualitative rating was more powerful than quantitative eye tracking measures or CPT performance in discriminating relatives of schizophrenic patients from comparison subjects. Between-family correlations of neurocognitive variables and the DSM-III-R schizotypal personality disorder symptom clusters suggested that CPT errors of omission are associated with "psychotic-like" and "deficit-like" schizotypal symptoms. Eye tracking measures were not significantly correlated with schizotypal symptoms.

Conclusions: These results suggest that eye tracking deficits in the relatives of schizophrenic patients are unrelated to other disturbances in visual attention and schizotypal symptoms. They imply that these two components of a schizophrenia-related phenotype should be considered as largely independent factors in genetic studies of schizophrenia.

NR187 Tuesday, May 23, 12 noon-2:00 p.m.

Laboratory and Clinical Measures of Spatial Working Memory in Schizophrenic Patients and Controls

Richard S.E. Keefe, Ph.D., Psychiatry, Bronx VAMC, 130 West Kingsbridge Road, Bronx NY 10468; Sonia E. Lees Roitman, M.D., Rachel L. DuPre, Philip D. Harvey, Ph.D.

Summary:

Background: Results from neuropsychological tests that purport to measure the functioning of the prefrontal cortex (PFC) are often misinterpreted in psychiatric patients. Since many of these tests are highly complex, they are vulnerable to generalized deficits and typical clinical factors such as reduced motivation, uncooperativeness, and anergia. Simple, easily administered tests sensitive to dysfunction of the PFC are sorely needed. Simple working memory functions can be measured by tests that activate a neural network that includes the PFC.

Method: Twenty schizophrenics and 10 normal controls were examined to compare a computerized laboratory version of a visual working memory test that determines performance by measuring eye position data when a subject is asked to recall where a stimulus had previously been presented, and a version that requires subjects simply to indicate with a pen where a stimulus had been presented.

Results: In the laboratory version only, eye position data from 10 schizophrenics could not be analyzed due to artifacts such as head movement, restlessness, and excessive blinking. Schizophrenics were significantly less accurate than controls on both working memory tasks. Performance on the pen-and-paper version of the task was correlated with performance determined by eye position data ($r = 0.59$, $p < .05$).

Conclusions: An easily administered pen-and-paper working memory task may be useful as a clinical tool for measuring working memory functions in schizophrenics and other psychiatric patients.

NR188 Tuesday, May 23, 12 noon-2:00 p.m.

Negative Symptoms in Schizophrenia Are Differentially Related to Cognitive Impairment

Philip D. Harvey, Ph.D., Psychiatry, Mt. Sinai School of Med., One Gustave Place, New York NY 10029; Janel Lombardi, M.A., Martin Liebman, M.A., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

Negative symptoms in schizophrenia are reported to be more stable within patients over time than positive symptoms and more strongly correlated with the severity of cognitive impairments. Since cognitive impairment in schizophrenia is also quite stable over time, the question arises as to whether negative symptoms in schizophrenia, or at least some subset, are just an alternative manifestation of cognitive impairments. In order to address this question, 63 chronic schizophrenic patients (mean age 45, mean length of consecutive inpatient stay 15 years) were assessed at two intervals separated by one year. Severity scores for negative and positive schizophrenic symptoms (assessed with the PANSS), and cognitive impairments (assessed with the MMSE) were collected. The stability coefficient for negative symptoms was substantial ($r = .61$, $p < .001$), while the cross-temporal correlation for positive symptoms was not significant. When the influence of cognitive impairments was residualized with regression analysis, the cross temporal correlation for negative symptoms changed drastically ($r = -.38$, $p < .05$). Path analyses indicated that some individual negative symptoms at the follow-up assessment were completely accounted for by cognitive impairment (e.g., poor rapport) and others were completely unassociated with cognitive impairment (e.g., blunted affect). These data indicate that some of the crucial characteristics of negative symptoms may actually be due to the overlap between negative symptoms and cognitive impairments. Certain negative symptoms may be indistinct from cognitive impairments while others appear unrelated to these impairments. This heterogeneity requires more careful study and underscores the complex role of cognitive impairment in schizophrenia.

NR189 Tuesday, May 23, 12 noon-2:00 p.m.

Age Disorientation in Chronically Hospitalized Mood Disorder Patients

Philip D. Harvey, Ph.D., Psychiatry, Mt. Sinai School of Med., One Gustave Place, New York NY 10029; Janel Lombardi, M.A., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

Studies of chronic schizophrenic patients have found that 20% to 30% of these patients misstate their age by five years or more and that these patients are notable because of global intellectual impairments and changes in the structure of their cerebral cortex. It is not clear if these deficits are specific to schizophrenia, because chronic mood disorder patients were not previously studied. Thirty-two patients with mood disorders who had been hospitalized for more than 10 consecutive years were examined. Six (19%) of the patients were age-disoriented and those patients manifested global intellectual impairment (mean MMSE = 16) compared to the age-oriented patients (mean MMSE = 23), $t = 2.52$, $p < .01$. No differences in premorbid functioning, age of onset, or treatment history were found. When the patients were seen for a reevaluation the next year, all six age-disoriented patients were still age-disoriented and two of the nondisoriented patients appeared now to be disoriented (kappa = .89, $p < .001$) The prevalence of age disorientation and its association with global cognitive impairment were completely consistent with earlier studies of chronic schizophrenic patients. Previous continuum conceptions of psychotic disorders have suggested that affective disorders and schizophrenia may exist on a continuum marked by differences in affect expression and gender distribution. These data suggest that outcome is another crucial dimension to consider, in that poor outcome cases may be very similar across the affective/schizophrenic nosological distinction.

NR190 Tuesday, May 23, 12 noon-2:00 p.m.

Event-Related Brain Potentials in Schizophrenia During Visual Information Processing

Esther F. Rabinowicz, Ph.D., Biopsychology, NYS Psychiatric Inst., 722 West 168th Street, New York NY 10032; Gerard Bruder, Ph.D., Craig Tenke, Ph.D., James Towey, Ph.D., Delores Malaspina, M.D., Jack M. Gorman, M.D.

Summary:

Objective: Event-related brain potentials (ERPs) were used to study electrophysiologic correlates of *visual* information processing abnormalities in schizophrenia. ERPs provide a continuous, time-locked record of brain potentials associated with early sensory-attentional processing (N1 and N2) and late cognitive evaluation (P3). By recording ERPs during a visual numerosity task, we sort to determine whether performance abnormalities of schizophrenic patients were related more to early or late stages of cognitive processing.

Method: Nine psychotic patients from the Schizophrenia Research Unit at New York State Psychiatric Institute (DSM-III-R consensus diagnosis: seven schizophrenia, one schizoaffective, and one psychotic NOS/schizotypal disorder), and 16 nonpsychiatric controls were tested. ERPs were recorded from 30 electrode sites while subjects were engaged in a dot enumeration task with lateralized presentation of stimuli to the left or right visual field.

Results: 1) patients had markedly smaller negative potentials in the region of N1 and N2 (130-320ms) when compared to controls ($F = 10.72$; $df = 1, 23$; $p < .005$); 2) this group difference in negativity was greatest at posterior sites where N1 and N2 were largest ($F = 6.48$, $df = 1.2, 27.6$; $p < .025$); 3) patients' reduced amplitude of negative potentials was associated with poorer accuracy of dot enumeration ($r = -.75$, $p < .05$); 4) there was no significant difference in P3 amplitude between groups.

Conclusions: The reduction in visual N1 and N2 amplitude, but not P3 amplitude, in patients agrees with prior findings for schizophrenic patients in visual tasks. Although preliminary, our findings support the conclusion that a deficit in early sensory processing and/or attentional allocation contributes to impairments of visual information processing in schizophrenia.

NR191 Tuesday, May 23, 12 noon-2:00 p.m.

Assessing the Effects of Medication on Task Performance in Schizophrenia

Esther F. Rabinowicz, Ph.D., Biopsychology, NYS Psychiatric Inst., 722 West 168th Street, New York NY 10032; David R. Owen, Ph.D, Raymond A. Knight, Ph.D., Xavier Amador, Ph.D., Jack M. Gorman, M.D.

Summary:

Objective: We recently reported that performance on the Dot Enumeration Perceptual Organization Task (DEPOT), which assesses numerosity and form judgments to the same dot stimuli, strongly suggested deficiencies in the short-term visual memory of patients with schizophrenia. The present study sought to replicate these findings and to determine the effects of medication on DEPOT performance.

Method: A new sample of subjects (18 schizophrenic patients, eight schizoaffective patients, and 18 nonpsychiatric controls) was administered DEPOT. A subsample (14 schizophrenics, four schizoaffectives) was tested both on and off haloperidol. All patients were recruited from the schizophrenia Research Unit at New York State Psychiatric Institute, and were DSM-III-R consensus diagnosed.

Results: 1) All critical findings on DEPOT corroborated our original study. 2) Medication had no effect on number performance for either group. Schizophrenic patients performed form discriminations better on medication, but nonschizophrenic patients were affected in the opposite direction, improving off medication ($p = .11$). (3) A response delay manipulation interacted with diagnosis and medication status ($p = .05$).

Conclusions: The replication strengthens our confidence in the utility of this paradigm for testing schizophrenic patients' cognitive deficits. These findings suggest that visual processing deficits in schizophrenia are unaffected by medication status, and apparently reflect enduring cognitive deficiencies. The sample sizes are small, but the trend for differences among the psychotic groups is interesting and bears further exploration. These results indicate that medicated schizophrenic patients can be used in future studies of deficit specification.

NR192 Tuesday, May 23, 12 noon-2:00 p.m.

The Economic Benefit of Clozapine Treatment of Patients in Partial and Outpatient Care Facilities

Michael J. Reinstein, M.D., Psychiatry, University Hospital, 1116 North Kedzie, Chicago IL 60615; Lynn Jones, R.N., Amir Poreh, Ph.D., Sangarapillai C. Mohan, M.D.

Summary:

In a recent study, Meltzer (1993) reported that schizophrenic patients show a significant reduction in economic costs and the number of hospitalizations after being treated with clozapine. The current study set out to replicate the above study with a sample of patients treated in partial care facilities ($n = 40$). Analysis of the data indicates that schizophrenic patients who received clozapine showed considerable improvement in cost and number of hospitalizations after six months of treatment. The data also provide information regarding the drop-out rate of patients. The role of background variables such as age of onset, age of patients, and education are discussed in light of Revicki et al. (1990) and Meltzer et al. (1993).

NR193 Tuesday, May 23, 12 noon-2:00 p.m.

Re-Examination of Clozapine Treatment on Quality of Life in Chronic Schizophrenic Patients

Michael J. Reinstein, M.D., Psychiatry, University Hospital, 1116 North Kedzie, Chicago IL 60615; Amir Poreh, Ph.D., Sangarapillai C. Mohan, M.D., Lynn Jones, R.N.

Summary:

In the past few years a number of studies have reported that clozapine has remarkable effects on both the symptoms and adaptivity of chronic schizophrenic patients. Meltzer, Burnett, Bastani, and Ramirez (1990), for example, report a significant increase in scores on the Quality of Life Scale (QLS, Heinrichs et al., 1984) after six months of clozapine treatment. Additionally, they report that 21 of the 38 patients evidenced a decrease in Brief Psychiatric Rating Scale's (BPRS) negative symptoms and were successful in obtaining a payed volunteer job. The current study attempted to replicate Meltzer's work and to reassess the effects of clozapine on schizophrenic patients. Unlike previous studies, the patients were recruited from partial care facilities and were retested after a four-month interval. The results of the current study show that four of the 15 patients were able to participate in volunteer jobs after they were introduced to clozapine. Additionally, the results show that the sum BPRS and the Scale for Positive Symptoms (PANS) scores significantly declined ($t = 3.5$, $p = .008$; $t = 5.2$, $p < 0.001$), whereas the sum QLS and the Scale for Negative Symptoms (SANS) scores remained relatively unchanged ($t = -.56$, $p = .609$; $t = 1.1$, $p < 0.34$). The results are consistent with Lindstrom (1988) and provide a more conservative perspective regarding the benefits of clozapine in the treatment of chronic schizophrenic patients. The current study also suggests that additional factors, other than medication, may play an important role in the treatment of schizophrenic patients.

NR194 Tuesday, May 23, 12 noon-2:00 p.m.

Diabetes and Dementia in Schizophrenic Patients

Dharmbeer Sinha, M.D., Psychiatry, Chief Ambulatory Psychiat, 1 Freedom Way, Augusta GA 30910; Sukdeb Mukherjee, M.D.

Summary:

Recent studies of elderly chronic schizophrenic patients have drawn attention to a high rate of severe cognitive impairments that clinically resemble dementia. Neuropathological studies indicate that this is not accounted for by a comorbid presence of known dementing disorders, such as Alzheimer's disease. Studies in nonpsychiatric subjects have found that diabetes mellitus is associated with impaired cognitive functioning. We therefore examined whether diabetes contributes to cognitive impairment in elderly schizophrenic patients.

The sample comprised 71 schizophrenic patients at the Augusta VA Medical Center. All were men and their mean age was 57.6 years. Sixteen (22.5%) were diagnosed to have type II diabetes mellitus. Mini-Mental State Examination (MMSE) total score was less than 24 in 33 (46.5%) of the patients, and less than 18 in 12 (12.7%) patients. There was no significant difference between diabetic and nondiabetic patients on MMSE total score or any of the subscale scores. When the two most recent fasting blood glucose levels were examined, glycemic status was not related to cognitive status.

The findings are consonant with the view that cognitive dysfunction is integral to the schizophrenic disease process and not a consequence of medical comorbidity.

NR195 Tuesday, May 23, 12 noon-2:00 p.m.

The Neuropsychological Dysfunction of Frontal Lobe in Male Schizophrenic and Maniac Patients

Youngnam Park, M.D., Dept of Psych, Keimyung U Sych of Med, 194 Dongsan-Dong, Taegu 00172, Korea; Hwag-Heui Lee, M.D.

Summary:

Objective: There have been contradictory reports of neuropsychological tests in schizophrenia and mania. This study was designed to evaluate the neuropsychological dysfunction of frontal lobe in male schizophrenia and manic patients, using neuropsychological tests sensitive to frontal lobe function.

Method: Wisconsin card-sorting test (WCST), Stroop color word test, Verbal fluency test, and Maze learning test were administered to hospitalized male schizophrenia (N = 17), mania (N = 9), and normal controls (N = 16), diagnosed by DSM-III-R criteria. All participants were under age 40.

Results: Schizophrenic and manic groups had significantly lower overall performance than normal control group. There were no significant differences between schizophrenia and manic groups in the performance of WCST, Verbal fluency test, and Maze learning test. However, the schizophrenic group performed significantly poorer than manics in the Stroop color test.

Conclusion: These results suggest that there seems to be a significant frontal lobe dysfunction not only in schizophrenia but also in manic patients. The frontal lobe dysfunction might be related to certain psychotic symptoms, not to a specific diagnostic entity.

NR196 Tuesday, May 23, 12 noon-2:00 p.m.

Event-Related Potentials Indices of Language Processing in Schizotypal Personality Disorder

Margaret Niznikiewicz, Ph.D., Psychiatry Brockton VAMC, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Martha E. Shenton, Ph.D., Larry J. Seidman, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: Language processing in individuals diagnosed (DSM-IV) with schizotypal personality disorder (SPD) was investigated using the N400 as an index of language processing. This is the first study to use event potential (EP) measures of semantic difficulties in an SPD group. Our lab has found impaired performance in SPD subjects on the California Verbal Learning Test and semantic clustering. P300 amplitude in SPDs was intermediate between control and schizophrenic (SZ) groups. In the previous study, Sz patients were found to have larger and more delayed N400 to both congruent and incongruent sentence endings suggesting an inefficient use of context to select a proper item in the semantic network. Given these findings, we designed a study to examine the N400 component in SPD individuals. If the similarities found between the SPD and Sz groups existed also for neural processes indexed by the N400, a similar pattern of results would be expected for the SPD group as the one found previously for Sz group. We report here initial data.

Methods: Thirteen Sz patients, controls, and five SPD individuals read, and listened to, 200 sentences; one-half made sense (congruent condition) and the other half did not (incongruent condition). The ERPs were recorded to the target, final words in sentences.

Results: SPD subjects, compared with both Sz and control subjects, showed N400 latency and amplitude intermediate between the control and schizophrenic group in both the visual and auditory modality. In the visual, congruent condition, the N400 latency peaked at 340 msec in control, at 352 msec in SPD, and at 412 in Sz subjects; the N400 peak amplitude was 2.9 microvolts in

control, .4 in SPD, and .8 microvolts in Sz subjects. In the visual, incongruent condition, the N400 latency was 388 msec in control, 398 msec in SPD, and 428 msec in Sz subjects; the N400 amplitude was 2.1 microvolts, .2 and −1.5 microvolts, respectively, in the three groups. In the auditory, congruent condition, the N400 latency was 270 msec in control, 280 msec in SPD, and 316 in Sz subjects; the N400 amplitude was 1.1 in control, −.4 in SPD, and −1.0 microvolts in SZ subjects. In the auditory, incongruent condition, the N400 latency was 300 msec in control, 342 msec in SPD, and 364 msec in Sz subjects. The N400 amplitude was −1.8 in control, −1.9 in SPD, and −2.5 microvolts in Sz subjects. The results are significant at a trend level ($p < .1$). Thus, these preliminary data confirm the trend toward the same type of language impairment as found earlier in Sz patients.

Conclusions: These preliminary data suggest that the abnormal N400 component linked to a dysfunction in semantic memory found in schizophrenic patients may also be found in SPD individuals. This further suggests common factors among schizophrenia spectrum disorders.

NR197 Tuesday, May 23, 12 noon-2:00 p.m.

Cognitive and Symptom Correlates of Illness Management Skills in Chronic Schizophrenia

Michael B. McKee Ph.D., Psychiatry, NYH-Cornell Medical Ctr., 21 Bloomingdale Road, White Plains NY 10605; Thomas E. Smith, M.D., Sally J. Mackain, Ph.D., James W. Hull, Ph.D., Maryann Yanulis, Ph.D., Donna T. Anthony, M.D., Marianne S. Goodman, M.D.

Summary:

We hypothesized that psychotic symptoms and cognitive variables (attention, memory and executive function) would predict performance on measures of illness management skills. We are able to report preliminary data on the first 12 schizophrenic patients who have completed the study. Patients with estimated IQ below the borderline range or a serious medical illness were excluded from the study. A highly significant negative correlation was found between negative symptoms and patients' store of general information about symptom management ($r = -.73$, $p < .001$). In particular, this relationship was seen for the symptoms of flat affect ($r = -.71$, $p < .001$), anhedonia ($r = -.63$, $p < .01$), and alogia ($r = -.49$, $p < .05$). No relationship between positive symptoms and the illness management assessment was observed. A significant relationship was found between a measure of ability to retrieve verbal information from reference memory and patients' store of information about symptom management ($r = .80$, $p < .01$). Performance on a word list learning task correlated with patients' ability to solve illness management problems ($r = .64$, $p < .05$). A test of capacity to focus attention also correlated with problem-solving ability ($r = .72$, $p < .05$). The data suggest that differential patterns of relationships exist between negative symptoms, cognitive factors, and an in-vitro measure of illness management skills. Identifying such patterns in populations of inpatient schizophrenics may be useful in selecting candidates for illness management skills training programs.

NR198 Tuesday, May 23, 12 noon-2:00 p.m.

Aging on the Wrong Side of the Brain

Ede Frecska, M.D., Psychiatry, V.A.M.C., 79 Middleville Road, Northport NY 11768; Miklos F. Losonczy, M.D., Richard S.E. Keefe, Ph.D., Michael Davidson, M.D., Jeffrey Sparks, R.N., Kenneth L. Davis, M.D.

Summary:

Background: Previous cross-sectional and longitudinal neuroimaging studies of progressive changes in ventricular size in schizophrenia have yielded inconsistent results. Most of these studies did not subclassify patients according to the outcome of the illness.

Objective: This cross-sectional study provides analysis of the age-related relationship of ventricular measures in good outcome, poor outcome schizophrenic patients, and normal control subjects.

Method: The lateral ventricular, frontal, and posterior horn VBRs in the CT scans of 128 chronic schizophrenics and 79 control subjects were planimetrically, and volummetrically examined. The schizophrenic patients were subgrouped to poor outcome "Kraepelinian" ($N_1 = 58$) and relatively good outcome "non-Kraepelinian" ($N_2 = 70$) patients.

Results: Significant enlargement of all three ventricular regions were found in the combined schizophrenic group, when compared to control subjects. The Kraepelinian patients were entirely responsible for the observed difference. All parts of the ventricular system showed significant increase with age in every group. The Kraepelinian schizophrenic group distinguished itself from the comparison group by significantly larger slope of the age dependent enlargement of every ventricular measure. The two hemispheres of Kraepelinian schizophrenics show divergence in aging as reflected in the age-dependent increase of the left-minus-right differences: the left hemisphere ages more rapidly than the right.

Conclusion: These data indicate that there may be some left biased degenerative element to the disease process in the poor outcome schizophrenic group.

NR199 Tuesday, May 23, 12 noon-2:00 p.m.

Quantitative Autoradiography of a Novel Cocaine Binding Site Related to the Serotonin Transporter in Schizophrenia and Suicides

Donald C. Ohuoha, M.D., NIH, NIDA, ARC, CPRB, 4940 Eastern Avenue Bldg C 267, Baltimore MD 21224; F.I. Carroll, M.D., Thomas M. Hyde, M.D., Joel E. Kleinman, M.D., Richard B. Rothman, M.D.

Summary:

Recent studies have identified a novel cocaine binding site measured under 5-HT transporter assay condition with [125I]RTI-55. The function of this binding site in psychiatric diseases such as schizophrenia and suicide is under investigation. To test the hypothesis that SERTsite2 is distinctly different from the classic SERT we chose to compare the binding of SERTsite2 and the classic serotonin reuptake site SERT, in schizophrenics, suicide patients (cocaine intoxication often leads to depression and suicide), and neuroleptic-treated nonschizophrenic patients, to control for neuroleptic effects. In this study, we report the localization of a novel cocaine binding site (SERTsite2) possibly related to the serotonin transporter labeled using [125I]RTI-55 under SERT assay condition (blocker = 100nM GBR12935) in human basal ganglia. Previous experiments established that paroxetine has a high affinity for the classic serotonin reuptake site (SERT, K = 0.149) while it's affinity for SERTsite2 was much lower (Ki = 1354). In this assay 50nM paroxetine was used to block [125I]RTI-55 binding to SERT, thus permitting the selective labeling of SERTsite 2. Slides were preincubated for 30 min. in 55mM sodium phosphate buffer containing 50nM paroxetine and 100 nM GBR12935, washed briefly and then incubated for four hours at 4oC in 55mM sodium phosphate buffer containing 0.01nM [125I]RTI-55, 100nm GBR12935 and 50 nm paroxetine. Nonspecific binding was obtained by incubating consecutive slides in the same solution but in the presence of 10uM GBR12909. Slides were then washed three times for five minutes in buffer (10mM Tris, 150 mM NaCl, 0.1% BSA, pH 7.0), quickly rinsed in cold deionized water and air dried. Slides were then exposed to 125I sensitive film with standards in an X-ray cassette for one week. Classical SERT binding was obtained in consecutive slides by incubating in a solution

containing 2nM [3H]citalopram in buffer (Tris, 50mM, 150mM NaCl, pH 7.4) for 60minutes at room temperature. Nonspecific binding was obtained in the same solution but in the presence of 1uM imipramine. Slides were washed for 5min in cold buffer quickly rinsed in cold deionized water and air dried. Slides were then placed adjacent to tritium sensitive film and sealed in an X-ray cassette for 28 days at 4oC. Binding quantification was performed with a Macintosh computer image analysis system. Analysis of the autoradiograms indicated a 35% decrease in the nucleus accumbens of the SERTsite2 in the suicide group and a 30% decrease in the schizophrenic group when compared to controls. No such decreases were noted in the classic SERT site in the basal ganglia. These results further indicate that SERTsite2 is different from the classic serotonin reuptake site, and may be implicated in the pathophysiology of schizophrenia, suicide attempts, and cocaine euphoria.

NR200 Tuesday, May 23, 12 noon-2:00 p.m.

Lack of Sustained Elevation of Plasma Prolactin in Schizophrenic Patients Treated with ICI 204, 636 (Seroquel™)

Mark B. Hamner, M.D., RH Johnsson Medical Ctr, VAMC, 109 Bee Street, Charleston SC 29401-5703; Lisa A. Arvanitis, M.D., Barbara G. Miller, M.S., Chris G.G. Link, M.D., Walter W. Hong, M.D.

Summary:

ICI 204, 636, a dibenzothiazepine with affinity for multiple brain receptors, is a potential atypical antipsychotic. Like clozapine, ICI 204, 636 has higher affinity for central 5HT2 than D2 receptors (IC_{50} = 148 nM and 329 nM, respectively) and greater activity at limbic than at striatal dopamine receptors, suggesting that ICI 204, 636 may have low extra-pyramidal side effect (EPS) liability. Early clinical studies support the animal behavioral and electrophysiological data that predicted that ICI 204, 636 would have antipsychotic efficacy with reduced EPS. ICI 204, 636, like clozapine, does not produce sustained elevations in plasma prolactin (PRL) after short-term administration in rats. We investigated the effects of ICI 204, 636 on PRL in three, six-week, multicenter, double-blind efficacy and safety trials. Study 6 (109 patients) compared ICI 204, 636 (75 to 750 mg/day) with placebo, while Study 8 (286 patients) compared low (75 to 250 mg/day) and high (75 to 750 mg/day) doses of ICI 204, 636 with placebo. PRL was measured on Days 0, 21, and 42. Mean PRL decreased in all treatment groups in both studies. There were no significant differences between treatment groups in least squares means change from baseline to final observation (ANCOVA). Study 7 (201 patients) compared ICI 204, 636 with chlorpromazine (both groups, 75 to 750 mg/day), and PRL was assessed weekly. The decrease in PRL in the ICI 204, 636 group was significantly greater than the decrease in the chlorpromazine group at the final observation. These results suggest that ICI 204, 636 does not produce sustained elevations of PRL and support ICI 204, 636 atypical profile.

NR201 Tuesday, May 23, 12 noon-2:00 p.m.

Risperidone in the Long-Term Treatment of Patients with Schizophrenia in Sweden

Eva Lindstrom, M.D., Psychiatry, Uppsala University Hosp., Uppsala, Sweden; Bo Eriksson, B.Sc., Anders Hellgren, Lars Von Knorring, M.D., Goran Eberhard, Ph.D., Philippe Lemmens, Ph.D.

Summary:

Sixty-three patients with chronic schizophrenia entered an open-label trial of risperidone after participating in a short-term study of risperidone versus haloperidol; 32 of the 63 patients completed one year of treatment and 19 of the 32 completed two years. The mean dose of risperidone was 9.4 mg/day in the one-year follow-up and 8.0 mg/day in the two-year follow-up. Significant reductions from baseline in mean scores on the total Positive and Negative Syndrome Scale (PANSS) ($p < 0.01$), one each of five PANSS factors ($p < 0.01$), and on the Clinical Global Impression scale ($p < 0.01$) were found at the end of one year. Severity of extrapyramidal symptoms (scores on the Extrapyramidal Symptom Rating Scale) was significantly reduced at the end of one year ($p < 0.05$). Significant reductions in psychopathology and adverse effects were also noted after two years. Social functioning (modified Strauss/Carpenter scale) was improved after one and two years ($p < 0.05$ at two years). Time spent in hospitals was significantly reduced during the first year of treatment ($p < 0.05$). It is concluded that treatment with risperidone for one and two years is associated with significant reductions in the severity of schizophrenia and extrapyramidal symptoms, in improved social functioning, and in a reduction in days spent in hospital.

NR202 Tuesday, May 23, 12 noon-2:00 p.m.

MRI in Familial Schizophrenia

Tonmoy Sharma, M.D., Psychological, Inst. of Psychiatry, Decrespigny Park Denmark Hill, London SE5 8AF, England; Godfrey D. Pearlson, M.D., Patrick E. Barta, M.D., Lewis Shon, Hugh Gurling, M.D., Robin M. Murray, M.D., Qiang Li, M.D.

Summary:

Two well-replicated observations which speak most directly about etiological risk factors in schizophrenia are the increased risk to relatives and evidence of minor degrees of structural abnormalities demonstrated with brain imaging. The relationship between genetic liability to inherit the illness and the presence of structural brain abnormalities is unclear. We carried out magnetic resonance imaging of the brain in 16 families with two or more relatives affected with schizophrenia. Regional brain volumes were measured in 34 schizophrenic subjects, their 56 unaffected first-degree relatives, and 39 matched normal comparison subjects using a new 3D method of MRI image analysis. The schizophrenic subjects exhibited significantly smaller whole brain and cortical grey matter volumes and larger lateral ventricular and putamen volumes than their relatives and normal comparison subjects. The relatives as a group did not show any significant differences when compared to controls. However, when 11 relatives who were presumed transmitting parents were compared to comparison subjects they showed evidence of significant lateral ventricular enlargement but there were no differences in total cortical or regional volumes. These findings show the influence of genetic factors on brain structure in multiplex families with schizophrenia.

NR203 Tuesday, May 23, 12 noon-2:00 p.m.

Differential Change in Caudate Volumes with Antipsychotics

Miranda H. Chakos, M.D., Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks NY 11004; Jeffrey A. Lieberman, M.D., Jose Ma. Alvir, D.P.H., Robert Bilder, Ph.D., Manzar Ashtari, Ph.D.

Summary:

We performed volumetric assessments of caudate nuclei volumes in a group of eight schizophrenic patients who had MR scans after chronic neuroleptic treatment (Scan-1) and were subsequently treated with clozapine for several months and re-scanned (Scan-2). These patients were compared to schizophrenic patients who had two MR scans after receiving chronic neuroleptics (N = 7). Multivariate analysis of variance (MANOVA) with treatment group as a between-subject factor and with time

(Scan-1, Scan-2) and hemisphere (right,left) as a within-subjects repeated measures, revealed a significant group by time interaction which remained significant after covarying for age and height ($F = 10.9$, $df = 1$, $p = 0.007$). Paired comparisons showed that patients whose treatment was changed to clozapine had 10% decrease in caudate nuclei volumes at the second scan [paired $t = -4.00$, $df = 8$; $p = 0.0052$; Scan-1 mean caudate volume = 6.66 (1.09)cc; Scan-2 mean caudate volume = 5.96 (0.63)cc]. Patients who remained on chronic neuroleptics had a 8% increase in caudate volume at the second scan [paired t test = –2.00, df = 6, p = 0.09; Scan-1 mean caudate volume = 5.42(0.58)cc; Scan-2 mean caudate volume = 5.87(1.09)cc]. These findings suggest that typical and atypical medications can change caudate morphology in schizophrenic patients and that the effects may be mediated by D2 receptor activity.

NR204 Tuesday, May 23, 12 noon-2:00 p.m.

A Neuroendocrine Method of Antipsychotic Dose Reduction in Schizophrenia

Clayton E. Curtis, B.A., Psychiatry, VAMC, 130 W. Kingsbridge Road, Bronx NY 10468; Marci Mann, M.S., Kathy Piscani, R.N., Gail Burr, R.N., Robert J. Hitzemann, Ph.D., Jack Hirschowitz, M.D.

Summary:

The bromocriptine growth hormone test (BGHT) has been used as a neuroendocrine index of D2 receptor occupancy for the purpose of antipsychotic dose adjustment. The goal of this study was to use the BGHT in a sample of schizophrenics to find the minimum antipsychotic dose with the maximum therapeutic effect. At baseline, subjects had been either stabilized on 20 mg/day of haloperidol (n = 30) or were medication free (n = 23) for at least 14 days. Then subjects were randomly assigned to one of four treatment groups. Subjects on placebo (n = 6) or a dose that resulted in a haloperidol plasma level of 10 ng/ml (n = 23) served as control groups and subjects titrated to 50% (n = 5) or "just" 100% (n = 19) blockage of the BGHT served as experimental groups. Baseline symptom assessments were compared to assessments made when subjects were at the desired haloperidol level or putative receptor occupancy level.

Even though the 50%, 100%, and 10 ng/ml groups resulted in very different mean haloperidol plasma levels (<0, 1.5, and 9 ng/ml, respectively), they were equally effective in positive psychotic symptom reduction. All three groups showed significant symptom reduction compared to the placebo group. Although the differences did not reach significance, 25% of both the 50% and the 100% occupancy subjects combined, compared to 13% of the 10 ng/ml subjects showed at least a 30% reduction in positive symptoms, while in 71% and 74% of those subjects, there was no significant change. Contrary to prediction, there were no differences found in ratings of extrapyramidal side effects or tardive dyskinesia. Findings indicate that plasma levels of haloperidol much lower than conventionally used result in effective D2 receptor blockage and subsequent symptom reduction.

NR205 Tuesday, May 23, 12 noon-2:00 p.m.

P3 Topography in First Episode Psychosis

Dean F. Salisbury, Ph.D., Psychiatry 116A, Harvard Medical School, 940 Belmont Street, Brockton MA 02401; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: To examine P3 at the first episode of psychosis in an effort to determine whether P3 asymmetry was present and, if so, would topography discriminate first-episode schizophrenia-like psychosis from first-episode mania-like psychosis.

Method: P3 was recorded in 27 subjects suffering their first psychotic episode (nine schizophrenia-like, 18 mania-like). Subjects covertly counted infrequent target tones (1.5 kHz, 97 dB, 15%) presented in trains of standard stimuli (1 kHz, 97 dB, 85%) against 80 dB white noise.

Results: Groups differed in P3 topography (Group x Side interaction in P3 integrated voltage from 300-400 ms; $F(1,25) = 4.43$, $p = .046$). The schizophrenia-like group showed smaller P3 voltage over the left temporal area (2.45 μV) than over the right (3.77 μV). In contrast, the mania-like group showed larger P3 voltage over the left temporal area (4.29 μV) than over the right (3.38 μV).

Conclusions: The presence of a left-sided deficit in P3 voltage in first-episode schizophrenia-like psychosis, but not in first-episode mania-like psychosis, suggests that underlying abnormalities of left temporal lobe may be present at the first episode of schizophrenia, and furthermore, that these structural abnormalities may be at least partly responsible for the manifestation of schizophrenic symptoms.

NR206 Tuesday, May 23, 12 noon-2:00 p.m.

Effects of Cholinergic Antagonism in Young Schizophrenic Patients

Zafar A. Sharif, M.D., Psychiatry, Columbia University, 80-45 Winchester Boulevard, Queens Village NY 11427; Ahmad Raza, M.D., Fabien Tremeau, M.D., Peter A. Rao, M.D.

Summary:

We conducted an acute challenge study to examine the differential effects of selective muscarinic and nicotinic antagonism on positive and negative symptoms and memory function in young schizophrenic patients (mean age 35.7 ± 6.2). Scopolamine (3.6 μg/Kg i.v.) was used for muscarinic antagonism and mecamylamine (7.5 mg PO) for nicotinic antagonism. Subjects were maintained neuroleptic free for a minimum of two weeks and were tested on two days separated by at least 72 hours. Assessments (10-item orientation, Bushke Selective Reminding Test, BPRS and the thought disorder scale of Morengo and Harrow), were performed at baseline and after drug administration. All procedures were videotaped for subsequent rating by an independent rater blind to drug administration. To date we have conducted seven scopolamine and five mecamylamine challenges. No significant mean differences were detected in pre- and post-drug administration ratings of positive symptoms, negative symptoms, and thought disorder as assessed by the Harrow scale. Both drugs caused significant reductions in Bushke score (scopolamine $p = .016$; mecamylamine $p = .03$). Individually, one patient showed marked worsening of thought disorder on scopolamine and another became totally withdrawn and mute after mecamylamine. These observations are consistent with either a threshold effect or heterogeneity in the illness. We believe this is a useful paradigm for evaluating the role of the cholinergic system in the pathogenesis of these symptoms in schizophrenia and are currently examining a new cohort using higher doses.

NR207 Tuesday, May 23, 12 noon-2:00 p.m.

Schizophrenia: Thought Disorder and Context

Thomas H. Jobe, M.D., Psychiatry, University of Illinois, 912 South Wood St., Chicago IL 60612; Kristin E. Rappole, B.A., Nina D. Uziel, B.S., Fransisco Lopez III, B.S., Martin Harrow, Ph.D., James R. Sands, Ph.D.

Summary:

Objective: Computational Neuroscience has developed models of schizophrenic thought disorder that emphasize the role of context. Crucial for these theoretical models is whether a) schizo-

phrenics fail to *take in* the context and lose vital cues that guide thought processes (they don't respond to the question), or b) whether schizophrenics take in the context, but *go astray* in processing contextual information (their response is partially influenced by the question and partly by other irrelevant personal material).

Method: We assessed 39 schizophrenics and control groups of 16 schizoaffectives, 23 bipolars, 18 other psychotic patients, and 55 nonpsychotic patients. Patients were tested at the acute phase of hospitalization using standardized measures of thought disorder and newly developed measures of context, pre-tested for inter-rater reliability.

Results: 1) Most psychotic patients showed awareness of the original context in their responses. 2) However, schizophrenic and bipolar patients were significantly more likely than nonpsychotics to later stray from the context ($p < .01$). 3) Sixty-five percent of patients who strayed from the context showed severe thought disorder on other standardized tests. 4) Only 13% of patients not showing contextual difficulty were thought disordered.

Implications: 1) Schizophrenics did not differ from other groups in their ability to take in the context. 2) They shared with bipolar patients a strong tendency to later stray from the context and introduce their own irrelevant personal material. 3) Our data do not support the view that schizophrenics' strange comments are based on their not responding to, ignoring, or not "hearing" the immediate questions or stimuli.

NR208 Tuesday, May 23, 12 noon-2:00 p.m.

Use of Risperidone in Neuroleptic Refractory Schizophrenics in a State Psychiatric Center

Jean-Pierre Lindenmayer, M.D., Psychiatry, New York Univ Med Center, 60 Remsen Street, Brooklyn NY 11201-3453; Marc Vital-Herne, M.D., Franklin S. Simon, M.D., Adel Iskander, M.D., Alex Kartachov, M.D.

Summary:

Risperidone is a newly introduced atypical antipsychotic with both antidopaminergic and antiserotonergic affinity. Its efficacy for positive and negative symptoms with few extrapyramidal side effects has been established with acute, neuroleptic responsive patients. Its efficacy in schizophrenic patients refractory to typical neuroleptics is not established at this time. We report data from a systematic review of treatment refractory schizophrenic inpatients placed on risperidone since its introduction in a state psychiatric center. Eighty-two DSM-III-R schizophrenic inpatients (mean age: 45 years; range: 19-67) who satisfied specific inclusion criteria for clozapine treatment were included in the study. Measures included the Brief Psychiatric Rating Scale at baseline, the Clinical Global Impression Scale (CGI) at point of outcome, a 12-item side effect checklist, and four treatment outcome measures derived from systematic chart reviews assessed at four weeks prior to the switch to risperidone and after 16.8 weeks of risperidone treatment (range 3-33 weeks). Mean dosage of risperidone was 7.9 mg daily (range 1-16 mg). 27.0% of patients were rated as much improved, 37.0% as minimally improved, while 36.1% showed no change or were worse after risperidone. The main area of improvement was seen in positive symptoms, followed by negative symptoms. The incidence of side effects was remarkably low. These results will be compared to treatment response data to clozapine in similar chronic nonresponder populations.

NR209 Tuesday, May 23, 12 noon-2:00 p.m.

Validity of Family History: Method for Identifying Schizophrenia Related Disorders

Ge Li, M.D., Psychiatry, Bronx VA Medical Center, 130 W. Kingsbridg Road, Bronx NY 10468; Jeremy M. Silverman, Ph.D., Christopher Smith, Larry J. Siever, M.D., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Objectives: We examined the validity of the family history method for identifying schizophrenia-related disorders (SRD) by comparing diagnoses obtained by family history and family study methods.

Methods: Psychiatric diagnostic information on 277 first-degree relative of 47 probands with psychiatric disorders (Research Diagnostic Criteria [RDC]: schizophrenia = 35; schizo-affective disorder [SAD] = 7; major depression = 5) was obtained through telephone interview with family informants. Relatives were diagnosed using the Family History RDC (FH-RDC) which includes three *psychotic* schizophrenia related disorders (*P*-SRD): schizophrenia, chronic SAD, and chronic unspecified functional psychosis (CUFP). In addition, we used criteria for schizophrenia-related personality disorders (SRP), derived from DSM-III criteria for schizotypal personality disorder (SPD) to identify SPD and paranoid personality disorder (PPD). Of the 277 relatives, 190 (68.6%) were also examined in face-to-face interviews and diagnosed independently according the RDC and DSM-III-R for personality disorders.

Results: The sensitivity of FH-RDC for *P*-SRD was 0.69 (11/16), and specificity was 1.0 (174/174). Five relatives who met a *P*-SRD by the family study-interview (schizophrenia = 2, chronic SAD = 2, CUFP = 1) did not receive a *P*-SRD diagnosis by the family history method. Of these, three met the criteria for SRP and two met no schizophrenia-related disorder by family history. The sensitivity of SRP for SPD/PPD was 0.34 (13/38) and the specificity was 0.91(124/136).

Conclusion: The FH-RDC has adequate sensitivity and excellent specificity for the psychotic schizophrenia related disorders. In addition, while the specificity for SRP was good, modification of the criteria may be needed to improve its sensitivity.

NR210 Tuesday, May 23, 12 noon-2:00 p.m.

Neural Circuit Analysis in Schizophrenia From PET

Monte S. Buchsbaum, M.D., Dept of Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Tse-Chung Wei, Jacqueline Spiegel-Cohen, M.S., Erin A. Hazlett, Ph.D., Mehmet M. Haznedar, M.D., Christina T. Luu, B.A.

Summary:

Differences between normals and schizophrenics in the connections in the thalamocortical or frontostriatal circuits have been postulated to explain differences in sensory modulation. A possible approach to studying these circuits is the examination of correlation coefficients between metabolic rates in key structures within the circuits as assessed by positron emission tomography (PET) with 18-fluoro-2-deoxyglucose (FDG). We explored regional correlations in the first sample and provide replication in a second sample of unmedicated schizophrenic patients illustrated with the first in-vivo circuit images. We examined two samples of subjects: 40 unmedicated or never-medicated schizophrenic patients and 15 normal control subjects studied with 7.8 mm resolution; and 18 unmedicated patients with schizophrenia and 25 age- and sex-matched controls studied with 4.5mm resolution and coregistered 1.2 mm thick SPGR MRI. Subjects received FDG positron emission tomography (PET). Patients and controls performed a continuous performance test during FDG uptake in Sample 1 and a California Verbal Learning Test in Sample II. MRI templates were obtained and coregistered for each subject in the second group. Cortical and subcortical structures comprising two circuits selected on the basis of theoretical models of schizophrenia were examined. In Sample I, the regions of interest were assessed with a stereotaxic coordinate method; the correlation of glucose metabolic rate (GMR) for each structure in each circuit with connected

structures was calculated and the correlation matrix tested with the Kullback test. In Sample II, the average MRI cortical edge was computed, nine midline points identified visually, and all PET scans morphed to the average MRI. For each circuit link the correlation coefficient between the metabolic rate of the chosen structure and all other pixels was computed and displayed on the coregistered average MRI. In both samples, thalamofrontal correlations were negative in schizophrenics and positive in normals. In the second higher resolution sample, frontostriatal correlation patterns in the schizophrenics are markedly different from those of the controls and are consistent with an abnormality in a major sensory control feedback loop.

NR211 Tuesday, May 23, 12 noon-2:00 p.m.

Onset, Coping and Recovery From Hallucinations in Daily Life

Philippe A.E.G. Delespaul, Ph.D., Social Psychiatry, Acad. Psychiatric Center, Postbus 616, Maastricht 6200MD, The Netherlands; Marten W. Devries, M.D.

Summary:

In the study of auditory hallucinations patients are generally asked on questionnaires or interviews to condense their experience into a description of their hallucinations. Accuracy, however, is elusive due to flawed memory and emotional coloring. Investigating hallucinations prospectively in the ecologically valid context of daily life circumvents this problem and provides a better description of the cognitive, emotional, or environmental factors that trigger, maintain, or end the hallucination process. Fifty ambulatory and hospitalized schizophrenic patients reported their visual and auditory hallucinations repeatedly along with measures of ongoing thought, mood, motivation, activities, and persons and places frequented over one week in the natural circumstances of daily life (Experience Sampling Method—ESM). Surprisingly, more subjects experienced visual hallucinations as opposed to auditory, but auditory hallucination moments were more frequent, longer, and more intense. We found no environmental trigger for hallucination episodes but anxiety was higher before, in most subjects. Recovery of moments of visual hallucinations was related to concentration on activities and withdrawal from social contexts. "Being alone" or "working" diminished hallucinatory intensity over the course of the episode. Such behaviors may be viewed as coping strategies. This paper discusses the implications of the interplay of emotions and behavioral coping strategy on the psychological management of hallucinations.

NR212 Tuesday, May 23, 12 noon-2:00 p.m.

MRI Correlates of the Auditory P3A and P3B Event-Related Potential Components in Schizophrenia

Brian F. O'Donnell, Ph.D., Psychiatry, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Hirokazu Ohta, M.D., Robert W. McCarley, M.D., Cynthia G. Wible, Ph.D., Ron Kikinis, M.D., Martha E. Shenton, Ph.D.

Summary:

Objective: We investigated the P3a and P3b components of the auditory event-related potential (ERP) in schizophrenics (SZ), and their relationship to frontal and temporal lobe MRI volumes.

Method: Fourteen right-handed, male chronic SZ patients were compared with 13 age-, gender-, and handedness-matched control subjects. In one paradigm, a simple oddball task was used to obtain a P3b component. To obtain both the P3a and P3b components we used an oddball paradigm which included novel, non-target sounds (all unique).

Results: SZ, compared with normal controls, showed, in the simple oddball paradigm, a 48% P3b reduction ($p < .01$), and a left < right temporal region asymmetry (group X side: $p < .05$). Controls showed, in the novel paradigm, a marked P3b amplitude reduction compared to P3b in the simple oddball paradigm, but SZ had a low P3b amplitude in both paradigms. SZ's P3b topography resembled their P3a, with a more frontal and more right distribution than the P3b of the control subjects. Correlations with quantitative SPGR MRI ROI volumes for frontal and temporal lobe structures in SZ showed a distinctive pattern for P3a in that amplitude at frontal sites was positively correlated with medial temporal lobe ROI volumes (anterior hippocampus-amygdala). In SZ, both P3a and P3b were correlated with left temporal lobe neocortical structures, while superior frontal gyrus volume was correlated with P3b but not P3a amplitude (p's < .05).

Conclusions: P3a and P3b both appeared vulnerable to abnormalities of the temporal lobe. Somewhat surprisingly, P3a at frontal recording sites was best correlated with volumes of medial temporal lobe structures, suggesting that this input to frontal cortex may influence amplitude.

NR213 Tuesday, May 23, 12 noon-2:00 p.m.

FDOPA PET Study of Dopamine Function in Schizophrenia

Joseph C. Wu, M.D., Psychiatry, University of CA Irvine, Room 163 Irvine Hall UCI, Irvine CA 92715; Neetika Khosla, B.S., Steven G. Potkin, M.D., Ahmed Najafi, M.D., Lori LaCasse, B.S., Eric A. Klein, B.S.

Summary:

Objective: The objective of this project was to assess dopaminergic function in schizophrenic patients compared with normal controls using positron emission tomography studies of FDOPA uptake.

Method: Ten schizophrenic inpatients (age = 24.5 ± 6.0, 9m, 1f) who met DSM-III-R diagnostic criteria for schizophrenia were studied compared to 15 normal controls (25.5 ± 9.7 yrs, 9m, 6f). Five of the patients were on placebo and the other five were in double-blind studies for which the code had not been broken. PET studies were performed on a Neuroecat IV system with FWHM of 7.6mm in-plane. Each subject received 2.0-4.0 mCi of 6-FD. Twelve ten-minute scans were performed. FDOPA uptake was determined (Martin et al. (1989)). FDOPA uptake was graphically represented pixel by pixel.

Results: The schizophrenics have a significantly lower FDOPA uptake in the right and left striatum compared to normal controls ($p < .05$).

Conclusions: There may be a suppression of presynaptic dopamine activity in these schizophrenic patients as a consequence of previous neuroleptic exposure. Further studies will need to be done to assess presynaptic dopamine activity in never medicated schizophrenics.

NR214 Tuesday, May 23, 12 noon-2:00 p.m.

Assessment and Treatment Selection for the Revolving Door Schizophrenic Inpatient

Peter Weiden, M.D., Psychiatry, St. Lukes Roosevelt, 910 9th Avenue, New York NY 10463; William M. Glazer, M.D., Yelena Braz, M.D., Ryan De Haas, B.A., Mona Sajous, C.S.W., Sharon Haznedar, R.N.

Summary:

Goals: To present data on the causes, patterns of relapse, and types of treatments selected for "revolving door" schizophrenic inpatients.

Methods: Consecutive schizophrenic admissions to an acute inpatient unit were screened for "revolving door" criteria. Patients had either 1) two hospitalizations in the last year, or 2) three

hospitalizations in the last three years. Patients were then assessed for probable causes of relapse for the index and prior two hospitalizations. Treatment selection, based on this information, was trichotomized to: 1) oral neuroleptic, 2) depot neuroleptic (either haloperidol or fluphenazine decanoate), or 3) atypical antipsychotic (either risperidone or clozapine).

Results: Thirty-two of 97 screened admissions met the above revolving door criteria. They were indeed "revolving," having an average of 1.8 (±.7) hospitalizations per year over the last three years and were only out of the hospital for five months (median) before index admission. Medication noncompliance was judged to be the most common reason for rehospitalization (n = 16, 50%), followed by medication nonresponse (n = 9, 28%). Patterns of relapse were established from history about prior hospitalizations for 10 of the 16 "noncompliant" relapses and four of the nine "nonresponse" relapses. Not surprisingly, medication recommendations were closely linked to the assessed reason for relapse (depot therapy [n = 17] with medication noncompliance; atypical antipsychotic [n = 12] with medication nonresponse [$\chi^2 = 26.9$, $p < .001$]). Most medication recommendations were accepted by patients before discharge (71% for depot and 66% for atypical).

Conclusions: Medication noncompliance and medication nonresponse, in that order, were judged to be the most common causes of relapse for "revolving door" schizophrenic inpatients. Both depot therapy and atypical antipsychotics were commonly recommended and ultimately accepted by about two thirds of patients. Choice between depot and atypical was driven by the assessed cause of relapse. In summary, it seems possible to identify "revolving door" inpatients, and to target specific medication interventions within the time frame of an acute inpatient admission.

NR215 Tuesday, May 23, 12 noon-2:00 p.m.

Neuropsychophysiologic Study of Severely Disturbed Children

Robert L. Hendren, D.O., Univ. of NM Sch. of Medici, Family Practice Bldg. 4th, 2400 Tucker NE, Albuquerque NM 87131; Janet Hodde-Vargas, Ph.D., Ronald Yeo, Ph.D., Luis Vargas, Ph.D., William Brooks, Ph.D., Corey Ford, M.D.

Summary:

The long-term objective of this study is to demonstrate that children and adolescents who develop schizophrenia show specific neuropsychological, anatomic, and physiologic marker abnormalities prior to or coincident with the onset of schizophrenia. The first phase of this project which has been to study 20 children between the ages of eight and 12 years classified with K-SADS assessment as having a schizophrenia spectrum disorder and 20 matched controls without a psychiatric disorder, has just been completed. Both groups underwent a battery of neuropsychological tests to assess general as well as frontal and temporal lobe functioning; volumetric measurements of specific brain regions were determined from magnetic resonance imaging (MRI); and proton magnetic resonance spectroscopy (MRS) of a portion of the frontal lobe was analyzed.

Analysis of the data from the first 12 subjects compared with matched controls revealed significant overall group differences for the morphometric measurements and for the neuropsychological measures, including differences for amygdala volume, mesial temporal volume, callosal area, anatomic asymmetry, and a test of story memory. MRS ratio comparisons from the left frontal lobe showed a trend toward significant difference in the ratios of NAA/CRE and CHO/CRE.

NR216 Tuesday, May 23, 12 noon-2:00 p.m.

Cerebral Ventricular Enlargement, Medication Adherence and Outcomes in Schizophrenia

Richard R. Owen, Jr., M.D., Psychiatric Services, 116A/NLR VAMC, 2200 Fort Roots Dr, North Little Rock AR 72114-1706; JoAnn E. Kirchner, M.D., Brian J. Cuffel, Ph.D., Ellen P. Fischer, Ph.D., Craig N. Carson, M.D.

Summary:

Objective: To examine the relationship between cerebral ventricular volume and symptom outcomes in schizophrenia.

Methods: VA patients in a longitudinal study of outcomes of care for schizophrenia were included in this analysis if computed tomographic (CT) head scan was done previously or during an index hospitalization. Diagnosis of schizophrenia was confirmed by Structured Clinical Interview for DSM-III-R. Lateral ventricle-brain ratio (VBR) was determined on CT scans using planimetry. Percent change from baseline to follow up in the average Brief Psychiatric Rating Scale (BPRS) scores was used to assess symptom outcome. Subjects reported medication adherence at six months on a five-point scale (lower scores indicating better adherence).

Results: Sixteen male subjects had all data available. VBR was inversely correlated with percent change (improvement) in BPRS item averages (Spearman's r = ; ms 0.52, $p < 0.05$). The correlation between VBR and poor medication adherence approached significance (Spearman's $r = 0.49$, $p < 0.06$). Poor adherence was inversely correlated with BPRS change (Spearman's $r = -0.50$, $p < 0.05$).

Conclusions: The inverse correlation of VBR and BPRS change is consistent with previous reports of ventricular enlargement predicting worse treatment response. Our results also suggest that medication non-adherence may play a role in the poor outcomes of pharmacotherapy in patients with ventricular enlargement.

NR217 Tuesday, May 23, 12 noon-2:00 p.m.

Relationships Between Temporal Lobe Areas and Subdivisions of Prefrontal Cortex in Schizophrenia: An MRI Study

Cynthia G. Wible, Ph.D., Psychiatry, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Martha E. Shenton, Ph.D., Ronald Kikinis, M.D., Ferenc Jolesz, M.D., Robert W. McCarley, M.D.

Summary:

Prefrontal abnormalities in schizophrenics have been reported in studies using magnetic resonance imaging (MRI). A method for subdividing the prefrontal cortex into anatomical areas to measure volume was developed for use with MRI. The schizophrenic subjects in this study were previously shown to have left-lateralized volume reductions in several temporal lobe areas. Fourteen chronic schizophrenic and 15 control male right-handed subjects were matched on age, IQ, and parental SES. A 1.5 Tesla magnet was used to obtain 1.5 mm thick slices through the entire brain. Prefrontal gray matter was segmented using semi-automated image processing and then edited and subdivided using an image editor on a SUN workstation. A MANOVA using the factors group (schizophrenic versus control), area (orbital, inferior, middle, superior, cingulate, and frontal-pole), and side (right or left) showed no significant effects between groups. Although none of the subdivisions of prefrontal cortex showed significant reductions in volume in schizophrenic subjects, the volumes of the left anterior portion of several temporal lobe areas were highly correlated with volumes of left orbital, inferior, and middle prefrontal regions in schizophrenic subjects but not controls. The volumes of some prefrontal and temporal areas in schizophrenic subjects may be

affected in a parallel manner by some neurodevelopemental or pathological process.

NR218 Tuesday, May 23, 12 noon-2:00 p.m.

Cognitive Vulnerability, Coping Style and Relapse in Paranoid Schizophrenics

Stefano Pallanti, Ph.D., Institute for Neuroscien., Vle Ugo Bassi 1, Florence 50137, Italy; Leonardo Quercioli, M.D., Rogerio S. Paiva, M.D., Aldo Ragazzoni, M.D., Adolfo Pazzagri, Ph.D.

Summary:

Alteration of P300 component in simple "oddball" tasks is one of the most replicable biological observation in schizophrenics. This finding has been considered as a nonspecific indicator of cognitive disturbances. Correlation between P300 alterations and clinical subtypes (such as residual symptomatology, positive or negative symptoms) was controversial.

The advantages of studying neurophysiological phenomena rather than symptomatological subtypes have been indicated as a strategy for understanding heterogeneity in schizophrenia. Prospective studies about cognitive vulnerability, life-events vulnerability and coping have not so far been conducted. In this study, a work in progress, we examine how these factors interact before a new psychotic episode starts. The present investigation, a two-step research started in 1990, studies the complex relationship between P300 measures, susceptibility to stressful life events, and subjective experiences of cognitive function.

Procedure: In the first phase, a group of 41 paranoid schizophrenic outpatients (31 male, 10 female) was assessed, during asymptomatic phase, for P300 measures, subjective experience of cognitive complaints and coping style (FBF), clinical symptoms (SANS, SAPS, BPRS) and social adaptability (DSM-III-R scale). P300 components were recorded through Fz, Cz and Pz using the oddball paradigm. The second phase proceeded after relapse. Clinical and subjective assessment was repeated for each patient, and life events of the previous six months were rated. All patients were under neuroleptic treatment.

Main Results: A higher rate of stressful life events correlated with larger P300 amplitudes and low FBF scores ($P < .01$). This correlation was lower particularly for events of the last two months before relapse when "independent" life events were considered. A positive correlation was found between low rate of stressful life events, reduced P300 amplitudes, low social adaptability, and low educational level ($P < .01$). No correlation emerged between clinical symptoms and other variables investigated.

NR219 Tuesday, May 23, 12 noon-2:00 p.m.

Electrocardiographic Signs of Psychosis in Adults and Children

Peter M. Fink, M.D., Psychiatry, Rush Pres. St. Luke's, 1725 W. Harrison Suite 744, Chicago IL 60612; Hector C. Sabelli, M.D., Linnea Carlson-Sabelli, Ph.D., Joseph v. Messer, M.D., Karen Walthall, B.S., Cynthia C. Tom, B.S.

Summary:

Newly developed computer methods demonstrate how different emotions produce relatively specific modifications in cardiac activity, including marked differences between schizophrenic patients and normal subjects [Carlson-Sabelli et al, *Proc. Internat. Systems Science Society,* 1994; Sabelli et al, in Abraham & Gilgen eds. *Chaos Theory in Psychology,* in press].

Method: Holter recordings of the electrocardiogram. Subjects included nine healthy adults, six patients with affective psychoses, with and without antipsychotic drug treatment, three schizophrenics, two normal children and one psychotic child. The timing of R-R intervals was studied with the recurrence method, a technique that generates visual representations (that are readily comparable) and numerical measures of patterning (that can be statistically analyzed).

Results: The patterns of firing obtained in psychotic subjects (whether schizophrenic or affective) were visually different from those of nonpsychotic subjects, allowing rapid differentiation between these two groups even by untrained observers. In psychotics, patterns of firing were more repetitious ($p > 0.05$ Mann-Whitney U test). Antipsychotic medications were not responsible for these differences. Normative values were similar in healthy children and adults; the psychotic child displayed the same changes as the psychotic adults.

Conclusions: There are significant differences in the cardiac activity of psychotic subjects that can be demonstrated with dynamic methods for electrocardiographic analysis.

NR220 Tuesday, May 23, 12 noon-2:00 p.m.

Schizophrenia and the Temporal Lobe: A Replication

Erin R. Gautier, B.S., Neurosciences, University of Florida, P.O. Box 100244 JHMHSC, Gainesville FL 32610; John M. Kuldau, M.D., Alexandra Weis, B.S., Christiana M. Leonard, Ph.D.

Summary:

Objective: Schizophrenia research has been characterized by difficulty in replicating findings. Previous studies of temporal lobe abnormalities in schizophrenia have indicated decreased left superior temporal gyrus (STG) volume. We attempted to replicate this finding and to relate volumetric brain differences in schizophrenics to behavioral variables.

Method: Subjects: 11 males diagnosed with *DSM-III-R* schizophrenia (S) and 16 male controls (C), balanced for age, a quantitative measure of handedness, and parental education. All subjects received a volumetric brain MRI and the Lindamood Auditory Conceptualization (LAC) task. Volumetric measurements of the anterior STG were performed by two blind observers on reformatted, 1mm thick coronal sections.

Results: We confirmed the left anterior STG is smaller (C: $2.6 \pm 0.4cc^3$, S: $2.2 \pm 0.14cc^3$, $F = 7.47$, $p < .05$). Phonemic awareness, as measured by the LAC, was also lower and correlated significantly with the volume of the *right* STG ($r = 0.76$, $p < 0.05$) but not the *left* STG in schizophrenics. The LAC score also correlated significantly with degree of dextrality ($r = 0.89$, $p < 0.01$) in the patient group.

Conclusions: Decreased volume of the left STG is a robust finding in male schizophrenics and survives differences in patient samples and measurement protocols. The intricate relation between handedness, language skills, brain morphology, and psychopathology will be discussed.

NR221 Tuesday, May 23, 12 noon-2:00 p.m.

Automatic Inhibition in Schizophrenia of Auditory Processing During the Reading Aloud of Single Nouns

Jose V. Pardo, M.D., Psychiatry Service 116A, Veterans Admin Med Ctr, One Veterans Drive, Minneapolis MN 55417-2 300; Jonathan C. Uecker, M.D., Joel T. Lee, M.S.E.

Summary:

Objective: Does a loss of the normal automatic inhibition of auditory processing during self-generated speech cause auditory hallucinations in schizophrenia?

Method: Cerebral activation was measured in seven schizophrenic patients with positron emission tomography (PET) and the $H_2{}^{15}O$ bolus method for estimation of cerebral blood flow. The subjects were studied under two conditions: reading aloud vs. passive viewing of single, common, concrete nouns. The average

activation, during reading as compared to viewing, was calculated across subjects after stereotactic normalization. Planned comparisons involved paired *t*-tests of cerebral activation in primary auditory cortices.

Results: Activity within primary auditory cortices did not differ significantly between reading aloud and viewing conditions.

Conclusions: Schizophrenic patients, like normal controls, automatically inhibit auditory processing of self-generated speech. Therefore, these data rule out a loss of inhibition of auditory processing during vocalization as a mechanism of auditory hallucination in schizophrenia. (Supported by the Department of Veterans Affairs, USA; Scottish Rite Schizophrenia Research Program; and the Matt Kaul Fund)

NR222 Tuesday, May 23, 12 noon-2:00 p.m.

Linguistic Strategies Underlying Verbal Fluency Performance in Schizophrenia and in Controls Subjects

Philippe H. Robert, M.D., Pavillon J., CHRU Psychiatry, Hopital Pasteur 30 Av Voie, Romaine Nice 06002, France; Valerie Migneco, Dominique Marmod, Cecile Reuge, Guy Darcourt, M.D.

Summary:

There are probably different cognitive mechanisms underlying verbal word fluency performances. The aim of this study was to evaluate the linguistic strategies involved in a verbal word association task.

Population: Twenty-two schizophrenics patients according to DSM-III-R criteria and 22 controls subjects paired in age, sex, and education level were studied

Method: The subject is asked to produce in two minutes as many words as possible beginning with a given letter (three formal word fluency items) and of a given class (three categorical word fluency items). A linguistic strategy is defined as the association of at least three consecutive related words. Three types of linguistic strategies were defined: 1) formal strategies (at least three words related to the oral or written shape of the previous word or at least two words related by an homophonous link), categorical strategy (at least three words related to the meaning of the previous word) and automatic strategy (at least two words very often used consecutively in speech subjects).

Results: indicated that/

- schizophrenic patients produce far fewer words than control subjects
- schizophrenic patients use less strategies than control subjects
- there is a correlation between the number of produced words and the number of strategies.

NR223 Tuesday, May 23, 12 noon-2:00 p.m.

Oxidative Injury at the Onset of Psychosis

Sridhar Gowda, M.D., 3818 Shoal Creek Court, Martinez GA 30907; Sukdeb Mukherjee, M.D., Sahebarao Mahdik, Ph.D., Elezabeth E. Correnti, M.D., Russell E. Scheffer, M.D.

Summary:

Plasma levels of thiobarbituric acid reactive substances (TBARS) were examined in 20 drug-naive patients in a first episode of nonaffective psychosis (mean duration of psychosis 4.8 days) and 17 normal controls. TBARS levels were significantly higher in the patients than in normal controls ($P < .01$), and unrelated to age and sex. High TBARS was associated with lower RBC activity of the antioxidant enzyme glutathione peroxidase ($P < .05$) and a greater severity of negative symptoms.

Considering the very short duration of psychosis, the findings suggests that oxidative injury to membrane lipids precedes the onset of manifest psychosis. Because the brain is enriched in long chain polyunsaturated fatty acids, preferred substrates for membrane lipid peroxidation, it can preferentially suffer from such injury. The findings suggest that oxidative injury might be involved in the schizophrenic disease process, particularly with respect to the development of negative symptoms. They also suggest the need for more systematic studies of oxidative injury and the role of antioxidant treatment in schizophrenia.

NR224 Tuesday, May 23, 12 noon-2:00 p.m.

Schizophrenia: Neuroleptics and Negative Symptoms

John D. O'Brien, M.D., 160 E 38th Street Apt 21-H, New York NY 10016-2612; Barbara A. Cornblatt, Ph.D., David B. Schnur, M.D., Adam Smith, Ph.D., Ilisse R. Perlmutter, M.D., Michael Obuchowski, M.A., Elizabeth A. Amiel, M.D., Douglas F. Munsey, M.D., Myrna Rasmussen, Ph.D., Gregory Osgood, B.A.

Summary:

Objective: As part of a neurodevelopmental study of schizophrenia, recent onset and chronic patients with schizophrenia were compared across several clinical and neurocognitive variables.

Method: Twenty-four recent onset patients (age range 13.6-36.8 years, mean = 18.9 years; duration = 0.8 years) undergoing first hospitalization were compared with 13 chronic adult patients (age range 19.4-54.4 years; mean = 33.5 years; duration = 14.1 years). All patients received a DSM-III-R diagnosis of schizophrenia. This study examines the extent to which treatment response differs between the two patient groups.

Clinical state for all patients was assessed using the PANSS, which rates positive and negative symptoms and general psychopathology. Ratings were conducted within a week of admission and then repeated, approximately four weeks later, after stabilization on neuroleptics.

Results: In terms of clinical profiles, the two groups were highly similar, with positive symptoms and general psychopathology showing significant improvement with treatment. No decrease in negative symptoms was found in either group. However, after four weeks of treatment, a significant relationship was found between severity of negative symptoms and medication dose ($r = .57$; $p = .003$) for recent onset but not chronic patients.

Conclusions: Depression and extrapyramidal side effects did not appear to be explanations for the medication/symptom pattern. These findings suggest that the relationship between negative symptoms and medication may differ depending on phase of illness.

NR225 Tuesday, May 23, 12 noon-2:00 p.m.

CSF Antibodies to Heat Shock Protein-60 in Schizophrenia

David H. Strauss, M.D., Psychiatry, Columbia University, 722 West 168th Street Unit 101, New York NY 10032; Yutaka Ogino, M.D., David J. Printz, M.D., Jack M. Gorman, M.D., Saudi A. Sadiq, M.D.

Summary:

Objective: To examine the presence of antibodies to the 60kDa human heat-shock protein (hsp60) in the CSF of patients with schizophrenia, other neuropsychiatric diseases, and controls.

Background: Schizophrenia shares a number of clinical characteristics with known autoimmune diseases, and aberrant autoantibody production has been described in schizophrenia. The significance of such immune reactivity in schizophrenia remains uncertain but may suggest a direct or indirect role for autoimmunity in disease pathogenesis. By Western blot, at serum dilutions of 1:10,000, IgG antibodies to the 60 kDa human heat-shock protein

are seen in 44% of patients with schizophrenia and approximately 20% of patients with rheumatological or infectious diseases. CSF reactivity to hsp60 has not been examined.

Methods: Antibody reactivity to recombinant, affinity-purified hsp60 was tested in patients with schizophrenia, other psychiatric diseases, multiple sclerosis, CNS inflammatory and infectious disorders, other neurological disorders, and normal subjects. Western blot was performed using CSF at a 10 ug/ml concentration of IgG.

Results: CSF from three of seven patients with schizophrenia reacted with hsp60 by Western blot. By contrast, only one of 50 patients with other diseases or controls reacted with hsp60 (Fisher's p = 0.0045, one tailed.)

Conclusion: In schizophrenia, findings of CSF antibodies to hsp60 are consistent with previously reported data on serum reactivity to this antigen. In controls, lower reactivity to hsp60 occurred in CSF. This may suggest more specific immune reactivity to hsp60 in patients with schizophrenia.

NR226 Tuesday, May 23, 12 noon-2:00 p.m.

Corpus Callosum in Schizophrenia

Lisa A. Rowe, B.S., Neuroscience, University of Florida, P.O. Box 100244 JHMHSC, Gainesville FL 32610; John M. Kuldau, M.D., Erin R. Gautier, B.S., Christiana M. Leonard, Ph.D.

Summary:

Variation in corpus callosum (CC) morphology has been implicated in schizophrenia, but subregions have yet to be examined.

Objective: To quantitatively compare subregions of the corpus callosum in schizophrenics and control participants.

Method: Subjects: DSM-III-R diagnosed schizophrenics and 10 controls, matched for age, sex, and handedness. Volummetric MR images, 1.25 mm thick, were obtained using a Siemens 1-tesla magnetom scanner.

Results: No gross abnormalities were found in either group. The CC was subdivided along two axes: rotation of the mid-sagittal image along the a.) AC-PC line, and b.) intrinsic CC axis. Reliability estimates ranged from .82 to .97. Statistical analyses corrected for variation in head size. Though the total CC area was not different in the two groups, the rostrum was 50% larger in the schizophrenics, using either method [a.) $t = -2.38$, $p = .03$; b.) $t = -2.89$, $p = .02$].

Conclusions: These results suggest that the rostrum may be larger in schizophrenics than normals. Fibers from the rostrum connect the orbitofrontal cortex, a region important for social and affective integration, that may develop abnormally in schizophrenia.

NR227 Tuesday, May 23, 12 noon-2:00 p.m.

Catatonia From Neuroleptics and NMS: Two Entities?

Monika A. Koch, Psychiatry, SUNY Stony Brook, Health Science Ctr T-10, Stony Brook NY 11794; Georgios Petrides, M.D., Andrew J. Francis Jr, M.D.

Summary:

Objective: To determine presence of catatonic signs in NMS [neuroleptic malignant syndrome].

Methods: NMS cases were identified retrospectively by screening for elevated CPK, exposure to neuroleptics in the week prior to onset of symptoms, and significant motor, autonomic, or mental status changes. Twenty-two cases met at least two of eight published sets of research criteria for NMS. In five cases, a Bush-Francis Catatonia Rating Scale [requiring ≥2 signs for catatonia] had been performed concurrently; in the remaining 17, catatonic signs were retrospectively identified.

Results: 21/22 patients with NMS met research criteria for catatonia. Of these, two patients with ≥12 signs of catatonia also met 7/8 sets of research criteria for NMS. Autonomic signs were present in all patients, and CPK-levels ranged from 367-5515 mg/dl. In all cases neuroleptics were discontinued and the symptoms resolved. No patient received "specific" treatments such as dantrolene or bromocriptine.

Conclusion: Symptoms of NMS and catatonia overlap, so that differentiation is often impossible. This supports the hypotheses of similar pathophysiology (Fricchione, 1985) and a "neuroleptic toxicity spectrum" (Kontaxakis, 1989). Since catatonia and NMS may be indistinguishable, the data support White et al.'s (1991) recommendation to avoid neuroleptics in catatonia.

NR228 Tuesday, May 23, 12 noon-2:00 p.m.

A Comparison of the Efficacy of Clozapine and Risperidone in Treatment Refractory Schizophrenia

Ahmad Raza, M.D., Psychiatry, Creedmoor Psych. Center, 80-45 Winchester Blvd., Queens Village NY 11427; Tzippy Ettinger, B.A., Zafar A. Sharif, M.D., Fabian Tremeau, M.D., Peter A. Rao, M.D.

Summary:

We retrospectively examined the response to risperidone in treatment refractory schizophrenic inpatients who had been treated with clozapine (>300mg/day for > six weeks). We identified three responders to clozaril (BPRS reduction >30% from baseline) and five nonresponders who subsequently received risperidone (at least 6mg/day for > six weeks). Treatment outcome to risperidone was determined by a review of the medical records and rating individual positive and negative symptoms as better, unchanged, or worse with corroboration from interviews with the treating psychiatrists. A final judgment on global clinical response was made using a five-point CGI (improvement) scale. Only one of five clozaril nonresponders showed minimal improvement with risperidone, three of the five remained unchanged, and one experienced marked worsening. In the clozapine responsive group, one of three patients displayed an equivalent response to risperidone, one patient showed a markedly better response to risperidone, while the third patient had significant deterioration. This study suggests that clinical response to clozaril predicts the response to risperidone in treatment—refractory schizophrenia while patients resistant to clozaril are likely to be resistant to risperidone as well. In view of a more favorable side effect profile, risperidone should probably be the first line treatment for this group of patients.

NR229 Tuesday, May 23, 12 noon-2:00 p.m.

Laboratory Stressors in Schizophrenia and Mania

David B. Schnur, M.D., Psychiatry, Mt. Sinai School of Med, 79-01 Broadway, Elmhurst NY 11373; Rachel Yehuda, Ph.D., Scott P. Smith, M.A., Jean Franklin, M.D., Venecia M. Marte, Monica C. Dinu, M.D.

Summary:

Objective: We compared psychophysiological and neurochemical reactivity to laboratory stressors in schizophrenic, manic, and normal subjects to inform on the role of environmental stress in these disorders.

Method: The effects of mental arithmetic with and without auditory distraction (MA, MAD) and the cold pressor test (CP) were examined in schizophrenic, manic, and normal subjects. Skin conductance level (SCL), heart rate (HR), and plasma cortisol, 3-methoxy-4- hydroxyphenylglycol, and homovanillic acid were assessed at baseline, and after each laboratory manipulation.

Results: Preliminary analyses of SCR and HR in 10 schizophrenic, eight manic, and eight control subjects indicated that HR

tended to be higher in the schizophrenic group throughout the study ($p < .1$) with differences attaining significance during MA and CP ($F[2,25] \geq 4.4$; $p < .05$). Manic patients reacted similarly to controls. No significant between-group differences emerged in SCR nor were there group-by-condition interactions for either psychophysiological measure.

Conclusions: HR differences may distinguish schizophrenic, manic, and control subjects, but reactivity to laboratory stressors (indicated by interaction effects) appears to be similar in all three groups. Additional analyses of neurochemical measures will be presented and the theoretical implications of these findings will be discussed.

NR230 Tuesday, May 23, 12 noon-2:00 p.m.

Schizophrenia, Dopamine, Transforming Growth Factors-Beta and Excitotoxins

Murray A. Cowen, M.D., Nathan Kline Inst., Orangeburg NY 10962; Maurice R. Green, M.D., David N. Bertollo, B.A.

Summary:

The dopamine and glutamate-excitotoxic theories of schizophrenia are currently the most popular, but attempts to unify them have been less than convincing. There is a linkage which involves transforming growth factor(s) beta (TGF-beta). Dopamine regulates TGF-beta synthesis and secretion by tanycytes and tanycyte-like cells in the hypothalamus and medial temporal area, and TGF-beta potentiates glutamatergic synapses by inhibiting glutamine synthetase which is essential for the inactivation of glutamate. Tanycytes and tanycyte-like cells are similar to the radial glia that control most embryonic brain development, and they direct the embryogenesis of each of the neuronal systems that have been reportedly abnormal in schizophrenics. Unlike radial glia, they continue to maintain and regulate neurons throughout life (1). Thus, despite its excitotoxic potential, TGF-beta is probably the major inducer of nerve growth factors which maintain cholinergic and dopaminergic neurons. There is now considerable evidence that TGF-beta is markedly increased in the cerebrospinal fluid of schizophrenics during acute psychotic exacerbations, but is normal during remissions of the psychoses. It has been implicated as a major psychotogenic agent in AIDS dementia, and may also promote the paranoid psychoses that accompany early Alzheimer's disease.

NR231 Tuesday, May 23, 12 noon-2:00 p.m.

Do Thoughts About Abstinence Predict Future Drug Use in Cocaine Dependent Schizophrenics?

Lisa J. Roberts, M.A., Research, VA Medical Center, 11301 Wilshire Blvd B151Z, Los Angeles CA 90073; Andrew L. Shaner, M.D., Thad A. Eckman, Ph.D.

Summary:

Clinicians often attempt to predict the likelihood of successful treatment by relying on the patient's expressed desire to quit using drugs. The information is easy to obtain and has face validity. This study was conducted to determine whether such reports by cocaine-dependent schizophrenics actually predict future cocaine use. In a prospective study, 86 cocaine-dependent schizophrenics were assessed at study entry using the Thoughts About Abstinence Scale (TAA) and urine toxicology. The TAA asks subjects to endorse one of six abstinence goals. Additional items measuring "desire to quit," "expected success," and "perceived difficulty in avoiding relapse" were assessed on 10-point Likert scales. Follow-up data regarding TAA and cocaine use were collected three, six, and 12 months after study entry. TAA responses were modestly predictive of subsequent drug use. However, this relationship could be explained on the basis of the highly significant concurrent correlation between Thoughts About Abstinence items and drug status, and the modest autocorrelation within each domain. These results suggest that among cocaine dependent schizophrenics, reported motivation (as measured by TAA) does not predict future cocaine use. Thus, clinicians should avoid predicting outcome based on motivational attributions. Instead, they should focus on engaging and maintaining dually diagnosed patients in treatment.

NR232 Tuesday, May 23, 12 noon-2:00 p.m.

Suicide Among Psychiatric Hospital Inpatients

Alec Roy, M.D., Psychiatry, New Jersey Medical School, 185 South Orange Avenue, Newark NJ 07103; Veronika Solt, M.D., Ronald J. Draper, M.D., Matthew J. Pitera, M.D., S. Hassan, M.D., Rakesh K. Bansil, M.D.

Summary:

We compared 37 inpatients of a psychiatric hospital who committed suicide with 37 age- and sex-matched inpatient controls. Significantly more of the suicides had made a previous attempt (23 vs 13, $p < 0.02$) and suffered from schizophrenia (28 vs 12, p, 0.0005). Only six patients committed suicide on the ward. A third of the patients, the majority schizophrenic, committed suicide after having been in the hospital over a year. When the schizophrenic suicides ($N = 28$) were compared with living schizophrenic controls ($N = 13$) the only significant difference was that more of the schizophrenic suicides had made a previous suicide attempt (60.7% vs 15.4%, $P < 0.007$) and had made two or more previous attempts (238.6% vs 0%, $P < 0.05$). These results suggest that in the psychiatric hospital setting the inpatient at risk for suicide has previously exhibited suicidal behavior, suffers from schizophrenia, and that the risk of suicide may remain high among long-stay schizophrenics. The schizophrenia findings are of note as neuroendocrine challenge studies with the serotonin agonist M-CPP, and treatment responses with atypical neuroleptics, as well as postmortem studies, suggest serotonergic dysfunction among schizophrenics. Also, follow-up studies of schizophrenic patients have reported that low CSF 5-HIAA is associated with suicidal behavior during follow up.

NR233 Tuesday, May 23, 12 noon-2:00 p.m.

Dopamine Receptor Structure: Psychiatric Applications

Curtiss J. DuRand, M.D., Psychiatry, ENRM VA Medical Center, 200 Spring Road, Bedford MA 01730; Richard C. Kaiser, M.D., Martha Teeter, Ph.D.

Summary:

G protein-coupled receptors are products of one of the largest families of genes, representing 1% to 2% of the human genome. It has been said that they function to modulate the mind. They are targets of at least 50% of therapeutic agents in medicine.

Although the large structural and functional database now available for these and related proteins is not sufficient to define their three-dimensional structure, this database can be integrated to build and test plausible structural models.

Our databased structures of dopamine receptors provide explanatory pictures of many of their known functions. They are being used to:

- design mutagenesis experiments;
- explain some effects of human mutation on function;
- study possible receptor-receptor interactions, drug effects, and differences between receptor subtypes; and
- explore various conformational states such as high and low affinity for agonists and states that activate G proteins.

Results of some of these uses will be presented.

NR234 Tuesday, May 23, 12 noon-2:00 p.m.

Glucose Metabolic Rate of the Basal Ganglia In Schizophrenia

Lina S. Shihabuddin, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Christina T. Luu, B.A., Mehmet M. Haznedar, M.D., Kenneth L. Davis, M.D.

Summary:

Most neuroimaging studies have found decreased metabolic rates in the basal ganglia of schizophrenic patients. This study examined the basal ganglia using PET with 18-F-2-deoxyglucose (FDG) in a completely new cohort of 19 patients with schizophrenia and 25 healthy matched controls. Subjects were scanned with our new high resolution (4.5 mm FWHM) scanner. Patients were off all psychoactive medications a minimum of two weeks. All subjects were screened by history, psychiatric interview, physical exam, and laboratory testing. Controls with a history of mental illness in a first-degree relative were excluded. During the FDG uptake period, all subjects performed a modified version of the California Verbal Learning Test (CVLT). The glucose metabolic rates were determined using a stereotaxic method based on a template from the Matsui and Hiranu atlas. The metabolic rates in the caudate and the putamen were significantly lower in the schizophrenic patients compared to the controls ($F = 7.80$, $p < 0.01$), more on the right than on the left. In addition, there was loss of the normal left-right asymmetry in schizophrenics. These findings further suggest right basal ganglia pathology in schizophrenia and are consistent with our previous finding that neuroleptics increase the metabolic rate in the right putamen in schizophrenics.

NR235 Tuesday, May 23, 12 noon-2:00 p.m.

A Clinical Update on Olanzapine: Atypical Antipsychotic

Winston G. Satterlee, M.D., CNS/GI/GU/Medical, Eli Lilly & Company, Lilly Corp Ctr Drop Code 2128, Indianapolis IN 46268; Charles M. Beasley, Jr., M.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.

Summary:

Olanzapine structurally a thienobenzodiazepine, has demonstrated in-vitro affinity for serotonin (5-HT)2a, 5-HT2c, dopamine (D)2, D4, D1, muscarinic (particularly M1), α1-adrenergic, and H1 receptors. This broad receptor profile includes high affinity for D2 and D4 receptors and greater activity at 5-HT2a than at D2 receptors. An earlier trial in 335 patients showed that olanzapine was statistically superior to placebo for both positive and negative symptoms of schizophrenia.

In a randomized, double-blind, multicenter clinical trial designed to test the efficacy and safety of olanzapine, 152 schizophrenic patients were randomly assigned to 1 or 10 mg/d of olanzapine or placebo (Pbo). When baseline and endpoint scores were compared, the 10mg dose of olanzapine (–7.7) was statistically significantly superior to Pbo (–0.4) relative to mean change in BPRS total. When baseline to endpoint mean changes for BPRS positive, PANSS total, PANSS positive, and PANSS negative scores were compared, olanzapine (10mg) was statistically significantly superior to Pbo and few treatment emergent extrapyramidal symptoms occurred in patients on olanzapine. Olanzapine (1mg dose) was not significantly different than Pbo in terms of efficacy.

Olanzapine's receptor profile, efficacy, and its safety profile strongly suggest that olanzapine is a very promising atypical antipsychotic agent.

NR236 Tuesday, May 23, 12 noon-2:00 p.m.

Five-Year Follow-Up of Outcome in a Prospective Study of First-Episode Schizophrenia at Hillside Hospital

Julia A. Becker, M.D., Psychiatry, Hillside Hospital, P.O. Box 38, Glen Oaks NY 11004; Amy R. Koreen, M.D., Miranda H. Chakos, M.D., Steve Geisler, M.D., Jose Ma. Alvir, D.P.H., Margaret Woerner, Ph.D., Jeffrey A. Lieberman, M.D.

Summary:

Objective: To determine five-year clinical outcome in first-episode schizophrenia.

Method: In a prospective study at Hillside Hospital 118 schizophrenic patients admitted for their first episode of psychosis were followed for up to five years. Subjects were diagnosed by DSM-III criteria (75% schizophrenia; 8% schizoaffective, manic; 17% schizoaffective, depressed). Fifth-two percent were male, 48% were female, and mean age (S.D.) was 25.2 ± 6.6 years. Ethnicity included 41% Caucasians, 37% African Americans, 14% Hispanics, 8% Asians, and 4% "other."

Results: The median time to recovery among the 107 patients who remitted was nine weeks. Cumulative relapse rates were 16% at year 1, 51% at year 2, 64% at year 3, 74% at year 4, and 78% at year 5. By the first year 11 of the 15 patients who relapsed were not on neuroleptics. During year 2 there were 13 of the 26 relapsed patients who were off medication. During the third year there were four of six patients who were off neuroleptics. All of the relapsed patients during the fourth and fifth years were taking neuroleptics. Survival analysis, which used neuroleptic status as a time-dependent covariate, estimated a five-times higher rate of relapse after discontinuing neuroleptic compared to patients remaining on medication. Seventy-nine percent never married, 13% had a first marriage, 1% had remarried, and 8% had separated or divorced.

Conclusion: The data demonstrate a high percentage of relapse. The relapse rate is less than seen with chronic schizophrenics withdrawn from medications, and in a small sample of the population there also appears to be a good outcome without relapse.

NR237 Tuesday, May 23, 12 noon-2:00 p.m.

Retention by Florid and Never Florid Schizophrenia Spectrum Patients

Avraham Calev, Ph.D., Psychiatry, SUNY at Stony Brook, Health Sci. Ctr. T10 020, Stony Brook NY 11794

Summary:

Three groups of patients diagnosed with DSM-III-R as schizophrenic, schizoaffective, and schizophrenoform, and a group of hospitalized patients lacking positive symptoms and meeting DSM-IV criteria for schizophrenia, but not DSM-III-R criteria, were assessed using Calev et al. (1983) immediate and delayed categorized word list recall tasks. The tasks were matched for discriminating power (Chapman and Chapman, 1978). Testing took place within three years since first admission. They were either drug free or on neuroleptics only, or on both neuroleptic and anticholinergic drugs. All were free of florid symptoms during testing. Patients on anticholinergic drugs performed worse than other patients, and patients' performance was generally lower than that of normals. All DSM-III-R schizophrenia spectrum patients performed worse on delayed than immediate recall, repeating former findings which suggested rapid forgetting in schizophrenia. DSM-IV hospitalized schizophrenics not meeting positive symptoms criteria, showed no evidence of worse delayed than immediate recall, although performing generally worse than normals. The possibility that negative symptoms without psychosis are associated with global cog-

nitive deficits, whereas DSM-III-R schizophrenia is associated also with milder and specific memory deficits, is discussed.

NR238 Tuesday, May 23, 12 noon-2:00 p.m.

A Controlled MRI Study of Tardive Dyskinesia

Christian L. Shriqui, M.D., Psychiatry, Robert-Giffard, Hosp 2601, de la Canardiere, Beauport Quebec QC G1J 2G3, Canada; Lawrence Annable, D.S., Gilles Bouchard, M.D., Pierre Grondin, M.D., Marie Dufour, M.D.

Summary:

Alterations in brain iron have been suggested to play a role in the development of TD which has been associated with MRI findings of shortened left caudate T2 relaxation time in patients with TD. We examined for differences in the signal intensity of basal ganglia structures in a group of dyskinetic and non-dyskinetic schizophrenic patients and in a neurological control group. The study included 62 chronic neuroleptic-treated DSM-III-R schizophrenic patients (51 men, 11 women); 44 patients met RDC criteria for at least mild TD (36 men, 8 women) and 18 (15 men, 3 women) were without TD, and 30 neurological control patients (10 men, 20 women). The age of the schizophrenic patients ranged from 28 to 64 years (median = 46 years) and of the neurological controls from 22 to 76 years (median = 46 years). Duration of neuroleptic treatment in schizophrenic patients ranged from three to 45 years (median = 23 years). Schizophrenic patients had a stable psychopathology and neuroleptic dose for at least three consecutive months before scanning. TD was assessed using the AIMS. MRI scans were acquired using a 0.5-T GE MR Max System unit. A first sequence in the transaxial plane consisted of continous 5-mm thick slices throughout the brain using a spin-echo technique with cardiac gating for proton density and T2 weighted images. A variable echo (VE) pulse sequence (TR = 1180 msec., TE = 20,100,180 and 260 msec.) and an inversion-recovery (IR) sequence (TR = 1180 msec., TI = 400 msec., TE = 20,40 and 60 msec) were also required to calculate T1 and T2 values. Schizophrenic patients with TD were compared to those without TD and to neurological controls with respect to T1 and T2 relaxation times in the caudate nucleus, putamen, globus pallidus, and thalamus (left and right) by means of analysis of covariance controlling for gender and age. No significant ($p > 0.10$) differences were observed between schizophrenic patients with TD and those without TD or neurological controls with respect to the T1 and T2 relaxation times.

NR239 Tuesday, May 23, 12 noon-2:00 p.m.

Neuropathological Study of 101 Elderly Schizophrenics: Preliminary Findings

Julia A. Golier, M.D., Psychiatry, Bronx VA Medical Center, 116A 130 W. Kingsbridge Road, Bronx NY 10468; Michael Davidson, M.D., Vahroum Haroutunian, Ph.D., Peter Powchik, M.D., Dushant Purohit, M.D., Daniel Perl, M.D., Kenneth L. Davis, M.D.

Summary:

Objective: To examine the role of known dementing illnesses in the cognitive dysfunction seen in some schizophrenic patients, the brains of 101 elderly institutionalized schizophrenics were studied.

Method: Brain tissue was examined for the presence of known dementing diseases and Alzheimer's disease (AD) related pathology using a standardized protocol developed by the Consortium to Establish a Registry for Alzheimer's disease (CERAD). Cognitive impairment was rated according to the Clinical Dementia Rating (CDR) Scale on a scale of 0 to 5 (0 represents no cognitive impairment, 5 represents a terminal level of dementia).

Results: The prevalence of primary CERAD neuropathologic diagnoses are as follows:

Diagnosis	N	Mean CDR (S.D.)	Mean age (SD)
Normal	37	2.0 (1.2)	72.7 (12.6)
Definite AD	6	2.8 (0.8)	81.8 (8.3)
Probable AD	4	3.2 (0.5)	85.0 (2.7)
Possible AD	29	2.2 (1.1)	82.1 (10.9)
Vascular	15	2.7 (1.2)	77.8 (8.9)
Parkinson's	2	4.0 (0.0)	78.0 (8.5)
Tumor	3	1.0 (0.0)	70.3 (17.6)
Other	5	2.6 (0.9)	82.8 (6.2)

These results suggest that elderly institutionalized schizophrenics can have moderate to severe cognitive impairment even in the absence of comorbid dementing illnesses. More than a third of the cases had neocortical neuritic plaques in numbers too few to warrant a diagnosis of definite AD. Among these patients no significant correlation was found between the number of neuritic plaques and cognitive impairment, after controlling for age.

Conclusion: The severe cognitive impairment seen in some elderly schizophrenics can not be fully accounted for by histopathologically identifiable causes of dementia and requires further study.

NR240 Tuesday, May 23, 12 noon-2:00 p.m.

The Validation of the Scale of Functioning for Schizophrenic Subjects

Mark H. Rapaport, M.D., Psychiatry, UCSD UN Cal San Diego, 8950 Villa Jolla Drive Ste2243, La Jolla CA 92037; James Bazzetta, M.A., Dilip V. Jeste, M.D., Sidney Zisook, M.D., William B. Perry, Ph.D.

Summary:

We present reliability and validity data for the Scale of Functioning (SOF) in schizophrenic and schizoaffective patients. This 15-item scale can be used with both inpatients and outpatients. We will describe data from over 180 younger and older psychotic subjects. The ICC for the SOF equals .94. Data from two separate orthogonally rotated factor analyses are presented, which document that the five factors identified in the initial analysis are present in a replication analysis and 70% of the variance is accounted for by these factors. The SOF is also highly correlated with a number of existing instruments including the Pfeffer Disability Scale ($r = .77$, $p < .0001$); the Quality of Well Being scale ($r = .3$, $p < .04$); the Dementia Rating Scale (DRS) total score ($r = .51$, $p < .03$); the Dementia Memory Subscale of the DRS ($r = .55$, $p < .02$); the Global Social Adjustment Scale ($r = .30$, $p = .05$); BPRS total score ($r = .3$, $p = .05$); PANSS total score ($r = .49$, $p < .0001$); SANS total score ($r = .54$, $p < .0001$). These data demonstrate that this 15-item scale designed for psychotic inpatients and outpatients is reliable and valid.

NR241 Tuesday, May 23, 12 noon-2:00 p.m.

Spatial Relationships of Neuroanatomic Landmarks in Schizophrenia

John R. DeQuardo, M.D., Dept of Psych, U of MI Medical Center Rm, 1500 E Medical Center Drive, Ann Arbor MI 48109-0116; Fred L. Bookstein, Ph.D., William D.K. Green, Ph.D., James A. Brunberg, M.D., Rajiv Tandon, M.D.

Summary:

The authors sought to investigate the sites and extent of structural neuropathology in schizophrenia demonstrated on mid-sagittal MRI scans utilizing a new technique of morphometric analysis. Utilizing a technique (image averaging and shape analysis) of morphometric analysis that allows the identification of averaged

anatomy via joint registration on multiple landmarks simultaneously, MRI scans obtained in the mid-sagittal plane were analyzed for 14 patients with schizophrenia, with variable levels of chronicity, and compared with 14 neurologic controls. The relation between averaged landmark configuration in the two groups was visualized as a deformation. The data suggest that the neuroanatomic abnormality in schizophrenia is circumscribed (focal), involving primarily the region of the posterior corpus callosum, upper brainstem and superior cerebellum, and secondarily the thickness of the corpus callosum all along its length. There were no large-scale abnormalities noted, although the patients with schizophrenia had significantly smaller brains. The findings are consistent with prior studies suggesting involvement of limbic structures, the corpus callosum, and the cerebellum in the illness. Complementing the "region of interest" method of investigating morphometric abnormalities, this method should contribute to defining the precise location and spatial relationship between relevant structural brain abnormalities in schizophrenia, and will educate future research efforts in the area.

NR242 Tuesday, May 23, 12 noon-2:00 p.m.

Affective Reactivity and Family History in Schizophrenia

Nancy M. Docherty, Ph.D., Psychiatry, Yale University, 34 Park Street Room 247, New Haven CT 06519; Ellen S. Grosh, M.D., Bruce E. Wexler, M.D.

Summary:

Objective: Associations between measures of affective reactivity of cognitive functioning in schizophrenia and family psychiatric history were examined in two separate samples.

Method: We assessed affective reactivity of positive formal thought disorder symptoms, first in 29 acute inpatients and then in 10 stable outpatients. We also administered paired-word dichotic listening tests of perceptual asymmetry to the outpatient sample, using affectively neutral and affectively negative words as stimuli.

Results: In both studies we found that thought disorder was greatly exacerbated by negative affect in those patients with a family history of schizophrenia (SFH), and not in those without the family history (SNFH). In the outpatient study, we also found that right ear advantage was more markedly diminished on the affectively negative task than on the neutral task in the SFH but not the SNFH subjects, indicating a probable increase in left hemisphere impairment in response to negative affect only in the SFH subjects.

Conclusion: These findings support the hypothesis that cognitive symptoms and left hemisphere impairment in schizophrenia are exacerbated by negative affect, and that this affective reactivity of impairment is associated with a familial form of the disorder.

NR243 Tuesday, May 23, 12 noon-2:00 p.m.

Affective Reactivity and Startle in Schizophrenia

Nancy M. Docherty, Ph.D., Psychiatry, Yale University, 34 Park Street Room 247, New Haven CT 06519; Christian Grillon, Ph.D.

Summary:

Objective: This study explored the relationship between reactivity of language symptoms to affect in schizophrenia, and physiological reactivity to acoustic stimuli.

Method: Ten stable schizophrenic outpatients each provided two speech samples: one on affectively negative topics and one on affectively positive topics. These were analyzed using an established method for assessment of communication disturbances. We also measured startle amplitude in response to repeated acoustic stimuli. For the analysis, subjects were divided into high vs. low startle groups (n = 5 per group).

Results: A two-way (group X condition) repeated measures ANOVA on the language ratings revealed more disorder in the affectively negative speech than in the affectively positive speech for the whole sample, $F = 6.10$, $p < .04$. The low-startle subjects showed levels of overall language disorder comparable to the high-startle group, $F = .03$, *ns.* However, there was a significant group X condition interaction effect, $F = 6.56$, $p < .04$. Deterioration of language in the affectively negative condition occurred only in the high-startle subjects.

Conclusion: Affective reactivity of language may be associated with a more global reactivity to sensory and affective stimuli which is present in some but not all schizophrenic patients.

NR244 Tuesday, May 23, 12 noon-2:00 p.m.

Longitudinal Evaluation of Very Chronic Inpatients with Common Psychometric Instruments

Cheryl K. Cantrell, M.D., Psychiatry, Delaware State Hospital, 1901 N. Dupont Highway, New Castle DE 19720; Eric S. Cole, Ph.D.

Summary:

Objective: The Brief Psychiatric Rating Scale (BPRS) (1), Global Assessment of Functioning (GAF) Scale (2), and Mini-Mental State Examination (3) are widely employed measures in both the clinical and research domains of psychiatry. The present investigation analyzed these measures relative to differentiating subgroups of psychiatric inpatients.

Methods: Thirty-seven chronic psychiatric inpatients were evaluated longitudinally over a 29-month period using the BPRS, MMSE, and GAF. The results were analyzed and tabulated into four diagnostic subgroups roughly described as psychotic, demented, both, or neither.

Results: Mean scores for the diagnostic subgroups were not significantly different on the BPRS, but were different on the MMSE and the GAF ranking of subgroups. Ranges and standard deviations of the mean MMSE scores were significantly larger in psychotic patients than in nonpsychotic patients although the grand means of the two groups did not differ significantly.

Conclusion: The GAF and MMSE differentiate diagnostic subgroups in this population better than the BPRS. Psychotic patients show more scatter in their MMSE scores over time than nonpsychotic patients, regardless of presence of dementia. Longitudinal testing with these instruments may assist the clinician in resolving diagnostic puzzles.

NR245 Tuesday, May 23, 12 noon-2:00 p.m.

Neuroleptics, Olfactory Sensitivity and Schizophrenia

Pinkhas Sirota, M.D., Abarbanel Men Hlth Ctr 6A, 15 Keren Kayemet, Bat-Yam, Israel; Israel Ben-David, M.D., Karen Luca-Haimovici, M.D., Joseph Zohar, M.D., Ruth Gross-Isserrof, Ph.D.

Summary:

Olfactory sensitivity to two odorants, iso-amyl acetate and androstenone, was assessed in 19 schizophrenic patients and 10 nonschizophrenic control subjects (five healthy subjects, four OCD patients and one MDD patient). Tests were performed during a drug-free period and three weeks after initiation of neuroleptic drug therapy. There were two main findings: 1) a significantly reduced olfactory sensitivity to iso-amyl acetate in drug-free schizophrenic patients as compared to nonschizophrenic controls; 2) a significant reduction in olfactory sensitivity induced by commonly used neuroleptic treatment. Is the reduced olfactory sensitivity due to previous long-term exposure to neuroleptic drugs or

is it due to an inborn defect associated with the pathophysiology of the disorder? Further studies with drug-naive schizophrenic patients are needed to elucidate this question.

NR246 Tuesday, May 23, 12 noon-2:00 p.m.

Stress Response Symptoms in Alzheimer's Disease Caregivers

Deborah B. Marin, M.D., Dept of Psych, Mount Sinai Med Center, Box 1230 1 Gustave Levy P1, New York NY 10029; Rachel Yehuda, Ph.D., Cynthia Green, Ph.D., Maureen Fusco, M.S.N., Bella Baruch, B.A., Kenneth L. Davis, M.D.

Summary:

Introduction: Caregiving for a family member with Alzheimer's disease (AD) is a very stressful experience. We explored the extent to which caregivers endorse symptoms associated with other traumatic stress responses.

Methods: Caregivers completed scales evaluating symptoms that result from the focal "trauma" of caregiving: Mississippi PTSD scale, Impact of Events Scale (IES), Dissociative Experience Scale, and a coping scale. Comparison groups were Holocaust survivors, second generation Holocaust survivors, and age-matched controls. Caregivers endorsed significantly higher scores on the Mississippi than controls, but were significantly lower than survivors with PTSD. Caregivers' Mississippi scores were comparable to survivors without PTSD and second generation survivors, all of whom were significantly higher than controls. Caregivers' IES scores were significantly higher than controls, which were attributable primarily to extremely high avoidance scores. In contrast, caregivers did not show more dissociation than controls. No difference in coping was observed among groups.

Conclusion: Caregiving for AD may be associated with a circumscribed symptom complex resembling that observed in other groups with chronic exposure to primary or secondary stress. It may be of clinical utility to conceptualize the experience of AD caregiving on the stress response spectrum along with the intergenerational stress response and secondary post-traumatic syndromes.

NR247 Tuesday, May 23, 12 noon-2:00 p.m.

Caudate Size in Geriatric Depression

George S. Alexopoulos, M.D., Department of Psychiatry, NYH-WD, Cornell UMC, 21 Bloomingdale Road, White Plains NY 10605; Barnett S. Meyers, M.D., Rotimi Bajulaiye, M.D., C. Elkin, M.D., Philippe J. Khouri, M.D., T. Kakuma, Ph.D.

Summary:

Objective: Reduced caudate size has been reported in younger depressives. Geriatric depression often occurs in patients with cognitive impairment and medical illnesses. These clinical characteristics of geriatric depression may either influence or be influenced by the size of the caudate. This study sought to identify the relationship between size of caudate and: 1) characteristics of geriatric depression; and 2) specific cognitive impairments.

Design: The subjects were 44 elderly patients with major depression by RDC and a wide range of cognitive impairment (Mattis DRS, Median: 134, Range: 99-144). Medical health was assessed with the Philadelphia Multiphasic Assessment Instrument. Specific cognitive impairments were assessed with the Mattis-Kovner verbal recognition memory test, the French Benton (visual retention), the Multilingual Aphasia Examination (visual naming, fluency, comprehension), the Purdue pegboard, and Trials A and B. The volumes of the left and right caudate were assessed using a stereologic method. MRI was also qualitatively assessed using the CERAD protocol.

Results: Univariate assessment indicated significant associations between small caudate size and poor medical health (right: r_s = 036, $P < 0.02$; left $r_s = 0.32$, $P < 0.04$), disability (right: $r_s = 0.34$, $P < 0.02$; left: $r_s = 0.24$, $P < 0.11$), and overall cognitive impairment (right: $r_s = 0.42$, $P < 0.009$; left: $r_s = 0.36$, $P < 0.02$). Preliminary analysis using structural equations suggested that poor medical health contributed directly to cognitive impairment. In addition, poor medical health contributed to small caudate size and caudate size contributed to cognitive impairment. Multiple regression using the Mattis DRS subscores as the independent variables showed that low volume of the right caudate was associated with impairment in construction subscores ($P < 0.02$), while the low volume of the left caudate was associated with impairment in both construction ($P < 0.05$) and memory ($P < 0.002$). When scores of tests for specific cognitive impairments were used as independent variables, low right caudate volumes were associated with impaired visual retention (Benton) ($P < 0.03$), while low left caudate volume was best determined by both visual retention (Benton) ($p < 0.009$) and visual naming ($P < 0.02$). There were no significant associations between volumes of the caudate and CERAD scores.

Conclusions: Small caudate size is most likely to be found in geriatric depressives with high medical morbidity and cognitive impairment. Findings relating low caudate volumes to specific cognitive impairments led us to advance the hypothesis that impairment of the caudate-frontal system can disrupt visual attention, visual scanning and/or motor planning leading to memory and construction impairment. Experiments testing this hypothesis need to take into consideration that in depressives, effortful processes are more likely to be impaired than automatic processes.

NR248 Tuesday, May 23, 12 noon-2:00 p.m.

Differential Characteristics of Early Versus Late-Onset Panic Disorder

Javaid I. Sheikh, M.D., Dept Of Psychiatry, Stanford Univ Sch of Med., 300 Pasteur, Stanford CA 94305-5546; Pamela J. Swales, Ph.D.

Summary:

Our group has previously reported that older panic disorder patients, age 55 and above, who have the onset of panic attacks at a late age (age 55 or later), manifest less avoidant behavior compared to same age panic disorder patients whose panic attacks began at a younger age (1). Based on findings in the literature that cognitive appraisal of panic attacks may play a major role in the development of avoidance in panic disorder patients (2), we hypothesized that the late-onset panic disorder (LOPD) patients (onset of panic disorder at or after 55) may also manifest less fearful cognitions during their panic attacks compared to similar age early-onset panic disorder (EOPD) patients (onset of panic disorder before 55). Our sample taken from ongoing treatment studies, consisted of 50 patients, age 55 and above, of which 40 were EOPD patients and 10 were LOPD. All patients were cognitively intact, and the diagnosis of panic disorder was made using the Structured Clinical Interview for Diagnosis based on the DSM-III-R (SCID). At baseline, all patients were administered the Stanford Panic Appraisal Inventory (1) consisting of 20 items with scores ranging from 0-10 on severity of commonly observed fearful cognitions during panic attacks. As hypothesized, LOPD patients showed significantly lower scores on this measure compared to EOPD patients (LOPD: M = 36.20, SD = 24.32 vs. EOPD: M = 82.00, SD = 45.84, $p < 0.005$). The data are consistent with earlier findings of less severe symptomatology in LOPD. Implications of these findings for phenomenological and treatment research will be discussed.

NR249 Tuesday, May 23, 12 noon-2:00 p.m.

Depression Predicts Mortality in Frail Elders

Steven C. Samuels, M.D., Psychiatry, University of PA., 3600 Market Street, Philadelphia PA 19104; Ira R. Katz, M.D., Patricia A. Parmelee, Ph.D., Alice A. Boyce, M.A.

Summary:

Objective: This retrospective study examines the relationships between depression, disability, physical illness, and mortality in the long-term care elderly.

Method: 116 depressed elderly (age 84.23 +/– 5.77; 99.1% white; 81% female; 56.9% nursing home; 43.1% apartments; HAM 18.28 +/– 5.27) were evaluated with the Hamilton (HAM), Montgomery Asberg (MA), Geriatric Depression Scale (GDS), Cumulative Illness Rating Scale (CIRS), and Physical Self Maintenance Scale (PSMS). Factor analyses utilized Principal Components Analyses and Varimax Rotations. Survival analyses utilized Cox proportional hazard models.

Results: HAM correlated with GDS ($r = .596$, $n = 116$, $p < .001$) but not CIRS ($r = .197$, $n = 35$, ns) or PSMS ($r = -.153$, $n = 51$, ns). MA correlated with GDS ($r = .715$, $n = 104$, $P < .001$) but not with CIRS ($r = .325$, $n = 35$, ns) or PSMS ($r = -.025$, $n = 51$, ns). Factor analyses of HAM yielded a four-factor solution (47.2% of the variance): core depression, anxiety, insomnia-hypochondriasis, and cognitive-ideation. MA yielded two factors (54.3% of the variance): core depression and anxiety. All factors except HAM anxiety correlated significantly with GDS; none increased with CIRS or PSMS. The HAM core depression factor (coefficient = .312, SE = .142, $p < .05$), MA total score (coefficient = .044, SE = .018, $p < .05$) and MA core depression factor (coefficient = .474, SE = .145, $p < .05$) predicted mortality. HAM and MA core depression factors remained significantly associated with mortality when controlling for cognition, physical illness, and disability.

Conclusions: The HAM and MA are valid and specific depression measures in the residential care elderly. The HAM and MA core depression factors (but not the other factors) were associated with increased mortality even when controlling for ratings of cognition, physical illness, and disability.

NR250 Tuesday, May 23, 12 noon-2:00 p.m.

Salivary Cortisol and Daily Events in the Aged

Steven C. Samuels, M.D., Psychiatry, University of PA., 3600 Market Street, Philadelphia PA 19104; Patricia M. Furlan, M.A., Ira R. Katz, M.D.

Summary:

Objective: This study sought to determine if measures of cortisol in saliva could represent a noninvasive measure of HPA axis function sensitive to activities of daily living in the nursing home elderly.

Method: Seven male nursing home residents (age 85.79 +/– 9.00) with mild depression (GDS 10.57 +/– 4.44) and moderate cognitive impairment (MMSE 18.49 +/– 8.16) gave salivary cortisol samples before and after an assisted bath, and at corresponding times on the subsequent control day. Subjects were medically stable and had not taken medications that would influence cortisol production for at least three weeks.

Results: Subjects perceived the assisted bath as mild/moderately stressful (2.43 +/– 1.40 on a 1-5 scale; 5 = most). Repeated measures ANOVA of the bath and control days for a timepoint before the bath and four timepoints after the bath did not yield a bath effect ($F = 3.740$, $p = .101$), time effect ($F = .988$, $p = .433$), or bath-time effect ($F = .767$, $p = .557$). Repeated measures ANOVA of the post-bath times on the two study days yielded a strong trend toward a main bath effect ($F = 4.983$, $p = .067$), but no time effect ($F = .788$, $p = .516$), or bath-time interaction ($F = .456$, $p = .408$).

Conclusions: Although repeated measures ANOVA pre- and post-bath did not give a significant effect, repeated measures ANOVA of post bath measures suggest the value of further research in noninvasive measures of the HPA axis. Future research with a larger sample size would decrease the possibility of a type II error. Comparisons should be made between subjects with different degrees of cognitive impairment, depressive symptoms, and disability.

NR251 Tuesday, May 23, 12 noon-2:00 p.m.

Sertraline and Fluoxetine in Geriatric Depression

Robert D. Linden, M.D., Pharmacology Res. Inst., 3505 Long Beach Blvd, Ste 2F, Long Beach CA 90807-1903; Paul A. Newhouse, M.D., K. Ranga Rama Krishnan, M.D., Mildred Farmer, M.D., Burton J. Goldstein, M.D., Lawrence W. Lazarus, M.D.

Summary:

Twelve investigational sites participated in this 12-week, double-blind, parallel-group comparison of sertraline (50-100mg) and fluoxetine (20-40mg). All patients ($n = 235$; mean age 68.5 yrs.), met DSM-III-R criteria for major depressive disorder at baseline. Efficacy evaluations included investigator ratings [the Hamilton Depression Scale (HDS), Montgomery Asberg Depression Rating Scale (MADRS), and Clinical Global Impressions Scales (CGI)], patient self-ratings [Beck Depression Scale (BDI), Profile of Mood States (POMS)], and cognitive tests.

Intent-to-treat analysis indicates that both treatments are effective in the treatment of geriatric depression. Significant differences ($p \leq .05$) in favor of sertraline were seen at week 2 on the HDS ratings, CGI scales (Improvement, Severity and Efficacy Index), as well as on the Montgomery Asberg Depression Rating Scale, and the Beck Depression Inventory. These findings suggest that sertraline may have advantages over fluoxetine early in treatment.

Significant differences ($p \leq .05$) in favor of sertraline were also observed on the number of correct responses on the Digit Symbol test and on the number of items recalled on the Shopping List Task. These findings may reflect improvement of depression affecting performance on these two measures of cognitive function.

NR252 Tuesday, May 23, 12 noon-2:00 p.m.

MRI Signal Hyperintensities in Geriatric Depression

Blaine S. Greenwald, M.D., Psychiatry, Hillside Hospital, 75-59 263 St Lowenstein Res, Glen Oaks NY 11004; Elisse Kramer-Ginsberg, Ph.D., K. Ranga Rama Krishnan, M.D., Manzar Ashtari, Ph.D., Peter M. Aupperle, M.D., Mahendra C. Patel, M.D.

Summary:

Signal hyperintensities on T-2 weighted and proton density (intermediate) magnetic resonance scans have been implicated in geriatric, and particularly late-age onset, depression; however limited studies have employed age-matched normal controls.

Objective: To reliably rate periventricular and subcortical signal hyperintensities on MRI scans in elderly depressives and age-matched normal controls to examine whether such "lesions" 1) discriminate depressed and normal groups and 2) are associated with any clinical variables.

Methods: Elderly DSM-III-R depressives ($n = 48$) and controls ($n = 39$) participated in an MRI study that included T-2 weighted and intermediate MR images of the head. Scans were evaluated in random order by research psychiatrists (KRRK, BSG) blind to diagnosis and trained in the application of hyperintensity rating scales (Fazekas; Boyko) that assess periventricular, deep white matter, and subcortical gray matter regions (interrater reliability = .90).

Results: Elderly depressed patients (mean age +/- SD = 74.6 +/ - 6.1; 33F/15M) manifest significantly more severe hyperintensity ratings in the subcortical gray matter (Boyko criteria) ($p < .05$, than age-matched controls. Deep white matter hyperintensity ratings were significantly higher in subjects with hypertension ($p < .05$). Significant differences were not identified between early- and late-onset depressed patients matched for current age and cerebrovascular disease risk. Logistic regression in both the total and depressed groups revealed that cerebrovascular risk and age significantly predicted severity of deep white matter hyperintensities ($p \leq .02$).

Conclusions: Findings are consistent with prior neuroimaging studies that implicate the basal ganglia in depression and geriatric depression, and demonstrate an association between cerebrovascular risk and subcortical hyperintensities. Data support the conceptualization that subcortical cerebrovascular disease—earmarked by MRI hyperintensities—is associated with or predisposes to depression in at least a subgroup of the elderly. However, it appears that when cerebrovascular risk is controlled, the postulated relationship between late age-at-onset and hyperintensities may be diminished or lost.

NR253 Tuesday, May 23, 12 noon-2:00 p.m.

Survival Time Among Demented Hospice Patients

Patricia Hanrahan, Ph.D., Psychiatry, University of Chicago, 5841 S. Maryland Avenue MC3077, Chicago IL 60637; Daniel J. Luchins, M.D.

Summary:

Alzheimer's disease is the fourth leading cause of death (Katzman, 1976). Family and professional caregivers favor hospice care for the terminal stage of dementia, yet less than 1% of patients enrolled in hospice have a primary diagnosis of dementia (Hanrahan & Luchins, 1995). The major obstacle to hospice care identified in our previous research was the difficulty in predicting survival time. Because of the variable survival time in dementia, it is difficult for these patients to meet a key hospice enrollment criteria: a six-month survival time. We have established and replicated criteria to enroll end-stage dementia patients in hospice which include the characteristics of end-stage dementia and a history of medical complications related to the dementia. Data on 40 patients in two cohorts have been collected from ten hospices over four years. Our enrollment criteria have proven feasible in that the average survival time among the 40 patients was 6.4 months. Within the second cohort, predictors of survival time included impairments in activities of daily living, (R square = .29, $p < .05$), and reduced interest in or ability to eat (R squared = .50, $p < .01$). Data on service costs further support the feasibility of this mode of care; average costs have been well within the Medicare reimbursement limit.

NR254 Tuesday, May 23, 12 noon-2:00 p.m.

ENA 713 in Alzheimer's Disease: Safety and Tolerance

Neal R. Cutler, M.D., Calif. Clinical Trials, 8500 Wilshire Blvd 7th Floor, Beverly Hills CA 90211-3109; John J. Sramek, Pharm.D., Jerome F. Costa, M.D., Ravi Anand, M.D.

Summary:

Objective: To determine the maximum tolerated dose (MTD) of the acetylcholinesterase inhibitor ENA 713 in AD patients.

Method: Fifty AD patients (NINCDS criteria, mean age 67.8) were randomized to receive ENA 713 bid (n = 20), ENA 713 tid (n = 20), or placebo (n = 10) for a nine-week, double-blind dose escalation phase followed by a one-week placebo washout. For the two ENA 713 groups, 2mg/day was given on Days 1-3 and 3mg/day on Days 4-7 followed by daily doses of 4mg, 5mg, 6mg, 7.25mg, 8.5mg, and 10mg for Weeks 2 through 7, respectively, and 12mg/day for Weeks 8 and 9.

Results: Three patients on active drug discontinued due to adverse events. One patient (later found to have a history of atrial arrhythmias) discontinued at 4mg/day (tid regimen) after experiencing atrial fibrillation, and one each at 8.5mg/day (bid regimen) and 12mg/day (tid regimen) discontinued due to nausea and vomiting. Up to 12 mg/day was otherwise well tolerated, with patients experiencing primarily mild to moderate adverse events, including headache, nausea, dizziness, abdominal cramps, and diaphoresis. The total incidence of adverse events between patients treated with ENA 713 versus placebo was similar, but patients treated with ENA 713 tid experienced a significantly higher ($p < 0.05$) incidence of nausea (55%) than did patients on placebo (10%), with no statistically significant difference between the nausea incidence in tid and bid (40%) regimens.

Conclusion: No MTD was defined, but patients tolerated doses 100% higher than those used in a previous Phase II study with minimal effects (6 mg/day; bid regimen), suggesting that ENA 713 can be administered to AD patients in higher doses which may show greater potential for clinical efficacy in AD.

NR255 Tuesday, May 23, 12 noon-2:00 p.m.

A Longitudinal View of Late-Life Onset Depression and Dementia

Angela Pedraza, M.D., Memory Disorder Center, Neuro Institute, 201 East Sample Road, Pompano Beach FL 33064; Jacqueline Valdes, Ph.D.

Summary:

Objective: The longitudinal course of cognitive performance for patients presenting with major depression for the first time in late life was examined.

Method: Six patients with late-onset depression were followed over a three to four year period. As part of their work-up at a memory disorder center, all patients were followed by a neurologist, psychiatrist, and neuropsychologist on a yearly basis. Patients also received yearly neurodiagnostic testing (i.e. MRI, EEG) and blood work. Cognitive performance was evaluated yearly utilizing the Mini Mental State Examination (MMSE) and comprehensive neuropsychological testing.

Results: All patients initially evidenced cognitive impairment on neuropsychological testing. At one-year follow-up, after appropriate pharmacotherapy, patients evidenced improved cognitive performance on both neuropsychological testing and the MMSE. However, one to two years later, increased cognitive impairment was again evident and most patients were diagnosed with a dementing illness. In addition to memory impairment, neuropsychological profile patterns were also less typical of Alzheimer's disease and involved more visual perceptual/constructional impairments and less language based deficits such as anomia. Six case studies are presented.

Conclusions: Results support the postulate that late-life depression in some patients may represent the first symptomology of a dementing disorder, and that initially reversible cognitive impairment may be only temporary.

NR256 Tuesday, May 23, 12 noon-2:00 p.m.

Side Effects of Antidepressants in Very Old Nursing Home Residents

Melinda S. Lantz, M.D., Psychiatry, Jewish Home & Hospital, 120 West 106 Street, New York NY 10025; Eric N. Buchalter, D.O., Vincent Giambanco, R.P.H.

Summary:

Depression and depressive syndromes are common among elderly residents of long-term care facilities. There has been increased attention to the diagnosis and treatment of depression in this population. In addition, antidepressants are increasingly used for syndromes such as chronic pain, anxiety, agitation, and insomnia. While the potential benefits of these agents are great, little is known of the side effects and adverse events associated with antidepressant therapy in the very old. We surveyed all residents of a 514-bed nursing home who were treated with antidepressant agents over a 36-month period (N = 120). Side effect and adverse drug reactions were assessed by retrospective chart review. Parameters reviewed included weight change, and behavioral, cardiovascular, gastrointestinal, hepatic, renal, and hematological effects. Seventy-nine (66%) residents were being treated for depression or a depressive syndrome, while 41 (34%) received antidepressants for alternative indications. Side effects, including adverse events requiring discontinuation of the medication were more common among residents with dementia, who were more likely to suffer weight loss during therapy. In addition, those residents who did not meet criteria for a depressive syndrome appeared more likely to experience side effects. Behavioral side effects, including mood lability, aggression, and psychosis occurred most frequently among those treated with SSRIs.

NR257 Tuesday, May 23, 12 noon-2:00 p.m.

The Meaning of Global Assessment of Functioning Scores in Geropsychiatric Inpatients

Debra L. Karch, Ph.D., Horizon Ment. Hlth Manag., 2220 San Jacinto Blvd Ste 320, Denton TX 76205; William S. Edell, Ph.D.

Summary:

Objective: To examine the meaning of GAF scores in geropsychiatric inpatients.

Method: Inpatients (N = 305) on geropsychiatric units (mean age = 75.8) across 11 med/surg hospitals and informants participated in an outcome measurement study. Instruments administered at a time of admission included the Mini-Mental State Exam (MMSE), Geriatric Depression Rating Scale (patient and informant versions), Philadelphia Center Morale Scale, Health Status Questionnaire, GAF Scale (completed by admitting psychiatrist), and an admission questionnaire measuring demographic characteristics, current functioning, and physical and instrumental activities of daily living (PADL/IADL).

Results: GAF scores were significantly related only to MMSE scores and PADL's. Stepwise multiple regression examining MMSE and PADL subscales as independent variables and GAF score as dependent variable yielded two variables (ability to walk and language functions on MMSE) that accounted for a significant proportion of the variance (22.1%). Mean GAF scores for patients low on both variables, high on one and low on the other, or high on both was 19, 25, and 33, respectively. Level of depression, morale, health status (including role limitations attributed to emotional problems and mental health), and current functioning as rated by informant did not correlate significantly with GAF scores.

Conclusions: Despite explicit instructions on the GAF scale to consider the patient's psychological, social, and occupational functioning and to *not* include impairments in functioning due to physical or environmental limitations, ratings in geropsychiatric patients appear related to the patient's ability to walk and use language.

NR258 Tuesday, May 23, 12 noon-2:00 p.m.

A Scale to Measure Severe Cognitive Impairment

Peter V. Rabins, M.D., Department of Psychiatry, Johns Hopkins Hospital, 600 N Wolfe St, Baltimore MD 21287-7279; Cynthia Steele, M.P.H.

Summary:

An 11-item scale to measure cognitive function in persons with severe cognitive impairment was developed and administered to 42 subjects with dementia and Mini-Mental State Exam (MMSE) <14. The Severe Impairment Rating Scale (SIRS) had two-week re-test reliability of r = .976, p < .0001. Inter-rater reliability for two raters was (r = 992, P < .0001. Chronbach's alpha = 0.76. The SIRS score correlated with both the Glasgow Coma Scale (r = .85, p < .0001) and the MMSE (r = xxx, p < .0001) supporting its validity. A ceiling is present at MMSE score of 5 and a floor effect on the Glasgow Coma scale of 10. The SIRS is a reliable and valid scale to measure function in persons with very severe cognitive impairment.

NR259 Tuesday, May 23, 12 noon-2:00 p.m.

Venlafaxine in Depressives Post-Cerebrovascular Aneurysm or in Hypertension

Ben Zimmer, M.D., Psychiatry, Allegheny General, 320 E. North Avenue, Pittsburgh PA 15212; Mary Brilmyer, R.N.

Summary:

Objective: Because primary care physicians' and psychiatrists' caution regarding the hypertensive potential of venlafaxine may prevent its use as a first-line thymoleptic, especially in patients with anergic depression following CVA, we were anxious to study the efficacy and safety of this agent in post-stroke and/or hypertensive, depressed patients.

Method: An open-label study of all post-stroke or hypertensive, depressed patients who met DSM IV criteria for major depression and who received venlafaxine as part of their treatment in the late life depression clinic of the Allegheny General Hospital and Allegheny Neuropsychiatric Institute. Efficacy was measured by two clinician mutual agreement on the clinician global impression (CGI). Measure and safety was measured by pre- and post-drug clinic vital sign measures.

Results: 18 patients, nine women, $\bar{X}$ age 71.9 and nine men, $\bar{X}$ age 72.3, entered the study. No patients developed sustained hypertension despite a mean 4.5 months of venlafaxine at a mean dose of 125 mg per day. Four of 18 actually showed a decrease in BP. Only 3/18 worsened on CGI measures; one patient showed no improvement. Fourteen on 18 showed good improvement.

Conclusion: Venlafaxine can be used as a first-line thymoleptic even in post-stroke depressives or those with hypertension.

NR260 Tuesday, May 23, 12 noon-2:00 p.m.

Neuropsychological Deficits and P300 Latency in Elderly Non-Demented Depressives

Balkrishna Kalayam, M.D., Department of Psychiatry, NY Hospital-Cornell, Med., 21 Bloomingdale Road, White Plains NY 10605-1504; Gregory G. Brown, Ph.D., Robert C. Young, M.D., George S. Alexopoulos, M.D., Frank E. Musiek, Ph.D.

Summary:

Objective: A subgroup of elderly non-demented depressives have marked slowing in performance of neuropsychological tasks that persist with recovery. P300 latency for event-related potentials is also prolonged in elderly depressives with pseudo-dementia compared to controls. We report preliminary findings in non-demented depressed patients for P300 latency that was increased compared to controls, and associated with decreased performance on tasks of initiation/perseveration (I/P) on the Mattis Dementia Rating Scale (MDRS).

Method & Results: Symptomatic elderly depressives (N = 14; Mini-Mental Score > 24; mean age ± SD = 73.7 yrs ± 7.6 yrs) and controls (N = 10; 71.1 yrs ± 4.9 yrs) were assessed using

the MDRS and P300. Latency for P300 was longer in patients (Mean ± SD = 370.2 ± 44.8 ms) compared to controls (315.6 ± 27.7 ms; $p < .01$; anova). In the patient group P300 latency was negatively correlated with I/P scores on the MDRS ($R = -.688$; $p < .01$). There was no relationship between P300 latency and MDRS scores for attention, memory, construction, and conceptualization. The results were accounted for by endogenous more than sensory components, as the groups had comparable P2 latency and differed in their P2-P3 interval ($p < .01$; anova).

Conclusion: Increased latency for P300 in elderly depressives may be associated with difficulty in I/P. Frontal lobe dysfunction has been implicated in both increased P300 latency and impaired I/P.

(Supported by MH01051)

NR261 Tuesday, May 23, 12 noon-2:00 p.m.

Elderly Attitudes on Being Told the Diagnosis of Alzheimer's Disease as Compared to Terminal Cancer

Suzanne Holroyd, M.D., Blue Ridge Hospital, Drawer D—6 East, Charlottesville VA 22901; Diane Snustad, M.D., Zona Chalifoux

Summary:

Objective: Controversy exists whether all Alzheimer's disease (AD) patients should be told their diagnosis, yet no research has been done examining attitudes of the elderly on this topic.

Method: In this study, 156 elderly persons (mean age = 79.7 years) read vignettes of two patients, one with AD and one with terminal cancer, and then answered questions regarding these illnesses.

Results: The majority (N = 124, 79.5%) responded they would want to know if they had AD, but this was significantly fewer (Fisher exact test, $p = 0.0002$) than those who would want to know if they had terminal cancer (N = 143, 91.7%). Interestingly, among those with spouses, even significantly fewer subjects would want their spouse to be told if the spouse had either illness. For AD, only 65.7% (N = 69) would want their spouse to know (Fisher Exact Test, $p = 0.0083$), whereas for cancer, 80.2% (N = 77) would want their spouse to know ($p = .0006$ Fisher Exact Test). No demographic variables distinguished between subjects who did or did not want to know diagnoses for themselves or their spouses. Reasons some subjects gave for being told the diagnosis included consideration of suicide.

Conclusion: Although these results may support disclosure of diagnosis for most patients with AD, clinical and ethical issues remain in individual cases. Implications for clinicians are discussed.

NR262 Tuesday, May 23, 12 noon-2:00 p.m.

Low-Dose Risperidone for Dementia Related Disturbed Behavior in Nursing Homes

Richard J. Goldberg, M.D., Dept. of Psychiatry, Rhode Island Hospital, 396 Eddy street, Providence RI 02903-4923; Jenna S. Goldberg

Summary:

Many nursing home residents have dementia with behavioral problems. These patients, however, are often unresponsive to or are unable to tolerate the extrapyramidal side effects of standard neuroleptics. Clozapine has greater efficacy in these patients than standard agents, but it has limited use in the elderly because of sedative and anticholinergic side effects and the need for weekly monitoring of white blood cell counts. Risperidone may be better tolerated in the elderly because at low doses it poses little risk of extrapyramidal side effects and has no adverse effect on blood elements. Sixty-four nursing home patients with a primary diagnosis of dementia (55% with Alzheimer's type and 20% with multi-infarct type) were treated with 0.25 mg to 0.5 mg of risperidone twice daily, and after six months their behavior was rated by the nursing staff. According to global ratings of effectiveness, risperidone was very helpful in 41% of the patients, moderately helpful in 26%, slightly helpful in 16%, and not helpful in 17%. The greatest improvements occurred in physical agitation, verbal outbursts, physical aggression, depressed mood, anxiety, abnormal movements, and eating problems. Overall, risperidone was well tolerated and nursing staff viewed it as an effective drug that improved a broad range of behavioral disturbances.

NR263 Tuesday, May 23, 12 noon-2:00 p.m.

Prevalence of Psychiatric Illness in VA Nursing Home Residents

Joel E. Streim, M.D., Psychiatry, Setion Geriatric Psych, 3615 Chestnut St, Philadelphia PA 19104-6006; Ira R. Katz, M.D., Steven I. Chavin, M.D., Patricia A. Parmelee, Ph.D., Andrea R. Tucker, B.A., Suzanne Difilippo, B.A.

Summary:

Objective: The purpose of this study was to determine the prevalence of depression and psychosis in VA nursing home residents with and without dementia.

Methods: We conducted psychiatric evaluations on 159 veterans residing at the 240-bed VA Nursing Home Care Unit (VANHCU) in Philadelphia. Cognitive status was assessed with the Blessed Information-Memory-Concentration test; depression was assessed with the Geriatric Depression Scale; both depressive and psychotic symptoms were identified by a structured interview derived from the Schedule for Affective Disorders and Schizophrenia. For this sample of VANHCU residents, the mean age (SD) was 73.9 (10.87) years; 98.1% were male; 52.2% were African American, 45.9% Caucasian, and 1.8% other races and ethnic backgrounds.

Results: For the total sample, the prevalence of dementia was 61.6%, major depression 17.6%, depressive symptoms 30.8%, and psychotic disorder 4.4%. In comparing the demented to the cognitively intact residents, major depression was present in 16.3% and 19.5%, respectively; other depressive symptoms were found in 5.0% and 26.3%; and psychotic disorders in 4.1% and 4.9%, respectively. 81.1% of VANHCU residents had diagnosable psychiatric disorders, comparable to prevalence rates reported in studies of non-VA nursing homes. However, African American VANHCU residents had a significantly higher prevalence of dementia compared to Caucasians (72.3% vs 47.9%, $p = .0018$) and African Americans with dementia tended to have lower rates of depression than Caucasians with dementia (20.0% vs 25.7%, ns).

Conclusion: These findings suggest the need for further epidemiologic studies to identify subgroups of nursing home residents that may differ in their mental health service needs.

NR264 Tuesday, May 23, 12 noon-2:00 p.m.

A Double-Blind Comparison of Sertraline and Nortriptyline in the Treatment of Depressed Geriatric Outpatients

William J. McEntee III, M.D., Future Hlth Care Res Ctr, 1217 E Avenue South #209, Sarasota FL 34239-2329; David J. Coffey, M.D., William Bondareff, M.D., Murray Alpert, Ph.D., Ashok B. Raj, M.D., Stephen A. Rappaport, M.D., Myron F. Weiner, M.D.

Summary:

Twelve investigational sites in the United States participated in this double-blind, parallel-group study to evaluate the relative

safety and efficacy of sertraline and nortriptyline in the treatment of geriatric depression. Following a one- to two-week placebo washout, patients were randomized to 12 weeks double-blind treatment with either sertraline (50-150mg) or nortriptyline (25-100mg). All patients (n = 204; mean age 68 yrs.), met DSM-III-R criteria for major depressive disorder. Efficacy evaluations included investigator ratings, patient self-ratings, and cognitive tests.

Both sertraline and nortriptyline were effective in treating geriatric depression (intent-to-treat analysis). Hamiltion Depression Scale ratings declined 56% for the sertraline-treated group and 49% for the nortriptyline-treated group, with significantly more patients showing clinically significant response to sertraline than to nortriptyline at week 12 ($p < .05$). Differences between the treatment groups were most evident on measures completed by patients, with sertraline-treated patients reporting significantly ($p \leq .05$) greater improvement in their overall quality of life. On the POMS scale sertraline-treated patients reported significantly ($p \leq .05$) more improvement than nortriptyline-treated patients on five subscales. The sertraline group also exhibited significantly ($p < .05$) greater improvement in their performance on the Digit Symbol and the Shopping List Task.

NR265 Tuesday, May 23, 12 noon-2:00 p.m.

Predictors of Improvement in Cognitive Functioning in Geropsychiatric Inpatients

William S. Edell, Ph.D., Horizon Men Hlth Manage., 2220 San Jacinto Blvd, Ste 320, Denton TX 76205; Debra L. Karch, Ph.D.

Summary:

Objective: To identify predictors of improvement or decline in cognitive functioning in geropsychiatric inpatients.

Method: Changes in Mini-Mental State Exam (MMSE) scores of three or greater from admission to discharge were used to identify inpatients on geropsychiatric units (mean age = 75.8) across 11 med/surg hospitals who significantly improved ($n = 68$) or declined ($n = 30$) in cognitive functioning. Instruments administered included the Geriatric Depression Rating Scale (patient and informant versions), Philadelphia Center Morale Scale, Health Status Questionnaire, GAF Scale (completed by admitting psychiatrist), an admission questionnaire measuring demographic characteristics, current functioning, and physical and instrumental activities of daily living (PADL/IADL), and a medical record form at discharge.

Results: Average change in MMSE score was +4.8 for improvers and −7.6 for decliners. Patients who improved in cognitive functioning were younger (74.8 vs. 79.3) and had greater capacity to do IADL's at admission (e.g., use telephone, handle money, take own medicines). Groups did not differ at admission on total MMSE score (18.4 vs 18.9), GAF score, level of depression, health status (including role limitations attributed to emotional problems and mental health), current functioning as rated by informant, morale, education level, sex, life stressors, PADL's, medications, motivation for treatment, or number of prior hospitalizations. Patients showing improvement at discharge were less likely to be assigned a primary diagnosis of cognitive disorder (25% vs. 53%).

Conclusions: Inpatient treatment may impact negatively on cognitive functioning among very old patients who are largely unable to do IADL's even with some assistance.

NR266 Tuesday, May 23, 12 noon-2:00 p.m.

Hearing Impairment and Psychiatric Illness in the Elderly

Sandhya Panguluri, M.D., Psychiatry, Walter Reuther Hospital, 30901 Palmer, Westland MI 48185; Venkataramana S. Lingam, M.D., Norma C. Josef, M.D.

Summary:

Objective: To study the association between hearing impairment and any particular psychiatric disorder in mentally ill elderly.

Method: One hundred two records of newly admitted patients who had audiometric screening in a state geriatric facility were reviewed. Audiometric screening was done with pure tones and hearing impairment was graded as mild, moderate, severe, and profound. All patients, based on psychiatric diagnosis, were divided into three groups: 1) affective symptoms, 2) psychotic symptoms, and 3) Miscellaneous. Data were analyzed by using regression analysis, chi square, and student's t test.

Results: Forty-two percent were found to be hearing impaired. Hearing impairment was found to have a direct correlation with advanced age. No difference in sex distribution was found. Analysis of the data did not show any statistically significant association of hearing impairment with any particular psychiatric illness.

Conclusions: In this study the incidence of hearing impairment in the mentally ill is comparable with that of the general population. Lack of reliable information regarding sequence of events obscured any possible etiological relationships. Further research into social and psychological problems of the chronically hard of hearing is needed.

NR267 Tuesday, May 23, 12 noon-2:00 p.m.

Risperidone in Geropsychiatry: Review of Experience in Two Teaching Public Hospitals

Stephen M. Aronson, M.D., Psychiatry, Wayne State University, 2350 Londonderry Rd, Ann Arbor MI 48104; Venkataramana S. Lingam, M.D., K.A. Hasanat, M.D.

Summary:

Risperidone is a novel antipsychotic which is increasingly replacing traditional neuroleptics for several indications in psychiatry. Although extensively studied in several clinical settings, it has not been adequately studied in the elderly. Elderly patients pose psychopharmacologic challenges due to poorly-understood pharmacodynamic changes, sensitivity to side effects, and interactions with concomitant medications. Given the inadequacy of treatments for behavioral symptoms in dementia, and the large number of elderly treatment-resistant patients with chronic axis I disorders, there is clear need for more efficacious, less toxic, cost-effective therapies.

We reviewed the records of 20 patients age 65 and over who received risperidone at two public hospitals. We examined psychiatric diagnosis, indications for risperidone, and response to treatment using the Clinical Global Improvement (CGI) scale. Eleven males and nine females were studied. Mean age was 72.11 ± 6.3 years. Diagnoses included organic delusional disorder (7), schizophrenia (6), bipolar (4), MDD with psychotic features (2), and schizoaffective (1). Mean risperidone dose was 3.55 ± 2.1 mg. CGI scores of 19 patients improved on risperidone. Twelve patients were rated as much improved, seven mildly improved, and one no change. Mean CGI change was 1.58 ± 0.6. The drug was well tolerated.

Our findings suggest that risperidone is an effective therapeutic agent in several neuropsychiatric disorders in the elderly. Controlled studies in specific diagnoses in this population are needed to better characterize this agent's potential role in geriatric psychopharmacology.

NR268 Tuesday, May 23, 12 noon-2:00 p.m.

Diagnostic Criteria For Alcohol-Induced Dementia

David M. Smith, M.D., Psychiatry, Portland VA Medical Ctr, 116A-P PO Box 1034, Portland OR 97207; Roland M. Atkinson, M.D.

Summary:

Introduction: Despite studies implicating alcohol as an etiologic factor in 21% to 24% of dementia cases, no clear criterion standard exists for alcohol-induced persisting dementia. Potential diagnostic criteria have not been systematically studied in patients referred to a dementia clinic.

Methods: A research assistant administered standardized assessment instruments for alcohol use disorders and quantity of use to 20 consecutive veterans referred to a dementia clinic and to a control group of 18 non-demented veterans. A psychiatrist blind to the alcohol assessment, administered a coded neurological exam and cognitive screening instruments.

Results: Nine of 20 demented veterans, but only four of 18 in the non-demented cohort had histories of heavy alcohol use defined by at least five drinks/day for at least one year. Alcohol history was rarely documented in the medical charts. Veterans in the dementia cohort with heavy alcohol use were significantly more likely to have gait ataxia, limb ataxia, and polyneuropathy. Boston Naming Test scores were significantly higher for demented veterans with heavy alcohol use compared to other demented veterans.

Conclusion: Alcohol history is often ignored in dementia evaluation. This study provides evidence of potential diagnostic criteria to distinguish alcohol-induced dementia: ataxia, polyneuropathy, and less impairment of naming ability.

NR269 Tuesday, May 23, 12 noon-2:00 p.m.

Psychiatric Components of Failure to Thrive in the Elderly

Ira R. Katz, M.D., Section on Geriatric Psyc, Univ of Pennsylvania, 3600 Market St Rm 810, Philadelphia PA 19104; Patricia A. Parmelee, Ph.D., Alice A. Boyce, M.A., Andrea R. Tucker, B.A., Suzanne Difilippo, B.A.

Summary:

Objective: Failure to thrive in the elderly is an often terminal state characterized by clinical, metabolic, and physiological deterioration.

Methods: To further characterize this state, we investigated the relationship of affective and cognitive symptoms with selected laboratory measures in 157 older subjects (average age (sd) 86.2 (5.6), 64% female, 45% from a nursing home, and 55% from a congregate apartment facility). For purposes of data reduction, we performed a factor analysis with Varimax rotation on 24 routine clinical laboratory measures, and found that a solution with eight factors accounted for 66.5% of variance. Two of the factors were of specific interest: one (14.9% of variance with significant loadings from total protein, cholestesterol, albumin, transferrin, calcium, and triglycerides) was related to protein calorie nutritional (PCN) status; another (10.5% of variance with loadings from sedimentation rate, platelets, alkaline phosphatase, and (–) albumin) was related to acute phase (AP) processes. Patients with depression were characterized by lower factor scores, suggesting subnutrition, on the PCN factor, while those with moderate degrees of cognitive impairment were characterized by higher scores, suggesting a modest activation of acute phase processes, on the AP factor.

Conclusions: These findings are consistent with subnutrition as a cause or effect of depression and with the activation of inflammatory processes in Alzheimer's disease.

NR270 Tuesday, May 23, 12 noon-2:00 p.m.

Alzheimer's Disease Patients Support Groups

Elizabeth G. Fine, M.S.W., Social Work, Mount Sinai Hospital, 1 Gustave Levy Place Box 1230, New York NY 10029; Deborah B. Marin, M.D., Lizette Williams, B.S., Richard C. Mohs, Ph.D., Kenneth L. Davis, M.D.

Summary:

Introduction: People with Alzheimer's disease (AD) may benefit from a support group in the same way as individuals suffering from other terminal illnesses. This study determined the feasibility and outcome of supportive group therapy for patients with mild AD for both patients and their caregivers.

Methods: Eleven AD patients met weekly for 1.5 hours with a social worker for six months. At baseline and at six months group members completed the Mini-Mental Status Exam, Geriatric Depression Scale, Cognitive Failures Questionnaire, and Personal Mastery Scale. Caregivers completed the Memory and Behavior Problems Checklist and Burden Interview. Members and caregivers also completed a satisfaction questionnaire.

Results: Members attended on average 75% of the sessions, with attrition of one individual. Members and caregivers were very satisfied with the group and members reported that the group enabled them to better cope with their illness. Pre and post scores on all scales were not significantly different from one an other.

Conclusions: A support group for mild AD is feasible and highly accepted by its members and their families. The lack of statistical results may reflect measurement limitations and small sample size. Future studies should include a control group, larger sample sizes, and other measures. A program that includes concurrent caregiver and patient support groups may result in more significant findings.

NR271 Tuesday, May 23, 12 noon-2:00 p.m.

Use of Clozapine in Mentally Ill Elderly

Jasveen K. Dhadli, M.D., Psychiatry, Walter Reuther Hospital, 30901 Palmer, Westland MI 48185; Aurelio Ortiz, M.D., Venkataramana S. Lingam, M.D., Norma C. Josef, M.D.

Summary:

Objectives: To review the safety and efficacy of clozapine in mentally ill elderly.

Methods: In this retrospective study 13 subjects on clozapine, in a geriatric facility, were studied. The age range was 61-74 years (two males and 11 females). The duration of illness was 30-46 years. The diagnoses were schizophrenia (9), mood disorder (3) and organic mental disorder (1). The effects of clozapine were evaluated on the following symptoms: delusions, hallucinations, and aggression. Clinical response was judged from progress notes written by treating psychiatrists and nurses.

Results: The length of treatment was one to 38 months. Dosages of clozapine were gradually titrated to the optimum response. The average dose was 450-500 mg/day. Minimal response was found in 15% of patients, mild response in 31%, moderate in 31%, and good response in 23% The most frequent side effects were lethargy (38%), constipation (31%) and seizures (15%). None of the patients had leukopenia.

Conclusions: This retrospective chart review suggests that clozapine is possibly useful in treating the mentally ill elderly. However, elderly may be at greater risk of developing side effects such as lethargy, constipation, and seizures. One observation from this study suggests that the risk of side effects can be minimized by increasing the dose slowly.

NR272 Tuesday, May 23, 12 noon-2:00 p.m.

Personality Dysfunction and Quality of Life in Old Depressives

Robert C. Abrams, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Sandra V. Horowitz, Ph.D., George S. Alexopoulos, M.D.

Summary:

Objective. Health-related quality of life is a broad concept encompassing medical disabilities and satisfaction in living. However, diverse populations may have specific predictors of quality of life. In this study we investigated relationships between personality dysfunction and quality of life in elderly depressives.

Design. Twenty-five cognitively intact men and women aged 63 to 85 who had been treated for major depression were studied. Subjects were evaluated using the Quality of Life subscale of the General Health Questionnaire (GHQ/QL-12), the Hamilton Depression Rating Scale (HDRS), the Cumulative Illness Rating Scale for Geriatrics (CIRS-G), the Social Support subscale of the Multilevel Assessment Inventory (MAI), and the Global Assessment Scale (GAS). Personality assessments included the Personality Disorder Examination (PDE), and the Neuroticism subscale of the Eysenck Personality Inventory (EPI).

Results. Both personality measures, EPI Neuroticism, and the total PDE dimensional score, were inversely correlated with GHQ/QL-12 ($p < .05$), as were scores on the CIRS-G ($p < .02$) and HDRS ($p < .002$). GHQ/QL-12 was positively correlated with GAS ($p < .04$) and social support scores ($p < .005$). Similar results were obtained using multiple regression models.

Conclusion. Dysfunctional personality traits may impact negatively upon quality of life in treated elderly depressives and might be considered with residual depression, medical burden, and social support in predictive models.

NR273 Tuesday, May 23, 12 noon-2:00 p.m.

Personality Disorders and Social Support in Old Depressives

Robert C. Abrams, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Sandra V. Horowitz, Ph.D., George S. Alexopoulos, M.D.

Summary:

Objective. Personality disorders may be risk factors for chronicity in geriatric depression. Mechanisms could involve the failure of individuals with lifetime personality dysfunction to maintain social supports in old age. To this end we investigated relationships among personality disorder symptoms, social support, and residual depression in treated elderly depressives.

Design. Twenty-six cognitively intact men and women aged 63 to 85 who had been treated for major depression were studied. Evaluation included the Cornell Scale for Depression in Dementia (CSDD), the Social Support subscale of the Multilevel Assessment Inventory (MAI), the Neuroticism subscale of the Eysenck Personality Inventory (EPI), and the Personality Disorder Examination (PDE).

Results. An inverse relationship was found between the social support score and: a) neuroticism ($p < .001$); b) the total dimensional score for cluster B personality disorders, including borderline, narcissistic, histrionic, and antisocial ($p < .07$); and c) a measure of residual depression, the CSDD ($p < .01$).

Conclusion. Low levels of social support may be at least independently associated with personality dysfunction and residual mood symptoms in treated elderly depressives. Since impaired interpersonal relationships lie at the core of the personality disorder construct, these individuals may lack the social connections which could contribute to recovery. Personality functioning and social support may both need to be considered in models for chronicity of geriatric depression.

NR274 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Prospective Long-Term Follow-Up Study of Divalproex Treatment of Bipolar Spectrum Illnesses

Frederick M. Jacobsen, M.D., 1301 20th St NW Suite 711, Washington DC 20036-6023; Lillian Comas-Diaz, Ph.D.

Summary:

Objectives: 1) To conduct an open, prospective, longitudinal investigation of low-dose divalproex (VPX) treatment of cyclothymic (CYC) and bipolar II (BP2) patients; 2) to compare these results to treatment responses of bipolar I (BP1) patients.

Method: CYC and BP2 patients began VPX 125-250 mg daily, and doses were increased if mood swings occurred. CGI and four-point mood-stabilizing scales were rated before and three to six months after starting VPX, and blood levels were drawn.

Results: 121 patients took VPX 125-500 mg/day for a mean of 19.6 months and showed a group mean ± SD decrease in CGI ratings from 4.3 ± 0.6 to 2.1 ± 1.0 ($p < 0.001$) and an increase in mood stability. CYC patients ($N = 34$) required lower mean ± SD VPX doses (276.5 ± 115.9 *vs* 382.6 ± 173.8 mg, $p < 0.01$) and blood levels (29.9 ± 13.7 *vs* 38.0 ± 15.1 μg/ml, $p < 0.05$) than BP2 patients ($N = 85$) for stabilization. Twenty-three CYC/BP2 patients complained of the side effects, of whom eight discontinued VPX. In contrast to the mild bipolars, a group of bipolar 1 patients ($N = 22$) needed significantly higher VPX doses (1319.4 ± 623.1 mg) and blood levels (78.4 ± 23.3 gmg/ml)($p < 0.001$) to stabilize.

Conclusions: 1) low-dose divalproex can stabilize mild bipolar illnesses; 2) the data support a previously described relationship between the severity of bipolar illness and the dose of divalproex required for stabilization, such that milder illness may stabilize with lower doses of divalproex (CYC < BP2 < Bipolar I).

NR275 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Severe Affective Illness and Refractory OCD

Frederick M. Jacobsen, M.D., 1301 20th St NW Suite 711, Washington DC 20036-6023

Summary:

Objectives: To determine if risperidone (RIS) can: 1) diminish psychosis, agitation, or rapid cycling in bipolar (BP) and unipolar (UP) illnesses; and 2) to augment pharmacological response in refractory obsessive compulsive disorder (R-OCD).

Methods: 20 outpatients suffering psychosis or agitation associated with DSM-IV BPI, BPII, or UP illness, and five R-OCD patients started open trials of RIS 1.0-1.5 mg/day. Doses were increased to a maximum of 6 mg/day based upon response. Target symptoms, Clinical Global Impressions, and YBOCS scales were given before and one to four weeks after starting RIS.

Results: 17 to 20 affectively ill patients (85%)(13 BP, four UP) showed complete or partial symptomatic improvement following treatment with mean ± SD RIS doses of 3.5 ± 1.9 mg/day. CGI group ratings decreased from 4.7 ± 0.8 to 2.5 ± 1.3 ($p < 0.001$) and benefits included decreases in agitation, psychosis, sleep disturbance, and rapid cycling. Ten patients complained of side effects; four of these discontinued RIS. R-OCD patients showed a mean decrease in YBOCS from 28.0 ± 8.7 to 15.6 ± 7.3 ($p < 0.05$) following the addition of a mean ± SD RIS dose of 3.6 ± 1.3 mg.

Conclusions: Risperidone may be useful in the treatment of psychosis, agitation, and cycling accompanying severe affective illnesses, and in enhancing response in refractory obsessive compulsive disorder.

NR276 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

T3 Suppression Test: A Better Way to Assess Hypothalamus-Pituitary-Thyroid Dysfunction in Depression?

Patricia R. Mourilhe, M.D., Psychobiology, The NY Hospital CUMC, 21 Bloomingdale Road, White Plains NY 10605; Peter E. Stokes, M.D., Chris Huston, Alexandra I. Barsdorf

Summary:

The TRH stimulation test is considered to be the most sensitive dynamic study of the hypothalamus-pituitary-thyroid (HPT) axis function, affected by thyroid hormones, negative feedback, and the central drive. Recently our laboratory has piloted assessment of thyroid axis suppressibility in depressed patients after a single dose of 3,000 mcg of T4. We now present new data of TSH suppressibility with a single dose of 50 mcg of T3. Four depressed patients (2F, 2M) received an oral a.m. dose of 50 mcg T3 after basal TSH, T4, and T3 were obtained. Repeat samples were obtained at 6, 10, 24, 48, and 72 hours post-dose. Seven normals and one patient following recovery (greater than 50% drop of HAM-D) underwent the same procedure. There was a 2.0-3x increase in serum T3 within six to 10 hours post-dose. TSH levels clearly decreased in all instances, achieving maximum suppression of approximately 50% at 24 hours. Recovery occurred within 48 to 72 hours.

The rapid recovery of TSH achieved with T3 suppression offers the advantage of allowing a suppression pattern to be analyzed while the patients are still depressed within the first week of admission. Although normals tended to achieve higher suppression, no significant relationship was found between the magnitude of suppression between the normal and depressive state. Data collection and analysis are continuing.

NR277 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Acute Neuroendocrine Effect of ECT on the HYPAC Axis

Patricia R. Mourilhe, M.D., Psychobiology, The NY Hospital CUMC, 21 Bloomingdale Road, White Plains NY 10605; Peter E. Stokes, M.D., Alexandra I. Barsdorf

Summary:

Previous data from our laboratory have described HPA response to ECT and shown that the hormonal response was inversely proportional to the pre-ECT level of HPA activity. We now examine new data regarding age-related duration of response to ECT. In this study, we want to address in humans the prior data in rats showing disinhibition of HPA activity after stress. This disinhibition appeared to be related to age and excess glucocorticoid-related hippocampal damage (Landfield) and persistent hippocampal glucocorticoid receptor down regulation (the cascade hypothesis [McEwen & Sapolsky]). Twenty-one patients have been studied in the current program. Findings to date reveal a more rapid rate of increase to peak serum cortisol levels post-ECT in patients 50 and older compared with patients younger than 50. Older patients also showed a less complete suppression of HPA activity post-dexamethasone, as evidenced by higher baseline (pre-ECT) cortisol levels than younger patients on DST. Preliminary findings support previous work done in this laboratory showing an inverse relationship between baseline HPA activity and post-ECT peak hormonal response. No significant relationship was found between age and duration of hormonal response post-ECT. Data collection and analysis are continuing.

NR278 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Efficacy of Sertraline for Treatment of Premenstrual Dysphoric Disorder

Kimberly A. Yonkers, M.D., Department of Psychiatry, UT Southwestern Med. Ctr., 5959 Harry Hines Boulevard, Dallas TX 75235-9101; Uriel Halbreich, M.D., Ellen W. Freeman, M.D., C.S. Brown, M.D., Teri B. Pearlstein, M.D.

Summary:

Objective: Studies of the psychobiology of premenstrual dysphoric disorder (PDD), a severe form of premenstrual syndrome, show abnormalities in markers of serotonergic transmission. Thus, agents that inhibit the reuptake of serotonin are likely to be effective for PDD. In this multicenter study, the serotonin reuptake inhibitor, sertraline, was compared to placebo in a double-blind, placebo-controlled, parallel design.

Method: Subjects were recruited from 12 academic centers. Women between the ages of 24-45 with regular menstrual cycles were eligible. All subjects met DSM-IV criteria for PDD and showed at least a 75% increase in at least five symptoms during the luteal compared with the follicular phase of the cycle. Concurrent psychiatric diagnoses were ruled out by SCID. After at least two cycles of baseline daily ratings to confirm the diagnosis, subjects were given placebo on a single-blind basis. Nonresponders were then randomized to either sertraline or placebo for three menstrual cycles. Evaluations were conducted during each premenstrual phase using the CGI and HRS-D and daily ratings. In addition, assessments were made of quality of life (Q-les-Q) and social adjustment (SAS-SR).

Results: 184 women were included in this preliminary completer analysis. A total of 68.4% of women on sertraline were treatment responders (CGI-I of 1 or 2) compared with 39.5% of women given placebo ($p < .01$).

NR279 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Are Post-Stroke Depressive Symptoms Frequently Non-Specific for Depression During the First Two Years After Stroke?

Tatsunobu Ohkubo, M.D., Psychiatry, University of Iowa, 200 Hawkins #2887 JPP, Iowa City IA 52242; Robert G. Robinson, M.D.

Summary:

Although depressive symptoms are common in patients with acute stroke, the diagnosis of depression may be complicated by the presence of somatic symptoms that are secondary to a medical illness. We have previously demonstrated that both somatic and psychological depressive symptoms in acute stroke were more frequent in patients with depressed mood than in patients without mood disturbance (Fedoroff et al., 1991). In the present study, we examined the longitudinal course of depressive symptoms in 139 patients who had follow-up evaluations at 3, 6, 12, or 24 months following acute stroke. The psychiatric examination included the Hamilton Rating Scale for Depression and a structured interview using the Present State Examination (PSE). Symptoms that were specific for depression (i.e., significantly more frequent in patients with depressed than nondepressed mood) varied with time following stroke. Diurnal mood variation, loss of energy, poor concentration, loss of interest, and hopelessness were significantly more frequent in depressed patients throughout the 24-month follow-up. In contrast, the frequency of number of vegatative symptoms such as early morning awakening and loss of libido, decreased eating, and symptoms related to self-attitude such as guilt feelings and suicidal thoughts were no longer significantly more common in depressed than in nondepressed patients after six months. These findings suggest dynamic changes in the clinical presentation of post-stroke depression, perhaps reflecting changes in the mechanism of these depressions over time.

NR280 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Sustained Antidepressant Effect of Phenylethylamine Replacement

Hector C. Sabelli, M.D., Psychiatry, Rush Pres. St. Luke's, 1725 W. Harrison Suite 744, Chicago IL 60612; Peter M. Fink, M.D., Jan A. Fawcett, M.D., Cynthia C. Tom, B.S.

Summary:

Phenylethylamine (PEA) is a neurohormone that maintains energy, attention, and mood. Short-term studies indicate that oral PEA rapidly relieves depression in 60% of major depressive episodes pretreated with low doses of selegiline to inhibit selectively MAO B, not requiring a low tyramine diet. We treated 14 women and 12 men who had major depressive disorder (N = 8) or bipolar disorder (N = 9) with selegiline (10 mg/day) plus PEA (5 to 60 mg per day according to clinical response). Eighteen subjects responded successfully to PEA treatment within days of onset. The antidepressant response to PEA had been maintained in 12 patients for 20 to 50 weeks; effective dosage did not change with time. There were no apparent side effects of euphoria.

In conclusion, PEA relieves depression in a sustained manner in a significant number of patients, including some unresponsive to the standard treatments. As the PEA metabolite phenylacetic acid is reduced in CSF, plasma, and urine in 60% of depressed subjects [Sandler et al *Clin Chim Acta* 1979;93:169-171; Sabelli et al *J Clin Psychiatry* 1986;47:66-70; Gonzalez-Sastre et al, *Acta Psych. Scand.* 1988;78:208-210], it is possible that PEA deficit may be the cause of a common form of depressive illness, and that PEA administration may represent a physiological treatment of depression, i.e. the replacement of the deficient chemical, much as insulin is used to treat diabetes.

NR281 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Antidepressant Response in Depressed Patients with Anxiety

James M. Russell, M.D., Dept of Psych, Univ of Texas Med Branch, 301 University Blvd. Rt D28, Galveston TX 77555-0428; Larry Koran, M.D., James P. McCullough, Ph.D., Daniel N. Klein, Ph.D., George A. Trapp, M.D.

Summary:

In a 12-week, double-blind, multicenter study comparing sertraline and imipramine in 638 chronic and double depressed individuals, these medications were effective in more than 60% of completed patients. More than half of these subjects had significant comorbid anxiety. This paper examines the effect of antidepressant treatment on these comorbid anxiety symptoms. All subjects were initially interviewed using a SCID-P and met diagnostic criteria for chronic major or double depression. Comorbid anxiety symptoms were determined with the SCID-P GAD rating at baseline and HAM-D anxiety scales at baseline, weeks 2,4,6,8,10 and 12. In preliminary analyses of 82 patients from one site, including 72 completers and 46 responders, the overall response rate and drop-out rate were not affected by the presence of comorbid anxiety symptoms. Subjects with comorbid anxiety symptoms took longer to respond (6.8 weeks) than subjects without comorbid anxiety (4.4 weeks). Therefore, it is important to treat depressed individuals with comorbid anxiety symptoms aggressively and to recognize that these patients may take longer to respond to antidepressant medications. An analysis of 638 study subjects will be performed to test these preliminary findings and examine response differences between imipramine and sertraline.

NR282 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Improvement in Winter Depression is Associated with a Phase Advance in the Dim Light Melatonin Onset

Katherine H. Thomas, M.D., Psychiatry, Oregon Hlth Sci. Univ., 3181 SW Sam Jackson Park Road, Portland OR 97201; Alfred J. Lewy, M.D., Robert L. Sack, M.D., Vance K. Bauer, M.A.

Summary:

Bright artificial light has been shown to be efficacious in treating winter depression. However, there is less consensus on the importance of the timing of light exposure. The phase-shift hypothesis of winter depression states that individuals with winter depression experience a phase delay in their internal circadian rhythms during the winter. According to this hypothesis, morning should be the most effective time to use light therapy, since this is the time when light would cause a phase advance in circadian rhythms.

To test this hypothesis, 41 patients with winter depression were studied over the course of four winters. Subjects were exposed to two weeks of morning light and two weeks of evening light, with a week of no light in between the two treatments. The order of light treatment was randomized among subjects. At baseline and at the end of each week of the study, severity of depression and circadian phase (by means of the endogenous melatonin rhythm) was assessed. In support of the phase-shift hypothesis, morning light treatment was more antidepressant than evening light treatment, and the response to morning light was associated with a significant advance in circadian phase.

NR283 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Prepubertal Suicidality and Parental Psychopathology

Ronald A. Weller, M.D., Ohio State University Hos, Dept of Psychiatry, 473 West 12th Avenue, Columbus OH 43210-1252; Parul Kapadia, M.D., Elizabeth B. Weller, M.D., Mary A. Fristad, Ph.D., Sheldon H. Preskorn, M.D.

Summary:

This study assessed suicidal behavior in hospitalized depressed children and determined its relationship to parental suicidal behavior and psychopathology. Subjects were 58 prepubertal children aged 5-13 consecutively hospitalized with diagnosis of major depressive disorder (MDD); 58 psychiatrically ill but not depressed children admitted to the same unit during the same time period and matched for age and sex served as a comparison group. Charts were reviewed to determine suicidal behavior in children and psychopathology in the parents. Data available for review included structured Diagnostic Interview for Children and Adolescents (DICA), Psychiatric Diagnostic Interview (PDI), physician admission and discharge notes, and social service notes including family history.

All levels of suicidal behavior were more frequent in MDD children. Suicide attempts were increased in the mothers (17% vs 10%) and fathers (10% vs 6%) of MDD children, but these differences were not statistically significant. Depressed children (n = 49) and comparison children (n = 26) with suicidal behavior were compared as to parental psychopathology. Almost all parents in both groups had some psychopathology. When specific diagnoses were compared, mothers of MDD children had significantly more MDD (60% vs 26%) and anxiety disorders (25% vs 4%) than mothers of comparison children. Although suicidal behavior was increased in the children with MDD vs. psychiatrically ill comparison children, suicide attempt rates did not differ significantly in their parents. Failure to find a difference may be due to the low ascertainment rate for suicide attempts in parents and/or the small sample sizes. Because of sample size it was not possible to determine whether suicidality in the child was specifically associated with increased psychopathology in the parents of MDD children. However, preliminary analysis did not indicate a difference between these two groups.

NR284 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Lithium Plus Desipramine Versus Desipramine Alone in the Treatment of Major Depression: A Controlled Study

Lawrence H. Price, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Angela C. Cappiello, M.D., Christopher J. McDougle, M.D., Robert T. Malison, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

Summary:

The efficacy of lithium augmentation is well documented in tricyclic-refractory depression. It has been hypothesized that enhanced presynaptic serotonin (5-HT) function after short-term lithium interacts with the sensitization of postsynaptic 5-HT receptors after long-term tricyclic use. To determine whether other mechanisms are involved, we evaluated the rapidity and magnitude of improvement of depressed patients given lithium with desipramine from the start of treatment, rather than after completion of a full course of desipramine.

Methods: 29 patients with DSM-III-R major depression were randomized to double-blind, placebo-controlled treatment with either desipramine+placebo or desipramine+lithium for four weeks. Treatment response was based on HAM-D scores and CGI global improvement.

Results: ANOVAs of the HAM-D scores demonstrated that desipramine+lithium was superior to desipramine+placebo at week 1 ($p < .005$), week 2 ($p < .007$), week 3 ($p < .027$), and week 4 ($p < .093$).

Conclusions: These data suggest that desipramine+lithium has a more rapid onset of action and slightly greater efficacy than desipramine alone. The mechanism of action of lithium-tricyclic treatment might be independent of the increased sensitivity of 5-HT neurons caused by chronic administration of tricyclic.

NR285 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Alpha-1-Acid Glycoprotein and Age in Major Depression

Robert C. Young, M.D., Westchester Division, Ny Hosp-Cornell Med Ctr, 21 Bloomingdale Road, White Plains NY 10605-1504; Ashok Patel, M.D., J.P. Bocksberger, M.D., Leonard Fensterheim, M.P.H.

Summary:

Serum alpha-1-acid glycoprotein (AAG) increases with age in the normal population, especially in women. Increase in AAG in symptomatic major depressives compared with controls has been reported. We therefore examined AAG values in major depressives and hypothesized increased values with age.

Methods: Inpatients who met DSM-III-R criteria for major depression and were in stable physical health were studied. Serum AAG was determined by rate nephelometry.

Results: Twenty-four patients were studied (age: mean 58.9 yrs ± S.D. 22.0 yrs; F/M:16/8). AAG was positively associated with age ($r_s = 0.45$; $p < .05$), particularly in females ($r_s = .59$; $p < .05$). Patients with recurrent episodes ($n = 17$) had higher AAG (78.0 mg/dl ± 29.5 mg/dl) than those with single episodes (49.6 mg/dl ± 14.6 mg/dl), taking age differences into account ($F = 5.36$; $p < .05$).

Discussion: Further investigation of relationships between AAG, age and, illness course in major depression is warranted. AAG binds psychotropic drugs and may contribute to pharmacokinetic sources of interindividual differences in treatment response. AAG m-RNA is present centrally, and a role for AAG as an endogenous ligand for tritiated imipramine binding sites has also been proposed. MH 40726

NR286 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Mania

Mauricio Tohen, M.D., Department of Psychiatry, Mclean Hospital, 115 Mill Street, Belmont MA 02178-1048; Carlos A. Zarate, Jr., M.D., Franca Centorrino, M.D., James D. Hegarty, M.D., Michael Froeschl, B.S., Silvina M. Zarate, B.S.

Summary:

Twelve patients with acute psychotic mania were treated with risperidone (2-6 mg/day) in a six-week trial. The patients, nine women and three men, with a mean age of 41 years, had a diagnosis of acute bipolar mania with psychotic features (SCID-P). Their mean baseline score was 80 on the 27-item modified Brief Psychiatric Rating Scale (BPRS) and 34 on the Young Rating Scale for Mania (YRSM). Nine patients completed three weeks of treatment, and seven patients completed six weeks. The reasons for discontinuation were refusal to continue in one patient, noncompliance in one, side effects (sedation, headaches, lethargy) in one, and failure to respond in two. At endpoint (last observation carried forward analysis), on the BPRS, seven patients showed a 50% decrease in scores and 12 patients a 25% reduction ($p < 0.01$); on the YRSM, nine patients showed a 75% reduction in scores and 10 patients had a 50% reduction ($p < 0.01$). Risperidone was well-tolerated and the status of no patient worsened during the trial. We conclude that risperidone is an effective and safe agent in the treatment of acute psychotic mania.

NR287 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Increased CSF Neural Cell Adhesion Molecule in Patients with Bipolar and Unipolar Mood Disorder

Macicj Poltorak, M.D., Neuropsychiatry, NIMH Bldg 10 Room 3N212, Bethesda MD 20892; Renee Wright, B.A., Mark A. Frye, M.D., Mark S. George, M.D., Peggy J. Pazzaglia, M.D., Robert M. Post, M.D., J.J. Hemperly, Ph.D., Shari Jerrels, B.A., William Freed, Ph.D.

Summary:

Neural cell adhesion molecule (N-CAM) is involved in cell-cell interactions during synaptogenesis, morphogenesis, and plasticity of the nervous system and may be a marker of brain remodeling or repair. In the central nervous system (CNS), N-CAM is composed of three polypeptides of 180, 140, and 120 kD MW. The 120 kD band is the most prominent component in CSF. Disturbances in synaptic restructuring and neural plasticity may be related to the pathogenesis of several neuropsychiatric disorders, including bipolar mood disorder and schizophrenia. Using the Western blot technique, we have recently found an increase in N-CAM in the CSF of patients with schizophrenia (Poltorak et al., 1994). We have, therefore, measured N-CAM in the CSF of mood disorder patients ($n = 36$: 16 bipolar I, 12 bipolar II, and eight unipolar depression) and normal controls ($n = 13$). There was a significant increase in N-CAM immunoreactive proteins, primarily the 120 kD band in the CSF of bipolar I patients and unipolar patients compared with normal controls ($p < 0.05$). Interestingly, CSF N-CAM significantly decreased as subjects were more depressed on the day of lumbar puncture ($r^2 = 0.4$, $p < 0.05$). Our results suggest the possibility of disturbances in N-CAM cellular function or abnormal N-CAM turnover in the CNS of mood-disordered patients.

NR288 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

The Ability of Ictal EEG Ratings to Detect Changes in ECT Relative Stimulus Dose in the Clinical Setting

Andrew D. Krystal, M.D., Dept of Psychiatry, Duke Univ Med Ctr, Box #3309 RM 54216 Red Zone, Durham NC 27710; C.

Edward Coffey, M.D., Richard D. Weiner, M.D., Tracy Holsinger, M.D., Thomas E. Sibert, M.D.

Summary:

ECT's therapeutic effectiveness appears to depend on the degree to which the stimulus intensity exceeds the seizure threshold (Dose). Unfortunately, maintaining a desired Dose clinically is confounded by a variable rise in seizure threshold that occurs over the treatment course. Recent evidence suggests that an algorithm based on ictal EEG data may be helpful in this regard. Ictal EEG indices have been found to differentiate ECT treatments on the basis of Dose in several research protocols but have not yet been tested for detecting the changes in Dose that occur clinically. As a result, we performed manual ictal EEG ratings for 50 clinically referred ECT patients with major depression who received ECT according to our standard clinical protocol, except that seizure threshold was determined both at treatment 1 and 6 to detect rises in seizure threshold (lowering of Dose). We found that a multivariate model of manual ictal EEG indices was a significant predictor of rise in seizure threshold ($p < 0.004$). Significant relationships to therapeutic response were also found. These results provide strong evidence that ictal EEG indices have significant potential as clinically applicable markers of ECT Dose.

NR289 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Improvements in Work and Social Disability in Depressed Patients Taking Bupropion Sustained Release

Josephine A. Mauskopf, Ph.D., Economics Research, Burroughs Wellcome, 3030 Cornwallis Road, Res. Triangle Park NC 27709; George P. Simeon, M.P.H., Jonathan R.T. Davidson, M.D., Ron Westlund, M.S.

Summary:

Objective: To measure the impact of depression and its treatment on patients' work and social disability.

Method: The Work and Social Disability Scale (WSDS), a five-category, investigator-rated scale was rated by psychiatrists at baseline and study termination in an eight-week, open, uncontrolled study evaluating the safety of a sustained release (SR) formulation of bupropion in 3,167 patients at 110 sites. To be included in the study, patients had to be 18 years or older, have a diagnosis of depression, and be considered appropriate for treatment with bupropion. The proportion of patients in each WSDS category was assessed at screen and termination. The percentage of patients improved at eight weeks was also measured.

Results: Of the patients entering the trial, 62.1 percent were markedly or severely impaired in their work or social activities, and only 5.5 percent were mildly or not impaired. After eight weeks of bupropion treatment, only 24.1 percent were markedly or severely impaired, and 47.1 percent were mildly or not impaired. In addition, 60.5 percent of patients had less disability at the end of the trial than at study entry.

Conclusions: The results show that depression results in significant functional impairment, particularly in the ability to work. This result, based on direct measurement, is consistent with the high published estimates of the indirect costs of depression based on secondary data. Functional status improved in patients treated with bupropion SR for eight weeks.

NR290 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Cognition and Psychosensory Features in Mood Disorders

Nutan Atre-Vaidya, M.D., Psychiatry, FUHS/The Chicago Med Ctr, 3333 Green Bay Road, North Chicago IL 60064; Michael A. Taylor, M.D., Michael Seidenberg, Ph.D., Alicia Perrine, B.S.

Summary:

Objective: Thirty percent to 50% of bipolar mood disorder patients are chronic, many have impairments in learning and memory, and about 30% have psychosensory features that may reflect temporolimbic sensitization. The relationship of cognitive deficits and psychosensory features as possible clinical markers of sensitization, and a potential underlying process of chronicity in bipolar patients has not been studied. The purpose of this study was to assess the relationship.

Method: We evaluated 23 bipolar mood disorder patients for the presence of psychosensory features using the Profile of Psychomotor Symptoms. We assessed psychopathology using screening and follow-up questions based on the SADS-L, SANS, and SAPS. We did cognitive assessments blind to psychiatric assessment, and tested: 1) general intelligence and language, 2) verbal and visual memory, and 3) visuospatial functioning.

Results: Bipolar patients showed significant impairment (1-2 standard deviation) compared to age-equivalent norms in verbal memory and learning. Cognitive deficits, especially memory, were significantly associated with psychosensory features and anhedonia, but not other psychopathology. The more psychosensory the features, the worse on all cognitive measures. In a multiple stepwise regression analysis, anhedonia and psychosensory features emerged as significant predictors of memory.

Conclusion: In bipolar patients, there is a relationship between psychosensory features and cognitive deficits that is independent of other psychopathology. These findings suggest that the pathophysiologic process responsible for cognitive deficits may also be expressed in psychosensory features.

NR291 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Tryptophan Depletion in Bupropion or Placebo Responders

Pedro L. Delgado, M.D., Dept of Pysch, Univ of Arizona Sch of Me, 1501 N Campbell Ave, Tucson AZ 85724; Louise J. Strayer, R.N., Karen Bachar, B.A., Rebecca L. Potter, M.D., Alan J. Gelenberg, M.D., Francisco A. Moreno, M.D.

Summary:

Brain serotonin (5-HT) 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 responding to and maintained on 5-HT reuptake inhibitors (SSRIs), but little change in those on desipramine or in drug-free symptomatic depressed patients (Delgado et al., 1990, 1991, 1994). This study investigates the response to TRP depletion in bupropion- or placebo-responders.

Method: In an ongoing study, 50 patients with major depression (DSM-IV) are randomized to double-blind treatment with placebo or bupropion (300-450 mg/day) over four to 10 weeks. Patients meeting response criteria for two weeks (50% decrease from baseline in the 25-item Hamilton Depression rating scale (Ham-D) with total ≤ 15) are depleted. Testing involves two two-day tests one week apart in a double-blind, controlled (full strength and quarter strength drink) crossover fashion. Each test includes a TRP-free, 15 amino acid drink day and a follow-up day. Patients and clinicians remain blinded as to medication status throughout testing. Behavioral ratings (Ham-D) and plasma (TRP levels) are obtained prior to, during and after testing. Depressive relapse is defined as a $\geq 50\%$ increase in Ham-D with total score ≥ 18.

Results: Data from the first eight treatment responders (bupropion N = 4 and placebo N = 4) shows that 1/4 bupropion-responders had a depressive relapse during TRP depletion while 3/4 placebo-responders relapsed. None relapsed during control testing. All patients who relapsed regained their improved status within 24 hours of testing.

Implications: Depressed patients who respond to placebo may be more vulnerable to alterations in 5-HT function than those on bupropion. In the context of prior TRP depletion studies in SSRI-treated and drug-free, symptomatic depressed patients, these results suggest that depression may not be caused by an abnormality of 5-HT function, but rather by dysfunction of other systems or brain regions modulated by 5-HT.

NR292 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Unilateral ECT Is As Effective As Bilateral ECT in Delusional Depression

Leon J. Grunhaus, M.D., Dept of Psychiatry, Sheba Hosp, Sheba Medical Center, Ramat Gan 52621, Israel; Atul C. Pande, M.D., Shmuel Hirschmann, M.D.

Summary:

It is still unclear whether a preferred treatment for major depressive disorder (MDD) with delusional features exists. In some clinical settings a combination of antidepressant and neuroleptic medications is selected, while in others, electroconvulsive therapy (ECT) is the treatment of choice. Bilateral ECT, reportedly the more effective treatment modality, has not been prospectively compared to unilateral ECT in the treatment of delusional MDD. This study reports on such a prospective and randomized comparison.

We found unilateral and bilateral electrode placement to be equally effective modalities for the treatment of MDD with delusional features. Forty-two patients (mean age 63.9) meeting the DSM-III-R criteria for MDD were included in the study. To be included patients were required to have a 17-item Hamilton Rating Score for Depression (HRSD) ≥ 18. Twenty-one patients met the additional criteria for MDD with delusional features. Patients were referred for ECT by their respective clinicians and underwent a thorough physical and laboratory examination pre-ECT. Patients in each category were allocated to either unilateral or bilateral ECT according to a randomization table. Treatment groups were stratified further according to the presence of delusions. All patients signed a consent for participation in research. ECT was performed according to the guidelines of the APA. Seizure threshold was measured during the first, fourth, and seventh ECT treatment. The electrical dose was fixed to stimulate patients with an electrical dose 150% over threshold. Eighty-eight percent of patients responded to the ECT course.

There were no differences in the rates of response between unilateral and bilateral groups for the whole sample or the groups stratified according to the presence of psychosis. We conclude that no difference in the rates of response between unilateral and bilateral treatements could be identified. The implications of these findings to clinical practice will be discussed.

NR293 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Attentional Disorders in Major Depressive Disorder: Result of a Comparative Study Using Computerized Tests

Jean-Georges Rohmer, M.D., Psychiatry, CHRU, 1 Place De L'Hopital, Strasbourg-Cedex 67091, France; Blandine Kastler, M.D., Michel Patris, M.D.

Summary:

It is generally acknowledged that patients suffering from major depression present various degrees of attention disorders.

Computerized tests, elaborated in our unit, are aimed at evaluating quantitatively various attention modalities (attention centered of one sensorial modality divided attention, selective attention and attention disturbance induced by various perturbers).

In this study, we tried to determine the attentional disorders in patients (15 cases) fulfilling the DSM-III-R criteria for major depressive disorder compared to normal subjects matched for age, sex, and study level. The first part of this study consisted of testing the drug-free patients recognized as depressed (MARS score > 25). Secondly, these subjects were evaluated again one month later under antidepressive treatment and after clinical recovery.

Our data showed globally low levels of the scores obtained by the depressed patient before treatment in all the tests. The mean reaction times were particularly increased, but the number of errors observed were similar to those of the healthy volunteers. These results can be explained as an adaptative strategy used by the patients in order to avoid errors.

In the second part of the experiment, the recovered patients have globally increased their performance. However, some attentional disorders seem to remain; the patients are still disturbed by aleatory stimuli and disynchronized information even with a good clinical recovery (Mean Madrs score < 5 and feeling by the patient of being well, not depressed).

From this we conclude that our tests are sensitive, and that standardized data collection allows studies of the cognitive tasks without bias due to nonstandardized stimuli.

The results obtained by the depressed patient still showed some deficits indicating a potential subclinical attentional vulnerability. If we compared these results to our preceding study concerning schizophrenic patients we can emphazize that the attentional disorders between these two pathologies are different.

NR294 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Double-Blind, Placebo Controlled Study of Light Therapy for SAD

Virginia A. Wesson, M.D., Hamilton Psych Hospital, 100 West 5th Street, Hamilton Ontario L8L 2B3, Canada; Anthony J. Levitt, M.D., Russell T. Joffe, M.D., Eleanor F. King, R.N.

Summary:

Objectives: Patterns of response to light box and head-mounted units (HMU) in SAD appear to differ. The current study employed a "no light" condition to compare response rates to the light box and the HMU against a plausible placebo.

Method: Forty-three subjects with major depression, seasonal subtype, were randomly assigned, in a double-blind manner, to receive two weeks of active light box (n = 9) or HMU (n = 12), or two weeks of placebo light box (n = 12) or placebo HMU (n = 10). The placebos emitted *no* visible light.

Results: Using ANOVA for repeated measures with change in total score on the 25-item HAM-D as the dependent measure, there was no significant main effect of light ($F = 0.20$, p = ns) or unit ($F = 0.50$, p = ns), and no interaction ($F = 0.21$, p = ns). Defining response as a 50% reduction in both the 17-item "typical" and eight-item "atypical" HAM-D scores, there was no significant difference in response rates between the four cells (Likelihood ratio $X^2 = 2.1$, df 4, p = ns), between patients receiving light (48%) vs. no light (41%; $X^2 = 0.2$, p = ns), between patients receiving the light box (38%) vs. the HMU (50%; $X^2 = 0.62$, p = ns).

Conclusions: The failure to detect any significant difference in efficacy between active and placebo treatments calls into question the specificity of light in light therapy for SAD. Methodological limitations, particularly small sample size, are discussed.

NR295 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

HPA Reactivity to Stress in Depressed Adolescents

Carrie M. Borchardt, M.D., University of Minnesota, Box 95 UMHC, 420 Delaware Street SE, Minneapolis MN 55455-0374; Amy Perwien, B.A., Gail A. Bernstein, M.D.

Summary:

Objective: This study examines whether depressed adolescents differ from normals in their hypothalamic-pituitary-adrenal reactivity to a blood draw stressor.

Method: Subjects were 16 medication-free adolescents with major depression (MD), anxiety disorder, and school refusal, and 16 matched normal controls. Subjects completed a structured interview as well as depression and anxiety ratings. Saliva samples for cortisol were collected immediately preceding, 30 minutes after, and 24 hours after the blood draw. All blood draws occurred between 3 p.m. and 4 p.m. to control for diurnal variation.

Results: Analysis of variance was used to examine the effect of group and time of sampling on cortisol levels. Analysis conducted on the control group only showed there was no effect of time of sampling on cortisol levels. Analysis conducted on the depressed group only showed there was a time effect on cortisol levels, with the baseline sample (24 hours later) being significantly higher than cortisols obtained around the time of the stressor ($F = 7.92$, d.f. = 2, $p = 0.002$). Analysis of variance conducted on the complete model examined effects of group ($F = 2.40$, d.f. = 1, $p = 0.132$), time ($F = 7.76$, d.f. = 2, $p = 0.001$), and group-time interaction ($F = 2.65$, d.f. = 2, $p = 0.079$).

Conclusions: Adolescents with MD and anxiety disorders suppressed cortisol around the time of the blood draw stressor.

NR296 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Mood, Motor and Cognitive Variability of Depression

Stephen K. Brannan, M.D., Psychiatry, UTHSCSA, 7703 Floyd Curl Drive, San Antonio TX 78284; Mahurin K. Rodrick, Ph.D., Janet L. Tekell, M.D., J. Arturo Silva, M.D., Helen S. Mayberg, M.D.

Summary:

Major depressive disorder impairs cognitive and motor functions, in addition to producing dysphoric mood, suggesting involvement of discrete but functionally interconnected limbic, paralimbic, and neocortical circuits. Expression of these clinical features is variable. Whether this variability is helpful in addressing treatment response has not been fully explored. Pretreatment regional cerebral glucose metabolism (via resting FDG PET scan), mood ratings (anxiety and depression), motor speed assessment, and a cognitive battery were performed in 25 nondemented (MMSE > 27 in all) hospitalized patients meeting DSM-III-R criteria for major depressive disorder. Patients were also classified by their six-week clinical response (as responder or treatment resistant).

All pretreatment measures differed significantly from a group of nondepressed controls. Motor and cognitive deficits were not related to depression severity. Slowed motor speed, however, did discriminate treatment-resistant patients from responders. Cognitive performance was more variable. The relationship of this clinical heterogeneity to regional metabolic changes in anterior cingulate, dorsal prefrontal, and ventral frontal cortex will be discussed.

This work supported in part by grants from NARSAD and Eli Lilly and Company.

NR297 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Relations of Personality to Depressive Subtypes

John B. Jolly, Psy.D., Psy/Cou, Missippi College, 200 S. Capitol Street, Clinton MS 39058; David C. Weisner, Ph.D., Thomas A.M. Kramer, M.D.

Summary:

Objective: This study examined the cognitive/personality model of Sociotropy (SOC) and Autonomy (AUT) (Beck, 1983) and the affect/personality model of Positive Affect (PA) and Negative Affect (NA) (Watson & Clark, 1984), and their relationships to two proposed depression subtypes (Beck, 1983).

Method: Eighty-four psychiatric inpatient adolescents completed a randomized packet of self-report measures that included the Personal Style Inventory II (PSI II), a modified Inventory for Clinical Features (M-ICF), the Positive and Negative Affect Scales-Expanded (PANAS-X) with trait instructions, and the Reynolds Adolescent Depression Scale (RADS).

Results: PA was significantly related (inversely) to AUT but not SOC scores, while NA was positively and nonspecifically related to both SOC and AUT scores. SOC was more strongly related to Sociotropic depressive symptoms (SOCCOM) than Autonomous depressive symptoms (AUTCOM), while AUT was more strongly related to AUTCOM than SOCCOM symptoms. PA was significantly related (inversely) to AUTCOM symptoms, while NA was significantly positively related to both SOCCOM and AUTCOM symptoms.

Conclusions: Findings support both personality models and their relationships to depressive subtypes. NA is nonspecifically related to depression, while PA differentiates subtypes of depression. AUTCOM depressive symptoms appear more depression-specific than SOCCOM symptoms.

NR298 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Seasonality of Admissions in Depressed Smokers

Dale A. D'Mello, M.D., Psychiatry St. Lawrence H, Michigan State University, 1210 W. Saagin AW, Lansing MI 48915; Charles Flanagan

Summary:

The influence of seasons on mood has been recognized since antiquity. A review of 611 consecutive admissions to a general hospital psychiatric unit in mid-Michigan examined the influence of cigarette smoking and psychiatric diagnosis upon the seasonal variation of admissions.

Among the smokers, admissions for depressive disorder (n = 151) peaked in the springtime. There was no appreciable seasonal variation in the rate of hospitalization among nonsmokers or among smokers in other diagnostic groups. These findings parallel previous reports regarding the influence of seasons upon admissions, symptom severity, clinical response, and suicide. The association between major depressive disorder and nicotine dependence will be explored. Possible therapeutic implications of comorbid depression and nicotine dependence will be presented.

NR299 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Dissociation and Major Depression

Alexis A. Giese, M.D., Psychiatry, University of Colorado, 4455 E. 12th Avenue Box A01115, Denver CO 80220; Steven L. Dubovsky, M.D., Marshall R. Thomas, M.D., Melissa Riemer, M.D.

Summary:

Dissociation occurs in a broad spectrum of psychiatric conditions; however, its significance in the presence of other disorders, particularly mood disorders, is unknown. We studied dissociation in 80 inpatients using the Dissociative Experiences Scale (DES) to determine if it is related to severity of depression (Hamilton Depression Scale), severity of psychosis (BPRS thought disorder subscale), or child abuse history. The subjects met criteria for major depression (nonpsychotic or psychotic) or schizophrenia.

Dissociative symptoms were common in depressed inpatients, but the mean DES was below reported means for dissociative disorders (mean DES = 26.0, SD = 21.5 vs. 36.1, SD = 10.1). Multiple regression analysis of the total cohort revealed that the DES correlates positively with Ham-D, psychosis score, and child-

hood sexual abuse. In the affective subgroup, the most significant predictors of the DES were sexual abuse history and Ham-D (adjusted $r^2 = 0.24$, $F = 16.3$, $p = 0.0002$ and adjusted $r^2 = 0.30$, $F = 11.1$, $p = 0.0001$, respectively); psychosis severity did not correlate with DES.

The results suggest that dissociative symptoms are common in depression and correlate with severity of depression and sexual abuse history, but not with psychosis. Further research is needed to address whether dissociative symptoms in the context of major depression represent a separable disorder or are part of the phenomenology of depression, especially for those abused in childhood.

NR300 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Physical and Sexual Abuse in Psychiatric Inpatients with a Diagnosis of Dysthymia

Shobhana B. Vora, M.D., Psychiatry, UMDNJ, 150 Bergen Street, Newark NJ 07103; Theresa M. Miskimen, M.D.

Summary:

Objective: Our clinical impression has been that there is an increased incidence of abuse in dysthymic patients. We hypothesize that past abuse may lead to dysthymia. Reports of abuse were compared between dysthymia and major depression.

Methods: This is a retrospective chart review of all patients admitted to the psychiatric inpatient unit of a university hospital with diagnosis of dysthymia (50 charts) or major depression (57 charts) from March 1991 to August 1994, excluding borderline personality disorder/traits.

Results: There were no significant differences among the two groups in race or gender, but there were significant differences in age. The dysthymia group was younger (N = 50: mean = 31.4 ± 10.152/N = 57: mean = 40.2 ± 15.959; P = 0.0008, t = –3.46). The dysthymia group reported a higher incidence of physical ($x^2 = 12.6$, P = 0.0001, df = 1) and sexual ($x^2 = 31.2$, P = 0.0001, df = 1) abuse but not verbal abuse ($x^2 = 3.0$, P = 0.083, df = 1). Multiple regression analysis to control for age revealed that the findings were not age dependent.

Conclusions: The results of this study highlight the need to address physical and sexual abuse issues, particularly with patients with a diagnosis of dysthymia. Possible explanations for the differences within the two groups will be discussed.

NR301 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Mini-Mental State Examination and Depression

Jonathan E. Alpert, M.D., Psychopharmacology, MA General Hosp WACC 815, 1500 Parkman Street Ste 815, Boston MA 02114; Lisa A. Uebelacker, B.A., Nancy E. McLean, B.A., Melissa Abraham, B.A., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Objective: The Mini-Mental State Examination (MMSE) is one of the principal methods for brief clinical assessment of cognitive status. Among depressed, elderly inpatients recent studies suggest an inverse relationship between MMSE scores and both depression severity and treatment response. We wished to examine the relevance of the MMSE in nonelderly outpatients with major depressive disorder (MDD).

Methods: The MMSE was administered to 148 outpatients (aged 18 to 65 years) who met DSM-III-R criteria for MDD on the SCID with pretreatment HAM-D-17 of ≥16. Subjects were then treated openly with fluoxetine 20 mg/day for eight weeks. MMSE scores were also obtained on 75 of these patients following treatment. Antidepressant response was defined as a sustained HAM-D-17 score of ≤7. Data were evaluated non-parametrically.

Results: Pretreatment MMSE scores did not correlate with depression severity or predict fluoxetine response and did not distinguish between patients who reported impaired concentration and those who did not. Subjects ≥50 years had lower baseline scores than younger patients, and men had lower posttreatment scores than women. Although statistically significant, these differences were of small magnitude.

Conclusions: While the MMSE allows for rapid assessment of mental status among neuropsychiatric patients, it does not appear to be a sensitive indicator of depression severity, concentration impairment, or likelihood of treatment response among otherwise healthy outpatients with major depression.

NR302 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

The Scope of Family Burden in Bipolar Affective Disorder: A Preliminary Report

Deborah A. Perlick, Ph.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; John F. Clarkin, Ph.D., Joanne Sirey, Ph.D., Lawrence H. Rockland, M.D., Elizabeth Pike, M.Ed.

Summary:

Objective: This study aims to determine the scope, correlates, and long-term impact of family burden on outcome in bipolar disorder. This is the first report of Time 1 data from an ongoing longitudinal study.

Method: Subjects were the primary caregivers of 109 patients consecutively admitted to psychiatric inpatient or outpatient services with RDC-diagnosed bipolar affective disorder. Caregivers were administered Platt et al's (1987) semi-structured interview assessing family burden regarding: 1) patient problematic behaviors, 2) patient role performance, 3) adverse effects on others. Patient clinical characteristics were assessed on the SADS.

Results: 92% of caregivers reported they were somewhat or greatly distressed in at least one of the three burden domains, 70% reported distress in two or more, and 44% reported distress in all three areas. To our knowledge this is a higher frequency of burden than has previously been reported among the family caregivers of the mentally ill. Chi square analysis showed greater burden among the caregivers of patients with current depressive vs. manic or no episodes ($p < .04$). Caregivers living in the same household as the patient and who were unmarried reported higher distress (p's < .04) in one or more domains.

Conclusions: Results demonstrate that caregiver burden is widely prevalent among family caregivers of bipolar patients. Additional work is needed to identify patient and family characteristics contributing to caregiver burden in bipolar disorder.

NR303 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A New Estimate of Gi Activity in Depression

John J. Mooney, M.D., Psychiatry, Harvard Medical School, 74 Fenwood Road Mass Men Hlth, Boston MA 02115; Jacqueline Samson, Ph.D., Nancy L. McHale, B.S., Jonathan E. Alpert, M.D., Martha A. Koutsos, M.D., Joseph J. Schildkraut, M.D.

Summary:

Objective: To present a new method estimating tonic inhibition of adenylate cyclase (AC) by the inhibitory G-protein Gi in depression.

Method: Basal AC activities and postreceptor-mediated AC activities—stimulated by guanine nucleotides (GTPγS) and aluminum fluoride (AlF_4)—were compared in mononuclear leukocytes (ML) and platelets (PL) from the same blood specimens obtained from depressed patients (N = 24) and controls (N = 19).

Results: Basal and postreceptor-mediated measures of AC activity were significantly greater ($p < .001$) in ML than in PL in

all subjects. In controls, differences between GTPγS or ALF_4-stimulated AC activities in ML and PL (i.e., values in ML minus values in PL) showed significant ($p < .05$) negative correlations with prostaglandin (PG)-stimulated AC activities and positive correlations with the ratio of PG-stimulated AC activities over basal AC activities ("fold-increase") in PL. These findings, in controls, resemble those of Cerione, et al. (1985) who examined the effects of Gi on hormonal stimulation of AC using purified components of the AC enzyme complex. Findings in depressed patients will be presented.

Conclusions: Since AC in ML is regulated by the stimulatory G-protein Gs but not by Gi, whereas AC in PL is regulated by both Gs and Gi, our procedure for subtracting values of postreceptor-mediated AC activities in PL from those in ML may offer a new method for estimating tonic inhibition of PL AC by Gi in depressive disorders.

NR304 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Family Experience of Stigma in Bipolar Disorder

Joanne Sirey, Ph.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Deborah A. Perlick, Ph.D., John F. Clarkin, Ph.D., Elizabeth Pike, M.Ed.

Summary:

Objective: Recent work with caregivers of individuals with mental illness found differences between spousal and parental caregivers on measures of expressed emotion and burden (Miklowitz et al., in press). The present study will be the first study to investigate stigma towards patients and stigma towards families in caregivers of patients with bipolar affective disorder.

Methods: 109 caregivers of individuals with RDC-diagnosed bipolar affective disorder and admitted to an acute psychiatric inpatient service were interviewed about their experience of the illness. They were administered a 15-item measure of stigma (Link et al, 1989). The associations between mean global scores and caregiver demographic characteristics were evaluated using ANOVAs. Perceived stigma levels were compared for patients with different bipolar diagnostic subgroups using t-tests.

Results/Conclusion: Caregivers perceive high levels of stigma towards both their family member patients and themselves. When caregivers were compared, spouses reported significantly more stigma towards families than parents or others family, $F(2,86) = 4.10$, $p = .02$. Differences between spouses and parents ratings were significant, Scheffe F-test = 3.52, $p = .05$. These differences reflect the role differences and suggest further exploration of caregiver experience and its impact on patient services use is necessary.

NR305 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Problem Awareness and Treatment Readiness in Dual Diagnoses Patients

Ihsan M. Salloum, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213; Howard B. Moss, M.D., Dennis Daley, M.S.W., Levent Kirisci, Ph.D., Musa Al-Maalouf, M.D.

Summary:

Problem awareness and treatment readiness are factors that may significantly contribute to the clinical course and outcome for dually diagnosed patients. The aim of the present study is to elucidate any differential patterns of problem awareness and treatment readiness among hospitalized patients with comorbid psychiatric and substance use disorders.

The Problem Awareness and Readiness for Treatment subscales of the Alcohol Use Inventory was administered to dually diagnosed inpatients (n = 67; males = 40; females = 27). A multivariate model approach to data analysis was employed. A significant interaction of voluntary admission status (VAS) x major depression disorder (MDD) x ethnicity was observed for the Problem Awareness factor ($p < .05$). African-American voluntary patients without MDD scored the highest. Similarly, there was a significant interaction of VAS x gender on Problem Awareness ($p < .05$) such that voluntary female patients scored highest. Two orthogonal Treatment Readiness factors were isolated. For the Anticipated Cure factor, significant interactions of VAS x MDD x ethnicity ($p < .05$) were found such that voluntary African-American patients independent of MDD scored highest. Also, a significant interaction of VAS x gender ($p < .001$) was found, with involuntary females scoring highest. For the Commitment to Treatment factor, only a significant effect of gender ($p < .05$) was found such that females scored higher than males.

These results suggest that demographics, administrative status, and psychopathology can affect both problem awareness and treatment readiness, thereby impacting upon clinical course and outcome.

NR306 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Sinus Bradycardia at Therapeutic Lithium Levels

Mary Joseph, M.D., Psychiatry, McGuire VAMC 116A, 1201 Broad Rock Blvd, Richmond VA 23249; Victor Vieweg, M.D., Antony Joseph, M.D.

Summary:

We present three new cases of patients with mood disorders taking lithium in therapeutic doses. Each subject developed sinus node dysfunction manifested primarily as sinus bradycardia (50 & below). We combine our three cases with 13 others from the literature to define the study population. Our findings, conclusions, and recommendations form the body of this report.

When bradycardia develops and/or patients develop cardiovascular symptoms or signs, we recommend cardiologic consultation and consideration of Holter monitor recording. Psychiatrists treating patients with lithium should have a low threshold to seek cardiologic evaluation when questions about lithium's effect on the cardiovascular system arise.

NR307 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Negative Symptoms in Patients with Depression and Pseudodementia

Igor I. Galynker, M.D., 46 Valley Ln, Chappaqua NY 10514; Teusink Paul, M.D., Burcescu Silviu, M.D.

Summary:

Objective: We recently reported that patients with dementia of the Alzheimer's type (DAT) manifest negative symptoms that correlate with the severity of cognitive impairment. This ongoing study evaluated whether negative symptoms are present in patients with depression and reversible dementia and the relationship between negative symptoms, cognitive impairment, and symptoms of depression.

Method: 13 patients with a DSM-IV diagnosis of major depression admitted to a geriatric psychiatry unit were evaluated for cognitive performance, depression, and positive and negative psychotic symptoms. Two groups of patients, with and without reversible dementia, were compared.

Results: There were no differences between the two groups on measures of depression. Nondemented patients scored significantly higher on the Mini-Mental Status Exam than those who were demented ($p < 0.0001$). Demented patients also showed significantly greater impairment on the Purdue pegboard task performed with the nondominant hand ($p < .05$) and with both hands ($p < 0.01$). The only significant finding in terms of negative symp-

toms was a higher SANS global score on the attention subscale ($p < 0.05$) for demented patients. However, this score is largely based on the number of errors occurring during mental status testing; thus, this finding may reflect differences in cognitive functioning between groups. In contrast to previous research on patients with (DAT), there were no significant correlations between measures of depressive symptoms, negative symptoms, and cognitive impairment.

Conclusion: These results suggest that pseudodementia of depression is clinically distinct from DAT.

NR308 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Risk Factors for Depression in Americans

Alec Roy, M.D., Psychiatry, New Jersey Medical School, 185 South Orange Avenue, Newark NJ 07103; Veronika Solt, M.D., John A. Williams, M.D., S. Hassan, M.D., Matthew J. Pitera, M.D.

Summary:

Objective: To assess risk factors predisposing to depression and recent life events in depressed American patients.

Methods: Forty depressed patients meeting DSM-III-R criteria for a major depressive episode were compared with 40 normal controls. Risk factors for depression were assessed and recent life events recorded.

Results: Before the onset of depression, significantly more of the depressed patients than controls had a poor marriage and were unemployed. The depressed patients had also experienced significantly more life events in the six months before the onset of depression. Among the depressed patients there was an interaction between life events and employment status; employed depressed patients had significantly more life events before the onset of depression than unemployed depressed patients.

Conclusion: Being unemployed and having a poor marriage before the onset of depression, and experiencing excess life events, are risk factors for depression in Americans.

NR309 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

The Use of Depression Rating Scales in Women with Postpartum Depression

Zachary N. Stowe, M.D., Department of Psychiatry, Emory University, P.O. Box AF, Atlanta GA 30322; Jacque C. Landry, B.A., Maryfrances R. Porter, Charles B. Nemeroff, M.D.

Summary:

Approximately 10% of postpartum women will experience a depressive episode during the first postpartum year. The debate continues as to whether or not these entities are unique syndromes. The addition of the modifier, 'postpartum onset' (onset within four weeks postpartum) to the DSM-IV may reduce the time of onset confound in earlier studies. The impact of DSM-IV criteria on clinician and self-report depression rating scales in postpartum women was studied.

All participants met DSM-III-R criteria for major depression, had symptom onset within six months postpartum, had not received treatment for the current episode of depression, and consented to the study. Seventy-one women completed the self-rated Beck Depression Inventory (BDI) and the Edinburgh Postnatal Depression Scale (EPDS) and were then interviewed by a psychiatrist (ZNS) who completed the Structured Interview Guide for Hamilton Depression Rating Scale (SIGH-D) blind to the self-rated measures. Subjects were divided by: 1) time of onset - PPD (<4 weeks) and MDE (>4 weeks and <6 months); and 2) index of recurrent episode of major depression.

Women with PPD had significantly higher ($p < 0.05$) total scores on self-report measures (BDI = 27 ± 8; EPDS = 21 ± 4; n = 41) compared with women with MDE (BDI = 22 ± 8; EPDS = 19 ± 3; n = 30). Similarly, women with PPD showed significant differences on individual rating scale items (guilt, anxiety) and were the only group in which the SIGH-D did not significantly correlate with the EPDS. Postpartum women experiencing a recurrent episode of depression (n = 27) endorsed more anhedonia, worthlessness, hypochondriasis, and guilt on self-rated measures.

These data underscore the potential unique clinical profile of early onset (<4 weeks) postpartum depression. The issue of index versus recurrent episode of depression warrants further study.

NR310 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Efficacy of Sertraline and Imipramine in Dysthymia

Maurizio Fava, M.D., Psychopharmacology Clinic, Mass Gen Hosp Bldg ACC815, 15 Parkman Street Ste 815, Boston MA 02114; James H. Kocsis, M.D., Richard C. Shelton, M.D., Lorrin M. Koran, M.D., Marc Hertzman, M.D.

Summary:

Background: There has been little systematic study of treatment for "pure dysthymia" (i.e. dysthymia without superimposed concomitant major depression) despite the prevalence of this disorder and the associated morbidity and functional impairment.

Objective: We wanted to conduct a large, multicenter, double-blind, placebo-controlled study of antidepressant therapy for "pure dysthymia."

Method: A total of 416 outpatients with DSM-III-R early onset, primary dysthymia of at least five years duration and no concurrent major depression were randomly assigned to treatment with sertraline (n = 136), imipramine (n = 140), or placebo (n = 140) for a 12-week initial treatment phase. The criterion for treatment response was a post-treatment CGI ≤ 2, but more stringent criteria were required for remission, i.e. a HAM-D ≤ 4 and a HAM-D item #1 score of 0 and no longer meeting criteria for dysthymia at the end of the study.

Results: Results of preliminary analyses revealed that both sertraline and imipramine were significantly more effective than placebo ($p < .05$) with no significant difference in efficacy between sertraline and imipramine. Sertraline was also superior to placebo for full remission. There were significantly more adverse events and more discontinuations for adverse events ($p < .003$) in the imipramine-treated patients compared with sertraline.

Conclusions: Both sertraline and imipramine may be effective treatments for patients with pure dysthymia, and sertraline seems to be tolerated better than imipramine. This is of clinical relevance since patients with milder forms of depression may be less likely to accept unpleasant side effects.

NR311 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Retention for Affective Material in Depression

Avraham Calev, Ph.D., Psychiatry, SUNY at Stony Brook, Health Sci. Ctr. T10 020, Stony Brook NY 11794

Summary:

It is widely accepted that depressives focus on negative memories and forget or repress positive memories (showing a mood-congruent affective tendency). Normals have an opposite positive bias in memory ("Pollyanna tendency"). Research evidence for depressives' negative bias in memory comes mainly from studies of retrieval of personal experiences during depression, or from studies of such retrieval during induced mood. In the present study, the hypothesis that depressives encode and remember negative emotion materials better than other materials was tested.

Contrary to the hypothesis, the results showed that severely depressed patients remembered more positive affect than negative affect words after a two-day delay. Depressives' overall mem-

ory performance and rate of forgetting were poor, similar to schizophrenics, and worse than normals. The results suggest that while memory performance during a depressive episode is poor, the memory consolidation process for affective information is normal. This conclusion is not incongruent with the finding that depressives show mood-congruent retrieval for previously learned personal (experiential) information.

NR312 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Survey of Prescribing Practices of Neuroleptics in the Maintenance Treatment of Bipolar Disorder

Helene Verdoux, M.D., Psychiatry, University Bordeaux, 121 Rue De La Bechade, Bordeaux Cedex 33076, France; Bruno Gonzales, M.D., Marc L. Bourgeois, M.D.

Summary:

Objective: The aim of the study was to examine patterns of prescribing neuroleptics in the maintenance treatment of bipolar (BP) outpatients, and the clinical and sociodemographical correlates of this prescription.

Method: A survey was mailed to all psychiatrists (n = 147) practicing in the public hospitals of Aquitaine region (Southwest France). They were asked to anonymously provide information on consecutive BP I outpatients they personally followed up.

Results: Psychiatrists who responded (29%) to the survey were representative of the total sample. Data were collected on 222 BP I outpatients: 67.6% received at least one neuroleptic (high-potency: 47.3%; low-potency: 35.1%; depot-neuroleptic:17.1%) Only 13.5% received lithium and/or anticonvulsants alone.

Presence of psychotic features, early age at onset, and low educational level were strong significant predictors of high-potency neuroleptic use. Psychiatrists rated 40% of patients treated with these drugs as refractory to lithium and/or anticonvulsants. Delay since last hospitalization was not associated with neuroleptic use.

Conclusions: Although a large percentage of BP patients receive at least one neuroleptic in their maintenance therapy, literature on this topic is scarce. It seems necessary to better assess the benefit-to-risk ratio of neuroleptics in the maintenance therapy of refractory BP disorders.

NR313 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Differential Prefrontal Rapid Transcranial Magnetic Stimulation in Depression: Preliminary Observations

Mark S. George, M.D., Bldg 10 Room 3N212, NIMH, 10 Center Drive, Bethesda MD 20892-0001; Eric S. Wassermann, M.D., Wendol A. Williams, M.D., Timothy A. Kimbrell, M.D., Peggy J. Pazzaglia, M.D., Ann M. Callahan, M.D., Mark A. Frye, M.D., Terence A. Ketter, M.D., Michael Hallett, M.D., Robert M. Post, M.D.

Summary:

Background: Transcranial magnetic stimulation (TMS) is a new technology where one can noninvasively place an electromagnet on the scalp and, by rapidly turning it on and off, stimulate underlying cortical neurons. In healthy controls, prefrontal rTMS on the left induces sadness and on the right happiness over the course of the day. Our group and others have been interested in whether this new technology might acutely or chronically affect mood in clinically depressed inpatients.

Methods: We are using rTMS in an initial acute exploratory and later in a chronic treatment mode. In five clinically depressed inpatients we administered rTMS on five consecutive mornings, varying the location each day randomly over either the right or left prefrontal cortex (each side twice in each subject) or the occipital cortex. Blinded (to region) nurses gathered 17-item Hamilton depression ratings in the morning immediately before and the evening following rTMS, which were compared to evaluate the acute effect of rTMS of different regions on depression symptoms. Apparent acute responders were given daily rTMS over the region associated with improvement.

Results: Preliminary findings suggest that left prefrontal cortex rTMS may be more effective than right prefrontal or occipital cortex stimulation in depressed patients. Depressed subjects tended to rate the rTMS as more painful than normal volunteers and several reported a mild headache.

Conclusions: These results suggest possible differential lateralized prefrontal regulation of mood in normal volunteers and depressed subjects. rTMS is a promising tool for noninvasively probing the neural substrates of emotion and addressing whether nonconvulsive stimulation can be applied as a treatment.

NR314 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Double-Blind Comparison of Fluoxetine, Bupropion and Placebo in Premenstrual Dysphoric Disorder

Teri B. Pearlstein, M.D., Butler Hospital, 345 Blackstone Blvd., Providence RI 02906; Andrea B. Stone, M.D., Sally A. Lund, M.D., Harriet Scheft, M.D., Caron Zlotnick, Ph.D., Walter A. Brown, M.D.

Summary:

Background: Three double-blind trials have reported efficacy of fluoxetine in women with premenstrual dysphoric disorder (PMDD). Nonserotonergic antidepressants have not been compared to serotonergic antidepressants or placebo in this disorder.

Method: Thirty-two women with PMDD were treated with single-blind placebo for one cycle and then randomly assigned to fluoxetine 20mg daily (n = 10), bupropion 300mg daily (n = 12), or placebo (n = 10), for two menstrual cycles. CGI, HAM-D, and GAS ratings were obtained premenstrually each of the three cycles.

Results: The three treatment groups differed significantly by CGI ratings at the end of treatment ($X^2 = 14.93$, $p < .001$). Fluoxetine was superior to placebo ($X^2 = 10.21$, $p < .001$) and bupropion ($X^2 = 7.79$, $p < .005$). ANCOVAs, using HAM-D and GAS as baseline covariates, demonstrated significant differences between the treatment groups at the end of treatment for HAM-D ($F = 4.99$, $p = .01$) and GAS ($F = 4.61$, $p = .02$) scores. Duncan tests demonstrated that fluoxetine was significantly superior to placebo by end-of-treatment HAM-D scores (mean 15 vs. mean 29, $p < .05$) and GAS scores (mean 72 vs. mean 58, $p < .05$). Mean HAM-D (23) and GAS (63) scores for bupropion were intermediate between, but not significantly different from, fluoxetine or placebo.

Conclusion: These results suggest that fluoxetine is superior to a nonserotonergic antidepressant in the treatment of PMDD.

NR315 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Survey of Gynecologic and Endocrine Abnormalities Among Women with Psychosis

Cassandra Morabito, Ph.D., Psychotic Disorders, McLean Hospital, 115 Mill Street, Belmont MA 02178; Mary H. Collins, M.D., Lisa S. Weinstock, M.D., Alexandra Levin, Mauricio Tohen, M.D.

Summary:

Clinical experience with chronically psychotic women indicates that many have gynecologic and endocrinologic abnormalities. Irregularities are manifested by hirsutism, irregular menstrual cycles, premenstrual symptoms, acne, and thyroid dysfunction. Current research is investigating the hormonal influence on affective and psychiatric symptoms. This generates the question of whether there is a comorbid gynecological problem among women with psychosis.

This prevalence was investigated by interviewing women with schizophrenia, schizoaffective, and bipolar disorder, mixed with psychotic features, who were admitted to McLean Hospital with a psychotic episode. A structured gynecologic-obstetric questionnaire was used, adapted from the University of Pennsylvania Gynecologic and Obstetric History Form and The Premenstrual Form.

Analysis of the answers to the questionnaire produced the following findings: menstrual cycles are irregular in length and duration of flow; severe cramps, premenstrual affective, and physical symptoms are common; and subjects reported premenstrual syndrome and menstrual symptoms in first-degree female relatives.

Implications of these findings and those from other studies are outlined. The authors argue that, along with medical history, social history etc., a menstrual history should be part of the psychiatric interview.

NR316 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Internal Consistency of DSM-III-R Personality Disorder Clusters in Middle and Late Adolescence

Daniel F. Becker, M.D., Menninger-SFBA, Mills-Peninsula Hospitals, 1783 El Camino Real, Burlingame CA 94010; Carlos M. Grilo, Ph.D., Martha L. Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Method: Subjects were 118 adolescents assessed with the Personality Disorder Examination at admission to the Yale Psychiatric Institute (mean age 15.7 years). Sixty-five of these subjects were independently reassessed with the same interview about three years later (mean age 18.8 years). Assessments were reliable (average kappa = .84). Internal consistency of the clusters was determined by Cronbach's alpha.

Results: At initial evaluation, internal consistency was adequate for Clusters B and C (with alphas .86 and .78, respectively), but not for Cluster A (alpha = .61). Three years later alphas were acceptable (.79-.86) for all three clusters.

Conclusions: The personality disorder construct has uncertain validity in adolescence. One possible indicator of construct validity of a syndrome is the internal consistency of its component symptoms. In middle and late adolescence, Clusters B and C show adequate internal consistency. Cluster A shows poor construct consistency during middle adolescence—although by late adolescence, these symptoms appear to coalesce to form an internally consistent syndrome.

NR317 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Neurological and Psychological Factors in BPD

Godehard Oepen, M.D., Psychiatry, Bedford Hosp. VAMC, 200 Springs Road, Bedford MA 01730; Catherine R. Kimble, M.D., Elizabeth F. Weinberg, M.D., Amy A. Williams, B.S., Mary C. Zanarini, Ed.D.

Summary:

We present preliminary data from an ongoing study aiming to shed light on both organic and psychological (trauma) variables in BPD, as part of Zanarini's McLean Study of Adult Development (MSAD). Forty female inpatients meeting DIB-R and DSM-III-R criteria for BPD, and 17 patients meeting criteria for another axis II disorder (OPD) were studied with a battery of structured interviews to gather information about childhood experiences and neurodevelopmental history. All also underwent a standardized neurological exam.

In logistic regression analysis, *early* organic factors ("prenatal drug exposure" p = .04; "childhood speech & language disorder" p = .02) significantly predicted a diagnosis of BPD, but the presence of neurological soft signs did not. A composite variable "vulnerable CNS substrate" was twice as frequent in BPD (87.5%) than in OPD (41.2%). There were high rates of abuse and neglect in both BPD and OPD patients, without significant differences in chi-square and regression tests. Significance and possible interaction of organic and psychological variables are discussed.

NR318 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Group Behavioral Therapy of OCD

Joseph A. Himle, M.S.W., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor MI 48109-0840; Randolph M. Nesse, M.D., Kathleen Krone, M.S.

Summary:

Previous research has demonstrated that individualized behavioral exposure and response prevention therapy is an effective treatment of obsessive compulsive disorder. In our prior preliminary report, seven-week group exposure and response prevention therapy was also found effective in reducing obsessions and compulsions. The present paper reports on a larger sample (n = 98) of treatment-seeking obsessive compulsives who received group behavioral therapy. As before, group exposure and response prevention significantly improved ratings of obsessions, compulsions, and depression. These improvements were maintained at three-month follow-up. Longer-term follow-up measures are also presented for some participants. In addition, a subsample of patients were given a longer course of treatment (12 weeks), which was not found to significantly enhance outcomes at the end of the group or at follow-up. These results confirm the efficacy of a seven-week behavioral treatment program administered in a group format.

NR319 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Relationships Between Personality and Neuropsychological Performance

Allen Y. Tien, M.D., Dept of Mental Hygiene Jo, Hopkins Sch of Public Hlt, 624 North Broadway, Baltimore MD 21205-1999; William Eaton, Ph.D.

Summary:

The biomedical model of mental disorders has focussed on "biological" measures of brain structure and function, sometimes in a reductionistic manner, but more comprehensive biopsychosocial models suggest greater complexity. Organic Unity Theory provides another perspective, stating that all mental processes and phenomena have physical correlates, although the reverse is not necessarily the case. In our work on studying relationships between schizophrenia and "spectrum" abnormalities, pilot data from 38 subjects showed relationships between normal personality domains and neuropsychological and attentional performance, and schizophrenia spectrum traits. Current data from 358 subjects in the 12-year follow up of the Baltimore Epidemiologic Catchment Area Survey sample include structured clinical assessment by psychiatrists using the WHO Schedules for Clinical Assessment in Neuropsychiatry (SCAN) with supplementary items for Axis II assessment, neuropsychological assessment using the Wisconsin Card Sorting Test (WCST), Continuous Performance Test (CPT), and other tests, and normal personality assessment using the NEO. A subsample is undergoing further assessment of oculomotor and attentional function as well as MRI measurement.

Factor analysis of the data shows interesting relationships between normal personality domains, especially the Openness to Experience domain, and WCST and CPT performance. One implication of these results is that cognitive and perhaps neurophysiologic abilities may underlie personality characteristics. Another is that personality traits have important effects on neuropsychological performance. However, both may be manifestations of varia-

tion in underlying brain neural network circuit structures and function. Patterns of variation in these domains may help define schizophrenia and improve understanding of etiology and treatment.

NR320 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Attentional Function in Schizotypal Patients

Andrea Bergman, Ph.D., Psychology, St. Johns University, Grand Central & Utopia Pkways, Jamaica NY 11439; Sonia Lees-Roitman, M.A., Gregory Osgood, B.A., Barbara A. Cornblatt, Ph.D., Larry J. Siever, M.D.

Summary:

Background: There is evidence that the boundaries of schizophrenia extend beyond chronic psychotic forms to include milder schizophrenia-related personality disorders. Much of this research has focused on establishing phenomenological, genetic, psychophysiological, and biological similarities between schizophrenia and schizotypal personality disorder (SPD). Attentional dysfunction has been reliably detected in schizophrenic populations as well as in a variety of at-risk populations, suggesting that abnormal attention is a promising indicator of a biological susceptibility to schizophrenia. However, few studies have been conducted investigating attentional dysfunction in clinical SPD patients.

Objective: The goal of this study was to examine the attentional functioning of SPD patients, patients with other personality disorders (OPD), and normal subjects assessed by the Continuous Performance Test-Identical Pairs version (CPT-IP).

Method: Subjects (N = 65) were assessed as part of ongoing psychobiological studies of mood and personality disorders in two medical centers; 23 subjects had a DSM-III diagnosis of SPD, 32 subjects had a DSM-III diagnosis of a personality disorder other than SPD; and 10 subjects served as normal controls. For all groups, attentional functioning was measured with the Continuous Performance Test-Identical Pairs version (CPT-IP), which includes both a verbal condition (4 digits) and spatial condition (nonsense shapes).

Results: Analyses of attentional functioning measured as D'indicate that SPD patients perform significantly worse than both OPD and normal subjects on the verbal condition ($F[2,62] = 8.0$, $p < .001$). In contrast, both SPD and OPD patients performed significantly worse than normal subjects on the spatial condition ($F[2,61] = 4.0$, $p < .03$).

Conclusions: These results indicate that SPD patients, like schizophrenic patients, have a global attentional deficit including both spatial and verbal processing. In contrast, OPD patients appear to have a specific deficit involving spatial processing, which has also been previously reported in a sample of patients with affective disorders. These results support the notion of a schizophrenia spectrum, with disorders ranging from chronic schizophrenia to milder, schizophrenia-related personality traits.

NR321 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Patterns of Obsessive Compulsive Symptoms in Tourette Subjects Are Severity Independent: A Discriminant Analysis

Christopher M. de Groot, M.D., Psychiatry, Ohio State University, 1670 Upham Drive Ste 130, Columbus OH 43210; Robert A. Bornstein, Ph.D., Matig R. Mavissakalian, M.D., Mark David Janus, Ph.D.

Summary:

The similarities and differences of obsessive and compulsive (OC) symptom expression in Tourette's syndrome (TS), chronic motor tic disorder (CMT), and obsessive compulsive disorder (OCD) have received considerable attention. Several recent studies have reported patterns of OC symptom expression apparently unique to the coexistence of tics or TS. The recognition of specific OC symptoms dependent on diagnosis has heuristic value with respect to both etiology and clinical rationales for both disorders. The current exploratory study examined the expression of OC symptoms between two disparate groups: a nonclinically-based TS sample with a broad range of OC symptoms and severity and a homogeneous OCD sample that had participated in a pharmacological investigation.

In contrast to the OCD subjects, the TS subjects tended to have more aggressive, sexual, and symmetry obsessions and more checking, counting, and touching/blinking compulsions, *independent of severity,* as measured by a standard obsessive compulsive clinician-rated inventory (YBOCS). Further, obsessive and compulsive symptoms were found to contribute to a discriminate function that significantly discriminated the two groups. Aggression, contamination, sexual, symmetry, somatic obsessions, and washing compulsions correctly grouped 91.4% of cases. The current study further supports the identification of a differential distribution of neuroanatomic lesions reflecting the OCD-TS spectrum.

NR322 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Self-Injurious Behavior in Personality Disorders

Antonia S. New, M.D., c/o Larry Siever, M.D., Mt. Sinai Sch of Med., 1 Gustave Levy Pl. Box 1230, New York NY 10029; Robert L. Trestman, M.D., Deana S. Benishay, M.A., Emil F. Coccaro, M.D., Larry J. Siever, M.D.

Summary:

Self-injurious behavior (SIB), defined as self-directed aggression without suicidal intent, is a prominent feature of many personality disorder patients. We hypothesized that SIB, like suicidal behavior, represents a form of self-directed aggression and may, like suicidal behavior and impulsive aggression, be associated with a decrease in central serotonin function in personality disorder patients. Fifty-two patients with DSM-III personality disorder who had undergone fenfluramine challenge as an assessment of serotonergic activity were studied.

The mean change in PRL in response to fenfluramine, deltaPRL, was lower in patients with a history of self-injurious behavior ($n = 12$; 9.8 ± 8.0), regardless of suicide history, compared to those without ($n = 40$; 18.1 ± 16.9; $t = 2.34$, df 39.9, $p < .03$). Among males only, the same pattern was observed, even though the finding was only at a trend significance, possibly because of the loss of power (SIB+: $n = 9$; 6.7 ± 6.1; SIB–: $n = 29$; 11.2 ± 7.7; $t = 1.82$, $df = 16.5$, $p < .09$). Although the number of women patients was not enough for meaningful statistical comparison ($n = 14$), the prolactin response to fenfluramine was decreased by 47% in women with self-injurious behavior ($n = 3$; 19.0 ± 5.6) compared to those without ($n = 11$; 36.0 ± 21.6). These data raise the possibility that a central 5-HT abnormality may be associated with self-directed violence and not necessarily with suicidal intent. There may also be gender-specific manifestations of serotonergic dysfunction.

NR323 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Clock Test, Depression and Alzheimer's Screening

Theodore Dreier, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Becca Levy, M.A.

Summary:

Objective: To determine the accuracy of a quantitatively scored clock test in screening for Alzheimer's dementia in a heterogeneous disturbed population and to evaluate the effects of depressive symptoms on test performance.

Method: Thirty randomly selected geropsychiatric inpatients were administered tests of clock drawing, clock setting, and clock reading (H. Tuokko et al *JAGS* 40:579 1992), the Hamilton Depression Rating Scale, and other tests of time perception. Subjects were diagnosed as either meeting NINCDS-ADRDA criteria for Possible Alzheimer's Disease (AD) or not (Non-AD).

Results: A MANCOVA analysis, with age as covariate, and errors on the clock test components as dependent variables, found a significant difference between the AD and Non-AD groups. Sensitivity ranged from 64% to 91%, specificity from 63% to 95%. Multiple regression analysis showed a significant effect of depression increasing the errors in clock drawing, but not in clock setting or clock reading.

Conclusions: This quantitatively scored clock test, containing three different types of tasks, continues to show promising potential as a screening test for Alzheimer's disease even in a disturbed heterogeneous population where identification of cases is more difficult. Delineating the effects of depression on one of the subtests may lead to further improvements in the clock test.

NR324 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

BPD Outcome in Outpatients: A Two-Year Follow-Up

Lynn Gaudreault, M.D., Psychiatry, Univ of Sherbrooke, 3001 12th Avenue Nord, Sherbrooke PQ J1H5N4, Canada; Nora Schneider, Ph.D., Antonio Andreoli, M.D.

Summary:

Significance: While several outcome studies have been conducted on borderline personality disorder (BPD) inpatients, little follow-up research has been designed to explore the evolution of BPD in outpatients. New investigations should be directed at clarifying this issue.

Methods: The present study was a prospective assessment of 29 DIB BPD patients referred with depression for intensive outpatient treatment. At intake, each subject was assessed on a battery of standardized instruments (HDRS, HAS, GAS, SCID-I, IPDE). Twenty-four subjects (82.7%) had two-year follow-up evaluation (HDRS, HAS, GAS, CGI, HSRS, clinical interview for long-term treatment characteristics).

Results: At that occurrence, 80% subjects exhibited fair to good GAS scores, and 47% had fair to good compliance with the psychiatric treatment they were assigned at discharge. We found more improvement and more psychiatric treatment in those subject with increased DIB scores ($p < 0.01$) and increased IPDE dimensional scores ($p < 0.01$).

Comment: These results suggest that BPD outpatients have better two-year outcome than BPD inpatients. In addition, this study indicates that a consistent number of outpatients with severe BPD pathology are suitable for specific long-term treatment.

NR325 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Pain Assessment Using Signal Detection Theory

Ingrid M. Kemperman, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Mark J. Russ, M.D., Tatsuyuki Kakuma, Ph.D.

Summary:

Objective: To determine whether previously reported differences in pain perception between two subgroups of self-injurious borderline patients may be explained by neurosensory factors and/or response bias.

Method: Thirty-four female inpatients meeting DSM-III-R criteria for borderline personality disorder were studied. Seventeen subjects reported usually feeling pain during self-injurious behavior (BPD-P), nine reported absence of pain (BPD-NP), and eight subjects had no history of self-injurious behavior (BPD-C). A pair of non-noxious and noxious heat stimuli were repeatedly applied in a random sequence to each forearm. The subjects rated the intensity of each stimulus on a categorical scale, and stimulus-response data were analyzed using signal-detection theory.

Results: Stimulus discriminability was lower in the BPD-NP group compared with the BPD-P group and the BPD-C group ($F = 8.13$, $P = 0.0014$). The response criterion was higher in the BPD-NP group compared with the BPD-P group and the BPD-C group ($F = 4.88$, $P = 0.014$). No differences between groups were found for the non-noxious stimuli.

Conclusions: The lower discriminability in the BPD-NP group is consistent with analgesia on a neurosensory basis. The higher response criterion (a function of psychological variables) in the BPD-NP group indicates that these patients are also more stoical. The absence of group differences for the non-noxious stimuli suggests that these conclusions are specific to pain (not simply temperature) perception.

NR326 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Substance Use and Secondary Borderline Personality

Paul S. Links, M.D., Psychiatry, The Wellesley Hospital, 160 Wellesley Street, Toronto Ontario M4Y1J3, Canada; Ronald J. Heslegrave, Ph.D.

Summary:

Objective: This paper presents new findings from a seven-year, prospective, follow-up study of a cohort of patients with borderline personality disorder (BPD) regarding the relationship between substance abuse (SA) and BPD.

Methods: Inpatients were screened for BPD, and of the 130 patients identified, 88 met criteria based on the Diagnostic Interview for Borderlines. At seven-years follow up, 81 (62.3%) were re-examined, two (1.5%) were deceased, six (4.6%) committed suicide, and 41 (31.6%) were unavailable.

Results: Subjects with BPD and SA were twice as likely to remain positive for BPD at follow up as subjects with BPD alone (relative risk = 2.19) and reported more self-destructive and suicidal thoughts and behaviors. A lifetime history of alcoholism significantly predicted episodes of alcoholism on follow up (chi square = 16.81, $p = 0.0001$); however, the level of initial borderline psychopathology did not predict subsequent episodes of alcoholism. Patients with a positive family history of SA showed better overall functioning than patients without a positive family history, based on McGlashan's Global Outcome Scale ($p < 0.01$) and their GAS score (73 vs 63, $p < 0.01$). Previous follow-up studies have found that borderline patients who obtain sobriety have some of the best outcomes.

Conclusions: These findings suggest an important interaction between SA and BPD such that removal of SA leads to resolution of BPD. In comorbid patients, SA may amplify a borderline predisposition.

NR327 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Personality Disorders in Pathological Gamblers Seeking Treatment

Peter Berger, M.D., Psychiatry, University of Vienna, Waehringer-Guertel 18-20, Vienna A1090, Austria

Summary:

Introduction: Early clinical observations of Moran stress the importance of personality pathology in pathological gamblers. The aim of the study was to assess the whole spectrum of personality disorders in pathological gamblers with a reliable instrument.

Method: Thirty-six male outpatients fulfilling DSM-III-R criteria for pathological gambling were examined by the author for pres-

ence of personality disorders with the International Personality Disorder Examination, a structured interview that has shown sufficient reliability. The interview allows formulation of DSM-III-R and ICD-10 diagnoses simultanously.

Results: Twenty-eight (77.8%) of the 36 pathological gamblers got a DSM-III-R diagnosis of a personality disorder and 12 of them got more than one diagnosis. Most frequent were borderline personality disorder (11 subjects, 30.6%) and passive-aggressive personality disorder (nine subjects, 25.0%). Only three patients had antisocial personality disorder. In ICD-10, 23 (63.9%) patients got a diagnosis of a personality disorder, impulsive (eight patients), and dissocial personality disorder (eight patients) as the most frequent.

Conclusion: The high frequncy of personality disorders indicates the importance of axis II in pathological gambling. Axis II pathology may play an important role in the development of pathological gambling and should be considered in the therapy of this disorder. In line with a study by Blaszczynski, et al., gamblers with antisocial personality disorder are relatively rare in clinical settings in contrast to epidemiological surveys.

NR328 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Epidemiological Survey of OCD and Syndromes in a Large French Clinical Sample

Elie G. Hantouche, M.D., SHU, Hopital Sainte Anne, 1 Rue Cabanis, Paris 75014, France; Marc L. Bourgeois, M.D., Myriam Bouhassira, M.D., Sylvie Lancrenon, Ph.D.

Summary:

Recent epidemiologic studies were conducted in general population, showing high prevalence rates of OCD (2-3%), although more investigation of OCD prevalence in clinical population is still warranted.

The prevalence of DSM-III-R diagnoses of obsessive compulsive disorder (OCD) and obsessive compulsive syndromes (OCS) is reported in 4,364 16-70-year-old, new, consecutive patients, consulting in outpatient psychiatry.

Point prevalence rates of 9.2% were recorded for OCD and 17% for OCS. Significantly different from nonobsessional patients, it was observed in OCD and OCS patients more male representation (41% vs 37%, $p = 0.007$), a younger current age (36 y vs 39 y, $p < 10^{-4}$), and age of disorder onset, and higher rate of celibacy (31.5% vs 28.6%, $p = 0.003$), more anxiety and depression comorbidity (50% vs 39%, $p < 10^{-4}$), a higher suicidal risk (17% vs 14%, $p = 0.04$-especially in OCS patients 18.3%), more chronicity (mean current episode duration 14.8 months vs 11.2 m, $p < 10^{-4}$), and higher rate of global functioning impairment (score at GAF 53.9 vs 57.9, $p < 10^{-4}$.

More sociodemographic, clinical, and psychometric data will be presented in the obsessional population ($n = 731$) and compared with recent epidemiological published studies concerning OCD.

NR329 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Phenomenological Profile of OCD Patients in Bahrain

Mohmed Khalil Al-Haddad, M.B., P.O. Box 26441 Adliya, Manama, Bhrain

Summary:

Fifty patients with a primary diagnosis of OCD were studied during 1994 from a phenomenological point of view in order to delineate the various forms and contents of obsessions and compulsions. An attempt was made to highlight the frequency with which the different forms and contents occur. Six types of obsessions were identified: doubts, thoughts, fears (phobias), image, impulses, and miscellaneous. Compulsive acts were classified into two types: yielding and controlling. The content of obsessions were classified in seven broad categories as relating to: dirt and contamination, germs, aggression, sexual, religious blasphomous, illness, and indicisiveness.

Thirty-eight percent of the patients displayed obsessional thoughts related to dirt and contamination, while 40% showed religious and blasphemous obsessional thoughts and doubts. Fifty-six percent of patients had compulsions, 36% of them were multiple, while 20% displayed only a single compulsion.

The paper describes the findings and emphasizes the role played by sociocultural and religious factors in shaping the character of an obsessional thought content.

NR330 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Quarter Century of Suicides in a Major Urban Jail: Implications for Community Psychiatry

Curtiss J. DuRand, M.D., Psychiatry, ENRM VA Medical Center, 200 Spring Road, Bedford MA 01730; James A. Haycox, M.D., Edward Federman, Ph.D., Gary Burtka, M.A., John Smith, M.A.

Summary:

This case series uses rigorous criteria to verify and examine all suicides in a representative large urban jail from the beginning of record-keeping in 1967 to 1992. Those charged with murder or manslaughter were 19 times more likely to suicide than inmates with other charges. Thirty-nine percent of the suicides were by persons charged with murder or manslaughter, constituting two percent of admissions (2/day). All thirty-seven suicides were by hanging, most occurring at night within 31 days of admission. Many had made prior attempts during incarceration.

People who committed suicide in jail differ dramatically from those who do so in lock-ups, suggesting that jail data be treated separately. Treatment of high-risk inmates and evaluation of all suicide attempts might well reduce jail suicide by a substantial proportion in this and similar populations.

NR331 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Positive Versus Negative Symptoms and Suicide Risk

Kalman J. Kaplan, Ph.D., Psychiatry, Michael Reese Hospital, 2929 South Ellis Avenue, Chicago IL 60616; Martin Harrow, Ph.D., Michael J. Reinstein, M.D., James R. Sands, Ph.D.

Summary:

Objective: The increased rate of suicidal activity over the last 15 years has proved a major challenge for practicing psychiatrists. The present research studies risk factors for suicide, exploring the relationship between positive and negative symptoms and overall functioning and later suicidal activity, and if these patterns vary with diagnosis.

Method: 98 schizophrenics and 117 nonpsychotic depressives were followed up 2.5 and 7.5 years after acute hospitalization. The patients were assessed for psychotic symptoms (hallucinations, delusions, first-rank symptoms), positive thought disorder, negative deficit symptoms, and suicidal activity (serious suicidal ideation, attempted suicides, or completed suicides), using standardized interviews and the National Death Index.

Results: 1.) Overall functioning 2.5 years after hospitalization tends to predict later suicidal activity for both the schizophrenics and depressives. 2.) Psychosis predicts suicidal activity five years later for the schizophrenic sample ($p < .05$) but not for the nonpsychotic depressives. 3.) Deficit symptoms predict later suicidal activity for the nonpsychotic depressives ($p < .01$) but not for the schizophrenics. 4.) These significant results hold even when level of overall functioning is controlled.

Conclusions: The results support an interactive model of suicide risk. Some risk factors for suicide are diagnosis-specific. These include psychosis and deficit symptoms. Other risk factors are diagnosis-free. These include overall post-hospital functioning.

TABLE. Mean Symptom Scores for Suicidal versus Nonsuicidal Schizophrenics and Depressives

	SCHIZOPHRENICS 7 year follow-up				NONPSYCHOTIC DEPRESSIVES 7 year follow-up			
2 year follow-up	no suicidal activity	suicidal activity	F	p	no suicidal activity	suicidal activity	F	p
Positive Symptoms								
Delusions	1.83(53)	2.38(16)	4.27	.04	1.30(79)	1.13(8)	.72	.46
Hallucinations	1.74(53)	2.25(16)	3.94	.05	1.08(79)	1.13(8)	.14	.71
Thought Disorder	2.38(52)	2.38(16)	.00	.98	1.78(78)	1.80(10)	.00	.95
Negative-Deficit Symptoms								
Concreteness	1.38(45)	1.50(14)	.65	.43	1.15(66)	1.50(6)	4.68	.03
Psychomotor Retardation	1.58(50)	1.20(15)	2.07	.15	1.06(71)	1.22(9)	3.22	.08
Negative Symptoms								
Poverty of Speech	.11(36)	.20(10)	.38	.54	.06(54)	.14(7)	.76	.39
Flat Affect	.29(35)	.20(10)	.19	.66	.21(56)	.14(7)	.12	.73
IQ	16.92(51)	15.06(16)	1.34	.25	18.59(74)	22.22(9)	3.70	.06

NR332 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Suicide Abuse and Dissociative Symptoms

Margaret L. Kaplan, Ph.D., Psychiatry, Montefiore Hospital, 111 East 210 Street, Bronx NY 10467; Gregory M. Asnis, M.D., Deborah S. Lipschitz, M.D.

Summary:

Research suggests that psychiatric patients with a history of childhood abuse are at greater risk for suicidal behavior (lifetime prevalence) than are nonabused patients. However, these positive findings may be due, in part, to the high rates of current abuse reported by adult victims of childhood abuse. This paper reports on a study that examines the independent contributions of childhood and adult abuse to the relationship between suicidality and abuse. Other issues addressed include, whether the nature of the suicidal behavior among abused patients differs from that of nonabused patients, and whether clinical characteristics might help to identify those abused patients that are at greatest risk for suicide attempts.

A total of 300 psychiatric outpatients were evaluated for histories of abuse, suicidal behavior, and clinical characteristics using self-report instruments and a face-to-face interview. Logistic regression analysis indicated that physical abuse (battering) in adulthood and histories of a combination of childhood and adult abuse were significant predictors of past suicide attempts and current suicidal ideation. Victims of abuse were suicidal at a younger age and reported more multiple suicide attempts than nonvictim controls. Among patients with a history of abuse, suicide attempters could be distinguished on the basis of higher levels of dissociation, depression, and somatization. The clinical relevance of these findings, especially in terms of identifying outpatients at risk for suicidal behavior, are discussed.

NR333 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Invasiveness of Sexual Abuse Predicts Suicide Attempts

Nicholas G. Ward, M.D., Psychiatry RP-10, Univ Of Washington, Seattle WA 98195; David Junker, B.S., Rama Oskouian, B.S., Bryan Hartzler, B.S., Albert Carlin, Ph.D.

Summary:

Objective: This study tests the hypothesis that more invasiveness of sexual abuse is associated with an increased risk of suicide attempt.

Method: All English-speaking patients in a university family practice clinic who were over 18 years old and who gave informed consent were included. A total of 210 patients completed a detailed questionnaire about types of childhood sexual abuse (e.g., extensive fondling, oral sex, forced intercourse, etc.), and suicide attempts. Invasiveness was determined by the 1) most invasive act and 2) number of different acts that occurred.

Results: More sexually abused than not sexually abused patients made suicide attempts (31.3% vs. 11.7%, $p < .001$). Within the sexually abused group, the risk of suicide attempt was higher in the forced intercourse than in the no forced intercourse subgroup (48% vs. 10.5%, $p < .008$). Within the forced intercourse group, the risk of suicide attempt was higher in those that experienced at least three other types of sexual abuse than in those who had fewer than three other types of sexual abuse (75% vs 23%, $p < .008$).

Conclusion: Although there is a greater risk of suicide attempts in those sexual abused, it is the forced intercourse subgroup that accounts for most of this risk, and within this group the addition of other forms of abuse further increases this risk.

NR334 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Suicide in Medical Students: 1989-1994

Lon R. Hays, M.D., Dept of Psych, Univ of KY Med Ctr, Rost St Annex 2 Room 206, Lexington KY 40536-0001; Todd R. Cheever, M.D., Pukar Patel, M.D.

Summary:

This descriptive study reports on medical student suicides from 1989-1994. A representative from the dean of student affairs office was contacted at all 126 U.S. medical schools to gain information related to medical student suicide. Responses were obtained from 102 schools. Fifteen medical student suicides were reported from August, 1989 through May, 1994. Fourteen suicides were by males (mean age, 25.9) and one was female. The suicides per year ranged from none in 1989-90 to five in 1992-93, with the rate/100,000 ranging from 0-11.7. Of the 15, 12 were Caucasian, two were Middle Eastern, and one was Hispanic. Thirteen were single, one was married, and one was divorced. Three of the suicides occurred during the first year of medical school, two during the second year, six during third year, and four in the fourth year. Two suicides were reported in February, August, October, and December, and none in June or July. Eight of the suicides were committed using firearms, six by overdose and one by jumping. Six of 14 students left a suicide note. Nine of 13 students were known to have a psychiatric or substance abuse history.

NR335 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Suicidal Ideation in Urban Medical Outpatients

Mark Zimmerman, M.D., Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence RI 02903; Jennifer D. Lish, Ph.D., David T. Lush, M.D., Neil J. Farber, M.D., Gary Plescia, M.A., Mary Ann Kuzma, M.D.

Summary:

Objective: To assess the prevalence of current suicidal ideation in urban primary care outpatients, and to compare suicidal and nonsuicidal medical patients on their demographic characteristics and their attitudes about mental health screening.

Methods: A consecutive series of 601 outpatients attending the faculty general internal medicine practice at the Medical College of Pennsylvania completed two questionnaires. This practice serves an urban, lower socioeconomic class population. One questionnaire (the SCREENER) screened for several different DSM-IV disorders and included three questions about suicidal

ideation. The second questionnaire assessed patients' attitudes about mental health screening.

Results: We found that 20 (3.3%) patients reported having thoughts of killing themselves. Patients with suicidal ideation were significantly younger (32.7 ± 12.7 years vs. 39.8 ± 15.2, $p < .05$), and more frequently divorced. Almost all (97.6%) patients indicated that their doctors should inquire about emotional health issues at some time, and the suicidal patients were nonsignificantly more likely to recommend inquiry about psychiatric symptoms at every visit (55.0% vs. 37.0%, $p < .11$). Only half of the suicidal patients reported a lifetime history of mental health treatment. The majority (70.2%) of patients believed that it would be easy to discuss mental health problems with their medical doctor. There was an interaction between suicidal ideation status, history of mental health care, and level of comfort in discussing psychiatric problems.

Conclusion: Suicidal ideation has a significant prevalence in an urban primary care patient sample; only half of the suicidal primary care patients ever had mental health treatment; and almost all patients indicated that it is appropriate for their primary care practitioner to evaluate them for psychiatric disorders.

NR336 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Female Panic Disorder Patients Manifest Greater Somatization Compared to Male Patients

Javaid I. Sheikh, M.D., Dept Of Psychiatry, Stanford Univ Sch of Med., 300 Pasteur, Stanford CA 94305-5546; Pamela J. Swales, Ph.D.

Summary:

Studies suggest the presence of higher somatization in panic disorder patients compared normal controls. To our knowledge, no investigation has looked at the gender-related differences in somatization among panic disorder patients. We are presenting a preliminary analysis of data in a small sample from ongoing studies of phenomenology of panic disorder. The purpose of this investigation was to determine whether women and men panic disorder patients exhibit differences in the degrees of somatization. Our sample consisted of 26 patients participating in a treatment study who met the DSM-III-R criteria for panic disorder based on the Structured Clinical Interview for Diagnosis (SCID). The sample included 16 males (age range 22-51, mean age = 37.5), and 10 females (age range 38-54, mean age = 48.9). They were evaluated using the Self-Report Inventory for Somatic Symptoms (SISS) before the start of treatment. Female patients manifested significantly higher Total Somatization Disorder Scores (TSDS) than male patients (mean = 12.50, sd = 7.60 vs. mean = 8.12, sd = 3.13; $p < .05$). Implications of these findings for future research will be discussed.

NR337 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Trichotillomania and Self-Esteem: A Survey of 62 Female Hair-Pullers

Jennifer L. Soriano, Psychiatry, Mass General Hospital, Bldg 149 13 Street OCD 9th Flr, Charlestown MA 02129; Richard L. O'Sullivan, M.D., Lee Baer, Ph.D., Katharine A. Phillips, M.D., Richard J. McNally, Ph.D., Michael A. Jenike, M.D.

Summary:

Objective: The psychological features of trichotillomania have received little empirical attention, despite the fact that sufferers commonly report negative self-image to be one of the most disturbing aspects of this disorder. We conducted this study to identify specific factors that predict self-esteem problems in hair pullers.

Method: Sixty-two females with trichotillomania or repetitive hair pulling were recruited through referrals to the Massachusetts General Hospital Obsessive Compulsive Disorder and Trichotillomania Clinics. Subjects completed self-report questionnaires assessing factors possibly related to self-esteem in hair pullers. The survey included questions related to hair-pulling symptoms, mood and anxiety symptoms, and body-image concerns. Self-esteem was assessed using the Rosenberg Self-Esteem Scale.

Results: Self-esteem was not directly related to age of onset of hair pulling or severity of hair loss. However, self-esteem was related to levels of depression and anxiety, frequency of hair pulling, and body dissatisfaction unrelated to hair pulling. High rates of anxiety, depression, and probable body dysmorphic disorder were found in the sample.

Conclusions: The negative impact of hair pulling on self-esteem, as well as the relationship between trichotillomania and anxiety, depression, and body image dissatisfaction, suggest that specific efforts should be made to address psychological features of trichotillomania in treatment.

NR338 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

A Long-Term Follow-Up Study of Somatoform Disorders

Michael Bach, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna A, Austria; Doris Bach, Ph.D., Ulrike Lupke, Ph.D., Ralph Schaible, Ph.D.

Summary:

The purpose of the present two-year follow-up study was to further validate different types of DSM-III-R somatoform disorders (somatization disorder, SOM; hypochondriasis, HYP; undifferentiated somatoform disorder, USD) by assessing their clinical course as well as their temporal relationship. A sample of 40 patients with somatoform disorders received an eight-week inpatient behavior therapy program. DSM-III-R diagnoses were assessed by SCID interviews before inpatient treatment and two years after discharge. At follow-up, 51% of the somatoform disorders were remitted (33% of SOM, 50% of HYP, and 83% of USD cases). Thirty-three percent of the patients with pretreatment SOM and 28% with pretreatment HYP met criteria of USD at follow-up. This diagnostic shift from other somatoform disorders toward USD during the course of illness gives evidence for the conceptualization of USD as a residual type of somatoform disorder. Thirteen patients (33%) exhibited an additional depressive diagnosis. However, neither the comorbidity of somatoform disorders and depression nor the pretreatment severity of illness (as determined by SCL-90-R scales of somatization and depression, the SCL-90-R global score, and the Whiteley Index for assessing hypochondriacal preoccupations) significantly predicted the clinical course of somatoform disorders. These results underline the independence of somatoform disorders despite high rates of comorbidity.

NR339 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Is Alexithymia Related to Somatization? A Factor Analytic Study

Michael Bach, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna A, Austria; Doris Bach, Ph.D., Martina De Zwaan, M.D.

Summary:

With regard to several methodological limitations in the assessment of alexithymia, uncertainty remains as to whether alexithymia and somatization are distinct psychological constructs or are overlapping, as suggested by the results of previous studies. In this study, 379 normal adults filled out the newly developed 20-item Toronto Alexithymia Scale (TAS-20) and a screening list for DSM-III-R somatoform symptoms (SOMS).

Significant positive correlations were found between the TAS-20 and the SOMS ($p < 0.002$). Subsequently, a correlation matrix consisting of items from both the TAS-20 and the SOMS was subjected to factor analysis, resulting in a four-factor solution with separate factor loadings according to these two scales (TAS-20: three factors, SOMS: one factor). These results were then replicated and cross-validated in an independent sample of 125 psychosomatic patients, revealing strongly comparable results. These findings provide evidence for the assumption that alexithymia and somatization reflect separate constructs that may occur simultaneously, but can be measured independently.

NR340 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Course of Psychological Variables in Whiplash Injury: A Two-Year Follow-Up with Age, Gender and Education Pair-Matched Patients

Bogdan P. Radanov, M.D., Psychiatry, Murtenstr 21, Berne 3010, Switzerland; Matthias Sturzenegger, M.D., Stefan Begre, M.D.

Summary:

Background: This study evaluated the course of psychological variables during a two-year follow-up in patients after common whiplash of the cervical spine.

Patients: From a sample of 117 patients with common whiplash referred from primary care and investigated on an average of 7.2 ± 4.2 days after trauma, a total of 21 suffered trauma-related symptoms during two years following initial injury. These patients (symptomatic group) were compared with 21 age, gender, and education pair-matched patients, who showed complete recovery from trauma-related symptoms during the two-year follow-up (asymptomatic group).

Methods: Both groups underwent standardized testing procedures (i.e. Freiburg Personality Inventory and well-being scale) at referral, and at three, six, and 24 months. At all investigations, neck pain and headache intensity were assessed.

Results: In the symptomatic group during follow-up, no significant change on ratings of neck pain or headache was found. Significant differences between the groups and significant deviation of scores over time were found on the well-being and nervousness scales. There was a lack of significant difference between the groups on the scale for depression, indicating possible somatic basis for change in psychological functioning in the investigated sample. With regard to scales of extraversion or neuroticism, there were neither significant differences between the groups nor significant deviation over time.

Conclusion: These results highlight that psychological problems of patients are a consequence rather than a cause of somatic symptoms in whiplash.

NR341 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Long-Term Outcome After Whiplash Injury: Follow-Up During Two Years with Patients Referred From Primary Care

Bogdan P. Radanov, M.D., Psychiatry, Murtenstr 21, Berne 3010, Switzerland; Matthias Sturzenegger, M.D.

Summary:

Background: Assessing the interrelationship between somatic and psychosocial variables and their relevance for long-term outcome using a nonselected, well-defined group of whiplash patients.

Patients: 117 patients from primary care with similar sociocultural background all involved in automobile accidents and who were fully covered by accident insurance.

Methods: Initial examination (mean = 7.2 ± 4.2 days after trauma) and follow-up examinations at three, six, 12, and 24 months after trauma. In all patients, initial features of accident mechanism, subjective complaints, and different aspects of patients' history were documented, and neurological, radiological, and neuropsychological examinations were performed. At follow-ups all patients underwent neurological examination and cognitive and psychosocial factor assessment. At two years, patients were divided into asymptomatic and symptomatic groups and then compared with regard to initial findings.

Results: 18% of patients still had injury-related symptoms at two years. The following significant differences were found with regard to baseline findings: Symptomatic patients were older, had higher incidence of rotated or inclined head position at the time of impact, had higher prevalence of pretraumatic headache, showed higher intensity of initial neck pain and headache, suffered a greater combination of symptoms, had a higher incidence of symptoms of radicular deficit and higher average scores on a multiple symptom analysis, displayed more degenerative signs (osteoarthrosis) on x-ray, scored higher with regard to impaired well-being and performed worse on tasks of attentional functioning, and showed more concern with regard to long-term suffering and disability.

Conclusion: Poor outcome in the long term after whiplash injury is primarily related to its initial severity.

NR342 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Comorbidity in Child and Adolescent Conversion Disorders

Atilla Turgay, M.D., Psychiatry, Scarborough General Hosp, 251 Queens Quay West #701, Toronto ON M5J 2N6, Canada

Summary:

There have been no published studies on comorbidity of child and adolescent conversion disorder. In this prospective, controlled, long-term, multicenter, clinical study, it was determined that 53.12 percent of 89 children and adolescents with conversion disorder suffered from other psychiatric comorbid disorders. The most common psychiatric comorbid disorders were other somatoform disorders (52.94 percent) and anxiety disorders (33.33 percent). One third of the children and adolescents with conversion disorder also met the criteria for another somatoform disorder. Most common comorbid somatoform disorder was found to be "psychogenic pain disorder." Many children and adolescents attributed the loss of functions to pain reactions. The majority of children lacked "indifference towards their symptoms" and bitterly complained about their loss of organ functions. The so-called "associated feature" of the disorder, "la belle indifference" was found to be associated with only about one third of the patients. There were significant differences in comorbid disorders between conversion disorders and a comparison group of age-, sex-, and SES-matched children and adolescents with conduct disorder ($p < 0.01$). The most common comorbid disorder in conduct disorder was ADHD.

Conversion disorders of childhood seemed to be closer to and overlapping with other somatoform disorders and anxiety disorders. Children and adolescents with comorbid conversion disorder and other psychiatric disorders required longer time in treatment and recovery than the patients with conversion disorder alone. The impact of the findings in this area requires some changes in our assessment and treatment of children and adolescents with conversion disorder.

NR343 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Are Antidepressants Effective in the Treatment of Chronic Pain?

David A. Fishbain, M.D., Pain Center, University of Miami, 600 Alton Road, Miami Beach FL 33139; Brian Cutler, Renee Steele Rosomoff, M.B.A., Hubert L. Rosomoff, M.D.

Summary:

Hypothesis: A recent meta-analysis of antidepressant (AD) treatment of chronic pain patients (CPPs), (Onghen 1992) demonstrated that ADs act through an analgesic effect and not via masked depression, manifest depression, sedation, and placebo effects. We wished to determine if an analgesic AD effect could be demonstrated for CPP diagnosed with SPD. SPD is DSM-III-R diagnostic term that implies lack of organic pathology to explain the CP.

Method: A Medline and manual computer search for studies utilizing ADs for the treatment of CP yielded 149 reports of which 16 had utilized CPP with a diagnosis of SPD. Of these reports eight had the minimum information necessary for the analysis: a P value comparing pain effect of ADs vs. placebo. For these studies, P levels were transformed into Z scores and combined for an overall Z score for which a P level and effect size was calculated. The number of hypothetical studies with findings of "no effect" required to render the overall P level nonsignificant was calculated. We also estimated the number of unpublished studies that might exist.

Results: The combined differences showed that AD decreased pain levels significantly more than placebo ($z = 5.90$, $p < 0.0001$). Effect size ranged from .28-.91 (mean .62). The number of unpublished studies required to make these results nonsignificant was 107. Number of nonsignificant studies reasonably argued to exist was 50.

Conclusion: (1) ADs are effective in the treatment of SPD associated CP; (2) Because previous studies indicate that the AD analgesic effect in CPPs is related to improvement in pain rather than improvement in depression, these meta-analysis results indicate that the validity of the SPD diagnosis as defined may be questionable. Because this study raises issues about the validity of the SPD diagnosis, physicians should use this diagnosis with great caution.

NR344 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Experience of Pain in Rheumatoid Arthritis: An Empirical Evaluation of the Contribution of Developmental Psychosocial Stress

Stephan Andreas Frost, M.D., Psychiatry, University of Berne, Murtenstrasse 21, Berne CH 3010, Switzerland; Bogdan P. Radanov, M.D.

Summary:

Background: Evaluation of the relevance of developmental psychosocial factors in pain experience.

Patients: 66 patients with rheumatoid arthritis (according to the ARA-criteria), all suffering from chronic pain according to IASP criteria.

Methods: Relationship between psychosocial aspects and pain intensity, affective and affective-evaluative dimensions of pain experience, and effectiveness of medication was assessed using structured biographical history, the State-Trait-Anxiety Inventory, and a subcontent of the Health Assessment Questionnare, following somatic parameters were assessed: 1.) Steinbrocker-radiological functional status, 2.) ACR-global functional status, 3.) Rheumafactor positive/negative, 4.) duration of illness.

Results: Different aspects of pain experience were significantly intercorrelated, and the investigated aspects of pain experience were correlated to different factors: 1) Pain intensity was only significantly related to the ACR global functional status; 2) Affective dimensions of pain were significantly correlated with a nurture score and the patient's relationship with their partner; 3) Effectiveness of medication correlated significantly with nurture score, stress score, partner's understanding of the patient's pain, duration of illness. Variables considered belonging to the pain-prone concept did correlate significantly with affective dimensions of pain and the effectiveness of medication but were not able to explain the main variance (18%, 45%).

Conclusion: Results suggest that the relevant aspects thought to be prominent in psychogenic pain have a similar origin to some degree, but are mediated by different factors more related to the actual psychosocial situation of the patient than to the former biographical experiences. Thus, results give evidence to reassess the meaning of developmental psychosocial stress in the context of chronic intractable pain.

NR345 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Do Normal Volunteers Know That They Are Not Psychiatrically Normal?

Clarice Gorenstein, Ph.D., Psychiatry, Univ. De Sao Paulo, LIM 23 FMUSP, Caixa Postal8091, Sao Paulo SP 01065-970, Brazil; Francisco Lotufo Neto, Ph.D., Marcio Melo, M.D., Valeria Lauriano, M.D., Laura Andrade, Ph.D., Valentim Gentil, M.D.

Summary:

"Normal" volunteers without lifetime psychiatric diagnosis, concerned about their usual levels of anxiety or irritability, were solicited by newspaper advertising and radio broadcasts. Subjects below the cut-off scores on the Self-Report Questionnaire (Harding *et al.*, 1980) were given an open psychiatric interview to exclude those meeting ICD-10 or DSM-III-R criteria for psychiatric disorders. They were then interviewed with the SCAN (Wing et al., 1990) to exclude those meeting its criteria for any lifetime psychiatric diagnosis. The remained subjects were defined as psychiatrically normal, despite their anxiety or irritability concerns.

From 275 subjects given the SRQ: 182 (66%) had scores higher than the cut-off. From the remaining 93, 59 were interviewed, and 39 (66.1%) met clinical diagnoses, six were excluded for lack of complaints, and only 14 met the established inclusion criteria. Thus, despite apparently clear request for *normal* volunteers with mild anxiety/irritability, upon careful evaluation of a total of 241 fully screened subjects, only 20 individuals (8.3%) did not present any psychiatric diagnosis. Of the 221 with positive scores, 199 (91.3%) have never received any psychiatric evaluation. These results confirm the need both for careful screening of "normal" subjects and for further psychiatric attention to our general population.

NR346 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

DSM-IV General Reliability Field Trials: Expert Phase

James W. Thompson, M.D., UMAB, IPHB Psychiatry, 645 W. Redwood Street, Baltimore MD 21201-1542; Allen J. Frances, M.D., Harold Alan Pincus, M.D., Michael B. First, M.D., Michael A. Flaum, M.D., J. Richard Hebel, Ph.D.

Summary:

Objective: To test the reliability of selected DSM-IV diagnostic categories.

Method: A group of videotaped patient interviews were produced, consisting of a standard DSM-IV diagnostic interview done by a psychiatrist. A large international field trial is in process, wherein psychiatrists and other clinicians will rate the tapes for diagnosis. In order to determine "best case" reliability figures and the typicality of the cases presented, experts in diagnosis rated

the tapes. In all, 50 tapes were rated by 200 psychiatrists and other experts at 20 sites. Kendall's coefficient of concordance (Kendall's W) was used to detect the level of agreement among clinicians.

Results: For patients who met criteria for schizophrenia, Kendall's W ranged from 0.49 to 0.66. When the first and second rule-out diagnoses were considered, agreement increased to from 0.54 to 0.86. Agreement on schizoaffective patients was low (0.30), but increased to 0.63 when the first and second rule-out diagnoses were considered. Agreement was very good (0.82 to 1.00) for patients with bipolar disorder.

Conclusions: DSM-IV reliability varies widely when only the working diagnosis is considered, but improves greatly when the top three diagnoses are considered. The large field trial will provide more definitive reliability figures and explanations of why reliability varies.

NR347 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Differential Diagnosis of Organic Psychosis and Schizophrenia in Patients with Psychoactive Substance Use Disorders

Richard N. Rosenthal, M.D., Psychiatry, Beth Israel Med. Center, First Ave at 16th Street, New York NY 10003; Christian Miner, Ph.D.

Summary:

Objective: To derive a model that discriminates between substance-induced psychosis [i.e., organic delusional disorder and/or organic hallucinosis (ODD/OH)] and schizophrenia in patients with prominent delusions or hallucinations in patients with psychoactive substance use disorders (PSUD).

Method: 211 psychiatric inpatients with PSUD were evenly sorted between those with consensus DSM-III-R diagnoses of schizophrenia and those with ODD/OH, and then into two data sets (A & B) by admission year. A discriminant function was derived by logistic regression to predict psychiatric diagnosis for Set A (N = 130), coded as a dichotomous criterion. The model was then tested using Set B (N = 81).

Results: For Set A, a discriminant function utilizing six predictors correctly classified 76.2% of all patients, including 83.1% of schizophrenics. Formal thought disorder and bizarre delusions significantly predict schizophrenia [odds ratio (OR) 3.55:1 and 6.09:1]. Suicidal ideation (OR = .32:1), IV cocaine abuse (.18:1), drug detoxification history (.24:1), or methadone maintenance (.18:1) demonstrate inverse relationships with a schizophrenia diagnosis. The model predicted the diagnostic status of 70.4% of patients in Set B, including 72.5% of schizophrenics.

Conclusions: The pattern of presenting symptoms and clinical history likely differs in patients with psychosis due to PSUD versus those with schizophrenia. The validated model presented here contributes to the differential diagnosis of schizophrenia and ODD/OH among patints with PSUD.

NR348 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Asperger's Syndrome in Later Life

Serge A. Mosovich, M.D., Psychiatry, Mt. Sinai School of Med., P.O. Box 1230 1Gustave Levy Pl, New York NY 10029; Lucille Horn, Ph.D., Valerie Minuchin, M.A., Bonnie R. Aronowitz, Ph.D., Eric Hollander, M.D.

Summary:

Despite difficulties in classification and diagnosis, prominent characteristics of autistic disorder include impairment of social and communicative behavior, impairment of cognitive functioning, and impulsivity. Milder forms of pervasive developmental disorders may be misdiagnosed, or emphasis may be placed on other deficits in communication and socialization. Asperger's syndrome, a category of pervasive developmental disorder, has received increasing scrutiny. Wing (1981), Nagy, and Szatmari (1986), and Tantam (1988), have delineated the characteristics of this disorder, including impairment in empathy, an extreme degree of social isolation, and difficulty understanding appropriate social rules.

We present seven cases of Asperger's syndrome presenting in later life, referred to us with behavioral symptoms of hyperactivity, poor impulse control, and attentional difficulties. Neuropsychological evaluation suggested dysfunctions in sociability, verbal and nonverbal expressiveness, and engrossing and idiosyncratic interests and clumsiness, all of which represent the current DSM-IV diagnosis of Asperger's syndrome. We present four cases at differing ages of diagnosis, their demographics, and their phenomenological findings. We hope to alert readers to clinical pitfalls and call attention to the existence of this little-known and fascinating disorder.

NR349 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Family and Genetic Studies of OCD

Margaret A. Richter, M.D., Neurogenetics, Clarke Institute of Psych, 250 College Street R-31, Toronto ON M5T 1R8, Canada; Richard P. Swinson, M.D., Russell T. Joffe, M.D., Farideh Badri, B.Sc., Elizabeth Billett, B.Sc., James L. Kennedy, M.D.

Summary:

Obsessive compulsive disorder (OCD) is a common psychiatric disease afflicting up to 3% of the population. A genetic etiology is likely, as suggested by twin and family studies and segregation analysis. In this family study we interviewed 36 probands meeting DSM-IV criteria for OCD, and obtained diagnostic information from the probands of all first-degree relatives using the Family Informant Schedule and Criteria (FISC), according to FH-RDC criteria. Results indicated that 17% of first-degree relatives met criteria for OCD. A further 17% had subclinical symptomatology (OCB).

Based on the strong evidence for inherited factors, and the role of the dopamine and serotonin systems in OCD, we typed the dopamine D3 receptor gene (DRD3) in 40 probands and controls. Chi-squared analyses of allele frequencies and genotypes revealed no significant difference between OCD subjects and controls. The 2 x 2 table of allele frequencies revealed a p value of 0.5, and for the 2 x 3 table of genotypes, $p = 0.2$. Typing of a functional polymorphism in the 5HT2A receptor gene is in progress. We conclude from the family study results that both OCD and OCB are strongly familial. The DRD3 polymorphism does not appear to be involved in the susceptibility to OCD.

NR350 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Exonic and Intronic Polymorphisms in the D3 Gene

Marc-Antoine Crocq, M.D., Psychiatry, Centre Hospitalier, 27 Rue Du 4 RSM, 68250 Rouffach 00110, France; Fabrice Duval, M.D., Alain Buguet, M.D., Sylvie Bisser, M.D., Antonia Mayerova, Ph.D., Jean-Paul Macher, M.D.

Summary:

Objective: The dopamine D3 receptor is a major target for antipsychotics and forms one subfamily with the D2 and D4 receptors. A few studies (Crocq et al. 1992, Mant et al. 1994) have shown a weak association between schizophrenia and homozygosity at a Bal I polymorphic site in the first exon of the D3 gene. However, this has not been replicated by others, and further studies are necessary.

Method: Using PCR we genotyped two di-allelic polymorphisms of the dopamine D3 gene, namely the known Bal I site in the first exon and a recently localized Msp I site in the fourth intron, in

Caucasians from France (n = 101) and Africans from the Republic of Congo (n = 56).

Results: At both loci, the predominant allele was different in Caucasians (Bal I allele 1: 0.67; Msp I allele 1: 0.52) and Africans (Bal I allele 1: 0.12; Msp I allele 1: 0.24). Within the African group, allelic frequencies did not differ between healthy subjects and 25 patients with trypanosomiasis (sleeping sickness).

Conclusions: Bal I allelic frequencies in the D3 gene display ethnic variations, even though schizophrenia is present in all human cultures. This suggests that if the Bal I locus is associated with schizophrenia, it might not be causative per se but instead is a marker that is linked to another causative mutation in some populations.

NR351 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Distribution of the TaqI Polymorphism of the Dopamine D2 Receptor in Korean Alcoholism Population

Min Soo Lee, M.D., Psychiatry, Korea University, 126-1 5-Ka Anam-Dong, Sungburk, Ku Seoul 136-705, Korea; Young Tae Kim, M.D., Dong-Il Kwak, M.D.

Summary:

The allelic distribution of TaqI polymorphism of the D2 dopamine receptor gene in alcoholism was examined in 25 Korean alcoholics and compared with Korean controls. In alcoholics, the numbers of alcoholics with A1A1, A1A2, and A2A2 were five (20%), 15 (60%), and five (20%), respectively, and in controls with A1A1, A1A2, and A2A2 were two (8%), eight (32%), and 15 (60%), respectively. The prevalence of the A1 allele in alcoholics was 80% and was 40% in controls. And the frequency of the A1 allele in alcoholics and controls were 0.5, and 0.24, respectively. There was significant difference in the frequency of the A1 allele between alcoholics and controls ($P < .05$).

These data suggest that the A1 allele is associated with alcoholism in a Korean population. However, the possibility that the gene is not a genetic determinant in the etiology of alcoholism cannot be definitely excluded, because of the intrinsic limitation of the method of analysis, the number of subjects studied, other contradictory findings by other studies, and similar increase in the prevalence of the A1 allele in the spectrum of disorders that share a common pathophysiologic genetic mechanism.

NR352 Tuesday, May 23, 3:00 p.m.-5:00 p.m.

Psychiatric Disturbances in Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy Disease

Docteur C. Spadone, Centre Hospitalier, Sainte-Anne, 1 rue Cabanis, Paris 75674, France; M.O. Krebs, J.M. Vanelle, M.F. Poirier, H. Chabriat, F. Guedj, H. Loo

Summary:

A new neurological pathology called CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy) has been identified as linked to a genetic defect on the 19th chromosome (Tournier-Lasserve et al., 1993, *Nat. Genet.*, 3, 256). Clinical features include transitory ischemic accidents, strokes, dementia, and migraine associated with white matter and basal ganglia hyperdensities on MRI.

Family studies exhibit an autosomal dominant transmission with a complete penetrance over 30 years old, when phenotypes are based on MRI results. Genetic diagnosis is based on a significant linkage between the disease and a chromosome 19 marker in the tested families. Interestingly, a high prevalence of psychiatric symptoms has been observed among CADASIL patients (the third type of symptoms in frequence). We attempted to characterize them.

Four patients with genetically defined CADASIL and four patients with putative CADASIL (on the basis of clinical history and MRI) have been evaluated using two general psychiatric scales (SCL-90-R and CPRS). All patients were also examined with a standardized interview (SADS-LA-R), which generates retrospective lifetime DSM-III-R diagnoses. Results showed high prevalence of bipolar mood disorders, familial or not, and anxiety disorders.

Further studies are needed to find out whether bipolar mood disorders and CADASIL are genetically linked, or whether mood disorders are symptomatic of cerebral lesion. Consequences for genetic studies in bipolar mood disorders will be discussed.

NR353 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Self-Reported Sexual Dysfunctions in Social Phobic Patients

Michael R. Ware, M.D., Dept of Psychiatry, Medical University of SC, 171 Ashley Ave, Charleston SC 29425; Naresh P. Emmanuel, M.D., Violetta D. Czepowicz, M.D., Michael R. Johnson, M.D., Rebecca Kapp, R.N., R. Bruce Lydiard, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the common sexual dysfuntions in social phobic male and female patients.

Summary:

Objective: A consistent data base on the effects of Axis I psychopathology on sexual functioning in psychiatric patients is lacking. There has been essentially no investigation into the sexual functioning of patients suffering from anxiety disorders. We speculate that social phobics (SP) will demonstrate diminished sexual desire and functioning as a group compared with normal controls.

Methods: The Sexual Function Questionnaire (SFQ) is a self-report instrument designed to measure treatment emergent changes in the area of psychosexual dysfunction including inhibited sexual desire, inhibited sexual excitement, and inhibited orgasm. To date, 38 unmedicated patients (23 male, 15 female) diagnosed with DSM-III-R social phobia using a structured clinical interview have entered psychopharmocology trials and have completed the SFQ at baseline. Data from a comparison group of 26 normal controls (six male, 20 females) has also been collected.

Results: Preliminary data analysis utilizing chi square demonstrates that as a group SP patients are significantly more likely to report a sexual dysfunction ($p = 0.045$), and less likely to have a satisfactory nonsexual relationship with their partner ($p = 0.042$) compared with normal controls. Further, female SP patients are significantly less likely to report having regular menstrual periods compared with controls ($p = 0.027$).

Conclusion: Unmedicated social phobic patients appear to be at significant risk for experiencing one or more sexual dysfunctions. Data analysis from an enriched SP patient and normal control population will be presented.

References:

1. Gitlin MJ: Psychotropic medications and their effects on sexual function: diagnosis, biology, and treatment approaches. *J Clin Psych* 55:406-413, 1994.

2. Harrison WM, Rabkin JG, Ehrhardt AA, et al.: Effects of antidepressant medication on sexual function: a controlled study. *J Clin Psychopharm* 6:144-149, 1986.

NR354 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Long-Term Treatment and Prevention of Relapse of OCD with Paroxetine

Martin Steiner, Ph.D., Clinical Develop., Smith Kline Beecham, P.O. Box 1510, King of Prussia PA 19406; William D. Bushnell, M.S., Ivan P. Gergel, M.D., David E. Wheadon, M.D.

Educational Objectives:

To evaluate the safety and efficacy of paroxetine, a selective serotonin reuptake inhibitor, in maintaining response and preventing relapse during long-term treatment of obsessive compulsive disorder.

Summary:

The SSRIs, including paroxetine, have been shown to be effective in the short-term treatment of OCD.

Objective: The purpose of this study is to evaluate the effectiveness of paroxetine during long-term treatment of OCD.

Method: All patients who met DSM-III-R criteria for OCD and had completed a 12-week study of paroxetine and placebo in the treatment of OCD (Study 116) and who, in the opinion of the investigator, would benefit from continued treatment, were eligible to participate in a 12-month extension (Study 126). The extension was divided into a six-month open-label phase with flexible dosing of paroxetine (20-60 mg/day), followed by a double-blind phase in which patients who achieved a therapeutic response were randomized to receive paroxetine or placebo.

Results: At baseline, the mean YBOCS Total score for the Study 116 population was 25.45. After 12 weeks, the mean improvement in YBOCS Total score for the cohort of patients (n = 263) eligible to enter the extension study was 5.70 points. Improvement continued during the open-label phase, with a mean improvement of 10.81 points at month 6. At that point, 104 patients met the criteria for a therapeutic response and were randomized in double-blind fashion to receive paroxetine (n = 53) or placebo (n = 51). The intent-to-treat survival analysis of time to relapse demonstrated significant treatment effect (p = 0.001) in favor of paroxetine, and a risk ratio of 2.7 with a 95% confidence interval. The mean time to relapse for the placebo group was 28.5 days compared to 62.9 days for the paroxetine group. Categorical analysis revealed that the percent of patients who relapsed also was significantly greater (p = 0.033) in the placebo group (30/51, 58.8%) than in the paroxetine group (20/53, 37.7%). Mean YBOCS Total scores were maintained or slightly improved in the paroxetine group but deteriorated over time in the placebo group.

Conclusions: The results of this study demonstrate that long-term treatment with paroxetine is effective in maintaining a therapeutic response and preventing relapse of OCD.

References:

1. Freeman CPL, Trimble MR, Deakin JFW, et al.: Fluvoxamine versus clomipramine in the treatment of obsessive compulsive disorder: a multicenter, randomized double-blind, parallel group comparison. *J Clin Psychiatry.* 55:301-305, 1994.

2. Tollefson GD, Rampey AH, Potvin JH, et al.: A multicenter investigation of fixed-dose fluoxetine in the treatment of obsessive-compulsive disorder. *Arch Gen Psychiatry.* 51:559-567, 1994.

NR355 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

A Fixed Dose Study of Paroxetine and Placebo in the Treatment of Panic Disorder

Martin Steiner, Ph.D., Clinical Develop., Smith Kline Beecham, P.O. Box 1510, King of Prussia PA 19406; Rosemary Oakes, M.S., Ivan P. Gergel, M.D., Daniel B. Burnham, Ph.D., David E. Wheadon, M.D.

Educational Objectives:

To appreciate the potential usefulness of paroxetine, a selective serotonin reuptake inhibitor, in the treatment of panic disorder.

Summary:

There is considerable evidence of comorbidity between major depression and panic disorder. A number of antidepressant drugs have been reported to be useful in the treatment of panic disorder; however, the only drug currently approved in the United States is a high-potency benzodiazepine (alprazolam).

Objective: This study was conducted to assess the safety and efficacy of paroxetine, a selective serotonin reuptake inhibitor, in the treatment of panic disorder.

Method: In this fixed-dose, parallel-design, 10-week trial, 278 patients who met DSM-III-R criteria for panic disorder (with or without agoraphobia) were randomized in double-blind fashion to receive paroxetine (10 mg, 20 mg, or 40 mg/day) or placebo. Patients assigned to 20 mg and 40 mg paroxetine were titrated to their respective dose levels.

Results: After 10 weeks of treatment, statistically significant differences were observed between paroxetine 40 mg and placebo for three of four primary efficacy variables: number of full panic attacks, percent of patients with no panic attacks, and CGI severity of illness. Statistical differences also were noted in a number of the secondary efficacy measures, including: Marks-Sheehan Phobia Scale, Hamilton Anxiety Scale, Montgomery-Asberg Depression Scale, and CGI global improvement. Paroxetine was well-tolerated and the adverse event profile in panic disorder patients was similar to that observed in depressed patients.

Conclusion: These results demonstrate the safety and effectiveness of paroxetine in the treatment of panic disorder.

References:

1. Rosenberg R: Drug treatment of panic disorder. *Pharmacol and Toxicol.* 72:344-353, 1993.

2. Modigh K, Westberg P, Eriksson E: Superiority of clomipramine over imipramine in the treatment of panic disorder: a placebo-controlled trial. *J Clin Psychopharmacol.* 12:252-261, 1993.

NR356 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Fluvoxamine Versus Clomipramine for OCD: A Double-Blind Comparison

Lorrin M. Koran, M.D., Psychiatry, Stanford Univ & Med, Rm 3362 Dept of Psych & Behav., Palo Alto CA 94305; Susan L. McElroy, M.D., Jonathan R.T. Davidson, M.D., Steven A. Rasmussen, M.D., Eric Hollander, M.D., Michael A. Jenike, M.D.

Educational Objectives:

To recognize and manage pharmacologic differences between fluvoxamine and clomipramine treatment of obsessive compulsive disorder (OCD) patients.

Summary:

The efficacy and safety of fluvoxamine (100 to 300 mg/day) and clomipramine (100 to 250 mg/day) were compared in a randomized, double-blind, parallel-group study of 79 patients with obsessive compulsive disorder (OCD) without coexisting depressive disorder. After a two-week placebo lead-in period, patients were randomized to fluvoxamine (37 patients) or clomipramine (42 patients) for 10 weeks. Efficacy was evaluated using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the National Institute of Mental Health Obsessive-Compulsive Scale (NIGH-OC), and Patient and Clinical Global Improvement Scales (PGI, CGI). Hamilton Depression scale (HAM-D) scores and somatic

symptoms (PSSC) were also assessed. Seventy-eight percent of fluvoxamine patients completed the entire study, compared with 64% of clomipramine patients. At the end of treatment, 56% of patients who received fluvoxamine were classified as responders, compared with 54% of patients who received clomipramine. Both groups showed steady improvement throughout the study; no statistically significant differences were observed between the groups for any efficacy variable at any time. A similar percentage of patients in both groups withdrew as a result of adverse events. No serious adverse events occurred with either drug. Insomnia, dyspepsia, and nervousness were more frequent with fluvoxamine, while dry mouth and postural hypotension were more frequent with clomipramine. This study demonstrated that fluvoxamine and clomipramine were equally effective in reducing OCD symptoms over a 10-week treatment period. However, the side-effect profile of fluvoxamine differs from that of clomipramine.

References:

1. Clomipramine Collaborative Study Group: Clomipramine in the treatment of patients with obsessive compulsive disorder. *Arch Gen Psychiatry* 48:730-738, 1991.

2. Goodman WK, Price LH, Rasmussen SA, et al.: Efficacy of fluvoxamine in obsessive compulsive disorder. *Arch Gen Psychiatry* 46:36-44, 1989.

NR357 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Cost Effectiveness of Fluvoxamine, Placebo and Cognitive Behavior Therapy Alone and in Combination in the Treatment of Panic Disorder

Richard J. Simpson, M.D., Health Center, Bridge of Allan, Fountain Road, Bridge of Allan FRQ 4EU, England; Donald M. Sharp, Ph.D., Kevin G. Power, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat panic disorder with or without agoraphobia in the most cost-effective way, including appropriate pharmacotherapy (e.g., SSRIs) alone or in combination with cognitive behavior therapy to assure a rapid onset of action and a persistence of effect.

Summary:

Objective: Well-controlled studies of drug therapy or cognitive behavior therapy separately or in combination are lacking in a number of indication areas in which these are often employed (e.g., panic disorder). This information is needed not only to establish efficacy, but also in order to develop factually based clinical-decision models for disease management using clinically relevant outcome variables.

Methods: 190 patients entered the study who met DSM-III-R criteria for panic disorder with or without agoraphobia and were randomly allocated to fluvoxamine (FL), placebo (PL), cognitive behavior therapy (CBT), FL + CBT, or PL + CBT. Patients (except CBT) received single-blind placebo medication for a one-week wash-out period, followed by a 12-week double-blind treatment phase. CBT was standardized and emphasized both gross exposure techniques and cognitive and behavioral panic management techniques. The FL, PL, and CBT received equal therapist contact time (30-60 min.). Measurements for treatment effect included: (for anxiety) the HAM-A, and a patient-rated scale (Sheffield Symptom Rating Test), the Fear Questionnaire (FQ) for avoidance, and panic attacks by a daily patient diary, and outcome variables to determine clinical relevance. Follow-up was obtained six months later.

Results: All active treatment groups showed a decrease in anxiety as measured by the HAM-A and the patient-rated scale, with the FL + CBT showing the earliest treatment effect (week 4). Phobic avoidance and number of panic attacks significantly decreased by week 12, with the FL + CBT again showing the largest response (83%). Treatment effects were observed in spite of a relatively large placebo response in the PL group on some measures of general anxiety, probably due to the increased therapist contact time. The FL group showed the highest proportion of patients (83%) achieving a clinically relevant outcome on the HAM-A and the FQ at end point. At the six-month follow-up, the FL + CBT group showed the best persistence of effect in the outcome variables, maintaining clinically relevant treatment gains with fewer intervening therapies (20%). The CBT + PL and PL alone groups had a higher proportion (43%) of patients who received subsequent treatment during the follow-up phase.

Conclusions: FL shows efficacy in panic disorder. All the active treatment groups showed therapeutic gains, with the FL + CBT showing the earliest onset of action and the longest persistence of effect, and the FL group showing the most clinically significant changes in core symptoms at end point. These results are similar to those reported in studies with imipramine and CBT in depression. Taking into account the earlier onset of action, fewer intervening therapies, and a persistence of clinical improvement six months later, suggests that FL + CBT can be cost-effective in treating panic disorder.

References:

1. Barlow DH, et al.: Behavioral treatment of panic disorder. *Beh Therapy,* 20:261-282, 1989.

2. den Boer JA, Westenberg HG: Serotonin function in panic disorder: a double-blind placebo-controlled study with fluvoxamine and ritanserin. *Psychopharm.* 102:85-94, 1990.

NR358 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

CSF Serotonin: Diagnostic and Seasonal Differences

Timothy D. Brewerton, M.D., Dept of Psych, MUSC, 171 Ashley Ave, Charleston SC 29425-0002; R. Bruce Lydiard, M.D., Michael R. Johnson, M.D., James C. Ballenger, M.D., Mark D. Fossey, M.D., James E. Roberts, Ph.D.

Educational Objectives:

To recognize the implications of recent findings showing diagnostic and seasonal variations in levels of CSF serotonin in humans.

Summary:

Objective: Although the indole neurotransmitter serotonin (5-hydroxytryptamine, 5-HT) has been of major interest to psychiatry since the 1950's, its direct measurement in CSF has been elusive given instrumental and methodological limitations.

Method: Using an enzyme immunoassay method, we measured CSF 5-HT concentrations in 77 drug-free subjects (55 females, 22 males), including normal controls (NC) ($n = 18$) and patients with DSM-III-R-defined obsessive compulsive disorder (OCD) ($n = 10$), generalized anxiety disorder (GAD) ($n = 17$), panic disorder (PD) ($n = 25$), and bulimia nervosa (BN) ($n = 7$). After four days of a low monoamine diet and overnight bedrest, CSF was obtained from each subject (12th-25th cc's).

Results: In a two-way analysis of covariance (ANCOVA) using diagnosis and season as grouping variables and gender as a covariate, we found a significant difference by diagnosis ($p \leq 0.008$) in all subjects and in women only ($p \leq 0.03$). In the total group, significant post-hoc differences were seen, with the OCD and GAD groups having significantly lower CSF 5-HT levels than the NC, PD, and BN groups ($p \leq 0.05$). We also found a significant difference by season in all subjects ($p \leq 0.025$) and a trend in women only ($p \leq 0.06$). Post-hoc differences were found for winter vs. summer and fall, and for spring vs. fall ($p \leq 0.05$).

Conclusions: To our knowledge this is the first report of 1) lower concentrations of CSF 5-HT in patients with OCD and GAD

compared with controls, and 2) seasonal differences in CSF 5-HT concentrations. These data contribute to our increasing understanding of 5-HT's roles in anxiety disorders and seasonal phenomena in psychiatry.

References:

1. Brewerton TD, Berrettini W, Nurnburger J, Linnoila M: An analysis of seasonal fluctuations of CSF monoamines and neuropeptides in normal controls: findings with 5-HIAA and HVA. *Psychiatry Res.*, 23:257-265, 1988.

2. Brewerton TD, Flament M, Rapoport J, Murphy DL: Seasonal variation of platelet 5-HT content. *Arch Gen Psychiatry* 50:409, 1993.

NR359 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Risperidone Versus Haloperidol in Treatment Refractory Schizophrenia: Preliminary Results

William C. Wirshing, M.D., Psychiatry, West LA VA Med Center, 11301 Wilshire Blvd Ward 210C, Los Angeles CA 90073; Donna Ames, M.D., Michele Palmer Bray, B.S., Barringer D. Marshall, Jr., M.D., Michael F. Green, Ph.D., Stephen R. Marder, M.D.

Educational Objectives:

To understand preliminary findings regarding the safety and efficacy of risperidone versus haloperidol in the treatment of refractory schizophrenia.

Summary:

Objective: Risperidone is a new antipsychotic agent that has demonstrated efficacy in the treatment of acute episodes of schizophrenia. However, it has not been studied in patients who are poor responders to conventional drugs. This ongoing double-blind study is designed to examine the safety and efficacy of risperidone when compared to haloperidol in treatment-refractory schizophrenic patients.

Method: To date 19 patients have participated in the study. After a week-long placebo washout, they receive four weeks of fixed dose risperidone 6mg or 15mg of haloperidol. The following four weeks dose can be adjusted either up or down. Patients are evaluated weekly using the PANSS, BPRS, UPDRS, AIMS, and Barnes Akathisia scales. Patients are followed for up to a year on open-label risperidone after completion of the double-blind phase.

Results: Three of the 10 haloperidol treated patients dropped prematurely from the study whereas all of the risperidone treated patients completed the initial eight weeks of the study. Seven patients in the haloperidol-treated group required medications for extrapyramidal side effects whereas only two risperidone-treated patients received side effect medication ($X^2 = 4.34$, $p = .04$). Both groups, had on average, 10%-15% improvement on the positive, negative, and general psychopathology subscales of the PANSS.

Conclusions: To date our preliminary results demonstrate that risperidone may be better tolerated in a treatment-refractory group of patients, perhaps due to its decreased liability of causing extrapyramidal side effects.

References:

1. Marder SR, Meibach RC: Risperidone in the treatment of refractory schizophrenia. *American Journal of Psychiatry,* 151:825-835, 1994.

NR360 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Cingulate Metabolism in Schizophrenia Spectrum

M. Mehmet Haznedar, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Benjamin V. Siegel, M.D., Larry J. Siever, M.D., Marja Germans, B.A.

Educational Objectives:

At the conclusion of this presentation the participant should understand the role of cingulate pathology and the concept of hypofrontality in schizophrenia spectrum illnesses.

Summary:

The relationship between schizotypal personality disorder (SPD) and schizophrenia has been supported by family studies. Anterior cingulate cortex (ACC) is of particular interest in schizophrenia, as it has been implicated in both attentional and affective behaviors, and postmortem studies have shown cytoarchitectural changes in schizophrenic subjects. In our current project we studied glucose metabolism using positron emission tomography (PET) in 12 SPD patients, 19 schizophrenic patients, and 21 normal controls. Patients were off all psychoactive medication for at least two weeks and all subjects had negative urine screens for drugs of abuse. Patients met DSM-III-R criteria for SPD or schizophrenia. During the 18-fluorodeoxyglucose uptake period all subjects performed the California Verbal Learning Test (CVLT), and then were scanned with our high-resolution (4.5mm FWHM) scanner. Cingulate glucose metabolic rate (GMR) was measured using a stereotaxic template developed from the MRI of 16 subjects. Twelve regions of interest from ACC to posterior cingulate cortex (PCC) were used to form an arch. Measurments of GMR in the medial frontal regions anterior to the ACC were done for comparison. GMR in the ACC was lowest in the SPD group and highest in the control group, with that of the schizophrenics falling between. In contrast, GMR in the PCC was lowest in the control group and highest in the SPD group, with that of the schizophrenics falling between ($F = 1.92$, corrected df = 16.68, 408.74, $p < .02$). This finding that patients with SPD exhibit hypofrontal and hypocingulate function as do schizophrenics, without possessing the potential artifacts of chronic hospitalization and neuroleptic treatment, suggests that these deficits may be related to a neuroanatomically based risk factor in schizophrenia.

References:

1. Siegel BV, Buchsbaum MS, Bunney WE, et al.: Cortical-striatal-thalamic circuits and brain glucose metabolic activity in 70 unmedicated male schizophrenic patients. *Am J Psychiatry* 150:1325-1336, 1993.

2. Buchsbaum MS: The frontal lobes, basal ganglia, and temporal lobes as sites for schizophrenia. *Schizophr Bull* 16;379-389, 1990.

NR361 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Efficacy of Clozapine Versus Haloperidol in a Long-Term Clinical Trial: Preliminary Results

John M. Kane, M.D., Department of Psychiatry, Hillside Hospital, 266th & 76th Avenue, Glen Oaks NY 11004; Stephen R. Marder, M.D., Nina R. Schooler, Ph.D., Daniel S.G. Umbricht, M.D., Donna Ames, M.D., William C. Wirshing, M.D., Robert Baker, M.D., Rohan Ganguli, M.D., Allan Z. Safferman, M.D., Michael Borenstein, Ph.D.

Educational Objectives:

To understand the utility of clozapine vs. haloperidol in schizophrenic outpatients who are partial responders.

Summary:

Objective: This 29-week, three-center trial was designed to compare the efficacy of clozapine (CLZ) to haloperidol (HPL) in schizophrenic outpatients who are partial responders to conventional compounds.

Methods: To date, 52 subjects have completed the double-blind comparison. Three clinical outcome criteria have been examined:

remission, improvement, and time to discontinuation for lack of efficacy. Remission is defined as meeting two of the following three criteria: have no more than mild symptomatology on any symptom in the Psychosis factor of the BPRS; the Clinical Global Impressions (CGI) Improvement is "moderately improved"; and the other BPRS items that were "moderate" at baseline are reduced by at least two scale points. Improvement is defined as 20% or greater improvement on the Psychosis factor of the BPRS.

Results: Initial survival analyses of the data on the 52 subjects (CLZ = 25, HPL = 27) reveal that a significantly greater proportion of patients met the remission criterion with CLZ (32%) compared to HPL (8%) (Mantel Haenzel $X^2 = 3.98$, $p < 0.05$ [df = 1]). A significantly greater proportion met the less stringent "improvement" criterion with CLZ (54%) than with HPL (8%) (Mantel Haenzel $X^2 = 11.08$, $p < 0.001$ [df = 1]). A significantly lower proportion was discontinued for lack of efficacy with CLZ (4%) than HPL (62%) (Mantel Haenzel X^2 15.83, $p < 0.001$ [df = 1]).

Conclusions: These preliminary results suggest that CLZ may be a superior alternative to continued conventional antipsychotic medication in outpatients with partially responsive symptoms.

References:

1. Kane JM, Honigfeld G, Singer J, et al.: Clozapine for the treatment-resistant schizophrenic: a double-blind comparison versus chlorpromazine/benztropine. *Arch Gen Psychiatry* 45:789-796, 1988.

NR362 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Long-Term Stability of Diagnosis and the Positive Negative Distinction in a Systematic Sample of Childhood and Adolescence Onset Schizophrenia

Michel Maziade, M.D., Hotel-Dieu Du Sacre Coeur, 1 Avenue Du Sacre Coeur, Quebec QC G1N 2W1, Canada; Nathalie Gingras, M.D., Stephane Bouchard, Ph.D., Benoit Gauthier, M.D., Guy Tremblay, M.D., Serge Cote, M.D., Chantal Merette, Ph.D.

Educational Objectives:

To review the four short-term longitudinal studies that are published on childhood-onset schizophrenia (EO-SZ); to learn about the similarities and differences between EO-SZ and adult-onset SZ and the implications for biological and genetic studies of schizophrenia.

Summary:

Little is known about the long-term outcome of childhood and adolescence onset schizophrenia (EO-SZ) and whether EO-SZ represents an etiologically separate form of schizophrenia (SZ). The present long-term epidemiological study over a period of 15.5 years aimed to tackle these two questions by means of: 1) a systematic sampling frame in a catchment area, 2) best-estimate DSM-III-R diagnoses made independently in childhood and in adulthood, 3) measures of the positive and negative symptoms through the CASH scale made separately in each period, 4) measures of nonpsychotic behavior disturbances (NPBD) and developmental problems prior to the appearance of SZ.

Sample: 33 consecutive referrals for SZ (mean age of onset: 13.5 years) to a regional center within a 22-year period.

Results: Data showed a) a high stability of DSM-III-R diagnosis until adulthood (mean age at follow-up: 28.5 years) but a weak continuity of the positive and negative dimensions; b) a poor long-term outcome of EO-SZ, a majority presenting a deteriorating course; c) an overrepresentation of males but little gender differences in clinical features and outcome; d) a bimodal distribution of age of onset of NPBD with a demarcation before the age of 7; e) a better long-term predictive power of age at onset of NPBD and developmental problems than of onset of psychosis. As a whole, DSM-III-R EO-SZ shows only quantitative differences with adult onset SZ. However, our data suggest that a distinction through the onset of preschizophrenic development or NPBD might be a promising way to disentangle genetic heterogeneity within EO-SZ.

References:

Asarnow RF, Asarnow RJ. Childhood-onset schizophrenia: editor's introduction. *Schizophrenia Bulletin,* 20(4): 591-597, 1994.

Maziade M, Raymond V, Cliche D, et al.: Linkage results on 11q21-22 in Eastern Quebec pedigrees densely affected by schizophrenia. *American Journal of Medical Genetics (Neuro-psychiatric Genetics),* in press.

NR363 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Olanzapine in the Treatment of Schizophrenia and Other Psychotic Disorders

Pierre V. Tran, M.D., MC 783, Eli Lilly Company, Lilly Corporate Center DC 2128, Indianapolis IN 46268; Charles M. Beasley, Jr., M.D., Gary D. Tollefson, M.D., W. Satterlee, M.D., J.G. Small, M.D., G. Besancon, D. Naber, T.M. Sanger, Ph.D., J. Bailey, A. Wood, K.A. Graffeo, Herbert Y. Meltzer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be informed about the mechanism of action, clinical pharmacology, clinical efficacy, and side-effect profile of olanzapine, a promising new "atypical" antipsychotic agent.

Summary:

Olanzapine, structurally a thienobenzodiazepine, is a putative "atypical" antipsychotic agent. In vitro studies have indicated that olanzapine has high affinity for 5-HT_{2A}, 5-HT_{2C}, D_4, D_1, D_2, muscarinic (particularly M_1), α_1, and H_1 receptors. In vivo binding studies, neuroendocrine studies and behavioral studies all suggest greater in vivo antagonism of 5-HT compared to D_2 receptors. Olanzapine selectively diminishes the spontaneous firing rate of A_{10} dopaminergic neurons without decreasing the rate of A_9 neurons on chronic administration suggesting antipsychotic activity with low potential for extrapyramidal symptoms.

Olanzapine has been shown to be superior to placebo in its efficacy against core positive and negative symptoms in two large placebo-controlled trials. In another dose-ranging haloperidol-controlled trial, it was found that increasing doses of olanzapine (up to 17.5 mg/day) produced increasing improvement in both the general psychopathology and negative symptoms of schizophrenia. The percentage of olanzapine-treated patients who discontinued from the study due to adverse events (10.9% across all olanzapine groups combined) was lower than the percentage of haloperidol-treated patients (14.8%). Treatment with olanzapine produced substantially less prolactin elevation and extrapyramidal symptoms when compared with haloperidol treatment. Experience to date suggest that olanzapine possesses many key characteristics of an "atypical" antipsychotic agent.

The acute phase (6 weeks) of a large (n = 1992) double-blind, olanzapine, and haloperidol trial in patients diagnosed with schizophrenia, schizophreniform disorder or schizoaffective disorder conducted in North America and Europe has more recently been completed. Results of this trial will be reported in detail.

References:

1. Moore NA, Callefaro DO, Wong DT, et al.: The pharmacology of olanzapine and other new antipsychotic agents. *Curr Opin Invest Drugs,* 2(4):281-293, 1993.

2. Tran PV, Beasley CM, Tollefson GD, et al.: Clinical efficacy and safety of olanzapine: A new atypical antipsychotic agent. American

Psychiatric Association Annual Meeting. Philadelphia, May 24, 1994.

NR364 Wednesday, May 24, 9:00 a.m.-10:30 a.m.

Fluid and Osmolyte Balance During Neuroleptic Malignant Syndrome

Ronald J. Gurrera, M.D., Psychiatry, Brockton DVAMC, 940 Belmont Street 116A, Brockton MA 02401;

Educational Objectives:

At the conclusion of this presentation, the participant should be able to provide more prompt and rational treatment of dehydration in patients with NMS based on a better understanding of its pathophysiology in this disorder.

Summary:

Diaphoresis and dehydration frequently occur together in neuroleptic malignant syndrome (NMS), but their pathophysiologic roles are uncertain. Dehydration may cause or contribute to NMS or be a consequence of untreated neuroleptic-induced extrapyramidal symptoms and fever, or diaphoresis may produce dehydration. In this study retrospective data were systematically collected from a large NMS case series for a 21-day period centered on the date of maximal clinical intensity ("peak date" ± 10d). Nonparametric one-way ANOVAs were used throughout. Twenty-eight patients (34 episodes) met NMS diagnostic inclusion criteria; of these, 20 patients (20 episodes) received intravenous hydration (IVH) at some point during the study period. Patients who received IVH had higher serum smolality ($p = .00003$) and greater calculated free water deficit ($p < .0044$) than those who did not, indicating that IVH was clinically appropriate. Patients with diaphoresis as an NMS feature had higher serum osmolality ($p < .00022$) than those without it, and were more likely to require IVH (Fisher exact test, $p = .009$). Patients who exhibited polydipsia during their episode had higher serum osmolality ($p < .41 \times 10^{-7}$) and greater free water deficit ($p = .77 \times 10^{-6}$) than those without polydipsia, indicating intact osmoreceptor function and suggesting that inadequate water intake was not the cause of dehydration. Urine specific gravity did not differ between any of these groups ($p < .25$ for all comparisons). These results indicate that clinically significant dehydration is a frequent concomitant of NMS, diaphoresis is associated with clinically significant dehydration, and central osmoreceptor function appears to be intact in NMS but renal osmoregulation may be impaired.

References:

1. Rosebush P, Stewart T (1989) *Am J Psychiatry,* 146:717-725.

2. Levinson DF, Simpson GM (1986) *Arch Gen Psychiatry,* 43:839-848.

3. Gurrera RJ, Chang SS, Romero JA (1992) *J Clin Psychiatry,* 53:56-62.

NR365 Wednesday, May 24, 12 noon-2:00 p.m.

Body Dysmorphic Disorder is Comorbid with Major Depression

Andrew A. Nierenberg, M.D., Clin Psychopharmacology U, Massachusetts General Hos, 15 Parkman Street WACC 815, Boston MA 02114; Katharine A. Phillips, M.D., Junko Kaji, B.A., Jonathan E. Alpert, M.D., John J. Worthington III, M.D., Maurizio Fava, M.D.

Summary:

Background: Body dysmorphic disorder (BDD) is preoccupation with imagined or slight defects in appearance that have been found by our group to appear as a comorbid condition in 13.8% of patients with atypical depression (Phillips et al. 1994).

Objective: The purpose of this study was to evaluate the prevalence of BDD in a separate cohort of patients with typical and atypical major depressive disorder.

Methods: 172 consecutive drug-free outpatients with major depressive disorder (MDD) who entered into a study of fluoxetine adjuncts were evaluated with the SCID-P, the ADDS, and a diagnostic module for BDD. Depressed subjects with comorbid BDD were compared with those without BDD with regard to demographics, depressive course, and other relevant measures. Unpaired t-tests and chi square statistics were used as appropriate.

Results: Fifteen (8.7%) subjects had a lifetime history of BDD. Those with comorbid BDD had an earlier age on onset of depression and longer duration of the current episode but did not have a greater number of episodes or greater severity of depression as compared with those without BDD. Both groups were similar with respect to age, gender, and marital status. There were a higher proportion of patients with BDD among the atypical depressives than nonatypical depressives (15% and 5.5%, respectively, $p = .024$). We also found that subjects with BDD had higher proportions of anxiety and personality disorders but not obsessive compulsive or eating disorders.

Conclusions: Our results indicate that BDD is frequently comorbid with major depression, is associated with an earlier age of onset of depression and longer duration of episodes, and is found more frequently in atypical depression.

NR366 Wednesday, May 24, 12 noon-2:00 p.m.

Does Degree of Insight in OCD Predict Improvement?

Jane L. Eisen, M.D., Butler Hospital, 345 Blackstone Blvd., Providence RI 02906; Steven A. Rasmussen, M.D., Katharine A. Phillips, M.D., R. Bruce Lydiard, M.D., Teresa A. Pigott, M.D.

Summary:

Objective: To determine whether insight in obsessive compulsive disorder (OCD) predicts response to selective serotonin reuptake inhibitors (SSRIs).

Background: A number of studies have demonstrated a range of insight in OCD. Based on these studies, DSM-IV has a new OCD subtype—OCD with poor insight. There is a paucity of data concerning the relationship between insight and treatment response.

Methods: Three sites participated in an insight study as part of a multisite OCD sertraline relapse study. A reliable pilot version of a rating scale developed to evaluate insight and degree of conviction, the Brown Assessment of Beliefs Scale (the BABS) was administered to 29 OCD probands at these three sites during the baseline visit and the week 16 visit. During this four-month period, patients were treated "openly" with sertraline using doses ranging from 50-200 mgs. daily. The Yale-Brown Obsessive Compulsive Rating Scale (the YBOCS) was administered at baseline and at 16 weeks. Spearman correlations between the BABS and YBOCS were conducted.

Results: Correlation between the baseline total BABS (minus the items on the BABS that are similar to YBOC items) and the percent change on YBOC from baseline to week 16 was 0.12. The mean YBOCS change was 14.1 ± 6 for those patients who had complete certainty about the accuracy of their obsessions ($n = 8$) vs. 13.2 ± 8.2 for those patients who had better insight ($n = 21$).

Conclusions: Poor insight as defined by the BABS overall score or by assessing conviction of beliefs alone did not affect response to sertraline.

NR367 Wednesday, May 24, 12 noon-2:00 p.m.

Remission and Relapse in OCD: A Two-Year Prospective Study

Jane L. Eisen, M.D., Butler Hospital, 345 Blackstone Blvd., Providence RI 02906; Steven A. Rasmussen, M.D., Wayne K. Goodman, M.D., Meredith Warshaw, Ph.D.

Summary:

Objective: To assess course of illness in obsessive compulsive disorder (OCD).

Background: OCD is a major psychiatric disorder with a lifetime prevalence of 2.5%. However, there has been no careful prospective study of patterns of remission and relapse, comorbidity, and changes in functioning and quality of life.

Methods: We conducted a naturalistic follow-up study of OCD over a period of two years. Sixty-five consecutive patients referred to two university-based OCD clinics were followed prospectively for 24 months. Sixty patients successfully completed assessments at baseline, 3, 6, 12, and 24 months from intake. Baseline assessments included structured interviews for both Axis I and II disorders, the Yale-Brown Obsessive Compulsive Scale (the YBOCS), and the Psychiatric Rating Scale (PSR), a six-point measure of symptomatic status. Follow-up measures included Global Assessment of Functioning (GAF), as well as the YBOCS, the PSR, and the LIFEUP, which evaluates diagnosis, treatment received, and psychosocial functioning.

Results: Of the 57 patients who entered the study at full criteria for OCD (YBOCS of >16), there was a 48% probability of achieving partial remission (YBOCS < 16 for eight consecutive weeks) by week 52 and an 11% probability of achieving full remission. The probability of subsequent relapse (returning to a YBOCS of >16) was 51% and 33%, respectively, for partial remission and full remission. Data on comorbidity, psychosocial functioning, and frequency of obsessions and compulsions will also be presented.

Conclusions: Almost half the subjects achieved partial remission from OCD over two years. However, only 11% reached full remission. For both types of remission, the relapse rate was quite high. This finding supports the notion that patients with OCD frequently have significant decrease in their symptoms although they rarely become symptom free.

NR368 Wednesday, May 24, 12 noon-2:00 p.m.

Avoidant Personality and Social Phobia Revisited

Vladan Starcevic, M.D., Psychiatry, Medical College of Penn, 3200 Henry Avenue, Philadelphia PA 19129; Brian B. Roberts, M.D., Eberhard H. Uhlenhuth, M.D.

Summary:

Objective: To develop clinically meaningful conceptualization of the relationship between social phobia (SP) and avoidant personality disorder (APD) in view of the fact that generalized subtype of SP (GSP) seems more prevalent in clinical samples of persons with SP.

Method: Fifty-two outpatients with the SCID-diagnosed, DSM-III-R SP were divided into two groups on the basis of the presence or absence of the SCID-II-diagnosed, DSM-III-R APD, and these groups were then compared.

Results: Twenty-three (44.2%) SP patients received a diagnosis of APD and all (100%) of them had GSP, as opposed to 22 (75.9%) GSP patients in the group without APD. Compared with the latter group, the group of patients with APD was characterized by the following significant differences: greater proportion of men, earlier onset of SP, younger age at the time of seeking treatment for SP, more fears of interactional situations (seven out of eight) than fears of performance situations (two out of eight), higher comorbidity rates, and higher scores on the harm avoidance scale of the Tridimensional Personality Questionnaire.

Conclusions: These results support the notion that SP with APD represents a more severe illness compared with SP without APD. As such, the comorbidity of SP and APD may have an adverse effect on the course and treatment of SP.

NR369 Wednesday, May 24, 12 noon-2:00 p.m.

Decrease in Worry During Treatment of GAD

Vladan Starcevic, M.D., Psychiatry, Medical College of Penn, 3200 Henry Avenue, Philadelphia PA 19129; Stephanie K. Fallon, M.D., Eberhard H. Uhlenhuth, M.D.

Summary:

Objective: To assess worry as an indicator of improvement during treatment of generalized anxiety disorder (GAD).

Method: Fourty-nine outpatients with a SCID-diagnosed, DSM-III-R GAD who participated in a drug treatment study of GAD, were administered the Penn State Worry Questionnaire (PSWQ) at baseline and after 12 weeks of treatment. The criteria for improvement were: 1) decrease on the Hamilton Anxiety Rating Scale (HARS) to a score below 15, or by over 50% for those patients whose baseline HARS score was between 15 and 30; 2) rating of "very much improved" or "much improved" on the Clinical Global Impressions—Change Scale (CGI-CS).

Results: There was a significant decrease ($p = 0.002$) in the PSWQ score among the 21 GAD patients who were considered improved. Of the 28 patients who were not considered improved on the basis of the HARS scores, 13 patients had a significant decrease ($p = 0.004$) in the PSWQ score, and they also met the CGI-CS criterion for improvement.

Conclusions: The criteria for improvement during treatment of GAD should be expanded to include a decrease in worry, especially since pathological worry is a defining feature of GAD. A decrease in the frequency and intensity of such worry might be a more sensitive, and a more relevant indicator of improvement than a decrease in global anxiety alone, as assessed by instruments such as HARS.

NR370 Wednesday, May 24, 12 noon-2:00 p.m.

The Prevalence of School Dropouts in an Anxiety Disorders Clinic Sample

Michael A. Van Ameringen, M.D., McMaster Psychiatric Unit, 3rd Floor Fontbonne Bldg, 50 Charlton Avenue E, Hamilton ON L8N 4A6, Canada; Catherine L. Mancini, M.D., Carol Wilson, M.Sc., Bridgette Hill

Summary:

Many anxiety disorders have their onset during childhood and adolescence causing significant disability in social and occupational functioning. Two-hundred-and-one patients meeting DSM-III-R criteria for a primary anxiety disorder completed a questionnaire to determine the impact that their anxiety disorder had on school functioning and/or premature withdrawal from school. They also completed self-report measures of anxiety, depression, and social adjustment.

Statistics Canada, in 1991, estimated that 18% of 20-year-old Canadians had not completed high school. In our study 49% ($n = 98$) reported leaving school prematurely, and 24% of those indicated that anxiety was the primary reason for this decision. Patients who had left school prematurely were significantly more likely to have a lifetime diagnosis of social phobia, a history of alcohol abuse/dependence, and a greater number of lifetime diagnoses than those who completed their desired level of education.

This study suggests that anxiety disorders are associated with higher dropout rates than are found in the general population. Further studies are required to determine methods for the early identification and treatment of anxiety disorders in school-age

children that would result in a lower overall rate of dropping out of school.

NR371 Wednesday, May 24, 12 noon-2:00 p.m.

Buspirone Augmentation of Selective Serotonin Reuptake Inhibitors in Social Phobia

Michael A. Van Ameringen, M.D., McMaster Psychiatric Unit, 3rd Floor Fontbonne Bldg, 50 Charlton Avenue E, Hamilton ON L8N 4A6, Canada; Catherine L. Mancini, M.D., Carol Wilson, M.Sc.

Summary:

Buspirone is an azapirone derivative and a 5-HT_{1A} partial agonist used in the treatment of generalized anxiety disorder. It has also been used to potentiate the antidepressant and antiobsessional effects of the selective serotonin reuptake inhibitors (SSRI's). We evaluated the efficacy of buspirone in the augmentation of social phobic symptom response to the SSRI's. Ten patients receiving a primary DSM-III-R diagnosis of generalized social phobia were included in the study. Eight out of the 10 patients had been on at least one other drug treatment for social phobia prior to being placed on the SSRI. SSRI treatment included two patients on paroxetine, three patients on fluoxetine, and five patients on sertraline. Patients obtaining only a partial response to an adequate trial of the SSRI received buspirone in addition to the SSRI for eight weeks in an open clinical trial. The mean dose of buspirone used at endpoint was 45 mg/day ± 10.8 mg. Seven patients (70%) were considered responders (moderate or marked improvement) and three (30%) were considered nonresponders (minimal improvement or no change). This study provides clinical evidence suggesting that buspirone augmentation may be a useful clinical strategy in social phobic patients who fail to respond to an SSRI.

NR372 Wednesday, May 24, 12:00 noon-2:00 p.m.

Predicting Patient Dropout in Panic Disorder

Naresh P. Emmanuel, M.D., Dept of Psych, MUSC, 171 Ashley Avenue, Charleston SC 29425-0002; Michael R. Ware, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

Summary:

Failure of patients to complete a research study is a problem affecting multiple aspects of human clinical trials. Patient drop out increases enrollment time, boosts costs in completing a study, and complicates data analysis. Our aim was to determine factors that predict patient drop out in a clinical trial evaluating the efficacy and safety of moclobemide versus placebo in panic disorder.

Subjects participated in a multicenter, double-blind, placebo-controlled study comparing moclobemide, a reversible monoamine oxidase inhibitor, with placebo in the treatment of panic disorder. The duration was nine weeks, which included a one-week placebo run-in. All subjects met DSM-III-R criteria for panic disorder based on a structured clinical interview. We defined dropouts as patients who did not complete the study. Twenty-nine of the 54 subjects dropped out. The Clinical Global Improvement Scale(CGI), Hamilton anxiety and depression scales, adverse effects, and basic demographics were the main assessment variables.

The CGI was one of the best predictors of patient dropout. Dropouts were significantly less likely to achieve a "much" or "very much improved" on the CGI compared with completers. Results of the factor analysis and methods to improve study completion rates will be discussed.

NR373 Wednesday, May 24, 12 noon-2:00 p.m.

Venlafaxine in Social Phobia: A Case Series

Naresh P. Emmanuel, M.D., Dept of Psych, MUSC, 171 Ashley Avenue, Charleston SC 29425-0002; Violetta D. Czepowicz, M.D., Gerardo Villarreal, M.D., Michael R. Johnson, M.D., Michael R. Ware, M.D., Robert N. Rubey, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D.

Summary:

Social phobia is a disorder characterized by extreme fearfulness in social situations that involve possible scrutiny by others. This disorder affects 13.3% (lifetime) of the population. Limited controlled trials have demonstrated the utility of monoamine oxidase inhibitors, benzodiazepines, and selective serotonin reuptake inhibitors in the management of social phobia. No drug is yet approved for the treatment of social phobia. We report our experiences with venlafaxine, a novel compound that inhibits the uptake of both serotonin and norepinephrine, in the treatment of social phobia.

This is an ongoing eight week trial that has currently enrolled 10 patients. All patients met criteria for a primary diagnosis of social phobia (DSM-III-R) using the Structured Clinical Interview. The Clinical Global Improvement Scale and the Duke Brief Social Phobia Scale were used to evaluate efficacy to treatment. Maintenance doses ranged from 75 mg to 300 mg.

Five of the 10 subjects were rated as "much" or "very much improved" (CGI = 1 or 2) by week eight based on the clinical global improvement scale.

This pilot study suggests that venlafaxine may be efficacious for the treatment of patients with social phobia

NR374 Wednesday, May 24, 12 noon-2:00 p.m.

A Comparison Study of Body Dysmorphic Disorder and OCD

Katharine A. Phillips, M.D., Butler Hospital, 345 Blackstone Blvd, Providence RI 02906; Craig G. Gunderson, B.A., Susan L. McElroy, M.D., Gopinath K. Mallya, M.D., William P. Carter, M.D.

Summary:

Background: Body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, is classified as a somatoform disorder but has been hypothesized to be related to OCD. Indeed, BDD is included in the Y-BOCS Symptom Checklist, and its transfer to the anxiety disorders' section was considered for DSM-IV.

Methods: We compared these disorders by assessing consecutive patients with DSM-III-R OCD (n = 53), DSM-IV BDD (n = 53), or both disorders (n = 33). Subjects were assessed with the SCID, the Y-BOCS, and a semistructured clinical interview.

Results: BDD and OCD did not significantly differ in terms of sex ratio; most other demographics, course, and impairment variables; Y-BOCS score; or lifetime prevalence of most disorders assessed. Although treatment response was not formally compared, 60% of open SRI trials in BDD subjects led to a clinically significant response vs. 7% with all other medications, similar to OCD. However, BDD patients were less likely to have ever been married (13% vs. 39%, p = .03) and more likely to have had suicidal ideation (70% vs. 47%, p = .02) or made a suicide attempt (22% vs. 8%, p = .03) because of their disorder. BDD patients also had an earlier onset of major depression (19 ± 7 vs. 25 ± 11 years, p = .002) and a higher lifetime prevalence of major depression (85% vs. 55%, p = .001), social phobia (49% vs 19%, p = .001), and psychotic disorder diagnoses (30% vs. 8%, p = .003). We also found that 15% of OCD patients had comorbid BDD.

Conclusions: These results suggest that BDD and OCD have many similarities but also some notable differences, and that they should be differentiated in clinical and research settings—e.g., by stratifying for the presence of BDD in OCD treatment trials.

NR375 Wednesday, May 24, 12 noon-2:00 p.m.

Diagnostic Instruments for Body Dysmorphic Disorder

Katharine A. Phillips, M.D., Butler Hospital, 345 Blackstone Blvd, Providence RI 02906; Katherine D. Atala, M.D., Harrison G. Pope, Jr., M.D.

Summary:

Background: Body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, is included in DSM-III-R and DSM-IV. However, BDD is not included in the Structured Clinical Interview for DSM-III-R (SCID), and reliable diagnostic instruments for the disorder have not been developed. This study presents data on a self-report diagnostic screening instrument for BDD (Body Dysmorphic Disorder Questionnaire [BDDQ]) and a clinician-administered, semistructured, diagnostic module for BDD (BDD Diagnostic Module), which is similar in format to the SCID.

Method: In consultation with other BDD researchers, self-report and clinician-administered diagnostic questions based on DSM-IV criteria for BDD were developed. Pilot data were obtained to further refine the instruments' questions. The instruments' test-retest reliability and validity were then determined. Sixty-six subjects filled out the BDDQ; of these, 51 were interviewed with the BDD Diagnostic Module by two of the authors in separate interviews on the same day, and the other 15 received the BDD Diagnostic Module from one author. The interviewers did not review the BDDQ until their interview was completed.

Results: With the BDD Diagnostic Module, a kappa of 0.96 was obtained for the test-retest reliability of a current or lifetime diagnosis of BDD in the 51 subjects who received two interviews; 28 (55%) of the cases were determined by both interviewers to have BDD. Using the Diagnostic Module as our gold standard, the BDDQ had a sensitivity of 100% and a specificity of 89% in the 65 subjects who received the instruments.

Conclusions: The self-report diagnostic screening instrument for BDD had excellent sensitivity and specificity, and the clinician-administered Diagnostic Module had excellent interrater reliability. These instruments, which are brief and easy to administer, may be useful in both clinical and research settings.

NR376 Wednesday, May 24, 12 noon-2:00 p.m.

A Double-Blind Placebo Controlled Study of Paroxetine and Clomipramine in the Treatment of Panic Disorder

Geoffrey C. Dunbar, M.D., Clinial R&D, Smith Kline Beecham, Third Avenue Harlow, Essex CM19 5AG, England

Summary:

???A double-blind placebo-controlled study of paroxetine and clomipramine in the treatment of panic disorder.

Patients (480) who met DSM-III-R criteria for panic disorder with or without agoraphobia were eligible, provided they had ≥three full panic attacks in the previous three weeks. They were randomized to receive paroxetine (10-60mg), clomipramine (10-150mg), or placebo. Medication was adjusted according to efficacy and tolerability over a period of 12 weeks. All patients could then enter a nine-month extension, but those who did not had their medication down-titrated over three weeks.

The primary efficacy variable was reduction in the number of panic attacks as assessed in the intent-to-treat population. There was a significant difference ($p \leq 0.05$) between paroxetine and placebo from week 3 onwards, in the number of patients with a ≥50% reduction in the frequency of panic attacks and those with zero panic attacks. There was also a significant difference in the mean number of panic attacks from week 9. There was no significant difference between paroxetine and clomipramine at any of the time points. Patients with adverse events (AE) were similar on paroxetine (73%) compared with placebo (68%), but AE were less frequent compared with clomipramine (89%). Dropouts due to AEs were 7% vs. 11% vs. 15%, respectively.

These data indicate paroxetine is effective in the treatment of panic disorder. It is as effective as the standard therapy clomipramine. Paroxetine is better tolerated than this tricyclic and less likely to lead to dropout.

NR377 Wednesday, May 24, 12 noon-2:00 p.m.

Cognitive Impulsivity Predicts Polysubstance Abuse in Hospital Inpatients

Kurt K. Hubbard, B.A., 240 Prospect Avenue #487, Hackensack NJ 07601; Sue Borgaro, M.A., Joel Lord, M.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D., David L. Pogge, Ph.D.

Summary:

Impulsivity is found in a variety of childhood and adult psychiatric disorders. Most commonly, children with conduct disorder and attention-deficit hyperactivity disorder are characterized as impulsive, but substance abuse disorders and certain personality disorders are also defined in terms of impulsive behaviors. Many research studies have suggested that impulsivity can be measured psychometrically with either personality inventories or behavioral tests such as the Continuous Performance Test (CPT). In specific, certain types of errors of commission on the CPT can be characterized as reflecting impulsivity. In this study, 110 adolescent psychiatric inpatients were interviewed with a structured diagnostic interview (the SCID), tested with the CPT, in both single-task and dual-task versions, and administered several personality inventories. On the single-task CPT adolescents with polysubstance abuse made significantly more "impulsive-type" errors of commission than the other patients, $t(108) = 2.13$, $p < .05$, while not differing in nonimpulsive errors of commission or errors of omission. This finding was even stronger in the dual-task CPT, ($t(108) = 2.63$, $p < .005$). Patients who abused alcohol alone were not elevated in their frequency of impulsive CPT errors, although subjects who abused drugs alone and not alcohol were elevated in those errors. Impulsive CPT errors of commission were uncorrelated with IQ measures, MMPI subscales, and scores on the Psychopathy Check List. These data support a link between cognitive-behavioral impulsivity and polysubstance abuse in adolescence, and that this link is more than the common presence of antisocial tendencies in impulsive and substance-abusing populations. A futher finding of interest was that drug abusers who had elevated frequencies of impulsive errors had relatively longer response latencies while performing the test, possibly suggesting that impulsivity is associated with failure to inhibit responses despite attempts to do so.

NR378 Wednesday, May 24, 12 noon-2:00 p.m.

Subclinical OCD in College Students

Marcia R. Morris, M.D., Student Health Care Cente, U of FL Student Hlth Care, PO Box 117500, Gainesville FL 32611-7500; Roger Blashfield, Ph.D., Babu Rankapalli, M.D., Wayne K. Goodman, M.D.

Summary:

Objective: Recent literature has suggested that obsessive compulsive (OC) symptomatology occurs in subclinical forms and correlates with increased levels of comorbidity. This study was designed to identify subclinical obsessive compulsive disorder (OCD) in a late adolescent population.

Methods: A self-report OCD screening test was administered to 1286 college students. This 12-item test was adapted from a portion of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). A subset of subjects with "high" and "low" scores for obsessive compulsive symptoms was interviewed for OCD, other anxiety disorders, and depression.

Results: Among the original sample of 1286, 24% were defined as having "high" scores for OC symptoms. Of 11 high scores interviewed, eight had subclinical OCD (i.e., definite obsessions and compulsions, but do not meet full OCD criteria for interference in functioning) and one subject had OCD. Of 17 low scorers, none had OC symptomatology. High scorers on the OCD screening test also reported significantly more anxiety and depressive symptoms than low scorers.

Conclusions: These preliminary data suggest that OC symptoms may be common in college students and that further study of subclinical OCD is warranted. Additional data will be presented based on a replication of this study.

NR379 Wednesday, May 24, 12 noon-2:00 p.m.

Pyridostigimine Induces Panic Attacks in Patients with Panic Disorder

Kishore M. Gadde, M.D., Psychiatry, Duke University Med Ctr, Box 3812, Durham NC 27710; Thomas W. Uhde, M.D.

Summary:

To investigate the status of cholinergic and adrenergic neurotransmitter systems in panic disorder, we challenged 15 patients with panic disorder and 15 age-, sex-, height-, and weight-matched normal controls with 1) a cholinesterase-inhibitor, pyridostigmine (1.8 mg/Kg, p.o), 2) an α_2-agonist, clonidine (100 mcg/sq.metre, p.o), and 3) both agents, on three separate days in a double-blind, randomized fashion. Pyridostigmine alone produced substantial panic symptomatology in the patient group, with 10 patients experiencing either full-blown panic attacks or limited-symptom panic attacks. Five patients experienced significant panic symptomatology with a combined challenge of pyridostigmine and clonidine. Pounding heart or palpitations, hot flashes, choking, chest discomfort, derealization, fear of dying, and dizziness were the most commonly reported panic symptoms. As expected, none of the patients experienced panic attacks in response to clonidine alone. Normal controls reported no significant panic symptomatology or increased anxiety on any of the study days. The pyridostigmine-induced panic attacks were reported by the patients to be similar to their typical panic attacks. In addition to behavioral responses, we also studied neuroendocrine and cardiovascular responses. Our data suggest that cholinergic neurotransmission may play a key role in the aetiology of panic disorder, and further studies in this regard are indicated.

NR380 Wednesday, May 24, 12 noon-2:00 p.m.

Early Loss and Separation in Social Phobia

Dominique Servant, M.D., Anxiety Unit, 57 Boulevard De Metz, Lille 59037, France; Georges Gauthier, M.D., Regis Beuscart, M.D., P. Jean Parquet, M.D.

Summary:

The present study examines the prevalence of early loss and separation in patients with social phobia compared with a group with panic disorder with agoraphobia (PDAG).

Method: Seventy-four consecutive patients with social phobia and 111 with PDAG were examined to assess the presence of loss and separation experiences in childhood. Loss comprises death of mother, father, or loss of one parent by divorce or serious health problem. Separation was considered to have been experienced if the patient or either of the parents had been away for three months or more. Each of these loss and separation variables was scored for 0-15 years of time period of the patients life.

Results: A history of loss and separation was observed in 12.3% of the social phobia patients and 39.9% of the PDAG patients. PDAG patients who experienced loss and separation had significantly greater rates of lifetime major depression (71%) than social phobia patients who experienced loss and separation (44%).

Conclusions: These findings suggest that early experiences that predisposed to all phobias were more important for agoraphobia than for social phobia. According to what is found in the literature, it is suggested that social phobia results from the combined effect of a stronger genetic influence and nonspecific environmental experiences.

NR381 Wednesday, May 24, 12 noon-2:00 p.m.

Multifamily Group Versus Group Behavioral Treatment of OCD

Michele T. Pato, M.D., Psychiatry, Rhode Island Hosp., 593 Eddy Street, Providence RI 02903; Barbara Van Noppen, M.S.W., Gail Steketee, Ph.D.

Summary:

Purpose: There is a growing literature on the efficacy of group behavioral treatment (GBT) for OCD. Preliminary findings, by Steketee and others indicate family involvement may improve outcome. We hypothesized that multifamily group behavioral treatment (MFGBT), would improve long-term efficacy.

Methods: OCD patients were studied using the YBOCS to measure OC symptoms and the Family Assessment Device (FAD) to measure family function. The findings were compared with those from out GBT-treated patients. Groups of six patients plus family members met for eight to 12 sessions of 90 minutes each. Sessions included assigned readings and education about OCD, family behavioral contracting, homework assignments and actual exposure and response prevention.

Results: A group of 13 OCD patients were treated with MFGBT and followed up for six months. YBOCS decreased from 23.7 to 14.5 (t (13) = 7.70, $p < .001$) and to 13.1 at follow-up (t (10) = 5.19, $p < .001$, from pretreatment). Another cohort, n = 5, with eight- to 24-month follow-up (n = 8) showed similar findings. MFGBT showed substantially better average effect sizes at post-test (1.19, n = 28) and follow-up (1.52, n = 18) than did GBT (.86, n = 83 and 74, n = 54) respectively. FAD scores for GBT did not improve post-treatment but at follow-up affective responsiveness and role functioning were significantly improved. In contrast, MFGBT lead to significant improvement at post-treatment in: problem solving, affective responsiveness, communication, behavior control, and general functioning. Only communication remained significant at follow up.

Conclusions: Analysis of effect size, even in these small samples, indicates that MFGBT may be more effective than GBT in immediate and long-term follow-up. The role of improving family functioning will be further elaborated.

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Clinical Characteristics of Panic Disorder with Sleep Attacks

Hisanobu Kaiya, M.D., Psychiatry, Nagoya Mental Clinic, 1-16 Tsubaki-Ch Recru Bld 3Flr, Nagoya Wakamura Ku 453, Japan

Summary:

The current study analyzed clinical history of 184 patients (77 female and 107 male patients) with DSM-III-R panic disorder (PD) or agoraphobia after panic attacks. Seventy-two (39%) of these patients showed panic attacks during sleep. Panic attacks during sleep preceded those during awakening in 15 patients (31%). Most panic attacks during sleep occured between two and five hours after falling asleep. Fifteen percent of patients with sleep attacks experienced dream at the attacks. The number of symptoms was smaller in sleep attacks than in awakening (6.0 ± 3.5 vs. 7.1 ± 3.4). Most patients (81%) claimed severer attack symptoms during awakening than sleep. Sleep attacks had less nausea or abdominal distress, and feeling dizzy, unsteady, lightheaded, or faint in comparison to awakening attacks. There were no significant differences in age of intake and onset, gender, family history of PD, and history of early separation between PD with and without sleep panic attacks. PD with sleep attacks had significantly more mental symptoms and unexpected attacks.

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New Phenomenological Dimensions for Subtyping OCD

Euripedes C. Miguel, M.D., Psychiatry, University Sao Paulo, Rua Valenca 91, Sao Paulo SP 01254-060, Brazil; 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: This study searches for new phenomenologic factors that can be useful in subtyping OCD. We sought to test the following hypotheses regarding intentional repetitive behaviors: 1) in OCD without ties (OCD Group), they are preceded by cognitive and autonomic phenomena, but not sensory phenomena; 2) in OCD with comorbid TS (OCD + TS Group), they are preceded by sensory phenomena, but less frequently by cognitive and autonomic phenomena.

Method: Twenty adult outpatients with OCD and 20 with OCD + TS were evaluated with a semistructured interview assessing sensory, cognitive, and affective experiences related to repetitive behaviors.

Results: The OCD + TS Group reported significantly more intentional repetitive behaviors preceded by sensory phenomena ($p = 0.001$) and not by cognitions ($p = 0.004$). The OCD Group tended to report autonomic anxiety more frequently associated to their repetitive behaviors ($p = 0.05$). The OCD + TS Group also reported significantly more cognitions without compulsions (pure obsessions) ($p = 0.001$) and sensory phenomena preceding . . . cognitions.

Conclusions: The dimensions studied (sensory, cognitive, autonomic phenomena) proved to be useful phenomenologic measures in demarcating OCD related and not related to TS. Therefore, we expect that these dimensions would be useful in subtyping OCD and may represent valid indicators of prognosis or treatment response.

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Pentagastrin Effects in Patients with GAD

Olga Brawman-Mintzer, M.D., Dept of Psych, Med Univ of S Carolina, 171 Ashley Ave, Charleston SC 29425-0742; R. Bruce Lydiard, M.D., Gerardo Villarreal, M.D., Rebecca S. Knapp, M.D., Naresh P. Emmanuel, M.D., James C. Ballenger, M.D.

Summary:

Cholecystokinin (CCK) is a mammalian brain peptide that acts as a neurotransmitter in the CNS. Intravenous administration of CCK-B receptor agonist CCK-4 (and its synthetic analog pentagastrin) to patients with panic disorder induces panic attacks in a dose-dependent manner at significantly higher rates than in normal control subjects. To further explore the role of the CCK system in anxiety disorders we examined the panicogenic/anxiogenic effects of CCK-B receptor agonist pentagastrin and placebo in seven patients with a DSM-III-R diagnosis of GAD and seven age- and sex-matched normal comparison subjects. Study subjects received in a single-blind fashion one infusion of placebo (0.9% NaCl) followed by an infusion of 0.6 μg/kg of pentagastrin. The panicogenic/anxiogenic effects of the infusion were assessed utilizing the Panic Symptom Scale (PSS) and Visual Analog Scale (VAS) for general anxiety. Heart rate and systolic and diastolic blood pressure were monitored as well. We found that GAD patients had a significantly higher tendency to develop panic attack (71%) following pentagastrin infusion compared with normal comparison subjects (14%) ($p = 0.031$). Patients with GAD were also significantly more likely to report increased anxiety than normal controls following pentagastrin infusion ($p = 0023$). Interestingly, GAD patients showed a significant pattern of attenuated diastolic blood pressure ($p = 0.039$) and heart rate response ($p = 0.055$) to pentagastrin infusion compared with normal controls, suggesting a weaker autonomic response to stress in patients with GAD. The significance of our findings will be discussed.

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Does Brief Dynamic Psychotherapy Reduce the Relapse Rate of Panic Disorder?

Ida M. Wiborg, Ph.D., Psychiatry, University of Oslo, Postboks 33 Gaustad, 0320 Oslo, Norway; Alv A. Dahl, M.D.

Summary:

Research has shown that as many as two-thirds of patients with panic disorder (PD) relapse after end of medication. The primary aim of our study was to test the hypothesis that a treatment that included medication combined with brief dynamic psychotherapy would be effective in reducing the relapse rate of PD. We were also interested to see if keeping patients as long as nine months on medication (clomipramine), would give better protection against relapse.

Forty-four subjects (aged between 21 and 49 years) who met DSM-III-R criteria for PD with or without agoraphobia were randomly assigned to two treatment cells: a drug cell (Group-D) and a brief dynamic psychotherapy plus drug cell (Group-D + P).

Subjects assigned to Group-D ($N = 24$) were given clomipramine and treated by their physicians after a manual worked out by the authors. All physicians (12) agreed on limiting their interaction with the patients to 'contact as usual.' Patients met weekly with their physicians for 12 weeks.

Subjects assigned to Group-D + P ($N = 20$) received clomipramine and brief dynamic psychotherapy, targeted specially at hypothesized panic-maintaining processes, given by the first author. Patients had 15 weekly sessions. To emphasize that psychotherapy was the important ingredient of the treatment, clomipramine was first introduced from the fourth week of treatment.

A comprehensive battery of measurements were gathered at baseline, treatment start, during treatment, and at the follow-ups at six, 12 and 18 months. Panic episodes and anticipatory anxiety were monitored daily by diary beginning two weeks before treatment start.

Randomization produced no significant differences between the two samples either demographically or clinically. Seventeen patients (71%) in Group-D and four patients (20%) in Group-D + P relapsed between end of medication at nine months and 18 months follow-up after a panic-free period ($p = .00223$). Relapse was defined as fullfilling DSM-III-R criteria for PD with or without agoraphobia. On all ratings, Group-D + P showed significantly

greater improvement than Group-D. All patients completed the treatment and the follow-ups.

NR386 Wednesday, May 24, 12 noon-2:00 p.m.

An Open Trial of Paroxetine in Social Phobia

Catherine L. Mancini, M.D., Dept of Psych 3G2, Chedoke McMaster Hospital, 1200 Main Street West, Hamilton ON L8N 3Z5, Canada; Michael A. Van Ameringen, M.D., Carol Wilson, M.Sc.

Summary:

To determine the efficacy of paroxetine in the treatment of social phobia, paroxetine was administered to 18 patients with a primary DSM-III-R diagnosis of social phobia, generalized type, in a 12-week, open, clinical trial. Treatment began at 10 mg of paroxetine daily and was increased according to clinical response and side effects. Patients completed self-report measures of social anxiety and avoidance, depression, and disability at baseline and at weeks 4, 8, and 12. Clinicians completed the Liebowitz Panic and Social Phobic Disorders Rating Form. All 18 patients completed the 12-week trial. Fifteen (83.3%) were considered responders (moderate or marked improvement) and three (16.7%) were considered to be nonresponders (minimal improvement or no change in their symptoms). All measures of social anxiety and phobic avoidance, depression, and disability showed a statistically significant change at end point. These findings suggest that paroxetine may be effective in the treatment of social phobia, generalized type, as has been suggested with other selective serotonin reuptake inhibitors. Controlled studies will be required to further investigate this preliminary finding as well as to compare it to other pharmacological treatments of social phobia.

NR387 Wednesday, May 24, 12 noon-2:00 p.m.

Quality of Life in Panic Disorder

Barbara S. Scupi, M.S., Room 3N212 Bldg 10, 9000 Rockville Pike, Bethesda MD 20892; Brenda E. Benson, B.S., Una D. McCann, M.D., Thomas W. Uhde, M.D.

Summary:

Research indicates that individuals who suffer from panic disorder with agoraphobia (PDA) experience a poorer quality of life than those with panic disorder without agoraphobia (PD). To determine factors that might contribute to this difference, we used the NIMH Panic Disorder Questionnaire to compare 175 patients with PD and 899 patients with PDA.

As expected, individuals with PDA were found to have greater life restriction in terms of greater agoraphobic avoidance and lesser employment. Additionally, patients with PDA reported increased generalized and anticipatory anxiety on several measures: generalized anxiety most of time, worry causing a panic attack, fear of panic attack causing avoidance, and anxiety causing avoidance. The PDA group also reported significantly greater sensitivity to some factors triggering panic attacks, including physiological factors (exercise, standing, pain) and psychosensory factors (bright lights, heat). Poor quality of life experienced by PDA individuals is associated with broader comorbidity and with increased sensitivity to internal and external panic triggers.

NR388 Wednesday, May 24, 12 noon-2:00 p.m.

Is PTSD and Etiological Factor in Addictive Behavior?

Jean-Michel Darves-Bornoz, M.D., Psychiatry, Hopital Universitaire, Clinique Psychiattrique Univ, Tours Cedex 37044, France; Isabelle Delmotte, M.D., Patricia Benhamou, M.D., Andree DeGiovanni, M.D., Philippe Gaillard, M.D.

Summary:

Clinicians have often noticed substance abuse in victims of trauma. On the other hand, substance abuse is frequently present in the comorbidity of psychiatric patients. We have designed a study to examine whether a link exists between these observations.

Ninety female psychiatric inpatients consecutively hospitalized in a university hospital department of psychiatry (18-84 years, mean age 39.4 years) were interviewed by three psychiatrists with a clinician-rated battery of instruments (among them the SI-PTSD, Structured Interview for Post-Traumatic Stress Disorder by Davidson et al.) and with a semistructured questionnaire related to social and clinical data (including items about a trend to addictive behavior such as alcohol abuse, drug consumption, eating disorders, sexual addictions, or repeated suicide attempts). The mean age at first hospitalization was 33 years (min 14, max 84) and the cumulated duration of hospitalization over their lives was in mean 7.6 months (min 1 day, max 60 months).

Trauma being defined as in the SI-PTSD, 27% of the patients had a single trauma and 31% several traumas over their lives. The study found a significant link between suffering from PTSD (30% of the sample) and a trend toward addictive behaviors as a whole (57% of the sample), especially alcohol abuse, drug consumption, and bulimic impulses. In addition, the patients with several traumas were more likely to develop addictive autoaggressive behaviors such as repeated suicide attempts. Moreover, no was found link between a trend toward addictive behaviors and having experienced a traumatic event without developing PTSD.

PTSD often complicates preexisting mental disorders. Since PTSD is linked to a trend toward addictive behaviors, as a whole and for each subtype of addiction, this study strengthens the pertinence of the concept of addiction and suggests that PTSD could be a predisposing factor for addictive behaviors among all the factors leading to addictions.

NR389 Wednesday, May 24, 12 noon-2:00 p.m.

PTSD, Spouse Abuse and American Indian Vietnam Veterans

Ilena M. Norton, M.D., Dept of Psych UCHSC, Univ N Pavilion, 4455 E 12th Avenue A011-13, Denver CO 80220; Spero M. Manson, Ph.D.

Summary:

Objective: To determine if PTSD is associated with domestic violence among American Indian Vietnam veterans.

Method: Forty American Indian Vietnam combat veterans from Southwest and Northern Plains tribes were interviewed at their respective reservations, using the SCID and the Conflict Tactics Scale. These veterans were oversampled for PTSD symptoms based on CIDI interviews of 600 American Indian veterans. The Fisher's Exact Test was used for all comparisons.

Results: Twenty-seven percent met the criteria for current PTSD and 22% for current alcohol dependence. Thirty percent reported any violence toward their wives or partners in the past year; 17.5% reported severe violence. Witnessing violence between parents during childhood was reported by 47.5%; 17.5% reported approving of men hitting their wives. PTSD was associated with any violence ($p = 0.008$) and severe violence ($p = 0.01$). Alcohol dependence ($p = 0.41$) and witnessing violence ($p = 0.31$) were not associated with wife abuse. Approving of violence was associated with any ($p = 0.02$) and severe ($p = 0.001$) violence.

Conclusions: PTSD, alcohol dependence, witnessing violence, and approval of violence have been associated with wife-beating in previous studies. In our study, only PTSD and approval of

violence were associated with wife-beating. This may be attributable to the small sample size, but also may be due to cultural differences in the origins of domestic violence.

NR390 Wednesday, May 24, 12 noon-2:00 p.m.

Tricyclics, Selective Serotonin Reuptake Inhibitors and Venlafaxine: Comparative Tolerabilities in Early PTSD Treatment

Neal A. Kline, M.D., Psychiatry 0603, Univ Calif San Diego, 9300 Gilman Drive, La Jolla CA 92093

Summary:

Objective: With several classes of antidepressants available for treating PTSD and comorbid depression—including tricyclics, SSRIs, and venlafaxine—how might initial tolerability compare across these three classes?

Method: Combat veterans with PTSD and depression seen at our Department of Veterans Affairs outpatient PTSD clinic were prospectively assigned to five cells: 1) imipramine, 2) doxepin, 3) sertraline, 4) fluoxetine, and 5) venlafaxine, with six subjects in each cell. Prior exposure to the medication in a proposed cell excluded membership, and the subject was assigned another cell. Exclusion criteria for this open-label pilot study were: active substance or alcohol abuse, bipolar affective disorder, psychotic disorders, and disorders reflecting brain damage.

Results: At the first return visit each subject was assessed with the Clinical Global Impression scale (CGI) for improvement. Scores for the imipramine group were: 2,2,3,4,6,6; doxepin: 2,2,2,2,5,6; sertraline: 1,2,2,3,3,5; fluoxetine: 2,2,3,5,5,6; and venlafaxine: 2,3,3,5,6,7. Each cell included "good and "bad" early tolerability ratings, in scatter patterns.

Conclusion: In the psychopharmacological treatment of PTSD and comorbid depression with "old-fashioned" tricyclics, "modern" SSRIs, and the newest agent, venlafaxine, early *tolerability*—not efficacy—did not uniformly improve with newer agents compared with older agents. Rather, heterogeneity of responses was the norm across all groups, suggesting the need to maintain a broad formulary from which to choose when medicating PTSD and depression.

NR391 Wednesday, May 24, 12 noon-2:00 p.m.

Clonazepam Treatment of Panic Disorder in Patients with Recurrent Chest Pain and Normal Coronary Arteries

Lawson R. Wulsin, M.D., Dept of Psychiatry, 231 Bethesda Ave (ML 559), Cincinnati OH 45267-0559; Rula Dawaher, B.A., Bernard D. Beitman, M.D., Richard J. Maddock, M.D., Victoria Wells, M.D.

Summary:

To examine the efficacy of clonazepam in chest pain patients with panic disorder and normal coronary arteries, we conducted a placebo-controlled, double-blind, flexible-dose (1-4 mg/d), four-week trial of clonazepam. All subjects had current panic disorder and a negative coronary angiogram or thallium exercise tolerance test within the previous year. Preliminary analyses (N = 28) show improvements of the clonazepam and placebo groups on all five outcome measures. Improvement in the clonazepam group (N = 13) was significant on the Hamilton Anxiety (mean change = –8.5, t = 3.4, p = .005) and the Clinical Global Impression scales (mean change = –1.5, t = 4.2, p = .001), but not on panic attack frequency, panic attack intensity, or the Zung Anxiety Scale. However, the placebo group (N = 14) significantly improved on the panic attack intensity (mean change = –1.9, t = 2.3, p = .04) and Clinical Global Impression (mean change = –.86, t = 2.8, p = .02) with trends on HAM A, panic frequency, and the Zung. The improvements in the clonazepam group were not significantly better than the improvements in the placebo group on any of the five outcome measures. These preliminary analyses do not support the efficacy of clonazepam in chest pain patients with panic disorder. Further analyses will examine the factors that predict good response.

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P1 Mid-Latency Auditory Evoked Potential in PTSD

Gregory M. Gillete, M.D., Psychiatry, Univ of Arkansas Med Sci, 4301 W Markham Street Slot 554, Little Rock AR 72205; Robert D. Skinner, Ph.D., Doyle H. Davis, M.S., Lisa Rasco, B.A., Frederick A. Boop, M.D., Edgar Garcia-Rill, Ph.D.

Summary:

Dysregulation of brainstem reticular formation (RF) noradrenergic locus coeruleus (LC) neurons, has been implicated in generating hyperarousal symptoms of post-traumatic stress disorder (PTSD). RF cholinergic neurons, which reciprocally synapse with LC neurons, are normally involved in REM generation, the latter putatively related to PTSD re-experiencing symptoms. A noninvasive measure of RF cholinergic activation is the P1 midlatency auditory evoked potential, which normally undergoes rapid habituation.

Objective: To study P1 habituation in PTSD as a measure of RF cholinergic involvement.

Method: We studied the P1 in a two-click paradigm (0.2Hz stimulation rate, 250 msec interclick interval) in nine CAPS- and SCID-assessed PTSD patients and five age-matched normals. All were drug-, alcohol-, and medication-free at least one week before study.

Results: PTSD patients showed decreased habituation of P1 compared to normals: mean %-amplitude (ratio of second-click P1 amplitude over first-click P1 amplitude) of 60% for patients vs. 2% for controls ($p < 0.001$, t-test). Among patients, CAPS re-experiencing symptom scores correlated significantly with extent of P1 habituation decrease ($P < 0.04$, simple regression), a correlation not found for CAPS avoidance or hyperarousal symptom scores.

Conclusions: These preliminary results suggest disinhibition of RF cholinergic neuronal substrates in PTSD and RF cholinergic involvement in modulating re-experiencing symptoms.

Supported by NSF grant RII8922108 and NIH grant NS20246

NR393 Wednesday, May 24, 12 noon-2:00 p.m.

The Multidisciplinary Study in Patients with Chest Pain of Undetermined Etiology

Indira M. Varia, M.D., Dept of Psych, Duke Univ Med Ctr, PO Box 3889 Erwin Road, Durham NC 27710; Thomas M. Bashore, M.D., Rex M. McCallum, M.D., Scott R. Brazer, M.D.

Summary:

Objective: The purpose of this multidisciplinary study was to determine the prevalence of psychiatric, cardiac, gastrointestinal, and rheumatologic diagnosis in consecutive consenting patients with CPUE.

Method: Of 2,222 patients undergoing cardiac catheterization at Duke University Medical Center from December 1990 to June 1991, 126 patients with chief complaint of chest pain had normal coronary artery. Sixty-two patients were excluded (unable to exercise); eight patients were lost to follow-up. Twenty-four patients consented for study were admitted to Duke Research Unit for three days, comprehensive, multidimensional, diagnostic assessment by a team consisting of a cardiologist, gastroenterologist, rheumatologist and psychiatrist. The assessment consisted of a cardiolight exercise study; esophageal motility study with edrophonium, acid profusion, and balloon distension testing; a 24-hour

ambulatory PH test; upper endoscopy; a structure rheumatologist evaluation; and structured psychiatric interview.

Results: The prevalence of disorder in each group were GI 67%; psychiatry 87%; cardiovascular 29%; and rheumatology 29%.

Conclusion: The study suggests high prevalence of psychiatric disorders, specifically anxiety disorder, in patients with chest pain of undetermined etiology.

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Comorbidity in Panic Disorder With and Without Agoraphobia

Alvaro Rivera, M.D., Salud Mental, Centro Salud Goya, O'Donnell 55, Madrid 28009, Spain; Susana Alfonso, M.D.

Summary:

Objective: To compare the patterns of comorbidity (Axis I and II, DSM-III-R) betwen panic disorder without agoraphobia and panic disorder with agoraphobia. This study may give us some answers concerning the evolution of these disorders as well as their classification and etiology.

Methods: Selected patients from emergency and outpatients clinic from the Hospital Clinico Universitario San Carlos de Madrid, following DSM-III-R criteria. Of 95 patients suffering panic, 60 had agoraphobia and 35 did not. SCID-UP was used as diagnostic tool for associated pathology, and SCID-II was used to determine personality disorders.

Results: No statistical differences were found between the groups, including the rate of mood disorders, hypochondria, somatization, alcoholism, and eating disorders, nor among personality disorders. Regarding anxiety disorders we only found an increased prevalence of simple phobia in the agoraphobic group.

Conclusions: Considering associated pathology as an indicator of severity, panic disorder with agoraphobia is not more severe than uncomplicated panic disorder. We do not observe that the presence of some personality disorders promotes its evolution to agoraphobia.

NR395 Wednesday, May 24, 12 noon-2:00 p.m.

PTSD After Moderate Head Injury

Deborah L. Warden, M.D., Psychiatry, Walter Reed Medical Ctr., Washington DC 20307; Lawrence A. Labbate, M.D., Andres M. Salazar, M.D., Rachael S. Nelson, M.D.

Summary:

Objective: To determine the incidence of post-traumatic stress disorder (PTSD) among patients with closed head trauma and amnesia for the event.

Method: Forty-five active duty service members (44 men and one woman, mean age, 27, SD = 7) who sustained moderate traumatic brain injury were enrolled in an outcome study. Inclusion criteria were post-traumatic amnesia greater than 24 hours and recovery to Ranchos Los Amigos level VII (oriented and cooperative) within 90 days of injury. Patients were administered a Present State Exam modified for use with head-injured patients, and additional questions regarding post-traumatic stress symptoms. Patients were evaluated at entry into study, at eight weeks, eight months, 14 months, and at 24 months.

Results: Of the sample, no (0%) patients met full criteria for PTSD, none met the DSM-III-R B (re-experience) criterion, and three (7%) patients met both C (avoidance) and D (arousal) criteria. These three patients also had clinical diagnoses of organic mood disorder, depressed.

Conclusion: Post-traumatic amnesia following moderate head injury may protect against recurring memories and the development of PTSD. Some patients with amnesia may develop a form of the syndrome without the re-experiencing symptoms.

NR396 Wednesday, May 24, 12 noon-2:00 p.m.

Assessment and Treatment of OCD

Juliana Lachenmeyer, Ph.D., Psychiatry, North Shore University, 300 Community Drive, Manhasset NY 11030; Kevin Handley, B.S.

Summary:

This study is part of a larger ongoing study of obsessive compulsive disorder. The assessment protocol measures level of functioning, pervasiveness of the disorder, and use of medication along with behavioral treatment. Patients referred to the Anxiety Treatment Program at North Shore University Hospital are administered the ADIS-R Structured Interview. Those who meet criteria for OCD are given the Maudsley, Y-BOC O-C Global Scale, the Neo-PI-R, and the WISPI. A functional analysis is made based on the relationship of symptoms to anxiety: either anxiety inducing or reducing. In addition, avoidance behavior and rituals are also assessed. A behavioral treatment plan is developed. Guidelines for referral have been established. At present 20 patients have been assessed; 50% are on medication; 20% of these were put on medication at the onset of behavioral treatment. Three patients had limited symptomatology: two had tricolotelomania. In addition, 40% were "checkers", 25% had OC Global functioning scores showing very severe symptomatology. After six months of treatment, 33% of these patients had symptom reduction to the minimal within normal range. Preliminary conclusions suggest that overall functioning prior to initiation of treatment is a good predictor of progress in treatment, whereas severity of specific symptoms and level of anxiety are not. Additional findings and implications for treatment will be discussed.

NR397 Wednesday, May 24, 12 noon-2:00 p.m.

Potentiation of Fluoxetine by Amunoglutethimide Steroid Suppression in OCD: A Case Report

Guy Chouinard, M.D., Psychiatry, LH Lafontaine Hospital, 1025 Pine Avenue West, Montreal PQ H3A1A1, Canada; Marie-Claire Belanger, R.N., Sarah Sultan, M.D., Linda Beauclair, M.D., Beverley E. Pearson-Murphy

Summary:

The involvement of serotonin in obsessive compulsive disorder has been hypothesized based on the observation that the serotonin reuptake inhibitor, clomipramine, and other SSRIs such as fluoxetine, sertraline, fluvoxamine, and zimelidine were efficacious in the treatment of obsessive compulsive disorder. Furthermore, clomipramine has been found to have a greater antiobsessive effect compared with other types of antidepressants, which preferentially block the uptake of noradrenaline over serotonin. There is evidence that steroids contribute to maintaining major depression, and that steroid suppression agents (aminoglutethimide, ketoconazole, and/or metyrapone) may lead to sustained improvement of depression in drug-resistant cases. We investigated this treatment approach by adding a steroid suppressant to fluoxetine in the case of a severe obsessive compulsive patient who was treatment-resistant. We found that this combination (aminoglutethimide, 250 mg qld and fluoxetine, 40 mg qam) significantly improved the patient's condition. Moreover, on each occasion over a four-year period when we tried to decrease either fluoxetine or the steroid suppressant, the patient started to relapse, suggesting that the steroid suppressant had a potentiating effect on the SSRI.

NR398 Wednesday, May 24, 12 noon-2:00 p.m.

Odors and Perceptions of Room Size

Alan R. Hirsch, M.D., Smell & Taste Treatment, 845 N Michigan Ave, Chicago IL 60611-2201; Jason J. Gruss

Summary:

Claustrophobia is common, with a lifetime prevalence of approximately 10%, and severely restrictive in modern society. Those so afflicted tend to be extremely sensitive to room size. While odors have been determined to effect other behavioral states, its effect on perception of room size has never been assessed. In order to study this, eight subjects were placed in a cylindrical space-deprivation booth 2.5 ft. in diameter by 4.5 ft. in height. Odors, including evergreen, barbecue smoke, tranquility, vanilla, buttered popcorn, seashore, charcoal-roasting meat, cucumber, coconut and green apple were presented in a randomized, double-blind fashion. Statistical analysis was performed based on Sign-Rank test for paired differences. The only odor to significantly affect the perceptions of room size in all subjects was barbecue smoke ($p < 0.05$), which caused their estimations of room size to shrink. In subjects with a normal ability to smell ($n = 7$), the only odor tested that significantly affected perceptions of room size was green apple ($p < .02$), which made the room seem larger. Use of the odor of barbecue smoke in agoraphobics and the odor of green apple in claustrophobics as part of the therapeutic armamentarium warrants further exploration.

NR399 Wednesday, May 24 12 noon-2:00 p.m.

Trauma History As a Predictor of Response to Moclobemide

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., John J. Worthington III, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

The present study examines the effect of trauma exposure as a predictor of response to pharmacological intervention with moclobemide, a reversible monoamine oxidase inhibitor in subjects with social phobia or panic disorder.

Method: Thirty-five subjects with social phobia and 30 subjects with panic disorder presenting to a psychopharmacological research clinic received SCID interviews to establish current and lifetime diagnoses. Sections of the KSADS-E and DICA-P were administered to assess for a history of childhood anxiety disorders. Information regarding trauma exposure and age(s) at trauma(s) was collected, as well as gender and age of onset of social phobia/panic disorder. The subjects received a 12-week trial of moclobemide.

Results: Forty-five percent of social phobia subjects and 33% of panic disorder subjects reported histories of trauma. Data will be presented assessing whether subjects with social phobia and/or panic disorder and a history of trauma respond differently to treatment with a reversible monoamine oxidase inhibitor than those without a history of trauma.

NR400 Wednesday, May 24, 12 noon-2:00 p.m.

Brain Abnormalities in OCD by Morphometric MRI

Hans C. Breiter, M.D., Psychiatry, Mass General Hospital, Building #149 13th Street, Charlestown MA 02129-3422; Michael A. Jenike, M.D., Lee Baer, Ph.D., Cary R. Savage, Ph.D., Scott L. Rauch, M.D., Pauline A. Filipek, M.D.

Summary:

Objective: A pilot MRI study of posterior brain volumes found less white matter in obsessive compulsive disorder (OCD) patients compared with controls. The current study evaluated whole brain volumes using MRI-based morphometry.

Method: Ten female OCD patients were matched with 10 female controls for age, weight, handedness, education, and verbal IQ. Scanning utilized a 3D volumetric protocol. Scans were blindly normalized and segmented using well-characterized, semi-automated, intensity contour algorithms. Volumes extracted included: cerebral hemispheres, cortex, white matter, diencephalon, caudate, putamen, globus pallidus, hippocampus, amygdala, third and fourth ventricles, corpus callosum, operculum, cerebellum, and brain stem. Other volumes included anterior to posterior neocortex with adjacent white matter, namely precallosum, anterior pericallosum, posterior pericallosum, and retrocallosum. Volumes differing between groups were correlated with Yale-Brown Obsessive Compulsive Scale scores and Rey-Osterieth Complex Figure Test measures.

Results: Significantly less total white matter was found in OCD patients, confirming our pilot result and expanding it to whole brain. OCD patients further showed greater total cortex and opercular volumes. OCD severity and nonverbal immediate memory correlated with opercular volumes.

Conclusions: These findings may indicate that OCD is a neurodevelopmental disorder, possibly resulting from impaired myelinization and/or inadequate cortical pruning.

NR401 Wednesday, May 24, 12 noon-2:00 p.m.

Single Site Findings in a Safety and Efficacy Study of CI-988 in GAD

John J. Sramek, Pharm. D., Calif. Clinical Trials, 8500 Wilshire Blvd 7th Floor, Beverly Hills CA 90211; Jerome F. Costa, M.D., Judith Bammert-Adams, Pharm. D., Alison E. MacPherson, B.A., Neal R. Cutler, M.D.

Summary:

Objective: To determine the efficacy of CI-988, a novel peptoid CCK_B antagonist, in patients with GAD. The present results are those of one site ($n = 32$) from a multicenter study ($n = 88$).

Methods: 16 patients were randomized to placebo and 16 to CI-988, and 29 patients completed all four weeks of study treatment. The primary efficacy measures were the Hamilton Rating Scale for Anxiety (HAM-A) and the Clinical Global Impression (CGI) scale.

Results: Patients on CI-988 showed a greater decrease ($p = 0.06$) in HAM-A scores than did patients on placebo at the end of the study, with mean change in HAM-A total at week 4 of −7.69 (−32.0%) for CI-988 and −4.19 (−18.6%) for placebo. There were no significant differences on the CGI between the two treatment groups. All adverse events were rated mild or moderate. One patient on CI-988 discontinued due to moderate abdominal pain; two patients on placebo discontinued for personal reasons. Our findings were not reflected in the overall multicenter results; the other two centers favored placebo and neither group, respectively.

Conclusions: Because CI-988 demonstrated acceptable tolerability and potential anxiolytic efficacy at this site, testing of higher oral doses may be warranted.

NR402 Wednesday, May 24, 12 noon-2:00 p.m.

HIV Illness and Testosterone Replacement Therapy: Mood and Anabolic Effects

Judith G. Rabkin, Ph.D., Psychiatry, Columbia University, 722 West 168th Street Unit 35, New York NY 10032; Richard Rabkin, M.D., Glenn Wagner, M.A.

Summary:

Goal: To assess effects of testosterone replacement therapy on mood, energy, weight gain, and body composition in HIV+ men with low normal or deficient testosterone levels and clinical symptoms of decreased libido, appetite/weight loss, and possibly low mood and low energy.

Method: To date, 81 men entered a 12-week trial of biweekly testosterone replacement therapy; 72 completed the trial, and 61 (85%) responded in terms of libido. Of the 53 who have so far completed a double-blind, placebo-controlled, discontinuation phase, 74% of those randomized to continue testosterone maintained their positive response, compared with 21% who maintained their response on placebo. Among 52 patients with an initial complaint of low mood, 64% were rated as much improved, while 23 of 37 (62%) completers who had low appetite at study baseline were much improved. Mean weight increased 3 lbs, and body cell mass (measured by bioimpedance analysis: BIA) for a subgroup of 12 men showed a statistically significant increase.

Conclusion: Testosterone appears to have both positive mood and anabolic effects for men with significant HIV illness, low serum testosterone levels, and clinical symptoms.

NR403 Wednesday, May 24, 12 noon-2:00 p.m.

Depression and Help-Seeking of Partners in the Heterosexual HIV Transmission Study

Cheryl Ann Kennedy, M.D., PO Box 73, Stockton NJ 08559-0073; Judith Abrams, Ph.D., Joan H. Skurnick, Ph.D.

Summary:

Objective: To explore factors in failure to seek help among those who reported depressive symptoms (Centers for Epidemiologic Studies-Depression scale [CESD] >= 16) in a couples study of HIV transmission.

Methods: From 1992-1994, as part of a large epidemiologic study, over 500 individuals in serodiscordant and seroconcordant couples from Northern New Jersey (NJ) and New York City (NY) completed the CESD, a structured interview, and a self-report questionnaire.

Results: Over 40% scored >=16 on the CESD, and of those, 45% reported seeking help from a mental health professional in the past six months (psychiatrist, psychologist, psychiatric social worker). The proportion of depressed individuals in NY who sought help (58%, 46/80) was significantly greater than in NJ (38%, 50/132), p = 0.005. Having a high school diploma was associated with help-seeking in NY and not in NJ (p = 0.02). HIV-positivity, gender, race, employment, being born outside the US and income were not apparent barriers to help-seeking.

Discussion: More than half of those who reported depression did not seek help, and traditional access barriers did not account for this. Medical providers must be aware of a high prevalence of depressive symptoms and hidden barriers that may prevent help-seeking in those with HIV and in their partners. Counseling opportunities must be available.

NR404 Wednesday, May 24, 12 noon-2:00 p.m.

Effects of Methylphenidate on HIV-Related Memory Dysfunction

Joel K. Levy, Ph.D., Psychiatry, Baylor College of Med., One Baylor Plaza, Houston TX 77030; Francisco Fernandez, M.D.

Summary:

Objective: To examine cognitive adjuvant effects of methylphenidate in HIV-infected patients with memory dysfunction.

Method: Twenty patients with impaired memory from a community-based clinic dedicated to HIV care enrolled in a memory enhancement program. Patients were randomized to receive memory compensation training with methylphenidate (N = 10) or placebo (N = 10). All subjects underwent four weeks training and an additional four-week blinded observation period. Memory function was assessed using "ecological" memory tasks and self-perception of memory instruments, at baseline and after the treatment period.

Results: A trend of improvement in functioning on practical measures of memory (memory notebook utilization: amount and quality of information entered) was found. There was also improvement in memory test performance in those receiving the active medication.

Conclusions: These are the first controlled psychopharmcotherapy data specific for HIV-related memory disturbance and were collected in a community-based research setting. Preliminary results support neurorehabilitation therapies in HIV disease. Results also suggest that methylphenidate is an effective cognitive adjuvant for this memory disturbance. From practical standpoints of encouraging adaptive function, promoting independence in medical regimen compliance, and continuing vocational pursuits, HIV-memory dysfunction should be detected early to compensate for this problem.

NR405 Wednesday, May 24, 12 noon-2:00 p.m.

New Pharmacological Approaches to the Treatment of HIV-1-Induced Cognitive Impairments

Benedetto Vitiello, M.D., Room 11-94, NIMH AIDS Office, 5600 Fishers Lane, Rockville MD 20857; Willo Pequegnat, Ph.D., Ellen Stover, Ph.D.

Summary:

Objective: HIV-1 has a high tropism for the central nervous system. HIV-1 infection is often associated with cognitive impairment, whose severity can range from subtle deficits in the early phases of the infection to frank dementia in overt AIDS. While the pathogenesis of HIV neurotoxicity infection remains unclear, attempts have been made to study potential pharmacological agents that may prevent, reverse, or delay the HIV-related cognitive failure.

Method: Through Medline searches and review of other unpublished sources (recent scientific meetings, workshops and seminars), all the available reports relevant to this topic were retrieved and critically reviewed. Focus was mainly, but not exclusively, on clinical reports. Preclinical data were also included if potentially relevant to clinical treatment.

Results: Zidovudine has been reported to both prevent and at least transiently reverse AIDS dementia, also with reduction of CNS lesions as seen on MRI and SPECT of the brain. Several other compounds have been proposed for the treatment of HIV-induced cognitive impairment, including psychostimulants (e.g., methylphenidate), dopamine agonists (e.g., bromocriptine), calcium channel blockers (e.g., nimodipine), cytokine blockers (e.g., pentoxifylline), NMDA receptor antagonists (e.g., memantine), and other potentially neuroprotective agents (e.g., peptide T). Peptide T is an octapeptide analogue of Vasoactive Intestinal Peptide and is supposed to counteract the neurotoxic effects of gp120. It is administered intranasally. Following preliminary uncontrolled studies, which have shown its safety and suggested possible efficacy, peptide T has been under investigation in a NIMH-sponsored, placebo-controlled trial that has enrolled about 200 patients and is currently being completed.

Conclusions: Several pharmacological approaches are currently under investigation that have therapeutic potential for HIV-positive patients at different stages of infection. The knowledge that is being acquired in this area may also be relevant to the treatment of other non-HIV-related types of dementia.

NR406 Wednesday, May 24, 12 noon-2:00 p.m.

A Survey of HIV/AIDS Awareness in One District Branch

Maria L.A. Tiamson, M.D., AIDS Management Prgm 2nd, Westchester County Med Ct, RM 2080 Macy Pavilion, Valhalla NY 10595; Michael Blumenfield, M.D.

Summary:

The AIDS epidemic is now well into its second decade. There is an increasing role for the psychiatrist in the treatment of HIV/AIDS patients.

Objectives: To survey the attitude, knowledge and experience of psychiatrists in one APA district branch.

Methods: A two-page survey was sent to all 600 members of the Westchester district branch, a northern suburb of New York City. It consisted of eight questions on important knowledge facts about the psychiatric aspects of HIV/AIDS, two questions assessing attitude towards treatment of people with HIV/AIDS, and 11 questions about clinical experience with this condition. Standard statistical analysis of the data received was performed.

Results: A total of 109 surveys were returned. Of the questions related to knowledge, the highest number of correct responses was 5/8, which was achieved only by 3.7% of the respondents. The median number of correct answers was 3/8 (31.2%); 6.7% of respondents had no correct answer. A total of 77% of the respondents would continue treatment even if they just found out that the patient was HIV(+); 25% of responding psychiatrists said they would inform a patient's sexual partner of his/her HIV status if the patient refuses to do so; 41% will continue to treat the patient and leave the responsibility of disclosure to the patient; while 26% would refuse to treat unless the patient informs his/her partner. Of the respondents, 53.2% have treated at least one patient with HIV/AIDS. Correlations between the attitudes, knowledge, and experience will be shown during the presentation.

NR407 Wednesday, May 24 12 noon-2:00 p.m.

Risperidone in the Treatment of Psychiatric Symptoms in Patients with AIDS

William S. Gilmer, M.D., 303 East Ohio, Chicago IL 60611; Stephen J. Ferrando, M.D., Jonathon D. Goldman, M.D.

Summary:

Patients with AIDS have been reported to experience a high incidence of extrapyramidal symptoms induced by dopamine-blocking agents. We report the results of risperidone treatment in 14 patients (aged 27 to 67 years; 13 men, one woman) with AIDS who required antipsychotic medication. HIV or mixed encephalopathy was diagnosed in 10 patients; primary mood disorders in six; secondary mania (presumed HIV) in six; trichotillomania in one; and histories of alcohol or other substance dependence in nine. Six patients had previously received dopamine-blocking agents such as haloperidol, perphenazine, thioridazine, prochlorperazine, and metoclopramide, all of which induced extrapyramidal symptoms. After receiving 1 to 3 mg of risperidone daily, clinical improvement was noted in 13 of the 14 patients, with minimal adverse effects. An acute oral dyskinesia 48 hours prior to death was noted in one risperidone-treated hospice patient with terminal AIDS who had recently received three other dopamine-blocking agents. We conclude that low doses of risperidone may be safe and effective in patients with AIDS who require antipsychotic treatment. However, advanced AIDS with severe encephalopathy and recent use of other dopamine-blocking agents may increase the risk of extrapyramidal symptoms in patients receiving risperidone.

NR408 Wednesday, May 24, 12 noon-2:00 p.m.

Suicidal Behaviors and Outcomes in HIV-1 Infections

Richard Douyon, M.D., Psychiatry, VAMC 116A, 1201 NW 16th St, Miami FL 33125; Joseph M. Mavica, D.O., Daniel Feaster, M.S., Karl Goodkin, M.D.

Summary:

As many as 98% of AIDS patients have a lifetime prevalence of mood disorders. About 20%-25% of HIV-1 infected patients attempt suicide. The relationship between suicidal risks and progression of HIV-1 infection is controversial. Some believe that the risk for suicide is higher in asymptomatic patients, but others argue that it is higher in patients with full-blown AIDS.

Objective: 1) to study the prevalence of suicidal ideations in a population of HIV-1 infected veterans, 2) to examine the relationship between suicidal spectrum behaviors and clinical progression of HIV-1 infection (using the CDC 1993 criteria) and to examine the relationship between depression, anxiety, and clinical progression of HIV-1 infection.

Methods: Seventy-eight male patients from the Special Immunology Services at the Miami Veterans Affairs Medical Center were diagnosed at baseline and assessed on consecutive visits using the following measures: the Beck Depression Inventory, the Spielberger Anxiety Scale, the Mini-Mental Status Exam, the University of Miami Bereavement scale, as well as the most recent CDC staging within six months of screening date. Treatment noncompliance was measured by the number of cancellations and no-shows. Patients were assessed for suicidal ideations by using item #9 of the Beck Depression Inventory. The data were summarized by means of ANOVA and Peason's correlation.

Results: 1) about 25% of our HIV-1 infected patients are suicidal, 2) suicide ideations have a deleterious effect on HIV staging, 3) depressed patients have more no-shows than cancellations, and 4) anxiety, bereavement, and cognitive impairment have no effects on clinical progression.

Conclusions: All HIV-1 infected patients should be evaluated for suicide and depression on a regular basis at any stage of the infection. Better predictors of suicide are needed. We will discuss the impact of our findings on suicidal ideations in the management and counselling of AIDS patients.

NR409 Wednesday, May 24, 12 noon-2:00 p.m.

Linking Community-Based Mental Health Services to an NIMH AIDS Research Center

David G. Ostrow, M.D., Prof of Psychiatry, Comm Health Behavior Prog, 1201 N Prospect Avenue, Milwaukee WI 53202; Kathleen Sikkema, Ph.D., Debra Murphy, Ph.D., Jeffrey A. Kelly, Ph.D., Kenneth Multhauf

Summary:

Objectives: To link community-based mental health services (MHS) to an NIMH-funded Center for AIDS Intervention Research, and to develop an HIV mental health screening protocol and treatment referral research program useful to community mental health caregivers.

Methods: MHS screening incorporated standardized measures administered by trained community caregivers. Collaborative alliances were forged between CAIR and community-based HIV medical providers to screen the majority of newly diagnosed Milwaukee HIV/AIDS clients. Research protocols translated needs assessment data into psychosocial/pharmacological treatment studies.

Results: Among the first 127 new outpatients screened, approximately 1/3 had an AIDS-defining illness. This sample was predominantly ethnic minority (60% black, 10% Hispanic), 80% male, and 50% male same-sex and 35% IDU risk behavior. Eight percent were already receiving MHS and an additional 36% requested referral to MHS, principally for depression. Also, 52% had BDI scores indicating probable clinical depression; 15% severe/extreme depression; 30% current substance abuse problems.

Among the first 150 patients referred, 57% were diagnosed with major depression, 3% bipolar disorder, 8% subsyndromal anxiety/depression, 7% ADC, 16% anxiety/panic, 25% substance abuse, 3% psychosis/delirium, 13% adjustment disorder, and 9% personality disorder. 20%-40% had comorbid substance abuse problems/disorders.

Discussion: AIDS/HIV service providers can collaborate in MHS research and provide referrals of patients in need of care for community-based treatment research.

NR410 Wednesday, May 24, 12 noon-2:00 p.m.

Animal Models for HIV-Induced CNS Dysfunctions

Floyd E. Bloom, M.D., Dept of Neuropharmacology, The Scripps Research Inst, 10666 North Torrey Pine Rd, La Jolla CA 92037-1027; Lisa Gold, Ph.D., Steven Henriksen, Ph.D., John Elder, Ph.D., Howard Fox, M.D., Tommy Phillips, Ph.D.

Summary:

HIV produces neuropsychological impairment through indirect and as yet undefined actions on neurons, presumably mediated through the abnormal secretory activity of virus infected macrophages, other CNS invasive immune cells, and capillary endothelial cells. Few animal model systems in use for the study of HIV pathogenesis have been extended to the analysis of the immunodeficiency-associated cognitive/motor complex. We have selected two experimental animal models, the simian immunodeficiency virus (SIV) and the feline immunodeficiency virus (FIV) (SIV and FIV). These viruses are, with HIV, members of the lentivirus subfamily of retroviruses with highly similar gene organization, biological properties, and clinical sequelae. We find consistent patterns of pathophysiological dysfunction in these animal models early in infection, well before the onset of generalized physiological decline, and which emulate features of disrupted human sleep EEG (Prospero-Garcia et al, PNAS, 1994) and neuropsychological performance (H. Fox and L. Gold, in preparation). Given these similarities, both SIV and FIV models may provide experimental systems for the study of vaccine development, infectivity, and virus sequence mutations, and for evaluating experimental therapeutic strategies (Supported by MH 47680).

NR411 Wednesday, May 24, 12 noon-2:00 p.m.

Psychiatric Comorbidity and General Hospital Use

Stephen M. Saravay, M.D., Psychiatry, Long Island Jewish MC, 270-05 76th Avenue, New Hyde Park NY 11042; Eliot Goldman, Ph.D., Simcha Pollack, Ph.D., Barbara S. Weinschel, M.D., Neil Grafstein

Summary:

Introduction: Medical patients with psychiatric and psychological disorders in general hospitals have extended hospital stays, utilize more general health services, and have increased rehospitalization rates for up to four years after discharge.

Hypothesis: This study tested the hypotheses outlined in our four-year follow-up study that 1) the influence of cognitive impairment on rehospitalization rates would diminish after four years, 2) depression and other personality variables would be sustained after four years.

Design and Setting: The records of a cohort analytic study of 273 medical and surgical inpatients who had been given psychological tests on index admission from June 1985 through June 30, 1986 at the Long Island Jewish Medical Center were examined eight years later. The number of medical/surgical readmissions and the number of days spent in the general hospital were obtained. Potential confounding variables were controlled for.

Results: Cognitive impairment did not predict increased hospital use at eight-year follow-up. However, subscales of the SCL-90 for depression were correlated with a higher rate of rehospitalization ($P = .002$) and total number of days hospitalized ($P = .006$) eight years later. Subscales for Anxiety, Hostility, and Interpersonal Sensitivity were also correlated with greater hospital use at eight years ($P < .05$).

Conclusions: Psychiatric and psychological comorbidity in medical inpatients is associated with increased hospital use for up to eight years after discharge. This association was evident for cognitive impairment within two years after discharge but not at later follow-up.

NR412 Wednesday, May 24, 12 noon-2:00 p.m.

Beside Data Collection Windows Pen Entry Notebook

James J. Strain, M.D., Psychiatry, Mt. Sinai School of Med, 1 Gustave Levy Place, New York NY 10029; Jeffrey S. Hammer, M.D., Ahron Friedburg, M.D., George Fulop, M.D.

Summary:

Introduction: No current system of computerized data entry of clinical information in consultation-liaison (C-L) psychiatry has been well received or has demonstrated that it saves the consultant's time. The inability to achieve accurate, complete, systematic collection of discreet variables and data entry in the harried C-L setting is a major impediment to the advancement of the subspecialty and health services research. The hand-held Notebook computer with Windows Pen Entry MICRO-CARES capabilities has permitted one time direct entry of data at the time of collection at the patient's side.

Data Elements: Variable choice and selection enhances the completeness and accuracy of data collection. For example, ICD-9, Axis III diagnoses maybe selected from a "look up" that at the same time automatically assigns the appropriate code and DRG number. Interventions are specified, including psychopharmacological agents that are selected from predetermined screens. Data elements can be added as required. A questionnaire builder allows the insertion of desired screening devices, e.g., Hamilton, Beck, MMSE. A patient narrative can be typed at the nurse's station, a chart note printed for the medical record, and the MICRO-CARES literature database perused with the printing of selected citations, abstracts, and in some cases, experts' commentaries for the consultee.

Results: The consultant's documentation time is halved using the Notebook Windows Pen entry MICRO-CARES software. From examining 82 traditional hand written consultation records, the direct entry Notebook data description was significantly more comprehensive and accurate. Consultees preferred typed written in contrast to hand written notes. Consultants unanimously felt the Notebook was an important assistant for documentation at the bedside.

Commentary: The cost of the hardware (about $2000) and software ($995) is less than that of an optical scanner and permits report generation and archival searches at the nurses' station without returning to the C-L office for scanning. Radio frequency or ethernet download from the Notebook permits direct data transfer to the C-L office archive computer without requiring secretarial time for scanning or manual data entry.

NR413 Wednesday, May 24, 12:00 noon-2:00 p.m.

Emergency Room's Service Use by Addicts Receiving Disability

Jeffrey G. Stovall, M.D., Psychiatry, VAMC-Westside, 820 S Damen Ave MP116A1, Chicago IL 60612; Linda S. Grossman, Ph.D., Sandra G. McRae, Ph.D., Janet K. Willer, Ph.D., Sarz Maxwell, M.D.

Summary:

Objective: We studied two hypotheses relating to service use patterns in VA hospitals: 1) Substance-abusing VA patients receiving disability benefits present at emergency rooms (ER's) because they have used their benefit money to buy drugs; 2) Scarcity of personal resources contributes to ER use.

Methods: We studied all psychiatric ER presentations (n = 1,448) during 1993 at the Westside VA hospital in Chicago, totalling the number of ER presentations and admissions according to the week of each month in which they occurred. A subsample of those admitted (n = 144) was further assessed for amount of VA disability money received and recent substance use.

Results: 1) From highest lowest, the frequency of ER visits and admissions occurred during the first week, followed by weeks 4, 3, and 2. 2) The same temporal pattern occurred for amount of benefit money received. 3). Significantly more ($p < .05$) of the patients seen in the ER during the first week were substance users (67%), compared to those seen during other weeks (50%).

Conclusions: These service-use patterns indicate that patients receiving most benefits, and substance users, have the highest ER utilization and the most admissions during the week following receipt of benefits. These findings support our hypotheses that high rates of disability payments to addicts contribute to increased service utilization. The higher rates of utilization at month's end, coinciding with depletion of resources, also support our hypothesis that veterans are more likely to present at the ER when financial resources are scarce.

NR414 Wednesday, May 24, 12:00 noon-2:00 p.m.

Referral Trends to an Inpatient Consultation/Liaison Service

Jill S. Meyer, M.D., Psychiatry, Lyons VAMC RWJMS, 151 Knollcroft Road, Lyons NJ 07939; Frank W. Favazza, M.D., William R. Mysels, M.D., Charles Englehart, Ph.D.

Summary:

There is often the need for psychiatric evaluation of hospital patients admitted for nonpsychiatric problems. Our study addresses this question of whether appropriate referrals are made from other services to the Consultation-Liaison Service at the Lyons VAMC. The referring services include medicine, including ICU, CCU, Alzheimer's unit, nursing home care units, intermediate care unit, neurology and surgery services. A total of 241 patient consultations of patients aged 55 and over were seen by the Consultation-Liaison Service between October 1994 and December 1994. The nursing home care unit and medicine service were the most frequent referrals, with 63% and 21% of the referrals. Psychiatric evaluation was assessed with regard to urgency of evaluation, psychiatric diagnosis, treatment recommendations, and compliance. Symptoms of agitation, aggression, depression, and anxiety, and evaluations of competency were the most common reasons for referrals for psychiatric evaluation. The time interval between the referring service's request and psychiatry Consultation-Liaison Service ranged between 1 hour and 21 days. The vast majority of referrals were considered appropriate.

NR415 Wednesday, May 24, 12:00 noon-2:00 p.m.

Chronic Fatigue and Traumatic Life Events

Peter Manu, M.D., Director of Medical Serv., Hillside Hospital, 75-59 263rd Street, Glen Oaks NY 11004; Rachel Yehuda, Ph.D., Earl L. Giller, Jr., M.D., Glenn Affleck, Ph.D.

Summary:

Objective: To determine the relation between traumatic, stressful life events, physical symptoms, psychiatric symptoms, and quality-of-life outcomes in patients with chronic fatigue.

Method: Cross-sectional study of 16 patients (10 women and six men; age range 31-61 years, mean 41.4 years, S.D. 9.3 years) with a chief complaint of chronic (six months or longer) fatigue. All patients received a comprehensive medical evaluation, a structured psychiatric interview, and a scored structured interview addressing 12 traumatic life events (e.g., childhood sexual abuse), completed a well-validated medical outcome study instrument assessing functioning and well-being, and had cortisol levels measured in urine collected over a 24-hour period (range 25-90 mcg, mean 51.9 mcg, S.D. 18.9 mcg).

Results: Trauma scores were significantly correlated with the number of major depressive symptoms ($r = .52$. $p = 0.04$). No statistical relationship was observed between trauma scores and the other measured variables (severity of fatigue, other physical symptoms, physical functioning, role functioning, social functioning, pain and urinary cortisol levels).

Conclusion: Traumatic, stressful life events do not influence the clinical presentation and functional impairment of patients with chronic fatigue, but may contribute to the etiology of chronic fatigue through the mediation of depressive symptomatology.

NR416 Wednesday, May 24, 12 noon-2:00 p.m.

Relationship Between Attention and Memory in PTSD

Julia A. Golier, M.D., Psychiatry, Bronx VA Medical Center, 116A 130 W. Kingsbridge Road, Bronx NY 10468; Rachel Yehuda, Ph.D., Barbara A. Cornblatt, Ph.D., Richard S.E. Keefe, Ph.D., Philip D. Harvey, Ph.D., Robert A. Levengood, M.D.

Summary:

Individuals with post-traumatic stress disorder (PTSD) show a wide range of memory impairments ranging from involuntary recollections to psychogenic amnesia. These memory dysfunctions are frequently accompanied by problems in attention and concentration. We have previously reported that combat veterans with post-traumatic stress disorder demonstrate circumscribed deficits in learning and memory. Although veterans with PTSD showed normal abilities in the functions of initial attention and immediate memory, cumulative learning, and proactive interference from previous learning, there were substantial deficits in retroactive interference, as revealed by a significant decrement in retention following exposure to an intervening word list. In the present study, we explored the extent to which changes in retroactive interference are associated with generalized attentional deficits. Combat veterans with PTSD (n = 15) and demographically comparable, normal comparison subjects (n = 12), were evaluated using a Continuous Performance Task in addition to the CVLT. The results again showed circumscribed, but not generalized, attentional deficits. The findings suggest that deficits in attention may underlie some of the memory impairments previously observed.

NR417 Wednesday, May 24, 12 noon-2:00 p.m.

An Intervention for Self-Injurious Behavior on an Inpatient Unit

Caron Zlotnick, Ph.D., Psychiatry, Brown University, 345 Blackstone Blvd, Providence RI 02906; Elizabeth B. Simpson, M.D., Michelle Kemp, M.A., M. Tracie Shea, Ph.D., Teri B. Pearlstein, M.D., Ann Begin, Ph.D., Ellen Costello, Ph.D.

Summary:

Background: Self-injury, a serious problem, is particularly challenging on an inpatient unit, as it causes great anxiety in staff and patients, may prolong hospital stay, and can precipitate an outbreak of similar behavior among others in the milieu.

Objective: To describe the implementation of a standardized cognitive behavioral intervention to self-injury on an inpatient unit and to provide descriptive data on the incidence of self-injurious behavior prior to and during the introduction of a treatment protocol.

Method: The intervention took place on a 12-bed ward that admits only female psychiatric patients. Prior to the introduction

of the cognitive-behavioral intervention, there was no uniform response by the unit staff to self-injurious behavior. Information regarding incidents of self-injury, suicide attempts, and action taken by the staff, were obtained from hospital records of incident reports.

Results: After an intervention for self-injurious behavior was introduced on an inpatient unit, there was a numerical decrease in the rate of self-injury, a decrease in the frequency of repeated incidents during one hospital stay, an absence of recurrence of the behavior in the same patient upon subsequent admissions, a decrease in the number of patients who self-injured and were examined by a physician, and a nonsignificant trend towards a decrease in the rate of self-injury.

Conclusions: Our finding, along with other findings, suggest that self-injurious behaviors on an inpatient unit can be managed more effectively, efficiently, and therapeutically with a cognitive-behavioral intervention.

NR418 Wednesday, May 24, 12 noon-2:00 p.m.

Adverse Impact of Sexual Trauma and Battering on Veteran Women's Mental Health

Marian I. Butterfield, M.D., Psychiatry, Durham VAMC & Duke, 508 Fulton Street, Durham NC 27705; Cedar Koons, M.S.W., Linda Barnett, Ph.D., Lori Bastian, M.D.

Summary:

Objective: To determine the impact of sexual trauma and battering on mental health in women veterans seeking primary care.

Methods: We surveyed 220 patients using the PRIME-MD and a trauma questionnaire to explore the impact of sexual trauma or battering on mental health.

Results: Mean age was 41, 47% were black, 46% reported trauma: 22% childhood sexual trauma, 18% rape (46% in military), 23% battering (31% in military). Those with sexual trauma (rape or childhood) were different from those without sexual trauma with respect to the following symptoms: depression 56% vs. 27% ($p < 0.001$), panic 25% vs. 5% ($p < 0.001$), somatoform 92% vs. 77% ($p <$ t0.001), eating disorder 22% vs. 11% ($p = 0.03$), alcohol abuse 19% vs. 10% ($p = 0.09$). Those reporting battering were different from those who did not with respect to symptoms of depression 65% vs. 27% ($p < 0.001$), panic 26% vs. 6% ($p < 0.001$), alcohol abuse 22% vs. 10% ($p = 0.03$), somatoform 90% vs. 79% ($p = 0.07$).

Conclusion: Many of the 1.2 million veteran women, like civilian women experience sexual trauma and battering throughout their lives. Service women are vulnerable to rape and battering in the military, which adversely affects mental health. The VA must continue to develop a culture sensitive to women's mental health needs.

NR419 Wednesday, May 24, 12 noon-2:00 p.m.

PTSD and Suicide in Urban Adolescents Exposed to Violence

Jill H. Rathus, Ph.D., Psychiatry, Monefiore Med. Center, 111 E. 210th Street, Bronx NY 10467; Gregory M. Asnis, M.D., Scott Wetzler, Ph.D.

Summary:

Violence poses a serious mental health threat to urban youth, may lead to post-traumatic stress disorder (PTSD), and may be a critical stressor for suicidal adolescents. The present study assessed these factors in an inner-city population of 33 adolescent outpatients with depressive symptoms at a large urban medical center. Participants had a mean age of 15.5 and were predominantly Hispanic & African American. Interviews included the Structured Clinical Interview for DSM-IV, the High Magnitude Stressor Events Structured Interview (Kilpatrick et al., 1991), the PTSD Symptom Scale (Foa, 1993), and the Beck Scale for Suicidal Intent. Findings indicate the most common violent events experienced are having lost relatives or close friends to homicide, witnessing domestic violence, and being physically abused by a caretaker (all reported by approximately 50% of participants). Another 1/3 to 1/8 report events such as physical or sexual assault, witnessing homicide, or witnessing the assault of a loved one. Diagnostically, 1/2 have lifetime histories of PTSD, with 1/3 meeting criteria for PTSD at time of evaluation. Finally, of those subjects who had made a suicide attempt (58%), those with a lifetime history of PTSD made significantly more dangerous suicide attempts in terms of intention to die ($F(1,15) = 9.34$, $p = .008$). Results will be discussed in terms of psychosocial stressors germane to a minority, urban, suicidal population; increased patient-treatment matching; and suicide prevention.

NR420 Wednesday, May 24, 12 noon-2:00 p.m.

PTSD in Cuban Refugee Children at Guantanamo Bay Naval Base, Cuba

Eugenio M. Rothe, M.D., Psychiatry, University of Miami, P.O. Box 016960 (D-29), Miami FL 33101; Capt. Jerry Rose, USN, Hector Castillo-Matos, M.D., Carlos A. Gonzalez, M.D., Lourdes Garcia-Iglesias, M.D., Ruben Busquets, M.D., Capt. Douglas J. Mason, USA

Summary:

Objective: This study was conducted to evaluate the degree of psychological trauma experienced by children and adolescents confined to the Guantanamo Bay Naval Base refugee camps after they attempted to escape Cuba in small boats and crafts in August, 1994.

Method: A preliminary sample of 69 children and adolescents and five adults were administered the Post-Traumatic Stress Disorder Reaction Index by Frederick & Pynoos (a standardized instrument to measure degree of psychological trauma). The instrument was administered in Spanish by four psychiatrists and one psychologist while the children were confined to the camps.

Results: Of the sample, 65.2% were boys, 34.8% were girls, and there were five adults (older than 18 years). Of the children, 78% presented enuresis, 11.6% encopresis, 88.4% crying spells, 97.1% sleep disturbances, 98.5% nightmares, 94.2% appetite disturbances, 72.5% aggressive behavior, and 17.4% suicidal ideations or attempts. The Global Trauma Score revealed that 82% of the boys and 95.8% of the girls presented the highest scores of (very severe) trauma and 18% of boys and 4.2% of girls had (severe) trauma. All five adults had (very severe) trauma scores.

Conclusion: These preliminary findings support our hypothesis that conditions of confinement at the refugee camps and other compounding factors (travel at sea and a tropical storm on Nov. 13, 1994) produced severe psychological trauma. A larger sample is presently being evaluated and factor analysis will be done when all the subjects are tested.

NR421 Wednesday, May 24, 12 noon-2:00 p.m.

Psychoendocrinology of Sexual Abuse in Women with Chronic Pelvic Pain

Christine Heim, Psychology, University of Trier, Universitatsring, 54286 Trier, Germany; Ulrike Ehlert, Ph.D., Juergen P. Hanker, Ph.D., Dirk H. Hellhammer, Ph.D.

Summary:

Chronic pelvic pain (CPP) is a common gynecologic complaint. In a large number of cases no obvious pathological causes of CPP can be found. The purpose of our study was to reveal endocrinological and psychological features of women suffering from idio-

pathic CPP. We examined (a) patients suffering from CPP without organic pathology and (b) pain-free infertile control patients. All patients underwent diagnostic laparoscopy in a general hospital. Endocrinological assessment included the measurement of (a) diurnal levels of free cortisol in saliva, (b) salivary cortisol response to administration of 100μg hCRF, and (c) salivary cortisol suppression after administration of 0.5 mg dexamethasone. Salivary cortisol was determined by immunoassay according to Dressendörfer et al. (1992). Psychological methods consisted of (a) a standardized interview on life events and (b) psychometric assessment of the extent of depression (SDS; Zung, 1986). Results revealed a decreased salivary cortisol release in the morning (CPP: 12.35 nmol/l; controls: 15.48 nmol/l; $p < .05$) and a blunted cortisol response to hCRF challenge in women with idiopathic CPP (basal: 5.70 nmol/l, peak: 19.52 nmol/l; controls: basal: 5.68 nmol/l, peak: 35.46 nmol/l; $p < .001$). The low-dose dexamethasone suppression test revealed a supersuppression of cortisol secretion in with CPP (CPP: peak: 1.02 nmol/l; controls: peak: 5.00 nmol/l; $p < .001$). Sixty-seven percent of patients with idiopathic CPP and 20% of control patients reported sexual and/or physical abuse experiences. The mean extent of depressive mood was within the normal range in both groups. With reference to results in post-traumatic stress disorder (Yehuda et al., 1991), we conclude that women with idiopathic CPP show reduced adrenal activity, which may be a consequence of trauma experience.

NR422 Wednesday, May 24, 12 noon-2:00 p.m.

Personality Change After Genocide: Disorders of Extreme Stress in Bosnians

Stevan M. Weine, M.D., Psychiatry, UIC Psychiatric Inst., 1601 West Taylor Street, Chicago IL 60612; Daniel F. Becker, M.D., Dolores Vojvoda, M.D., Emir Hodzic, Ph.D., Marie Sawyer, M.S., Leslie Hyman, C.I.S.W., Dori Laub, M.D., Thomas H. McGlashan, M.D.,

Summary:

Objective: The authors describe the first reported use of the SCID-DES (Disorders of Extreme Stress) instrument to assess for signs of personality change in Bosnian survivors of "ethnic cleansing".

Method: Twenty-four Bosnian refugees (12 males and 12 females; ages 13 to 59; mean age 34 years) were evaluated one year after resettlement in the U.S. They underwent systematic, trauma-focused, research interviews, including the SCID-DES instrument.

Results: Overall, this group of Bosnian survivors had been severely traumatized as a result of the Serbian nationalists' genocide-exposed to a mean of 16 types of traumatic experiences (range 7 to 24). However, no subjects met criteria for DES. Percent of subjects who met DES subcategory criteria were as follows: altered system of meaning (33%), somatization (29%), altered self-perception (25%), altered relationship with others (25%), altered regulation of affect (17%), altered attention/consciousness (17%), altered perception of perpetrator (0%).

Conclusions: The SCID-DES yields far lower rates of trauma-related personality change in Bosnian survivors of genocide then in adult survivors of prolonged early-life traumas. This is the first report indicating that the DES construct has better application to prolonged interpersonal early-life traumas (such as childhood incest and abuse) than to the prolonged communal traumas of genocide. Nonetheless, the SCID-DES instrument did document some post-traumatic changes in a number of realms of life experience. This suggests the need for a multidimensional approach to describing life changes in survivors of genocide.

NR423 Wednesday, May 24, 12 noon-2:00 p.m.

Assessing the Characteristics of Spouse Abuse in a Military Population

Charles D. Magruder, M.D., 2009 Alabaster Drive, Silver Spring MD 20904; Richard Croutharmel, M.S., Robert Mays, Ph.D., Vivian Sheliga, D.S.W., Ann E. Norwood, M.D., Alison Vawter, B.A.

Summary:

Objective: Spouse abuse is a serious public health problem. Some authors suggest that military populations may be at higher risk. In general, surveillance is lacking, but a program recently created by the military has made uniform data collection possible. This study presents information in this database for the U.S. Army from 1989 to the present.

Method: Information on cases is routinely collected on a standardized form. Denominator data were obtained from established sources and includes active duty and civilian women.

Results: The vast majority of substantiated cases, 4,000 to 6,000 per year involve abuse of the female partner. Incidence of this type of battering ranges from 13.0/1000 in 1991 to 16.0/1000 in 1990. There were 13.6 cases per 1000 women in 1994. No trends were noted. A total of 92% of the cases involved a minor physical injury. Enlisted women and women married to enlisted soldiers were at greater risk for abuse than female officers or women married to officers (O.R. = 11.5; 95% C.L. of 9.3 and 14.3). Information regarding incidence of abuse by geographic area, age, and ethnicity will also be presented.

Conclusions: Initial analyses indicate spouse abuse is a significant problem in this population. Preventive efforts should target enlisted couples.

NR424 Wednesday, May 24, 12 noon-2:00 p.m.

Weapons Collections Among VA Patients

Thomas W. Freeman, M.D., Psychiatry, VAMC #116-A, 2200 Fort Roots Drive, North Little Rock AR 72114-1706; Nichole Keesee, M.S.W., Carolyn Thornton, M.S.W.

Summary:

Thirty patients admitted to a post-traumatic stress disorder (PTSD) rehabilitation unit and 30 comparison patients admitted to acute psychiatric and substance abuse units were surveyed as to their habits of weapons use and collection, their use of substances, their PTSD and dissociative symptoms, and their history of spouse abuse. In addition, the spouses of 10 PTSD subjects were surveyed as to their husband's weapons collection and history of domestic violence. PTSD subjects had four times the number of guns as comparison subjects and engaged in a variety of potentially lethal behaviors with their weapons at a far higher rate than comparison subjects. Of the 30 PTSD patients, 14 had a history of suicide attempts. Those PTSD patients with histories of suicide attempts differed from PTSD subjects without a history of suicide attempts in terms of dissociative symptoms and other survey items.

NR425 Wednesday, May 24, 12 noon-2:00 p.m.

Successful Treatment of Paraphilic Sex Offenders

Eliezer Wiztum, M.D., c/o Dr. A. Rosler, Hadassah Unv Hosp., P.O. Box 12000, Jerusalem IS 91120, Israel; Ariel Rosler, M.D.

Summary:

We treated nine men with severe paraphilias (pedophilia [DSM-IV], with or without exhibitionism and/or voyeurism) with monthly injections of triptorelin (Decapeptyl-CR®), a long-acting gonadotropin-releasing (GnRH) analog that causes desensitization of GnRH

receptors, resulting in marked reduction of LH, FSH, and testosterone secretion. Age of the patients ranged between 22 and 43 years, and duration of their paraphilias between seven and 33 years. Three had been previously convicted, and two did not respond to cyproterone acetate therapy. All individuals requested therapy voluntarily, with a firm desire to "cure" themselves. Intensity of sexual drive (B.S.I. 53-Inventory Brief Symptoms), and three main complaints (Target Complaints Scale) were evaluated.

A marked improvement was observed in all nine patients after one to two months of therapy, whereas maximal effects were evident after four to 11 months. All said that their sexual interest and fantasies had decreased considerably, and their sexual drive was now well controllable. Although triptorelin caused a reduction of testosterone to prepubertal levels, married individuals continued to have sexual activity, albeit reduced. Androstenedione and DHEA-S were not influenced by therapy. Bone mineral density was unchanged after six to 12 months of therapy, although two patients had decreased values to start with, due to previous therapy with cyproterone acetate. Pedophilia may be a disorder basically associated with hypersensitivity to androgens, so that persistence of moderate sexual activity could be attributed to the effect of minimal testosterone levels, together with androgens of adrenal origin.

NR426 Wednesday, May 24, 12 noon-2:00 p.m.

Dissociative Amnesia: Evidence For Interhemispheric Disconnection

Godehard Oepen, M.D., Psychiatry, Bedford Hosp. VAMC, 200 Springs Road, Bedford MA 01730; Edward Federman, Ph.D., Lawrence R. Herz, M.D.

Summary:

An unusual male case of dissociative fugue was studied with particular reference to dissociative amnesia. A complex interaction of historical (abuse), developmental (cognitive impairment, immature EEG), social (threatened existence), psychodynamic (immature defenses), and neuropsychological factors in the development and resolution of the typical dissociative behavioral and memory pathology could be demonstrated. Psychiatric/psychodynamic assessment was complemented by brain imaging, EEG, repeated exam with extensive memory batteries, WAIS, MMPI, DES, and divided visual field paradigms. During claimed dissociative amnesia visuospatial performance was found to be enhanced relative to an otherwise subnormal performance profile, but levelled out after full return of memory. The anomalous performance in one modality was contrary to expected global learning effect and to an MMPI performance characterized by negativistic perseveration. It is here interpreted as a disconnection of ("social") left hemispheric from ("subjective") right hemispheric processes, with disinhibited hyperactivity of right hemisphere functions during the actual dissociation, and reestablished inhibitory balance after recovery (models by Wolff, Galin, Gazzaniga & LeDoux, Ross). Our biopsychosocial formulation leads to a testable model and assessment protocol for dissociative amnesia.

NR427 Wednesday, May 24, 12 noon-2:00 p.m.

The Prevalence of Dissociation in Inpatients

Virginia L. Susman, M.D., Westchester, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Beth Brodsky, Ph.D., Maura Lehr, M.S.W., Robert A. Grossman, M.D., Orli Avi-Yonah, Ph.D., Stephen Hurt, Ph.D.

Summary:

This study assessed the prevalence of dissociative disorders in a general inpatient population. One hundred and eight consecutively admitted patients consented and completed a screening packet of self-report instruments: Dissociative Experiences Scale (DES), Beck Depression Inventory (BDI), Personality Assessment Inventory, and a questionnaire addressing childhood physical or sexual abuse and lifetime substance abuse. Our design called for interviewing all who scored 15 or higher on the DES with the Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D).

Among the 108 subjects (50 male, 58 female) 71 scored 15 or higher on the DES. Thirty-five were interviewed, 18 were discharged before interview, one refused, and 17 were clinically judged to be too disorganized to be interviewed. Among the 35 who were interviewed, 17 had no SCID-D diagnosis and 18 met criteria for a dissociative, disorder (1 dissociative amnesia, 0 dissociative fugue, 2 depersonalization disorder, 3 DDNOS, and 8 MPD or dissociative identity disorder). We separated 4 others who met criteria but prominent organicity and substance abuse contributed extensively to their syndromes. Statistically significant differences between groups of those with and without SCID-D diagnoses were found in: mean DES score (27 vs 44, T= –2.34, p = .0291); Physical Abuse History (X^2 = 10.58, df = 2, p = .005); Sexual Abuse History (X^2 = 6.136, df = 2, p = .047); BDI score (27 vs 36, T = 2.08, p = .05).

NR428 Wednesday, May 24, 12 noon-2:00 p.m.

Trauma Associated Psychopathology in Alcoholics: Screening and Diagnosis

M. Kirsten Miller, M.D., 105 Kingsway Commons, Princeton NJ 08540-1612; Arthur A. Alterman, Ph.D., Pam Fawcett, M.Ed., E. Holub-Beyer, M.H.R., Delinda Mercer, M.S., Karen Clay, B.A., Joseph R. Volpicelli, M.D.

Summary:

It is well established that alcoholics frequently present with histories of adult and childhood trauma. However, little effort is routinely made to screen alcoholics for trauma-associated psychopathology such as dissociative disorders (DD). The objectives of this study were to evaluate the feasibility of accurately diagnosing DD among 50 walk-in outpatient alcoholics at the TRC and to obtain an impression of the prevalence and clinical relevance of trauma-associated psychopathology in this setting. Three modalities were used: 1) a standardized self-report instrument; 2) an interviewer-administered diagnostic instrument (DDIS); and 3) a psychiatric mental status exam. We found that, although alcoholism and DD can present similarly, (e.g. memory disturbances, affective lability, unusual behavior and impaired impulse control), routine screening for trauma-associated psychopathology such as DD and PTSD can be done successfully. We found that psychopathology associated with childhood sexual abuse was particularly important to diagnose early in treatment, because such pathology is sufficiently disruptive to threaten early treatment. Data will also be presented that suggest alarmingly high rates of rigorously defined childhood adult/or adult trauma (close to 3/4 of women and half of men) as well as of clinically significant trauma-associated psychopathology (nearly half of women and one-quarter of men). Finally, we will discuss the methods we found to be most effective for screening as well as for diagnosing trauma-associated psychopathology in alcoholics in clinical settings and comment on the question of exaggerated reporting of traumatic experiences.

NR429 Wednesday, May 24, 12 noon-2:00 p.m.

Psychiatric Diagnoses and Abuse Experiences of 45 Adult Pseudoseizure Subjects

Elizabeth S. Bowman, M.D., Department of Psychiatry, Indiana University, 541 Clinical Dr Room 291, Indianapolis IN 46202; Omkar N. Markand, M.D.

Summary:

Objective: This study sought to determine the occurrence of Axis I disorders and trauma experiences in adult pseudoseizure patients.

Method: Subjects were 45 adult seizure clinic outpatients of normal intelligence diagnosed with pseudoseizures by video-EEG. Trauma experiences were gathered by an unstructured interview and a trauma checklist. The Structured Clinical Interviews for DSM-III-R for Axis I disorders (SCID-P) and Dissociative Disorders (SCID-D) were administered to determine current and lifetime Axis I diagnoses.

Results: Subjects were 78% female, mean age 37.5 (SD 9.7) years. Current diagnoses included: any somatoform disorder, 98%; dissociative disorders, 91%;, affective disorders, 64%; post-traumatic stress disorder, 49%; non-PTSD anxiety disorders, 47%. A total of 82% had a lifetime diagnosis of a non-seizure conversion disorder; 82% reported trauma: sexual abuse, 67%; physical abuse, 67%; other significant traumas, 60%. The mean SCID-D score was 14.3 (SD 4.2), intermediate between scores previously reported for general psychiatric outpatients and for dissociative disorder patients.

Conclusion: Pseudoseizure patients have high rates of trauma and of psychiatric disorders found in traumatized groups. Patterns of psychiatric illnesses in dissociative disorder and pseudoseizure patients are similar. Clinicians should screen adult pseudoseizure patients for adult and childhood trauma, dissociation, depression, and PTSD.

NR430 Wednesday, May 24, 12 noon-2:00 p.m.

Validity of Family History Diagnosis of Alzheimer's Disease

Mohsen Aryan, Ph.D., Bronx VAMC, 130 W. Kingsbridge Road, Bronx NY 10468; Li Ge, M.D., Jeremy M. Silverman, Ph.D., Richard C. Mohs, Ph.D., Vahram Haroutunian, Ph.D., Kenneth L. Davis, M.D.

Summary:

Background: Family informants reports are routinely relied upon in many familial/genetic investigations of Alzheimer's disease (AD) to identify relatives with a primary progressive dementia (PPD), i.e., likely AD. This method has been found to have excellent reliability, but few studies have examined its validity, and none have used neuropathological diagnoses. In this study, we evaluated through family informants the dementia status of 74 deceased former nursing home residents who, at death, had an autopsy of the brain.

Methods: Neuropathologic diagnoses of definite and probable AD were assigned based on previously established research criteria (i.e., CERAD). Telephone interviews with family informants were conducted, blind to autopsy diagnosis, in most cases several years after death. The Alzheimer's Disease Risk Questionnaire was used to screen for a possible dementia. If suspected, we administered the Dementia Questionnaire (DQ). The DQ assesses, through informant report, the symptoms, course, and possible causes of a memory problem or cognitive deterioration. This information is used in order to determine the presence of dementia and where applicable, assign a diagnosis of PPD, based on DSM-III criteria for primary degenerative dementia.

Results: Agreement between family history and neuropathogical diagnosis was 73% (54/74). Of 48 elderly given a neuropathological diagnosis of AD, 35 were diagnosed as PPD (sensitivity = 0.729). Ten of the 13 elderly with neuropath AD but not called PPD were categorized as demented but assigned other causes. In addition, 19 of the 26 elderly not given a neuropath AD diagnosis were not called PPD by family history (specificity = 0.731).

Conclusion: The sensitivity and specificity of the PPD diagnosis for AD and the overall agreement between PPD and neuropathological diagnosis of AD are only slightly lower than many reports of those attained through clinical examination.

NR431 Wednesday, May 24, 12 noon-2:00 p.m.

Mechanisms of Programmed Cell Death in the Brain

Herbet W. Harris, M.D., Lab Neuroscience, National Inst. Aging, NIH Bldg 10 RM 6C103, Bethesda MD 20892

Summary:

Programmed cell death (apoptosis) is of central importance in many age-related degenerative processes. Interactions between cells and their extracellular matrix are critical to many cellular processes including differentiation and survival. Loss of contact with extracellular matrix can induce apoptosis. We demonstrate apoptosis in PC12 cells deprived of extracellular matrix adhesion, and we report that nerve growth factor (NGF) treatment greatly accelerates this process. Plating PC12 cells on agarose-coated dishes effectively blocks cell adherence. During the initial 24 hours of culture, 30% of the cells grown on agarose undergo apoptosis, while cells plated on collagen-coated surfaces maintain nearly 100% viability. Apoptosis of adhesion-blocked cells continued over the next 72 hours. Addition of NGF paradoxically accelerates apoptosis in nonadherent cells while inducing proliferation and differentiation of adherent cells. Both NGF and fibroblast growth factor induced apoptosis, while epidermal growth factor (which induces proliferation but not neuronal differentiation of PC12 cells) was far less potent. We investigated the nature of the signalling associated with NGF in nonadherent PC12 cells. Immunoblotting with antiphosphotyrosine antibodies revealed striking differences in the pattern of tyrosine phosphorylation induced by NGF in adherent compared with nonadherent cells, suggesting that NGF signalling is altered in nonadherent PC12 cells.

NR432 Wednesday, May 24, 12 noon-2:00 p.m.

Depression and Negative Symptoms in Alzheimer's Disease

William E. Reichman, M.D., Copsa Inst for Alzheimers, Disease & Related Disorde, UMDNJ-CMHC 671 Hoes Ln, Piscataway NJ 08854; Andrew C. Coyne, Ph.D., Satish Amirneni, M.D., Bruno Molino, B.S.

Summary:

Alzheimer's disease (AD) is the leading cause of intellectual decline in the elderly. Accompanying the neuropsychological deficits of AD are clinically significant behavioral features (e.g., delusions, aggression, sleep/wake cycle abnormalities, and depression). Many patients also display behaviors such as passivity, apathy, and lack of emotional reactivity. These may be conceptualized as "negative symptoms," analogous to the state described in schizophrenia. The present study: 1) compared the occurrence of negative symptoms in patients with AD and normal elderly controls; and 2) demonstrated that negative symptoms in AD patients are distinct from depression.

Subjects were 24 patients with clinically diagnosed probable AD by NINCDS-ADRDA criteria and 26 age-matched, healthy, elderly controls. All were free of medical illnesses or medication exposure that could cause negative symptoms. Subjects were administered the MMSE, Cornell Depression Scale, and a modified version of the Scale for the Assessment of Negative Symptoms (SANS) for use in AD patients (SANS-AD).

Results indicated that: 1) negative symptoms are more common in AD patients than in healthy elderly ($F[2,49] = 23.06$, $p < .0001$); 2) negative symptom scores are not correlated with depression scores in AD patients ($p > .05$); and 3) negative symptoms in AD are inversely correlated with dementia severity ($r = -0.40$, $p < .05$). Further research is required to determine the effects of negative

symptoms in AD on functional ability as a prelude to the development of effective interventions for these behavioral features.

NR433 Wednesday, May 24, 12 noon-2:00 p.m.

Relationship Between Melancholia and Personality Disorders

Eric D. Peselow, M.D., Psychiatry, NYU School of Medicine, 32 Bassett Avenue, Brooklyn NY 11234; Michael P. Sanfilipo, M.A., Faouzia Barouche, M.D., Gita Vaid, M.D., Alejandra Hallin, M.D., Ronald R. Fieve, M.D.

Summary:

The objective of our paper is to evaluate the relationship between melancholic/nonmelancholic depression and categorical and dimensional personality disorder diagnosis. The reason for this evaluation is that according to DSM-III-R criteria, one historical criterion for melancholia is the absence of a personality disorder, despite the fact that there is little evidence for or against this assertion.

Our method was as follows: We evaluated 355 patients who entered one of six double-blind, antidepressant/placebo trials over an eight-year period. These patients were all diagnosed as to whether they did or did not meet DSM-III criteria for melancholia. All patients prior to initiation of treatment (during the depressed phase) underwent a Structured Interview for DSM-III Personality Disorders (SIDP) to determine both dimensional personality traits and categorical personality diagnosis. Our results indicated that patients with melancholic depression had greater cluster A personality traits/diagnoses than nonmelancholics. Nonmelancholics tended to have greater cluster B personality traits/diagnoses than melancholics. We conclude that the statement that DSM-III-R melancholics have no personality disorder is incorrect.

NR434 Wednesday, May 24, 12 noon-2:00 p.m.

Effect of Cumulated Partial Sleep Deprivation on TRH Test Responses

Fabrice Duval, M.D., Psychiatry, Centre Hospitalier, 27 rue du 4eme RSM, 68250 Rouffach 00110, France; M. Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D., Jean-Paul Macher, M.D.

Summary:

Objective: The pathophysiologic mechanisms that underlie the blunted TSH response to TRH in depression remain uncertain. Recent studies have reported that sleep deprivation increases TSH concentrations both in normals and depressed patients. Due to the frequent sleep disturbances observed in depressive states, We hypothesized that decreases in total sleep time could stimulate TSH secretion and reduce pituitary TSH reserves leading to blunted response to TRH.

Method: We studied, in six healthy hospitalized volunteers, the effect of four nights partial sleep deprivation (PSD) on TSH and prolactin (PRL) response to TRH (200 μg iv administered at 10 AM). The TRH test was carried out three times: first at baseline (after a normal night) and then after the second and the fourth PSD. During the nights of PSD, the subjects slept from 10 p.m. to midnight and were then wakened.

Results: TSH and PRL responses to TRH were not significantly changed after two PSDs when compared with base-line values. However, the TRH-induced TSH and PRL responses were significantly decreased after four PSDs (both $p = 0.036$).

Conclusion: Our finding that cumulated PSD induces a blunting of TSH and PRL response to TRH may suggest that severe chronic sleep disturbance, even in the absence of major depression, could lead to a decrease of the pituitary responsiveness to TRH.

NR435 Wednesday, May 24, 12 noon-2:00 p.m.

Erectile Dysfunction in Sleep Apnea and Response to Continuous Positive Airway Pressure

Ismet Karacan, M.D., Psychiatry, Baylor College of Med., One Baylor Plaza Ste 710D, Houston TX 77030; Mehmet Karatas, M.D.

Summary:

Twenty-two men, whose average age is 54 years (27-73), with SAS and complaint of impotence were enrolled in this study. Each patient was evaluated in the sleep laboratory before and during treatment with CPAP. Tests included physical, psychological, and neurovascular examinations, along with polysomnography, nocturnal penile tumescence (NPT), and penile rigidity.

While 32% of 22 patients had normal NPT (psychogenic impotence), 68% had impaired NPT (organogenic impotence) before treatment with CPAP.

Patients were divided into three subgroups based on their NPT measures before and during CPAP. Seven patients (NN) had normal NPT patterns before and during CPAP. Ten patients (AA) had abnormal NPT patterns before and during CPAP. Five patients (AN) had abnormal NPT before CPAP but normal NPT during treatment with CPAP.

Before treatment with CPAP the three subgroups did not differ significantly with respect to average apnea duration (AAD) or the respiratory distres index (RDI). During treatment with CPAP, subgroup AN had a significantly shorter AAD and lower RDI than either of the other two subgroups ($p < .05$).

These results indicate that erectile dysfunction in patients with sleep apnea could be related to chronic cerebral hypoxia due to apnea, and CPAP may improve erectile dysfunction in almost one-third of this population.

NR436 Wednesday, May 24, 12 noon-2:00 p.m.

Academic Stress and Differential Changes in Immune Response

Sergio M. Gloger, M.D., Psychiatry, Catholic University, Marcoleta 352, Santiago 0068, Chile; Patricio Fischman, M.D., Isabel Caldumbide, M.S., Orietta Echavarri, M.S., Paulina Arias, B.S., Javier Puente, Ph.D.

Summary:

Objective: In association between stress and changes in immune competence has been suggested by previous reports. The aim of this study was to determine the effect on functional immune measures of an ongoing acute stressor placed at the end of a discrete period of cumulative academic demands.

Method: Psychological evaluation and blood samples were obtained from 42 healthy medical students a month prior to, and immediately before, the last and most dreaded of a series of final exams. Blastogenesis, the ability of lymphocytes to proliferate in response to mitogen stimulation, was performed by incubating ^{3}H-thymidine labeled T-cells with different concentrations of phytohemagglutinin (PHA). Natural killer cell activity (NKCA) was assayed by measuring the release of previously inserted ^{51}Cr from specific tumor cell lines (K562), at different ratios, following the lysis induced by the addition of NKC.

Results: Statistical analysis (two-tailed T-test for paired samples) revealed a significant reduction in the blastogenesis stimulation index at 5 mcgrs/ml of PHA (85.02 vs 47.93) between the basal academic stress and the acute exam situation ($p < .01$); NKCA (50:1 ratio) was found to be significantly increased at the acute exam situation (27.8 vs 38.1; $p < .003$).

Conclusions: The lowered mitogenic response in a group of young and healthy subjects further suggests that cellular immune-competence can be altered when facing even a commonplace, although intense psychosocial stressor. The increase in NKCA,

being a rapid first line immune response for acute antigenic challenges, suggests that, even in spite of a general decreased immune function, it may also represent a functional reserve when facing superimposed acute stressors. (Supported by FONDECYT Grant 1940640)

NR437 Wednesday, May 24, 12 noon-2:00 p.m.

Attributional and Defensive Styles: Do They Influence Immune Response?

Patricio Fischman, M.D., Psychiatry, Catholic University, Marcoleta 352, Santiago 0068, Chile; Sergio M. Gloger, M.D., Orietta Echavarri, M.S., Cristina Ramirez, M.S., Isabel Caldumbide, M.S., Cecilia Sepulveda, M.D.

Summary:

Objective: It as been reported that stressors alter immune function. Specific individual psychological traits may further and differentially modulate the direction and intensity of this immune response. Cognitive styles and intrapsychic defensive structures were assessed along with immune competence in an academic stress model.

Method: Forty-two healthy medical students were psychologically assessed using Peterson's Attributional Style Questionnaire (ASQ) and Bond's Defensive Style Questionnaire (DSQ). Immune competence was measured through blastogenesis. Students were evaluated a month prior to, and immediately before, the last of the final academic exams.

Results: Overall immune competence measured through the blastogenesis stimulation index significantly decreased (85.02 vs 47.93) ($p < 0.01$) between the basal period and the acute exam situation. A significant ($r = 0.32$) ($p < 0.05$) positive Pearson correlation coeficient for lineal relationship was found between the "internal" dimension (for causality of events) in the ASQ and the lymphocyte proliferation index. A significant ($r = -0.42$) ($p < 0.01$) negative correlation was found between the "self-sacrificing" cluster of defense mechanisms in the DSQ and blastogenesis.

Conclusion: A stronger inner sense of control illustrated by a cognitive attributional style that relies more on "internal reasons" for the cause of events, correlates positively with lymphocyte proliferation. This may suggest that, in contrast to the state of "learned helplessness" (heavier reliance on external attribution for causality), the aforementioned psychological trait may have a positive role in preserving immune competence in the face of an acute stressor. The heavier reliance on reaction-formation and pseudoaltruism as defense mechanisms clustered under the "self-sacrificing" dimension of the DSQ ("kind, helpful, masochistic, martyr type") may imply a less favorable immune response to an acute stressor. (Supported by FONDECYT Grant 1940640)

NR438 Wednesday, May 24, 12 noon-2:00 p.m.

Major Depression and Natural Killer Cell Activity: Relation to Severity and Past Antidepressant Medication

Antonio Andreoli, M.D., Psychiatry, Univ of Geneva, 8 Rue Du Decembre, Geneva CH 1207, Switzerland; Steve Keller, Ph.D., Theresa Q. Pascual, LP, John C. Bartlett, M.D.

Summary:

Significance: Over the last few years, decreased natural killer (NK) cell activity has been reported in psychiatric subjects with major depression (MD) (Irwin et al., 1990). Further research should be directed to determine whether such immune abnormality is a stable correlate of depressive mood in humans.

Methods: We studied 41 adult patients referred with major depressive episode (MDE) and 41 age- and sex-matched controls without past/present psychiatric disorder. All subjects were physically healthy and drug-free from at least six weeks. Each subject/control pair had immune evaluation (NK cell number and NK activity) and clinical assessment (HDS, HAS, GAS, interview for past antidepressant treatment) on the same day.

Results: MDE subjects had decreased NK cell number ($p < 0.05$) and cytotoxic activity ($p < 0.01$) compared with controls. In addition, there was an independent negative effect of age ($p = 0.05$) and severity ($p < 0.01$) and no effect of past antidepressant medication on the day-to-day adjusted variance of NK citotoxic activity in the MDE subgroup of the study sample.

Comment: The present study raised further evidence that depressed subjects have decreased NK cell number and function. Such an immune abnormality does not depend on previous AD treatment, but may be a correlate of increased age and severity in these patients.

NR439 Wednesday, May 24, 12 noon-2:00 p.m.

A Double-Blind Comparison of Sertraline and Clomipramine in Outpatients with OCD

Jean-Claude Bisserbe, M.D., c/o R. Wiseman, Pfizer Inc., 219 E. 42nd St. 3rd fl MS12, New York NY 10017; Robert L. Wiseman, Ph.D., Maureen S. Goldberg, R.N., Roger M. Lane, M.D.

Summary:

Objective: To compare efficacy, safety, and tolerability of sertraline and clomipramine in the treatment of obsessive compulsive disorder (OCD).

Method: Outpatients with DSM-III-R-defined obsessive compulsive disorder and scores of ≥20 on YBOCS, ≥7 on NIMH-OC, ≥4 on CGI-S, and ≤17 on HAMD (17-item) were randomized to sertraline ($N = 86$) or clomipramine ($N = 82$) once daily for 16 weeks. Initial daily doses of sertraline and clomipramine were 50mg. After a minimum of four weeks, these doses could be increased by 50mg increments every two weeks to a maximum of 200mg daily if the response was thought to be inadequate. Efficacy was assessed at the end of 1, 2, 4, 6, 8, 12, and 16 weeks of therapy using the YBOCS, NIMH-OC, CGI-S, CGI-I, and CAS scales.

Results: Mean baseline YBOCS, NIMH-OC, and CGI-S totals were 27.86, 10.13, 5.50, respectively, for sertraline; and 27.43, 9.93, and 5.52 for clomipramine. Sertraline demonstrated greater efficacy than clomipramine in the intention-to-treat patient group: mean baseline to final visit changes were −50.80% (YBOCS), −41.92% (NIMH-OC), −37.66% (CGI-S) for sertraline, and −42.94% (YBOCS), −33.84% (NIMH-OC), −29.29.96% (CGI-S), for clomipramine ($p < 0.05$). Mean final doses were 128.5mg sertraline and 90.1mg clomipramine. The number of patients withdrawing because of adverse events (all causalities) was substantially greater for clomipramine (25.6%) than sertraline (10.5%) ($p < 0.05$). The most frequent adverse events for clomipramine were dry mouth (19.5%), anxiety (17.1%), constipation (15.9%), and nausea (14.6%); and for sertraline, diarrhea (11.6%), nausea (11.6%), and headache (9.3%).

Conclusions: Sertraline was more effective than clomipramine. Its superior tolerability and lower rate of premature treatment withdrawal relative to clomipramine may offer considerable quality of life and compliance benefits in the long-term management of a chronic disorder such as OCD.

NR440 Wednesday, May 24, 12 noon-2:00 p.m.

A Double-Blind, Placebo-Controlled Study of Sertraline in the Treatment of Outpatients with SAD

Adam Moscovitch, M.D., c/o R. Wiseman, Pfizer Inc., 219 E. 42nd St. 3rd fl MS12, New York NY 10017; Robert L.

Wiseman, Ph.D., Maureen S. Goldberg, R.N., Roger M. Lane, M.D.

Summary:

Objective: To evaluate efficacy, safety, and tolerability of sertraline (STL) as a pharmaceutical treatment option in patients with seasonal affective disorder (SAD).

Method: Outpatients with seasonal pattern recurrent winter depression (DSM-III-R defined) and a SIGH-SAD total score ≥22 (≥12 on 21-item HAM-D, ≥10 on 8 atypical SAD items) were randomized in a double-blind, international, multicentre, parallel-group, eight-week, dose titration protocol to STL (N = 93) or placebo (PLC) (N = 94) once daily. The initial daily dose was 50mg STL or PLC-equivalent with dosage increases by 50mg increments every two weeks to a maximum of 200mg daily if response was suboptimal. Efficacy was measured at baseline (BLN) and at the end of weeks 1, 2, 4, 6, and 8 using the SIGH-SAD, Hamilton Anxiety (HAM-A), Clinical Global Impression for Severity (CGI-S), Hospital Anxiety (HAD-A) and Depression (HAD-D) factor, and Leeds Sleep Evaluation scales.

Results: Mean percent changes from BLN to final visit for primary outcome measures (intent-to-treat patients) are shown.

		SIGH-SAD	HAM-A	CGI-S	HAD-D	HAD-A	
STL	BLN	36.3	17.0	4.2	9.6	10.5	+p < 0.05, within group. *p < 0.05, **p < 0.01 between groups
	% Change	−51.8+*	−56.5+*	−38.3+*	−47.6+*	−37.9+**	
PLC	BLN	35.4	16.6	4.2	9.3	10.7	
	% Change	−42.7+	−41.8+	−28.2+	−28.1+	−19.7+	

Significant improvement over baseline was seen in both treatment groups. However, STL produced significantly greater response than PLC on all primary efficacy ratings. Overall, STL was well tolerated, with the most frequent PLC-adjusted adverse events (AEs) (all causalities) for STL being nausea (24.9%), diarrhea (16.2%), insomnia (13.0%), and dry mouth (10.8%). AEs were mostly mild to moderate and transient.

Conclusions: STL was demonstrated to be an effective and well-tolerated treatment option for SAD.

NR441 Wednesday, May 24, 12 noon-2:00 p.m.

An Open Pilot Study of Sertraline in the Treatment of Outpatients with Pedophilia

John M.W. Bradford, M.D., c/o R. Wiseman, Pfizer Inc., 219 E. 42nd St. 3rd fl MS12, New York NY 10017

Summary:

Objective: Pedophilia is a psychiatric disorder that is difficult to treat and often recurrent. Selective serotonin reuptake inhibitors (SSRI), which are known to decrease obsessive-compulsive behaviors, may be useful in the treatment of pedophilia. This study was undertaken to assess the safety and efficacy of sertraline, as a treatment for pedophilia.

Method: This was a 12-week, open-label, dose-titration pilot study. After obtaining written informed consent, otherwise healthy male outpatients over age 16, with a DSM-III-R diagnosis of pedophilia for at least six months, not currently on psychoactive medication or antiandrogen therapy, received an initial daily dose of 50mg sertraline. Based upon patient response and toleration, this was increased at two-week intervals by 50mg increments to a maximum of 200mg daily.

Results: Summary data from 19 patients are available; 16 patients completed the study, two withdrew owing to adverse events, and one was lost to follow-up. Marked improvement was observed on most sexuality scales. Despite the small sample, statistically significant baseline to last-visit changes (sign rank test) included Greenberg scores for fantasies of sex with young girls ($p < 0.05$), decrease in sexual activity ($p < 0.01$), decrease in penile tumescence to descriptions of pedophilia ($p < 0.05$), decrease in obsession on YBOCS ($p < 0.05$). There were also important decreases in the number of patients masturbating more than twice a week and in the number of patients who had fantasies of sex with young girls. The most common treatment related adverse events were: headache (nine patients), diarrhea, flatulence, nausea (five patients each), and insomnia (four patients).

Conclusions: Sertraline therapy is well tolerated and appears to be effective in the treatment of pedophilia.

NR442 Wednesday, May 24, 12 noon-2:00 p.m.

Outcome of Long-Term Psychiatric Hospitalization

Carol L.M. Caton, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, New York NY 10032; Alexander Gralnick, M.D., (Posthumously)

Summary:

Despite the persistent trend to restrict the length of psychiatric hospitalization, long-term hospital care is often the only alternative for patients who fail to benefit from brief hospitalization. Addressing the need for more empirical data on outcome of long-term hospitalization, we are reporting findings from a follow-up investigation of 100 consecutive admissions to a private psychiatric hospital who stayed six months or more. The typical patient was in late adolescence and had already experienced two prior hospitalizations. Many grew up in disorganized families with considerable parental pathology. The most common DSM-III-R diagnoses based on a SADS interview were major depression, schizophrenia or schizoaffective disorder, and conduct disorder. About half had concurrent substance abuse, Patients were reinterviewed two to three years post discharge. Among our findings are: 1) Fewer than one in three discharged "improved" were rehospitalized. Rehospitalization episodes were often associated with substance abuse. 2) Two-thirds of patients discharged "improved" remained in outpatient treatment for the entire follow-up period. 3) More than half were employed or attending school.

Findings suggest that a subgroup of the severely mentally ill may benefit from a longer hospital stay in which social rehabilitation and preparation for community living are emphasized.

NR443 Wednesday, May 24, 12 noon-2:00 p.m.

Are Meta-Analysis Reliable? The Evidence From Three Contradictory Meta-Analyses of Treatments in Panic Disorder

Larry V. Amsel, M.D., Biostatistics, Col. Univ Sch of Pub Hlth, 600 West 168th Street, New York NY 10023-3799

Summary:

Objective: Chalmers points out that if meta-analysis is to be scientific, it must at a minimum be reproducible. In this paper, we examine three meta-analyses of treatments for panic disorder (PD) published since 1990. In addition, we will compare these meta-analyses with a subsequent large-scale multicenter trial (n = 1168). Together these papers offer us the opportunity to examine the strengths and weaknesses of meta-analysis as it is currently practiced.

Method: A comprehensive literature review identified three meta-analyses of pharmacological treatments for panic disorder. For each meta-analysis we examined its scientific rigor using six criteria abstracted from the meta-analysis methodology literature. In particular: 1) the use of a written protocol, 2) study inclusion criteria, 3) treatment of "study quality," 4) data extraction, 5) multiple outcome variables, and 6) method of combining results.

Results: The effect size estimates of the three meta-analyses were significantly different, and the conclusions contradicted each other. Each one arriving at one of the three possible conclusions: 1) antidepressants are better than, 2) worse than, and 3) equal

to benzodiazepines for panic disorder. In methodology all the meta-analyses fell short in their rigor as measured by the above criteria. Interestingly the study that was most rigorous by these criteria also most closely agreed findings in a subsequent large multicenter (N = 1168) trial.

Conclusion: Meta-analyses are useful only when done rigorously, as defined in the methodology literature.

NR444 Wednesday, May 24, 12 noon-2:00 p.m.

A New Method for Quality of Life Assessment: Tableau d'Evaluation Assisstee de la Qualite de Vie

Denis Grabot, M.A., Lab Psychiatry, Universite Bordeaux, 121 Rue De La Bechade Centre C, Bordeaux 33076, France; Corinne Martin, M.D., Marc Auriacombe, M.D., Jean L. Tignol, M.D.

Summary:

The TEAQV (Tableau d'evaluation Assistee de la Qualite de Vie) is an instrument designed to standardize the collection of quality-of-life data among patients with chronic psychiatric or somatic diseases. This instrument is a two-part, seven-point scale (0 = extremely bad; 6 = excellent), self-rated, quantitative evaluation of a patient's quality of life at different time points in four areas (physical and psychological well-being, family relationships, professional activity). The first part is a one-time retrospective lifetime evaluation, while the second part is a current state evaluation that can be prospectively repeated. Time points are determined by important periods of the illness or treatment course. This instrument is administered by a trained interviewer in five to 10 minutes. The TEAQV has been used in different populations. Correlation coefficients between TEAQV current state and conventional scales were studied. Among 26 lung and heart-lung transplant patients, the correlation coefficients between TEAQV and the sickness impact Profile are: physical –.622; psychological –.406. Among 18 opioid-dependent patients in treatment the correlation coefficients between TEAQV and the Addiction Severity Index are: physical –.548; psychological –.763; social professional –.747; family –.341. Our early results with the TEAQV suggest that it may have the potential to be an easily used and helpful instrument for quality-of-life evaluation.

NR445 Wednesday, May 24, 12 noon-2:00 p.m.

Are Drug Research and Clinical Patients Similar?

Phebe M. Tucker, M.D., Psychiatry 5SP520, University of Oklahoma, 920 Stanton L. Young Blvd, Oklahoma City OK 73190; Lisa Goulden, Ph.D., Alfretia Scarborough, M.P.H.

Summary:

Objective: To compare pharmaceutical subjects and patients seeking treatment for the same disorder, examining demographics, personality variables, and general symptoms.

Methods: 21 subjects (16 females, five males) were recruited by newspaper ads and physician referral into a pharmaceutical protocol for panic disorder. Twenty-one outpatients (nine females, 11 males) treated in same university anxiety clinic for panic were selected from a database by stratification to include similar proportions with comorbid diagnoses in both groups. All had active panic disorder by full SCID. Initial 2 x 2 MANOVA identified group-by-gender main effects for demographics, BDI, State-Trait Anxiety Inventory, and SCL-90. As the research group had elevated MMPI-2 F-scale (infrequency), a 2 x 2 MANOVA for group by gender with F as covariate was performed on MMPI subscales to control for possible overreporting of symptoms. MANOVAs were followed by post-hoc T-Tests (significant for $P < .05$).

Results: Research subjects had significantly lower education and family income, independent of gender. Clinic males had higher MMPI-2 Psychaesthenia and SCL-90 Phobic Anxiety than clinic females. Research females had higher Trait Anxiety and MMPI-2 Psychaesthenia, Schizophrenia, and Social Introversion than research males and higher SCL-90 Interpersonal Sensitivity than clinic females.

Conclusions: Sampling bias may complicate pharmaceutical studies. Subjects, lacking financial resources, may participate expecting treatment and positive results. Gender may also influence subjectively reported outcome, as research females studied had greater baseline distress, including social mistrust.

NR446 Wednesday, May 24, 12 noon-2:00 p.m.

Published Research in Psychiatry: Who Pays?

Julio L. Jane, M.D., 500 Park Ridge Ct #U, Winston Salem NC 27104-3564; P. Murali Doraiswamy, M.D., Vincent Palese, PAC, Lorraine Vinci, M.S.

Summary:

Background: To study the extent of funded versus unfunded research in major psychiatric journals.

Methods: Survey of 143 original research articles published in 20 general and subspecialty psychiatric journals during one month in 1993. The corresponding authors were contacted to confirm sources of funding.

Results: 80% of journals surveyed had at least one unfunded article, and in half of the journals at least 25% of the articles were unfunded; 72% of published articles were supported by federal funds and 19% had no funding.

Conclusions: Over one quarter of all original studies published in psychiatry journals received no federal support. Increasing federal support for research in psychiatry will reduce pressures on academic faculty. We recommend that all published articles account for study costs to remove potential misconceptions that such costs are being passed on to patients or third party payers.

NR447 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Outcome in Schizophrenic Patients Switched From Clozapine to Risperidone

Robert Lynn Horne, M.D., Psychiatry, Univ NV School of Med, 44 Quail Run Road, Henderson NV 89014-2148; Forest Miller, Ph.D.

Summary:

Fourteen previously treatment-refractory schizophrenic patients were in remission while being treated with clozapine, but asked to be switched to risperidone to reduce treatment side effects and eliminate weekly blood tests and their costs. Risperidone was titrated 4 to 6 mg/day over three days while clozapine was withdrawn over periods ranging from 0 to 30 days (mean, 7.6 days). The risperidone dose was then adjusted according to patient response; the mean dose was 6.8 mg/day (range, 6-12 mg/day). Patients' mean Brief Psychiatric Rating Scale pathology scale scores increased from 15.5 while receiving clozapine to 17.7 after one month of risperidone treatment (n-9) or upon discontinuation of risperidone (n-5). According to scores on the Clinical Global Impression scale, two of these patients were much improved, one minimally improved, six unchanged, one minimally worse, and four much worse. Two of the five patients whose treatment with risperidone was discontinued had to be hospitalized briefly to reestablish clozapine treatment. Of the nine patients who were improved or unchanged at one month, none had relapsed after eight months of treatment with risperidone. Techniques for switching patients from clozapine to risperidone will be discussed.

NR448 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Use of Risperidone in a Private Psychiatric Practice

Robert Lynn Horne, M.D., Psychiatry, Univ NV School of Med, 44 Quail Run Road, Henderson NV 89014-2148; Forest Miller, Ph.D.

Summary:

Among 91 patients treated with risperidone (mean, 5.9 mg/day), primary diagnoses were schizophrenia in 31, depressive psychosis in 29, manic psychosis in 19, and organic psychosis in 12. Seventy of the patients were in remission while being treated with conventional antipsychotics, but asked to be switched to risperidone for more complete remission or fewer side effects. The other 21 patients were receiving no antipsychotic treatment. The 16-item Brief Psychiatric Rating Scale (BPRS) was completed for all patients at baseline and the BPRS and Clinical Global Impression (CGI) change scale at hospital discharge in the 42 inpatients (after a mean of 18 days) or after 30 days of treatment in the 49 outpatients. Of the 70 patients switched from another antipsychotic, 42 were very much or much improved (CGI scores) and 28 were minimally improved or unchanged; their BPRS total pathology scale score was reduced significantly from 27.9 to 16.1 ($p < 0.01$). Of the 21 patients not previously treated, 14 were very much or much improved and seven were minimally improved or unchanged; their BPRS scores were reduced from 29.9 to 19.0 ($p < 0.01$). These treatment outcomes were not significantly related to diagnostic group. The incidence of side effects (including EPS) was reduced during risperidone treatment. It is concluded that risperidone was safe and effective in this heterogeneous group of patients.

NR449 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Calcium Uptake into Platelets in Depression

Michael Berk, M.D., Psychiatry, WITS Medical School, 7 York Road Parktown, Johannesburg 2193, South Africa; Alphonce Nabiswa, M.D., Nicola H. Kirchmann, M.Sc.

Summary:

Uptake of $^{45}CA^{2+}$ into platelets and the effects of serotonin on uptake was studied in 15 drug-free patients with DSM-III-R major depression and 17 matched controls. Radioactive decay, proportional to calcium uptake, was measured by counts per minute (CPM) using a β liquid scintillation counter. The mean basal level of $^{45}Ca^{2+}$ uptake was significantly higher in the depressed group than in the controls ($P = 0.0246$, Mann-Whitney). Serotonin was associated with a significant decrease in $^{45}Ca^{2+}$ uptake in both groups ($P = 0.0075$, depressed; $P = 0.0012$, controls, Wilcoxon). The serotonin stimulated levels were not significantly different, however ($P = 0.299$, Mann-Whitney). There was a greater mean percentage decrease from the baseline in patients (30.3%) than in controls (14.1%), which tended toward statistical significance ($P = 0.0518$, Mann-Whitney). These results suggest dysregulation of calcium homeostasis in depression.

NR450 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Fluoxetine Treatment of Depression in Medical Students

Michael Berk, M.D., Psychiatry, WITS Medical School, 7 York Road Parktown, Johannesburg 2193, South Africa

Summary:

Many clinical trials are biased by the inclusion of low functioning indigent patients, which may result in poorer outcomes. Nineteen medical students (age 20 to 35) who met DSM-III-R criteria for major depression were treated in this open label study. The mean HAM-D score before treatment was 19.3 and this reduced to 4.6 after six weeks of treatment ($P < 0,01$.) Twelve patients went into remission (HAM-D < 7) and only one patient failed treatment defined as a less than 50% reduction in the HAM-D. Although open trials frequently have higher response rates, these results suggest that higher functioning patients may have markedly better response rates.

NR451 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Prevalence and Clinical Features of Akathisia in an Acute Inpatient Ward

Domenico Berardi, M.D., Psychiatry, University, Viale Pepoli 5, Bologna 40123, Italy; Annalisa Giannelli, M.D., Gloria Samory, M.D.

Summary:

Akathisia is a frequent side effect among patients on neuroleptic (NL) medications and is significantly associated with poor compliance and a worse outcome.

We have surveyed all patients admitted to the University Department of Psychiatry in Bologna (Italy) over a one-year period and treated with NL drugs ($n = 72$). We did not include only patients with a diagnosis of schizophrenia but we also included a number of patients with other diagnosis receiving NL drugs (e.g., patients with affective disorders, borderline personality disorders). All these patients have been evaluated weekly with a variety of standardized assessment instruments (e.g., BPRS, BARS, AIMS, Van Putten Scale, Simpson-Angus Scale). Fifteen patients (21%) suffered from akathisia, narrowly diagnosed: eight patients reported only inner restlessness, whereas seven also showed restlessness movements. Seven patients (10% of the sample) suffered from pseudoakathisia. Patients with akathisia tended to be older and female. The mean NL dosage, at the onset of akathisia, was 460 mg eq CPZ, as compared to 312 mg eq CPZ in controls. The prevalence of akathisia was higher in patients with affective disorders (32%) and borderline personality disorder (20%) than in schizophrenia and schizophrenia-like patients (16%). The implications of these results are discussed and recommendations for a rational prescribing of NL are outlined.

NR452 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Neuroleptic-Induced Changes in Plasma Methionine-Enkephalin Degradation

Marion E. Wolf, M.D., Psychiatry, VA Medical Center, 3001 Green Bay Road, North Chicago IL 60064; Barbara Lesley, R.N., Carol Frenkel, R.N., John Conran, M.D., Edward D. Bukowski, M.D., Aron D. Mosnaim, Ph.D.

Summary:

The suggested association of schizophrenia and other neuropsychiatric disorders with significant changes in central and peripheral mechanisms involving endogenous opioid peptides (e.g. endorphins and enkephalins) has raised interest in studying the different factors affecting the metabolism of these substances. Thus, we have examined the effects of various neuroleptics on the in vitro plasma degradation kinetics and half life of methionine enkephalin in samples from neuroleptic-free schizophrenic patients and drug-free healthy volunteers. Our results show significant pharmacokinetic differences between patient ($n = 15$) and control ($n = 20$) groups (initial velocity for methionine-enkephalin degradation, mean ± SD, and range of 1.19 ± 0.3 and 0.66-1.86, and 0.74 ± 0.1 and 0.54-1.04, respectively), with a substantial number of patients' samples (11 of 15) showing initial velocity values above that of the highest control. Whereas preincubation of plasma samples with different concentrations of either thiorida-

zine, chlorpromazine, or fluphenazine consistently resulted in decreased initial velocity and increased half-life values, there was some variability in these changes depending on the drug, its concentration, and the sample studied. No significant changes were recorded for lower drug levels (10^{-5} or 10^{-6}M). The possible relevance of these results with regard to the pharmacological effects of neuroleptics will be discussed.

NR453 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Listening to Antidepressants: Mood Improvement in Psychiatrically Normal Volunteers

Clarice Gorenstein, Ph.D., Psychiatry, Univ. De Sao Paulo, LIM 23 FMUSP, Caixa Postal8091, Sao Paulo SP 01065-970, Brazil; Valentim Gentil, Ph.D., Marcio Melo, M.D., Francisco Lotufo Neto, Ph.D., Valeria Lauriano, M.D.

Summary:

Panic disorder patients treated with clomipramine often describe themselves as calmer, less irritable, and more stable than prior to treatment. Antidepressants are known to reduce irritability, anxiety, and other affective symptoms in premenstrual dysphoric syndrome (Sundblad et al., 1992). To test the hypothesis that clomipramine is affective in reducing subclinical affective symptoms we conducted a double-blind, cross-over controlled trial of clomipramine (oral doses of 10-40 mg/day) and propanteline (active placebo) for five weeks in 13 psychiatrically normal volunteers selected from 275 responders to newspaper and radio requests for normal subjects. They did not reach cut-off scores in the Self-Report Questionnaire and did not meet lifetime or current psychiatric diagnosis criteria according to ICD-X or DSM-III-R as assessed by open psychiatric interview and Schedules for Clinical Assessment in Neuropsychiatry interview. However, they were concerned about their usual levels of anxiety or irritability. Significant improvement in the Clinical Global Impression scale was obtained in 80% of the subjects during clomipramine, and 30% during placebo ($p < 0.05$). Despite the small sample size this controlled trial suggests that it is possible to improve normal mood by low dose antidepressant drugs, confirming previous claims that optimizing mood by psychopharmacological means is truly possible (Kramer, 1993).

NR454 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Selective Serotonin Reuptake Inhibitor-Induced Sexual Dysfunction: Efficacy of a Drug (and Sex) Holiday

Anthony J. Rothschild, M.D., Harvard Medical School, McLean Hospital, 115 Mill Street, Belmont MA 02178-1048

Summary:

Numerous case reports and the results of a few controlled studies have documented sexual dysfunction in association with almost all antidepressants including the SSRIs. The purpose of the present study was to evaluate whether weekend drug-holidays would improve sexual functioning in depressed patients with SSRI-induced sexual dysfunction. Thirty outpatients (16 women, 14 men, mean ± SD age = 42 ± 6) who reported worsening of sexual functioning during SSRI treatment participated in the study. The subjects met DSM-III-R criteria for major depression, had responded to treatment with an SSRI with a post-treatment HDRS ≤ 10, and indicated that the sexual dysfunction was of sufficient magnitude that if not corrected they would choose not to continue taking the SSRI. Patients were instructed to discontinue the SSRI after the Thursday morning dose and to restart the SSRI (at their previous dose) on Sunday at 12:00 noon on four weekends. Ratings for depression (using the HDRS) and sexual functioning (using a 7-point scale; 1 = very much improved through 7 = very much worse) were performed in person on Thursday and by telephone on Monday morning. While only one of 10 patients on fluoxetine (Flu) reported "much" or "very much" improved orgasm function for at least 50% of the weekends, six of 10 patients on sertraline (Ser) (Fisher's exact; Ser vs. Flu, p = .03) and five of 10 patients on paroxetine (Par) (Fisher's exact; Par vs. Flu, p. = .07) reported improved orgasm function. Similarly, 50% of the patients on sertraline and paroxetine reported "much" or "very much" improvement in sexual satisfaction and libido for at least 50% of the weekends compared with none of the fluoxetine patients (Fisher's exact; Ser vs. Flu, p = 0.2; Par vs. Flu, p = .02). There were no statistically significant increases in mean HDRS scores after SSRI discontinuation. During the weekend drug holiday, 1/10 sertraline patients and 1/10 paroxetine patients had increases in HDRS scores from the 4-8 range to the 10-14 range. The improvement in sexual functioning in the paroxetine and sertraline patients (but not in the fluoxetine patients) is presumed to be due to the shorter half-lives of paroxetine and sertraline as compared to fluoxetine/nor fluoxetine.

NR455 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Safety and Tolerance of Fluvoxamine Versus Sertraline in Depressed Outpatients

Charles B. Nemeroff, M.D., Dept of Psych & Behav Sci, Emory Univ Sch of Med, 1639 Pierce Drive Ste 4000, Atlanta GA 30322; Philip T. Ninan, M.D., James C. Ballenger, M.D., John P. Feighner, M.D., John H. Greist, M.D., William Petterson, M.D.

Summary:

The safety and tolerance of fluvoxamine (LUVOX™) Tablets, 50-150 mg daily versus sertraline (Zoloft®), 50-200 mg daily, were studied in outpatients with DSM-III-R-defined major depressive disorder in a randomized, double-blind, parallel-group, multicenter study. After a one- to two-week placebo run-in, patients received double-blind treatment for seven weeks. Efficacy was evaluated primarily by the Hamilton Psychiatric Rating Scale for Depression (HAM-D). Secondary and supportive measures of efficacy included HAM-D factor scores, the Clinical Global Impressions Scale (CGI), the Hamilton Psychiatric Rating Scale for Anxiety (HAM-A), the Raskin-Covi Scale, and the Hopkins Symptom Checklist-56 (SCL-56). Safety evaluations included vital signs, clinical laboratory tests (hematology and biochemistry), the Sexual Symptoms Distress Index, monitoring of adverse events and concomitant medication. One hundred fourteen patients were screened for the study; 97 patients were randomized: 49 to fluvoxamine and 48 to sertraline. Eighteen fluvoxamine-treated and seven sertraline-treated patients did not complete the study. Mean HAM-D 21-item total score decreased 13.03 points (from a mean baseline score of 24.57) for fluvoxamine and 11.61 points (from a mean baseline score of 23.15) for sertraline (visit-wise analysis) over the seven-week period. There were no statistically significant differences between groups at any visit and at end-point for the primary efficacy variable (HAM-D 21-item total score). Secondary and supportive measures confirmed the results obtained with the HAM-D. Neither treatment was associated with any clinically important changes in laboratory values or vital signs. There were more overall complaints associated with sertraline than with fluvoxamine, although more fluvoxamine-treated patients discontinued due to adverse events. Sertraline was associated with significantly more sexual dysfunction complaints (libido decrease, sertraline 19.57% vs. fluvoxamine 6.12%; ejaculatory abnormality, sertraline 22.22% vs. fluvoxamine 5.26%) than fluvoxamine.

NR456 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Meta-Analysis of Studies on Carbamazepine Augmentation of Neuroleptic Treatment in Schizophrenia

Robert G. Stern, M.D., Psychiatry, Mt. Sinai Sch of Med., Box 1230 One Gustave Levy P1, New York NY 10029; Larry V. Amsel, M.D., Michael Davidson, M.D., John D. Davis, M.D.

Summary:

Objective: To date there is no consensus on the efficacy of carbamazepine as an add-on agent to augment the effects of neuroleptics in schizophrenic patients without frank seizures. This study used meta-analysis to determine if evidence exists to support the clinical efficacy of carbamazepine augmentation of neuroleptics in these patients.

Method: A comprehensive literature review of all studies using carbamazepine augmentation in psychosis was undertaken. Only those studies were analyzed which: 1) made appropriate diagnosis, 2) first treated patients with therapeutic doses of neuroleptic, and 3) then randomly assigned these subjects to augmentation with carbamazepine or placebo, in a double-blind study design. These criteria yielded seven studies acceptable for quantitative metaanalysis.

Results: Of the seven studies, four reported statistically significant improvement with carbamazepine augmentation over placebo augmentation, while three studies did not find a statistically significant difference. The meta-analysis of all seven studies yielded a Z statistic of 2.2, significant at the .05 level. The cumulative effect size had a point estimate of 0.26 with a 95% confidence interval of (0.03, 0.50), which indicates statistical significance.

Conclusion: Our meta-analysis found a statistically significant effect for carbamazepine augmentation. However, in a meta-analysis of seven or more studies the results are often highly statistically significant. In contrast, this meta-analysis was significant only at the .05 level. Moreover, the clinical significance of carbamazepine augmentation, as estimated by a combined effect size of 0.26, remains in question. We believe these results leave the question of carbamazepine augmentation open, and warrant a large multi-center trial to determine effectiveness of carbamazepine augmentation of neuroleptics for schizophrenic patients.

NR457 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Carbamazepine, Lithium and the Combination: A Bipolar Maintenance Trial

Kirk D. Denicoff, M.D., BPB, NIMH Bldg 10 RM 3N212, 10 Center Drive, Bethesda MD 20892; Earlian Smith-Jackson, R.N., Elizabeth Disney, B.A., Ali O. Syed, B.S., Gabriele S. Leverich, M.S.W., Robert M. Post, M.D.

Summary:

Objective: To compare the prophylactic efficacy of lithium, carbamazepine, and the combination and to identify possible clinical and biological markers of response.

Method: Fifty-two outpatients who met RDC criteria for bipolar I (n = 33) and II (n = 19) illness were studied in a randomized partial double-blind design for an intended one year of treatment with lithium or carbamazepine, a crossover to the opposite drug in the second year, and then a third year on the combination. Patients received detailed evaluations monthly and daily life chart ratings of the degree of functional incapacity associated with mania or depression.

Results: 13/44 (29.5%) failed lithium due to lack of efficacy, and two (4.5%) dropped out due to side effects. 13/45 (28.9%) failed carbamazepine due to lack of efficacy, and ten (22.2%) dropped out due to side effects (nine of the ten had rash). Seven out of 26 (26.9%) failed the combination. The percentage of patients who had marked or moderate improvement on the CGI scale was 33.3% on lithium, 31.5% on carbamazepine, and 50% on the combination. Substantial morbidity remained despite the use of antimanic or antidepressant adjuncts in 71.1% of patients on lithium and 74.2% on carbamazepine. A history of rapid cycling was associated with a poor outcome to both monotherapies.

Conclusions: These data suggest a high incidence of inadequate response to either mood stabilizer despite use of adjunctive agents as needed. Additional novel treatment regimens are need to better decrease affective morbidity.

NR458 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Negative Correlation Between Alpha-1 Acid Glycoprotein Plasma Level and Response to Haloperidol in the Acute Treatment of Schizophrenia

Ilan Levinson, M.D., Psychiatry, Beth Israel Medical Ctr., First Ave at 16th St 9 Fierma, New York NY 10003; Stewart B. Levine, M.D.

Summary:

Objectives: The authors investigated whether schizophrenic patients with varying blood levels of Alpha-1 acid glycoprotein (AAG) responded differently to a fixed dose of haloperidol.

Methods: AAG blood level was obtained from 17 newly admitted inpatients. All patients met DSM-III-R criteria for schizophrenia. All patients were medication free for at least three weeks and had no medical or drug abuse problems. Patients were started on haloperidol 5 mg P.O. BID, as well as benztropine 1 mg BID, and followed for a period of two weeks by BPRS scores.

Results: The mean AAG was significantly higher in nonresponders (X = 104.7) than in responders (X = 69.6) (P = 0.003). A significant negative correlation was found between AAG and the change noted in both BPRS and BPRS psychosis subscale (P = 0.0001). There was no correlation between initial BPRS scores and AAG level.

Conclusions: The study indicates that the efficacy of haloperidol in the first two weeks of treatment of schizophrenic patients negatively correlates with AAG level. Future research should clarify the importance of AAG as a factor in the neuroleptic treatment of schizophrenia.

NR459 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Double-Blind Randomized Study of Three Haloperidol Plasma Levels for Acute Psychosis

Philip G. Janicak, M.D., Research, Psychiatric Inst., 1601 West Taylor Street, Chicago IL 60612; Javaid I. Javaid, Ph.D., Rajiv P. Sharma, M.D., Anne M. Leach, M.D., S. Dowd, B.S., John M. Davis, M.D.

Summary:

Objective: The ideal therapeutic antipsychotic plasma level has remained elusive. Given haloperidol's (HPDL) widespread use, we attempted to confirm the results of earlier, retrospective fixed-dose studies by prospectively targeting patients to three HPDL plasma levels.

Methods: After washout, 91 acutely psychotic patients were randomly assigned (Phase A) to a low, middle, or high HPDL plasma level range under double-blind conditions. After two weeks of treatment at the assigned levels, nonresponders were randomly reassigned to continue as before or to change levels (Phase B).

Results: During the first phase, there were no significant differences in clinical outcome among these three groups. In the second phase, however, nonresponders in the low, middle, or high groups who were reassigned to or remained in the middle group demonstrated greater improvement than their counterparts who were not.

Conclusions: During phase A we found no differences in clinical response or side effects among the three groups. In phase B there was evidence of an optimal level for initial nonresponders. Our results suggest that low plasma levels of haloperidol (i.e., around 3-5 ng/ml) are effective for many patients and that middle levels (i.e., averaging about 10-12 ng/ml) may improve outcome in patients who do not demonstrate an early satisfactory response.

NR460 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

The Extrapyramidal Symptom Rating Scale: Revised Factor Structure

Lawrence Annable, D.S., Psychiatry, McGill University, 1033 Pine Avenue West, Montreal Quebec H3A 1A1, Canada; Guy Chouinard, M.D., Andree Ross-Chouinard, M.D.

Summary:

The Extrapyramidal Symptom Rating Scale (ESRS) has been shown to be valid and reliable for the assessment of neuroleptic-induced extrapyramidal symptoms and tardive dyskinesia (TD). Separate subscales of the ESRS assess the severity of drug-induced parkinsonism and akathisia, acute and tardive dystonia, and TD. We carried out principal components factor analysis with varimax rotation on the ESRS scores of 305 neuroleptic-treated chronic schizophrenic outpatients assessed by a single neurologist who was experienced in the use of the scale. Six factors emerged accounting for 67.1% of the variance in the items of the scale: 1) hypokinetic parkinsonism consisting of the items assessing bradykinesia, facial mask, gait and posture, and rigidity; 2) orofacial dyskinesia consisting of the items assessing dyskinesias of the jaw, mouth and lips, tongue and face; 3) trunk/limb dyskinesia consisting of the items assessing dyskinesias of the trunk and the upper and lower extremities; 4) akathisia; 5) tremor; and 6) tardive dystonia. This factor structure is consistent with the classical typology of movement disorders. Moreover, the factor structure for dyskinetic movements supports the hypothesis that orofacial and trunk/limb dyskinesias should be considered as distinct subsyndromes of TD.

NR461 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

ICI 204, 636 (Seroquel™): New Preclinical Research Data Confirm Atypical Antipsychotic Actions

Jeffrey Goldstein, Ph.D., Pharmacology, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850

Summary:

ICI 204,636, a dibenzothiazepine with affinity for multiple brain receptors, is a potential atypical antipsychotic. ICI 204,636 is active in behavioral and electrophysiologic tests considered predictive of antipsychotic activity and satisfies the following pharmacologic criteria, which are putative predictors of atypicality: 1) a higher affinity for central 5-HT_2 than D2 receptors; 2) limbic selectivity, as evidenced by depolarization inactivation of A10 but not A9 dopamine cells after chronic administration; 3) minimal dystonic liability in haloperidol-sensitized and drug-naive cebus monkeys; 4) transient elevations in prolactin after acute administration in rats.

New pre-clinical research findings further distinguish the atypical antipsychotic profile of ICI 204,636:

- In squirrel monkeys trained to discriminate clozapine from saline, ICI 204,636 produced dose-dependent increases in response on the clozapine associated lever with full substitution at the highest doses tested.
- In the prepulse inhibition (PPI) animal model of sensorimotor gating deficits in schizophrenic patients, ICI 204,636 restores PPI in apomorphine-treated rats with potency comparable to clozapine. Like clozapine but unlike haloperidol, ICI 204,636 also enhances PPI.
- Typical and atypical antipsychotics produce distinctly different induction patterns of neuronal Fos expression in the rodent forebrain. ICI 204,636, like clozapine, selectively increases the number of neurons that displayed Fos-like immunoreactivity in the limbic-related nucleus accumbens and prefrontal cortex, but not in the motor related dorsolateral striatum, the site of activity for haloperidol-like agents.
- In monkeys treated with amphetamine that exhibit asocial behavior, ICI 204,636 not only reverses stereotypy, but restores social behavior. To the extent that this model mimics both the positive and negative symptoms of schizophrenia, ICI 204,636 is predicted to exhibit enhanced antipsychotic efficacy.
- In the rat Paw Test (which discriminates between typical and atypical antipsychotics) ICI 204,636 is more effective in prolonging hindlimb retraction time than forelimb retraction time, a profile also shared by clozapine.

On the basis of the above results, ICI 204,636 exhibits pharmacological properties that distinguish it as an atypical antipsychotic agent, not only with respect to clozapine-like minimal EPS liability, but perhaps enhanced antipsychotic efficacy.

NR462 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Sertraline and Fluoxetine in Major Depression

Claudine Mertens, M.D., Psychiatry, St. Camillus Clinic, Pleispark 65, St. Denijs-Westrem B 9051, Belgium; F. Bartholome, P. Cosyns, M.D., H. D'Haenen, M.D., M. Van Moffaert, M.D.

Summary:

The objective of the study was to compare the short-term (8 weeks) and the follow-up (6 months) efficacy and toleration of sertraline (S) and fluoxetine (F) in depressed outpatients.

A total of 165 adult outpatients with DSM-III-R defined major depression were treated double-blind with either 50 mg S (n = 83) or 20 mg F (n = 82). These doses could be titrated to 100 mg or 40 mg respectively, if the response was inadequate after four weeks of treatment as determined by the investigator. Efficacy was assessed at the end of weeks 2, 4, and 8 using the MADRS, HAMD, CGI-S; responders had follow-up assessments at weeks 12, 16, 24, and 32, with the same scales. Responders were defined as ≥50% reduction from baseline HAM-D or MADRS, or score ≤10 and CGI ≤3.

Results: Both SSRIs produced similar efficacy from the intent-to-treat (ITT) analysis. Starting from a mean baseline MADRS of 24.5 for S and 23.1 for F, the mean % decrease to final visit (week 8) was 45% for S and 43% for F. The median baseline to week 8 changes for CGI-S were from markedly ill (score 5) to mildly ill (score 3) in both groups.

A further reduction of the scores was obtained from week 8 to the end of the study (week 32). A total reduction from baseline MADRS of 19.8 (–69%) was observed for S; and 18.3 (–65%) for F. On the CGI-S at the end of the study 79% of S patients were normal to mildly ill, compared to 81% of the F patients. Over 80% of patients were responders at the end of treatment in both treatment groups.

The final dosage was 50 mg in 64% of the sertraline and 20 mg in 63% of the fluoxetine treated patients. In both groups, 35% of the patients reported treatment-related adverse events (mostly nausea).

Conclusions: The results of this study demonstrate that S and F have a similar efficacy in the management of depression in outpatients and are well tolerated.

NR463 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Pharmacokinetic and Pharmacodynamic Interaction of Zolpidem and Fluoxetine

Antoni A. Piergies, M.D., CPA, Evanston Hospital, 2650 Ridge Avenue, Evanston IL 60201; Barbara Roth-Schechter, Ph.D., Pam Shinleber, R.N., Lisa McGarry, MT ASCP, Stephane Allard, M.D.

Summary:

Because early treatment of depression with selective serotonin uptake inhibitors (SSRI) can be associated with insomnia, nighttime administration of a sedative/hypnotic is often combined with an SSRI.

Objective: Evaluate pharmacokinetic (PK) and pharmacodynamic (PD) interactions between zolpidem 10 mg (Z) a short-acting hypnotic, and fluoxetine 20 mg (F), a SSRI.

Method: 24 male volunteers (mean age 23.5 yrs) received Z and F in the following open design: Z on night 1, a morning dose of F daily from day 2 thru day 18, and Z on night 18. Using HPLC, plasma levels of Z, F and norfluoxetin (NF) were determined throughout night 1 for Z, night 18 for Z, F and NF, on days 16 and 17 for F and NF. Morning Digit Symbol Substitution (DSST) and Buschke Modified Recall (BMR) tests were performed on days 1, 12, 18, and 19. Statistical analysis of data consisted of repeated measures of analysis of variance.

Results: There was no significant difference between night 1 (Z) and night 18 (Z and F) in AUC, C_{max} and $T_{1/2}$ of Z. There was no difference in C_{min} between day 16 and 17 for F and NF. There was a 3% to 4% increase in AUC and C_{max} of F and NF between day 17 (F) and day 18 (F & Z). There was no significant difference in the subjects' next day DSST and BMR after nighttime treatment of Z alone or in the presence of F.

Conclusion: Both Z and F were well tolerated alone or in combination. There were no clinically significant Pk or PD interactions between Z and F.

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Cost Benefit of Clozapine Regarding Activity Level

Veronica W. Larach, M.D., Psychiatry, Inst. Psiquiatrico, Lo Fontecilla 441 Las Condes, Santiago 27014, Chile; Patricia T. Munoz, M.D., Gladys N. Corral, U.N., Isabel E. Hanish, Ph.D.

Summary:

The cost benefit assessment of treatment with clozapine (CLZ) was prospectively studied in 42 DSM-III-R treatment resistant schizophrenic patients, with one-year follow-up treatment with clozapine: 34 men and 8 women, 35 ± 8 years of age, and 15 ± 7 years of illness, mean daily dose of CLZ = 375 mg. Direct costs were assesed involving hospitalizations, procedures, consultations, and drug costs. Clozapine treatment involves more costs in the first than in the second year because of the installation requirements and procedures for the first year of treatment. Analyses were made for the two previous years of treatment with typical neuroleptics, the first year of treatment with clozapine, and for a second hypothetical year, considering the observed trend of the first year of treatment with clozapine. Of 12 patients living in institutions, eight are living now with their families. From 2,325 hospitalization days observed in the previous two years to CLZ, 802 hospitalization days were observed with CLZ which includes treatment initiation. The patients' activity level previous to CLZ showed 76.3% of totally inactive patients, compared to 16.7% at the end of the first year of CLZ treatment. Direct costs appear to be two times greater than typical neuroleptics during the first year and 1.6 fold greater during the second year (20% less). When the productivity of the patients according to the activity level was considered, the cost of the first CLZ year was only 0.5 fold than the typical neuroleptic treatment; during the second year with CLZ it would be 15% less than the typical neuroleptic treatment if the same trend was to be maintained.

NR465 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of First Episode Psychotic Patients: A Double-Blind Multicenter Comparison with Haloperidol

R.A. Emsley, M.D., Univ of Stellenbosch, Tygerberg, South Africa; Robin McCreadie, M.D., Philippe Lemmens, Ph.D.

Summary:

Patients diagnosed as having provisional schizophreniform disorder (DSM-III-R) and psychotic symptoms requiring treatment with an oral antipsychotic agent were randomly assigned to receive risperidone (n = 99) or haloperidol (n = 84) for six weeks; the mean daily dose at end point was 6.1 mg of risperidone and 5.6 mg of haloperidol. The trial was completed by 80% of the patients in the risperidone group and 69% in the haloperidol group; significantly more haloperidol patients (15) than risperidone patients (six) withdrew because of adverse events or treatment insufficiency ($p < 0.05$). At treatment end point, 63% of the risperidone patients and 56% of the haloperidol patients were clinically improved, defined as a 50% reduction in total scores on the Positive and Negative Syndrome Scale (PANSS). Both treatment groups showed significant improvements on each PANSS subscale and on the PANSS-derived Brief Psychiatric Rating Scale ($p < 0.05$), with no significant between-treatment differences. Risperidone, however, was a safer drug than haloperidol; severity of extrapyramidal symptoms (scores on the Extrapyramidal Symptom Rating Scale) and their incidence were lower in the risperidone-treated patients; significantly fewer risperidone patients than haloperidol patients required antiparkinsonian medication ($p < 0.001$). It is concluded that risperidone is an effective and safe antipsychotic drug in first-episode psychotic patients.

NR466 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Risperidone Once Daily Versus Twice Daily

Barry D. Jones, M.D., Dept. of Psychiatry, McMaster University, 1200 Main St. West, Hamilton Ontario, Canada; Goedele deSmedt, M.D., Philippe Lemmens, Ph.D.

Summary:

Results of several controlled trials of risperidone in schizophrenic patients indicate that the optimal dose of risperidone is 4 to 8 mg/day given in two divided doses. The present study was designed to determine whether 8 mg of risperidone given once daily was as effective and safe as the same dose given twice daily in patients diagnosed as having chronic or subchronic schizophrenia with acute exacerbation. The six-week trial was completed by 77 patients assigned to twice-daily treatment and by 76 patients assigned to once-daily treatment. In both patient groups, Positive and Negative Syndrome Scale (PANSS) total and subscale scores, PANSS-derived BPRS scores, and scores on five PANSS symptom clusters improved significantly from baseline to treatment endpoint. Between-group differences in these scores, however, were not significant. The median time to first response was 14 days in both groups. Severity of extrapyramidal symptoms did not differ significantly between the two groups. It is concluded that 8 mg/day of risperidone given once daily is therapeutically equivalent to the same dose given twice daily.

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Are Study Dropouts Different From Completers?

Joyce R. Tedlow, M.D., Psychiatry, Mass General Hospital, WAC 815 15 Parkman Street, Boston MA 02114; Maurizio

Fava, M.D., Lisa A. Uebelacker, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: The aim of our study was to identify psychological and clinical predictors of failure to complete an eight-week open trial of fluoxetine in depressed outpatients.

Methods: Subjects consisted of 23 depressed patients who dropped out of a study involving open treatment with fluoxetine, 20 mg per day for eight weeks, and 23 subjects who completed the same study and were matched by age and gender. Diagnosis of major depressive disorder was made by SCID-P, and patients were required to have a score ≥16 at baseline on the 17-item Hamilton Rating Scale for Depression. All subjects were administered the SCID for personality disorders, the Anxiety Sensitivity Index, the Cook-Medley Hostility Scale, the Problem Solving Inventory, the Social Adjustment Scale (self-report), the Symptom Questionnaire, and the Composite Index of Quality of Life. Differences between completers and dropouts on the various measures were assessed with the Mann-Whitney U test, while differences in lifetime rates of Axis I and Axis II disorders were evaluated using a chi-square test.

Results: There were no significant differences between dropouts and completers on any of the measures we investigated. The two groups also did not differ in patterns of comorbidity.

Conclusions: We concluded that depressed patients who drop out of drug studies are clinically indistinguishable from completers. These data challenge the belief that subjects who drop out from psychopharmacological trials are more severely ill and impaired while completers are less ill.

NR468 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Treatment Response in Adults with ADD and Depressive Symptoms

Mady Hornig-Rohan, M.D., Depression Research Unit, Univ City Sci Ctr—8th F, 3600 Market, Philadelphia PA 19104; Jay D. Amsterdam, M.D.

Summary:

Objective: Some patients with adult attention deficit disorder (ADD) may actually present to the clinician as having chronic, treatment-resistant depression (TRD). The present study assessed treatment outcome with noradrenergic and/or dopaminergic agents in adults with ADD who initially presented as chronic depression.

Methods: 12 patients (10 men, 2 women; mean age 45.5 ± 12.8 years) presented with a DSM-IV diagnosis of MDD or dysthymia. All had a concurrent diagnosis of ADD. Six patients (50%) were resistant to at least two prior, adequate antidepressant treatments. We administered the Wender Utah Rating Scale (WURS), a validated self-report instrument for the retrospective identification of ADD with hyperactivity in adults. Patients were treated in naturalistic fashion with dextro-amphetamine, methylphenidate, a TCA, bupropion, or venlafaxine.

Results: Of the TRD patients, 66.7% showed complete resolution of MDD and ADD symptoms to one of the ADD treatments, while 33.3% had a partial response. 100% of non-TRD patients showed complete resolution of "depressive" symptoms to treatment. The eight depressed patients identified as "hyperactive" on the WURS included seven complete and one partial responder.

Conclusions: ADD can masquerade as MDD, and in particular, as chronic TRD. MDD patients should be evaluated for the presence of ADD symptoms to improve treatment response. Noradrenergic and/or dopaninergic agents may be selectively helpful for adult ADD presenting with affective symptoms.

NR469 Wednesday, May 24, 3:00 p.m.

Risperidone in the Treatment of Patients with Refractory Psychosis Due to Brain Injury

Kevin M. Furmaga, Pharm. D., Pharmacy Practice, University of Illinois, 833 South Wood Street, Chicago IL 60612; Ovidio A. DeLeon, M.D., Shobha B. Sinha, M.D., Thomas H. Jobe, M.D.

Summary:

Objective: This study was designed to evaluate the safety, efficacy, and pharmacokinetics of risperidone (R) and it's active metabolite 9-hydroxyrisperidone (RM) in patients with refractory psychotic symptoms (PS) resulting from brain injury.

Methods: R was administered to four medically complicated adult patients who fulfilled the DSM-IV criteria for "Psychotic Disorder Due To A General Medical Condition." Three patients developed PS following brain surgery and one after exacerbation of a hypercoagulation condition. Three patients failed previous trials with typical antipsychotics. Patients were assessed for psychiatric improvement and adverse drug effects. Serum was collected for measurement of steady-state trough R and RM concentrations (SC) at effective doses.

Results: Psychotic symptoms abated after R treatment in all patients without deterioration in cognitive function or neurologic adverse effects. Mean ± s.d. measures include: effective dosage = 4.5 ± 2.5 mg/day, time to response = 5.5 ± 4.7 days, SC(ng/mL): R = 0.42 ± 0.9, RM = 21.0 ± 4.5, moiety (R + RM) = 21.4 ± 3.8. Therapeutic response was maintained despite no measurable R in three patients.

Conclusions: a) R appears to be safe and effective in medically complicated brain-injured patients with refractory psychosis. b) R did not worsen cognitive or neurologic function. c) RM appears responsible for the therapeutic effects of R administration.

NR470 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Effects of Pentagastrin in Patients with Social Phobia and Panic Disorder and Healthy Volunteers

Una D. McCann, M.D., Room 3N212 Bldg 10, 9000 Rockville Pike, Bethesda MD 20892; Marilla Geraci, M.S.N., Shiyoko O. Slate, B.A., Diana Roscow-Terrill, M.S., Thomas W. Uhde, M.D.

Summary:

Pharmacologic challenge studies in patients with panic disorder have demonstrated that pentagastrin, a CCK_B agonist, induces anxiety and panic, and that patients with panic disorder are more susceptible to these effects than healthy volunteers.[1] Some neuroendocrine evidence suggests that social phobia, another anxiety disorder, may be related to panic disorder.[2] The purpose of the present study was to compare the effects of pentagastrin in patients with social phobia, patients with panic disorder, and healthy volunteers. Nineteen social phobics, 19 healthy volunteers, and ten patients with panic disorder received pentagastrin 0.6 ug/kg intravenously over one minute while participating in a structured social interaction task. Repeated measures of anxiety and panic were taken at baseline and up to two hours after drug administration. Patients with social phobia had greater anxiogenic responses to pentagastrin and were more likely to report panic attacks than normal volunteers (48% versus 16%, respectively). Pentagastrin induced slightly greater anxiety in patients with panic disorder than patients with social phobia, but the two groups did not differ in the incidence of pentagastrin-induced panic (50% versus 48%, respectively). These findings suggest that social phobia and panic disorder have significant overlap, and support the notion that brain CCK systems may be involved in anxiety.

NR471 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Selective Serotonin Reuptake Inhibitors Alter Metabolism of Clozapine

Franca Centorrino, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Judith Kando, Ph.D., Ross J. Baldessarini, M.D., Sheila A. Volpicelli, B.S., James G. Flood, Ph.D., Frances R. Frankenburg, M.D.

Summary:

Findings that serum clozapine (CLZ) and norclozapine (NOR) (assayed by improved LC-UV) were increased by fluoxetine (FLX) were extended in patients (N = 58) given CLZ plus FLX, sertraline (SRT), or paroxetine (PAR) for 60 days. Controls given CLZ alone (N = 29, 66% men; 269 ± 121 mg/day) or with an SRI (N = 29, 41% men; 279 ± 154 mg/day), were matched for age (34 ± 8.5 vs 36 ± 10 years) and CLZ daily dose (3.2 ± 1.6 vs 3.5 ± 2.4 mg/kg). Serum [CLZ + NOR] levels (16h post CLZ dose) were elevated with SRIs (158 ± 109%; $F_{1,56} = 6.7$, $p = 0.012$ for level/dose), with a difference between agents ($F_{3,54} + 2.8$, p 0.05) ranking: PAR (36 mg/d; 193%) SER (82 mg/d; 146%) = FLX (39 mg/d; 144%). Levels of CLZ, NOR (76% of CLZ), or their sum (controls, 420 ± 221 ng/ml) rose with CLZ dose (mg/d vs. [CLZ + NOR]: $r = + 0.471$ [58 df], $p = 0.0002$). All three SRIs elevated circulating concentrations of CLZ and NOR moderately and PAR had the largest effect.

NR472 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Symptom Changes During Drug Washout Periods in Patients with Treatment Resistant Schizophrenia

Anthony G. Kalinowski, Ph.D., Psychiatry, Harvard Medical School, 74 Fenwood, Boston MA 02115; Nancy J. Jaretz, R.N., Sarah K. Rosenbloom, B.A., Joseph Yin, Alan I. Green, M.D.

Summary:

Withdrawing psychotropic medications is often a prerequisite to psychopharmacologic research protocols. However, the practice of eliminating all neuroleptic and/or mood stabilizing medications even briefly, raises concerns about acute exacerbations of symptoms and threats to safety. To better understand the risks entailed in the withdrawal of neuroleptic and/or mood stabilizing medications we conducted a retrospective study of 20 inpatients with treatment-resistant schizophrenia (DSM-III-R) who went through a drug washout period prior to a study of clozapine. The sample consisted of seven males and 13 females with a mean age of 37 years and 14 prior hospitalizations starting at age 20. Patients were tapered off their neuroleptic and/or mood stabilizing medications over a period lasting 0 to 36 days, and were maintained drug-free on an inpatient unit (except for up to 4 mg/day of lorazepam or clonazepam) for an average of 33 days. An investigator-constructed checklist focusing on disruptiveness caused by behavioral dyscontrol, and positive, negative, and mood symptoms was used to review multidisciplinary progress notes from each patient's record for an average of 34 days prior to, and 33 days after, drug withdrawal. Despite the chronicity and severity of these patients' illnesses, there were no significant changes in the checklist subscale means or variances when the medications were washed out. Despite the non-significant changes, 10 patients did show some sustained increases in symptoms. Eight of the 10 patients with symptom worsening had gone through a tapering schedule of less than seven days.

NR473 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Differential Effects of Risperidone and Conventional Neuroleptics on Neurocognition: A Pilot Study

Terry E. Goldberg, Ph.D., Neuroscience Center, NIMH, St. Elizabeths, Washington DC 20032; David G. Daniel, M.D., David Pickar, M.D., Joel E. Kleinman, M.D., Daniel R. Weinberger, M.D.

Summary:

We performed a crossover study comparing the effects of risperidone with those of conventional high-potency antipsychotic agents on neurocognition in five patients with schizophrenia. Each phase of the study lasted six weeks. The mean risperidone dose was 6 mg/day. The other antipsychotic agents included haloperidol, fluphenazine, thiothixene, and perphenazine. At the end of each six-week period the patients were evaluated by means of IQ tests, verbal list learning, memory for stories, memory for designs, psychomotor speed, visual attention, visual perception of faces and lines, design drawing, fluency, naming, and abstraction. When receiving risperidone, patients had less impairment of attention and attained a greater number of categories on the Wisconsin Sort Test than when receiving the other antipsychotic agents. Patients receiving risperidone also performed better with coded symbols and numbers and displayed greater vigilance on the CPT. These findings may be explained by the lower incidence or severity of extrapyramidal symptoms (EPS) with risperidone than with conventional antipsychotics. The basal ganglion dysfunction that underlies EPS has been linked to attentional impairments in various neuropsychiatric disorders. These results are tentative and will be compared with findings from a larger study in which we compared the effects of risperidone and clozapine on neurocognition.

NR474 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Clinical Study of Nimodipine and Haloperidol

Kim Hyeongseob, M.D., Yongin Mental Hospital, 4 Sangha-Ri, Kusung-Myun, Y-Kun Kyunggido 449910, Korea; Whang Taeyeon, M.D., Han Ilwoo, M.D., Park Chongwon, M.D., Kim Jungun, M.D.

Summary:

This is a study of the clinical response (by BPRS and EPS scale) and plasma haloperidol, reduced haloperidol, 5-HIAA and HVA levels (by HPLC-UV and ECD detector) in combined use of haloperidol and nimodipine on male chronic schizophrenics (N = 120).

Nimodipine is a calcium channel blocker which has a CNS specificity and was added to stable dosage of haloperidol (mean = 25 mg/day) for five weeks. The dosages of nimodipine were 90mg/day (N = 11) and 45mg/day (N = 9).

Results: 1) Total BPRS score and thought, paranoid cluster scores revealed that those were sequentially decreased with the passing of time ($P < 0.05$). There were statistical differences in thought, paranoid cluster scores by nimodipine's dosage ($P < 0.05$). 2) The EPS and other somatic side effects (headache, vegetative symptoms, etc.) scores were decreased with the passing of time. 3) Plasma haloperidol, reduced haloperidol levels were increased by the 90mg of nimodipine at the 3rd and 5th week ($P < 0.05$). 4) Plasma 5-HIAA, HVA levels were not changed with the passing of time and dosage of nimodipine dosages.

Conclusion: There is the possibility that nimodipine has an effect on the adjunctive and treatment agent for treatment resistant schizophrenics, old aged psychotic patients prone to side effects of the antipsychotics.

NR475 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Olanzapine: A New Atypical Antipsychotic Medication

Naveed Iqbal, M.D., Psychiatry, Montifore Medical Center, 111 East 210th Street, New York NY 10467; Bruce J. Schwartz, M.D., Charles M. Beasley, Jr., M.D., Susan L. Hamilton, M.S., Carol W. Weinstein, M.D., Lloyd Goldsamt, Ph.D.

Summary:

Antipsychotic medications with serotonin 2 (5HT2) and dopamine (DA2) receptor antagonist properties have been found to be effective in the treatment of psychotic symptoms with a preferential efficacy for the negative symptoms. In addition, these 5HT2/DA2 antagonistic medications cause fewer extrapyramidal side effects (EPS), as well as reduce any existing EPS and/or tardive symptoms. However, clozapine, the prototypical 5HT2/DA2 antagonistic medication, despite its therapeutically superior efficacy over the typical neuroleptics, has several undesirable side effects, such as agranulocytosis and the lowering of the seizure threshold. As such, the development of newer antipsychotic medications with a greater safety profile is essential. One such medication in its late phase development is olanzapine. The initial analysis of 335 patients, treated at 22 sites for six weeks, revealed that olanzapine (12.5-17.5 mg qd) was more effective than haloperidol (10-20 mg qd) on both overall symptoms and negative symptoms of schizophrenia. Olanzapine was also found to have significantly less EPS than haloperidol. At our site, we treated 14 inpatients with outpatient follow-up for a variable period of time ranging from *three days to 1.5 years.* Case vignettes from our site will be presented and discussed in light of the overall olanzapine data, focusing on antipsychotic effects, EPS, adverse events, laboratory evaluations, and the safety profile of the medication.

NR476 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Prolactin Changes with Risperidone Treatment

David N. Osser, M.D., Mass. Mental Health, Harvard Med. School, 74 Fenwood Road, Boston MA 02115; Richard I. Shader, M.D.

Summary:

Twenty-nine inpatients (20 male, 9 female) mostly with neuroleptic-resistant schizophrenia were given risperidone and evaluated prospectively. Prolactin (PRL) levels were followed because of concern that pre-marketing data suggested large elevations. Twenty patients have completed three-month trials. At baseline on previous neuroleptic, mean BPRS was 53 (SD 12.5) and PRL was 29 ng/ml (SD 26). Normal PRL upper limit is 12 for men and 20 for women. At one month (mean dose 6 mg), BPRS was 47 (SD 14) and PRL had risen to 67 (SD 38). After three months (mean dose 7 mg), BPRS was 45 (SD 15, $p < 0.027$ compared to baseline, by paired t test), but PRL ($N = 16$) was still quite high at 60 (SD 30, $p < 0.0044$). PRL increases tended to be greater in five patients with past history of neuroleptic response: (58 vs 18 in nonresponders, $p < 0.07$). PRL elevation was highly correlated with improvement in BPRS in patients with history of previous response ($r = 0.92$), but not in those with neuroleptic resistance. Patients denied sexual or lactation disturbances on verbal inquiry. In conclusion, marked and sustained prolactin elevations, above previous increases, occur in both men and women on risperidone.

NR477 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Serotonin Dopamine Antagonists in Treatment of Cocaine Abuse

Faiq A. Hameedi, M.D., TRU, Yale School of Medicine, 34 Park Street, New Haven CT 06519; Conor K. Farren, M.D., Marc I. Rosen, M.D., H. Rowland Pearsall, M.D., Scott W. Woods, M.D., Thomas R. Kosten, M.D.

Summary:

Cocaine abuse is a major problem among patients with schizophrenia. Cocaine abuse is associated with significant disruption of serotonin and dopamine functions. A preclinical study by our group at Yale showed that pretreatment with clozapine, a serotonin-dopamine antagonist, decreases cocaine conditioned place preference in rats. Recently two clinical reports indicated that clozapine treatment may have reduced substance abuse in clozapine-treated schizophrenics. We conducted this study to evaluate the effects of clozapine pretreatment on behavioral and physiological effects of cocaine in humans. Three male volunteers with a history of more than 2 gm cocaine use per month received an acute dose of clozapine 0, 12.5, 25, and 50 mg orally in the AM on four separate days in a limited randomized double-blind design. Clozapine was followed two hours later by a single dose of intranasal cocaine 2 mg/kg. Preliminary results show that clozapine may have decreased cocaine induced "high" in these subjects by 13% to 42% at either a 25 or 50 mg dose. This decrease approached statistical significance with $p < 0.07$, (paired t test). Data from a larger sample will be presented. (Supported by NIDA grant P50-DA 04060, R18-DA 6190, K12 DA 0167 and K02-DA 0112)

NR478 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Clozapine Use in Treatment Refractory Mania and Psychosis

Jayendra K. Patel, M.D., Psych Mass Men Hlth Ctr, Harvard Medical School, 74 Fenwood, Boston MA 02115; Alan I. Green, M.D., Michael D. Banov, M.D., Mauricio Tohen, M.D., Alan F. Schatzberg, M.D., Jonathan O. Cole, M.D.

Summary:

We report here data from a 12-week, open-label study of clozapine in 23 treatment-refractory patients with bipolar ($N = 22$) or schizoaffective ($N = 1$) disorder. The group included 10 men and 13 women; mean age was 41.

Method: At study entry, patients had a manic psychosis refractory to adequate trials of lithium and neuroleptics. At baseline, a Structured Clinical Interview for DSM-III-R was used to confirm the diagnosis. Following withdrawal of other psychotropic medication (lorazepam permitted), patients were treated with clozapine, to a maximum of 550 mg/day. Outcome was assessed with the Brief Psychiatric Rating Scale (BPRS—using a 0-6 scale), Young Rating Scale for Mania (YRSM), and Clinical Global Impression Scale (CGI—with a 0-6 scale) performed every two weeks by trained raters.

Results: For the group as a whole, the mean percent improvements in BPRS, YRSM, and CGI (from pretreatment baseline to the last assessment) were 56%, 55%, and 38%, respectively. Twenty of 23 subjects demonstrated at least a 20% improvement on the BPRS. Fifteen subjects completed the entire 12-week protocol. Of these, mean percent improvement in BPRS, YRSM, and CGI was 70%, 72%, and 53%, respectively.

Conclusion: Data from this open label study suggest that clozapine as a monotherapy may be an efficacious treatment for patients with bipolar or schizoaffective disorder whose manic and psychotic symptoms are refractory to lithium and typical neuroleptics. Although these findings are consistent with other recent reports of open-label studies, double-blind studies will be required to conform them.

NR479 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Randomized Study of Yohimbine and Anetholtrithione on Salivary Secretion in Patients Treated with Tricyclic Antidepressants

Haleh Bagheri, Pharm.D, Pharmacology, Faculty of Medicine, 37 Allees Jules Guesde, Toulouse 31073, France; Laurent Schmitt, M.D., Michel Berlan, Ph.D., Jean Louis Montastruc, M.D., Paul Montastruc, M.D.

Summary:

Objective: This study was investigated to enhance salivary secretion of depressed patients treated with tricyclic antidepressants. One of the main side effects of tricyclic antidepressants is reduced salivary secretion due to their anticholinergic properties, resulting in a dry mouth and lack of compliance. Until now, few drugs have clearly demonstrated their efficacy in the treatment of this side effect. Acute administration of yohimbine, a selective antagonist for alpha 2 adrenoceptors, was found to increase salivary outflow in animals (0.4 mg/kg) as well as in healthy volunteers (14 mg). This acute effect was also observed at 10 mg in depressed patients treated with tricyclic antidepressants suffering from dry mouth.

Methods: We have investigated a lower dose of yohimbine (4 mg) to alleviate the occurence of some side effects. In Europe, anetholtrithione is widely used for the treatment of dry mouth. The present study was performed in order to evaluate the effect of yohimbine compared to anetholtrithione in ten patients treated with tricyclic antidepressants. Salivary secretion was estimated before the introduction of any of the treatment. They received in a cross-over randomized study, yohimbine (6 mg daily) or anetholtrithione (75 mg daily) during 5 days. On day 6, salivary secretion was estimated one and two hours after the ingestion of the drug.

Results: Compared to basal secretion and that induced by anetholtrithione, yohimbine significantly increased salivary secretion (Student's t-test): 108 ± 25 mg/2min for basal secretion, 175 ± 44 mg/2min and 163 ± 73 mg/2min, respectively, one and two hours after anetholtrithione (not significant), 404 ± 79 mg/2min and 366 ± 61 mg/2min, respectively, one and two hours after yohimbine ($p < 0.05$). Although yohimbine is known for anxiogenic properties, no patient suffered from anxiety or panic attacks.

Conclusion: This study demonstrates the interest of yohimbine (and other putative alpha 2 antagonists) in the treatment of dry mouth in patients treated by tricyclic antidepressants.

NR480 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Clozapine Treatment of Patients with Mental Retardation and Psychosis

Richard L. O'Sullivan, M.D., Psychiatry, OCD Clinic CNY 9 MGH East, Bldg 149 13th Street, Charlestown MA 02129; Mark L. Rubin, M.D., Jay Quintal, Psy.D., Lee Baer, Ph.D.

Summary:

Objective: Patients with mental retardation and comorbid thought disorders may require antipsychotic medication as frequently as a nonretarded psychiatrically ill patient. Despite clozapine's efficacy in treatment refractory schizophrenic patients, scant data exist on its use in patients with mental retardation and psychosis. We conducted a retrospective chart review to evaluate the clinical response to clozapine in a series of patients with mental retardation and treatment refractory psychosis treated in a mental retardation psychiatric clinic.

Method: A retrospective chart review was conducted on 23 consecutive patients with mental retardation and comorbid treatment refractory psychosis treated with clozapine for two to 12 months.

Results: Three patients discontinued clozapine within one week of treatment and were not included in the analysis. Clinical global ratings were significantly improved after clozapine treatment. Average mean doses of classical neuroleptics were significantly reduced. Mean corpuscular volume and monocytes decreased significantly from pre-clozapine levels, but no change in hematological parameters necessitated clozapine discontinuation. One patient had a seizure, treated successfully with anticonvulsant medication, allowing uninterrupted clozapine treatment.

Conclusion: Clozapine is a treatment option which may be successfully used in refractory patients with mental retardation and psychosis. Minor hematological changes were noted but did not adversely affect treatment.

NR481 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

The Combination of Paroxetine and Neuroleptics in the Treatment of Delusional Depression

Rocco M. Zaninelli, M.D., Clinical Research, Smithkline Beecham, Leopoldstrasse 175, 80804 Munich 00120, Germany; Manfred Wolfersdorf, M.D., Frank Konig, M.D., Thomas Barg, M.S.

Summary:

Objective: The standard treatment of "psychotic" or "delusional" depression (major depressive episode, severe with psychotic features according to DSM-IV) involves the combination of an antidepressant with an antipsychotic. Previous work addressing this topic has focussed on the tricyclic antidepressants; to date, there have been relatively few reports describing the combination of a selective serotonin reuptake inhibitor with an antipsychotic to treat delusional depression. We present the results of a pilot study in which paroxetine was combined with haloperidol or the nonphenothiazine neuroleptic zotepine.

Method: In this open study, 21 consecutively admitted inpatients with major depressive episode, severe with psychotic features were treated for 21 days with either the combination paroxetine 20 mg/d and haloperidol 2.5-10 mg/d (seven patients) or paroxetine and zotepine 50-300 mg/d (14 patients). Assessments were carried out at baseline and at weekly intervals using the 24-item version of the Hamilton Depression Scale (HAM-D).

Results: The mean score of the 24-item HAM-D decreased significantly from 45.7 at baseline to 20.6 at day 21 (Newman-Keuls test, $p < 0.01$). Eighteen patients (86%) were considered responders to combination treatment. During the treatment period, the mean score for a subset of HAM-D items (2, 17, 19, 23, 24) which we defined as the "delusion items" likewise decreased significantly, from 12.4 at baseline to 4.1 at day 21 ($p < 0.01$). There were no differences in the response rates between the two treatment groups, and significant adverse reactions to either combination were not observed.

Conclusion: Although this was an uncontrolled study, the results indicate that the combination of paroxetine with haloperidol or zotepine is a feasible and safe approach to treating delusional depression.

NR482 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Evaluation of Antimutagenic Activity of Phenothiazines

Jerzy Waldemar Leszek, M.D., Psychiatry, Medical University, Kraszewskiego 25, Wroclaw 50229, Poland; Kazimierz Gasiorowski, M.D., Katarzyna Szyba, Ph.D.

Summary:

Several reports have been published on the mutagenic and clastogenic effects of phenothiazine drugs widely used in psychiatric treatment. However, the data are conflicting, e.g.: several reports show the clastogenic and mutagenic activities of phenothiazines in mice bone marrows *in vivo* and in human lymphocytes *in vitro,* and on the other hand, the antimutagenic activity on the benzo(a)pyrene mutagenicity in the routine bacterial Ames test. We evaluated the mutagenic potential of chlorpromazine, fluphenazine, and fluphenazine capronate in the Ames test, with the use of TA 98 and TA 100 both in the presence and in the absence of the promutagen-activating fraction S9. None of the tested phenothiazines was mutagenic in the Ames test. The tested phenothiazines exhibited the antimutagenic influence on the standard promutagen, benzo(a)pyrene; the effect was relatively lower in the

case of chlorpromazine and fluphenazine (decrease of benzo(a)-pyrene mutagenicity by about 20%). The antimutagenic effect of fluphenazine capronate on benzo(a)pyrene was strongly dose-dependent in the range of the tested doses; i.e.: from 40-300 μmole/plate (the decrease ranging from 23% to 82%, respectively). Fluphenazine capronate also exhibited a low toxicity to bacterial cells. We concluded that the new form of fluphenazine (fluphenazine capronate), introduced for the prolongation of the therapeutic concentration of fluphenazine in human organisms is also strongly antimutagenic against the common environmental mutagen—benzo(a)pyrene. From this point of view, fluphenazine capronate could be recommended especially for the long-term therapy of severe psychiatric disorders.

NR483 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Pharmacoeconomic Evaluation of Depot Versus Oral Neuroleptic Therapy

Ronald P. Landbloom, M.D., Department Of Psychiatry, St Paul Ramsey Med Ctr, 640 Jackson Street, St Paul MN 55101-2502; James L. Roerig, Pharm.D., Beth A. Zander, B.A.

Summary:

Introduction: Clinical as well as research evidence indicated that a major cost involved in the treatment of schizophrenia and related illnesses is the cost of hospitalization and re-hospitalizations. Accumulated experience and research data indicate the major reason for re-hospitalization, is noncompliance with neuroleptic treatment. The continuous drug delivery system provided by depot neuroleptics can serve to reduce or eliminate the fluctuation in compliance and result in a realization of significant cost savings associated with reduced relapse related re-hospitalizations.

Methods: A patient population consisting of 60 patients (30 receiving haloperidol and fluphenazine decanoate, respectively) meeting DSM-IV criteria for schizophrenia or schizoaffective disorder was identified. A mirror design comparing the costs of hospitalization and outpatient treatment for the depot and prior oral treatment phases was conducted. Eligible patients received haloperidol or fluphenazine decanoate for at least one year.

Results: Forty patients have been identified to date. Twenty patients have met entry criteria for data analysis. Nine patients received fluphenazine and 11 received haloperidol. Preliminary analysis reveals the mean number of hospitalizations per year for oral therapy vs. depot therapy of 0.514 vs. 0.149, respectively. Completed data analysis will be presented.

NR484 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Clinical Predictors of Acute Risperidone Response in Schizophrenia, Schizoaffective Disorder, and Psychotic Mood Disorders

Paul E. Keck, Jr., M.D., Psychiatry, University of Cincinnati, POBox 670559 231 Bethesda Ave, Cincinnati OH 45267; Daniel R. Wilson, M.D., Stephen M. Strakowski, M.D., Susan L. McElroy, M.D., Danielle L. Kizer, B.S., Anthony Balestreri, B.S.

Summary:

Risperidone has been shown to be at least as effective as conventional antipsychotic agents in the treatment of patients with chronic schizophrenia and to cause fewer and less severe extrapyramidal symptoms. In the present study we evaluated the efficacy of risperidone in 49 patients with schizophrenia, 81 with schizoaffective disorder (58 bipolar type, 23 depressive type), and 11 with bipolar disorder. Each patient had received risperidone for at least two weeks. A moderate to marked treatment response was significantly ($p < 0.05$) associated with younger age, diagnoses of bipolar disorder and depressive-type schizoaffective disorder, a shorter duration of illness, and shorter length of hospitalization before receiving risperidone. Among patients with treatment-refractory schizophrenia, treatment response was sufficient to allow discharge from hospital in 26% of patients who had been in hospital for at least 10 weeks and in 11% of patients who had been in hospital for more than one year before being treated with risperidone. It is concluded that risperidone may be useful in patients with depressive schizoaffective disorder, bipolar disorder (in conjunction with mood stabilizers), and treatment-refractory schizophrenia.

NR485 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Randomized Double-Blind Trial of Risperidone Versus Clozapine for Treatment Resistant Chronic Schizophrenia

G. Bondolfi, M.D., Psychiatry & Adolescent, Prilly-Lausanne, Switzerland; P. Bauman, M.D., Michel Patris, M.D., J.P. May, M.D., U. Billeter, M.D., H. DuFour

Summary:

Risperidone has not been adequately studied specifically in treatment-resistant patients or adequately compared with clozapine for efficacy and safety. In the present study, we evaluated the efficacy and safety of these agents in 86 treatment-resistant outpatients at seven psychiatric clinics in Switzerland and France. Patients were randomly assigned to receive risperidone or clozapine for eight weeks after a seven-day wash-out period. Drug doses were stabilized at 6 mg/day risperidone and 300 mg/day clozapine and thereafter adjusted according to each patient's response; mean daily doses at endpoint were 6.4 mg and 291.2 mg, respectively. Investigators periodically assessed outcomes with the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression (CGI) Scale, and the Extrapyramidal Symptom Rating Scale (ESRS). Risperidone and clozapine had nearly identical therapeutic effects and both agents significantly ($p < 0.05$) reduced all PANSS subscale, CGI, and ESRS scores from endpoint to baseline. Risperidone had a faster onset of action and fewer patients in the risperidone than the clozapine group reported adverse events. It is concluded that risperidone and clozapine are not significantly different in most measures of effectiveness or safety in treatment-resistant schizophrenic patients.

NR486 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Cardiac Effects of Doxepin and Fluoxetine in Patients with Major Depressive Disorder

Brian Baker, M.B., Psychiatry, Toronto Hospital, 3D-ECW 399 Bathurst Street, Toronto Ontario M5T 2S8, Canada; Paul Dorian, M.D., Paul Sandor, M.D., Colin Shapiro, M.B., Marilyn Jane Irvine, Ph.D.

Summary:

Objective: To compare the effects of fluoxetine and doxepin on cardiac conduction (QRS duration, msec) and repolarization (corrected QT interval QTc, msec 1/2) in patients with major depressive disorder using the signal-averaged electrocardiogram.

Method: Randomized double-blind parallel-group six-week study; depression by structured interview (SCID) and 17-item Hamilton Scale (HAM-D). (≥18) QRS duration measured from filtered QRS vector; QT from unfiltered duration in x,y,z leads; total QT interval from first onset to last offset in any lead. Setting—teaching hospital. 41 patients entered, 39 available for analysis.

Results: Patients on doxepin (N = 19) (169 ± 42mg) were similar to fluoxetine (N = 20) (37 ± 18mg) on demographic variables, improvement in scales (eg. HAM-D, Montgomery-Ashberg) but volunteered more side effects ($p = .011$), especially dry mouth ($p = .0001$) and dizziness/lightheadedness ($p = .005$). Doxepin

increased heart rate (69 ± 13 to 80 ± beats per min; $p < .02$) and prolonged QTc (from 417 ± 36 to 439 ± 29 msec; $p < .03$). Fluoxetine had no effect on QTc or QRS duration. Multiple regression analysis revealed QRS interval was prolonged with increasing serum doxepin concentrations, whereas fluoxetine dose was negatively correlated with heart rate at week 6 ($p < .01$).

Conclusion: Using a sensitive measure, doxepin slows cardiac conduction and prolongs repolarization. Fluoxetine has no measurable electrocardiographic effects suggesting an increased safety margin for cardiac adverse effects.

NR487 Wednesday, May 24, 3:00 p.m.-5:00p.m.

Clinical Effects of Clozapine

Pierre-Michel Llorca, M.D., CH Valvert, Secteur 6, Boulevard Des Liberateurs, Marseille 13011, France; Christophe Lancon, M.D., Pascal Auquier, M.D., Thierry Boujerol, M.D.

Summary:

Objectives: We have realized an open study in a population of chronic schizophrenic inpatients treated with clozapine. The purpose of this study was to investigate the clinical response and the effect on extrapyramidal symptoms of this atypical antipsychotic.

Methods: Our sample is composed of 25 chronic hospitalized schizophrenics (18 males, 7 females; average age = 36.57, SD = 8.41) with an initial important symptomatology (average score on BPRS = 64.92, SD = 7.99). The weekly assessment was done using PANSS and EPRS during nine weeks. After a 15-day period of treatment adjustement, each patient reached a daily dose of 400 mg. Then the dosage was adjusted according to the clinical condition of the patients (range = 100-900 mg per day).

Results: Using the PANSS, we identified a statistically significant ($p < 0.05$) clinical improvement from the forth week of treatment for global score, positive, negative, and general psychopathology sub-scores. For EPRS a dramatic improvement ($p < 0.01$) has occured from the second week. We individualized a subgroup of seven good responders who showed an improvement of 20% or more on PANSS global score at the ninth week. This group showed a statistically significant ($p < 0.01$) more intense initial negative symptomatology compared to non-responders.

Conclusion: The improvement of extrapyramidal symptoms precedes the improvement of psychotic symptoms. The clinical efficacy concerns both positive and negative symptoms. In our sample, patients with intense negative symptomatology improve more than others.

NR488 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Predictors of Differential Response to Clozapine and Risperidone

David G. Daniel, M.D., 6404-P Seven Corners Place, Falls Church VA 22044; Terry E. Goldberg, Ph.D., Daniel R. Weinberger, M.D., Joel E. Kleinman, M.D., David Pickar, M.D., Lisa Lubick, MPP

Summary:

Clozapine and risperidone are novel antipsychotics with pharmacodynamic differences that may affect both antipsychotic efficacy and side effect profiles. Data are lacking to guide the clinician in the choice between the two agents. Twenty patients with schizophrenia or schizo-affective disorder who were clinically stable on clozapine at entry participated in a single-blind, randomized order, crossover comparison of six weeks on risperidone and six weeks on clozapine. They were rated on the PANSS, CGI, neuropsychological batteries, and side effect measures. Neither age, age of onset, length of illness, number of previous neuroleptic trials, nor diagnostic subtype predicted preferential clinical response. Differential effects on the "negative" but not "positive" symptom subscales of the PANSS and side effect measures such as subjective cognitive impairment, sedation, and nausea predicted patients' preference between the two treatments. The differential side effect profiles were consistent with differential effects at muscarinic dopaminergic, and histaminergic receptor subtypes.

NR489 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Comparison of Trazodone and Haloperidol for Treatment of Agitated Behaviors in Dementia

David L. Sultzer, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles CA 90024-1759; Kevin F. Gray, M.D., Ibrahim Gunay, M.D., M. Andrew Berisford, M.A., Michael E. Mahler, M.D.

Summary:

Objective: Agitated behaviors contribute substantially to the morbidity of Alzheimer's disease and other dementias. This study compared the efficacy and side effects of two medications for the treatment of agitated behaviors associated with dementia.

Methods: Twenty-eight elderly patients with dementia and clinically significant agitation were randomly assigned to double-blind treatment with either trazodone or haloperidol. The study included a one-week observation phase, a three-week dose adjustment phase, and a six-week extended treatment phase. The Cohen-Mansfield Agitation Inventory (CMAI), the Clinical Global Impression Scale (CGI), and a side effect checklist were used to measure clinical response.

Results: CMAI total scores in both treatment groups improved over the nine weeks of treatment ($p = .001$). There was no difference in improvement between medication groups. Seventy-one percent of the trazodone-treated subjects and 57% of the haloperidol-treated subjects were substantially improved on the CGI at the end of the study. Pacing, general restlessness, trying to get out of the building, and unwarranted accusations responded preferentially to haloperidol, whereas repetitive mannerisms, repetitive sentences, cursing/verbal aggression, and negativism/opposition to assistance responded preferentially to trazodone. Mean daily haloperidol dose was 2.5 mg and mean daily trazodone dose was 218 mg. Adverse effects were more common in the group treated with haloperidol.

Conclusions: Moderate doses of trazodone and haloperidol are equally effective for treatment of overall agitated behaviors in patients with dementia, but adverse effects are more frequent with haloperidol treatment. Specific symptoms may respond preferentially to a particular agent.

NR490 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Combined Lorazepam and ECT to Treat Catatonia

Georgios Petrides, M.D., Psychiatry, SUNY Stony Brook, Health Science Ctr T-10, Stony Brook NY 11794; George Bush, M.D., Andrew J. Francis Jr, M.D.

Summary:

Objective: Administration of benzodiazepines with ECT is traditionally avoided as they may impede production of adequate seizures, and perhaps impair the efficacy of the treatment. In catatonia, however, both lorazepam and ECT are known effective treatments. Whether these treatments can be combined is unknown.

Method: To date, we identified six patients with catatonia and various comorbidities treated with ECT (bilateral) and oral or parenteral lorazepam. In some cases, lorazepam was sequential, in others concurrent with ECT.

Results: Two patients whose catatonia had initially failed lorazepam before ECT responded to lorazepam when catatonia re-

emerged during a course of ECT. One patient on stable maintenance ECT for catatonia needed less frequent ECT after lorazepam was added. Two patients were treated with ECT and lorazepam simultaneously; their catatonic symptoms increased when lorazepam was discontinued. Finally, one patient failed lorazepam, then responded partially to ECT, and showed further improvement with maintenance lorazepam alone. We found no instance of deleterious effects of combined lorazepam and ECT in catatonia. Additional cases are being sought.

Conclusions: These cases suggest a facilitation of response with the combination of lorazepam and ECT in catatonia, and may imply a common mechanism of action.

NR491 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Rispiridone in Institutionalized Psychotic Patients Unresponsive to Conventional Antipsychotic Agents

Eugene G. Evans, Jr., M.D., Bryce Hosptial, 200 University Blvd, Tuscaloosa AL 35401

Summary:

Risperidone was given to 26 mostly elderly patients hospitalized from one to 18 years with various forms of continuous psychosis: schizophrenia in 13, schizoaffective disorder in eight organic dementias in three, and bipolar mania in two. All were unresponsive to or intolerant of conventional antipsychotics and, in one case, also to clozapine. Patients were evaluated at 19 and 29 weeks with the BPRS and the Abnormal Involuntary Movement Scale. Five patients discontinued the study, two because of noncompliance or death (unrelated to treatment), and one was unresponsive. Two patients improved sufficiently to be discharged: a 67-year-old man with catatonic schizophrenia who had been repeatedly hospitalized throughout most of his life but responded to 2 mg/day of risperidone and was discharged shortly after the 19th week of treatment; and another 67-year-old man frequently hospitalized with alcohol-induced persisting dementia who responded to 6 mg/day of risperidone and also was discharged shortly after the 19th week. Eight additional patients were much improved, including a 57-year-old woman hospitalized for 18 years with paranoid schizophrenia (who received 6 mg/day of risperidone) and a 58-year-old woman hospitalized for four years with severe schizoaffective bipolar disorder and violent or self-mutilative behavior (who received 8 mg/day of risperidone combined with lithium and carbamazepine).

NR492 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Chronic Benzodiazepine Use in a State System

Daniel J. Luchins, M.D., Department Of Psychiatry, Univ of Chicago, 5841 S Maryland Ave, Chicago IL 60637-2602; Mark Alexakos, MAPP

Summary:

As a quality improvement measure, we identified all patients in state operated facilities (approximately 500) who, during an entire four-month period, were prescribed daily, daytime benzodiazepines (BNZ). There were 222. As a comparison we identified 1951 patients who received no BNZ during this entire four-month period. We then examined the ratio of chronic BNZ to no BNZ patients to determine which factors were associated with chronic BNZ use.

Chronic BNZ use was more common in the mentally ill than those with developmental disabilities ($X^2 = 77$, df = 1, p = .0001) and within the mentally ill most common among schizophrenics ($X^2 = 8.6$, df = 2, p = .0001) and on geriatric units, and least common on forensic units ($X^2 = 10$, df = 4, p = .05). Chronic BNZ prescriptions were least likely to be written by board certified psychiatrists, board eligible psychiatrists were intermediate, and non-psychiatrists had the highest rate ($X^2 = 26.9$, df = 2, p = .00001). To address the issue of which factor might be most important, we carried out a logistic regression analysis and found board certification (R = .17, p = .002) and patients' age (R = .14, p = .0008) to be the only significant variable. The development of a computerized "medication alert" to help educate physicians who prescribe chronic, daytime BNZ will be discussed.

NR493 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Combined Desipramine and Fluoxetine Treatment in Refractory Depression

Helen L. Miller, M.D., Psychiatry, Yale Univ & West Haven, 950 Campbell Avenue, West Haven CT 06516; Pedro L. Delgado, M.D., Ronald M. Salomon, M.D., Robert M. Berman, M.D., Dennis S. Charney, M.D.

Summary:

The combination of a serotonin reuptake inhibitor and a tricyclic antidepressant is frequently used in patients with treatment refractory major depressive episode. However, there are few double-blind studies confirming the efficacy of this combination. We examined the combination of fluoxetine (FLU) and desipramine (DMI) in 12 depressed patients who had failed to respond to a therapeutic trial of at least six weeks of FLU, at a dose of at least 40 mg.

Method: Subjects who had a significant clinical depression, with a Hamilton Depression Rating Scale (HDRS) ≥20, were given a six-week drug washout, then treated openly with DMI for at least six weeks. DMI doses were titrated to achieve a therapeutic plasma level of 125 ng/ml or more. Subjects with a HDRS score ≥20 at the end of the DMI treatment were randomized to receive four weeks of either FLU 20 mg or placebo augmentation of DMI, in a double-blind study design. Plasma was obtained weekly for DMI levels and DMI doses were adjusted to maintain a steady plasma level by a pharmacist and a psychiatrist who did not have contact with the patients.

Results: Seven subjects were randomized to active treatment and five to placebo. One subject in each group had a therapeutic response (HDRS score ≤10 after four weeks of augmentation).

Conclusions: Combination of FLU and DMI does not appear to be an effective treatment for depression in patients who have failed to respond to a clinical trial of each drug itself.

NR494 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Ziprasidone: A Serotonin 2/D2 Atypical Antipsychotic?

Earl L. Giller, Jr., M.D., Associate Director CNS, Central Research Pfizer I, Eastern Point Rd, Groton CT 06340; James Heym, Ph.D.

Summary:

Ziprasidone, a 5 HT2/D2 receptor antagonist, shows potent effects in animal models thought to predict antipsychotic efficacy and a weak effect on motor activity. Its relatively low affinity for the alpha-1 adrenoreceptor predicts a low incidence of clinically significant hypotension, while its 5HT1 receptor agonist activity may result in improvement in mood. Thus, the preclinical pharmacology profile of this compound, along with positron emission tomography studies of normal volunteers, support ziprasidone's potential as an effective antipsychotic drug with minimal motor and dysphoric side effects.

Ziprasidone has been administered to about 375 schizophrenic or schizoaffective patients in controlled clinical trials. Symptom reduction in patients with acute exacerbation of psychosis will be presented. The overall incidence of adverse effects as well as specific movement disorder measures suggest that ziprasidone is well tolerated by patients with schizophrenia or schizoaffective disorder, with a low incidence of movement disorders.

NR495 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Predictable and Modest Inhibition of Desipramine Clearance by Sertraline at Low and High Doses

Lisa Von Moltke, M.D., Pharmacology, Tufts University, School of Medicine, Boston MA 02111; David J. Greenblatt, M.D., Richard I. Shader, M.D.

Summary:

When selective serotonin reuptake inhibitors (SSRIs) are coadministered with tricyclic antidepressants, a major consideration becomes the degree to which the SSRI elevates tricyclic levels. At recommended starting doses in vivo, fluoxetine or paroxetine (20 mg/day) inhibit desipramine clearance substantially more (about 300% to 600%) than 50 mg/day sertraline (about 20% to 40%). The results of these studies were correctly predicted by a model which uses in vitro microsomal inhibition constants, in vivo inhibitor plasma concentrations, and extrapolated hepatic inhibitor concentrations, to forecast the degree of impaired clearance in humans during concomitant drug administration. This model has now been applied to estimate the expected inhibition of desipramine at higher SSRI doses. At 100 and 150 mg/day sertraline, predicted increases are 53% and 84%, respectively. In two new investigations [1,2] using 150 mg/day sertraline, mean desipramine AUC increases of 54%[1] and 66%[2] were reported in humans. In contrast, predicted increases in desipramine AUC are >1000% with fluoxetine 40 and 60 mg/day, while with paroxetine 30 and 40 mg/day, predicted increases are 350% and 526%, respectively. Of clinical relevance: the predictable and modest inhibition potential of sertraline across a 50-150 mg/day dosing range is markedly less than the effects of either fluoxetine or paroxetine at their lowest recommended doses of 20 mg/day.

NR496 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Risperidone for Polydipsia and Hyponatremia in Schizophrenia

Iyad Y. Khreis, M.D., 2306 Hollyhock Dr, Columbia MO 65202; James R. Slaughter, M.D.

Summary:

Polydipsia with associated hyponatremia may occur in as many as 17% of chronic psychiatric patients (schizophrenia is by far the most common underlying mental disorder), but the diagnosis is often missed until severe hyponatremia causes generalized seizures. Early diagnosis and treatment are essential before the onset of water intoxication. The pathogenesis of this disorder is unknown, but in the presence of normal renal function the polydipsia is probably associated with defective function of antidiuretic hormone leading to abnormal thirst regulation.

We report on a schizophrenic patient with multiple episodes of acute polydipsia and hyponatremia for the past five years that were eliminated only after risperidone treatment. Risperidone improved the patient's psychotic symptoms, but appears to have specifically reduced compulsive fluid drinking apart from its effect on psychotic symptoms. Risperidone reduced the compulsion before it took effect on the psychotic symptoms, and the compulsion returned whenever risperidone was discontinued and the patient was taking only conventional antipsychotics.

NR497 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Carbamazepine: Associated Exfoliative Dermatitis with Severe Eosinophilia

Veronika Solt, M.D., Psychiatry, CMHC UMDNJ, 215 South Orange Avenue, Newark NJ 07103; Henry H. Kalir, M.D.

Summary:

Carbamazepine (CBZ), is a frequently prescribed medication for seizure disorder, which has been successfully used in psychiatric practice as a mood stabilizer. The most common minor side effects of CBZ are nausea, vomiting, drowsiness, dizziness, and ataxia. Serious, but rare adverse effects are hematologic toxicity, hepatitis, and exfoliative dermatitis. Acute confusional states most likely occur in combination with lithium or antipsychotic drugs.

We describe a case of severe eosinophilia, exfoliative dermatitis, and confusion eight weeks after initiation of CBZ treatment in a 57-year-old African American male receiving concomitant lithium and haloperidol therapy for schizoaffective disorder. The remarkable physical findings on hospital admission were : erythematous and confluent macular rash involving the trunk and all extremities, marked edema of hands and face, disorientation to all spheres, vital signs (T:102, P:128, BP:86/39 and R:18), and laboratory data (white blood cell count: 51,100 mm^3; eo:23%; ly:1%; and neut:62%). Following discontinuation of all medications a further increase of eosinophil count was noted to a maximum of 62% and worsening of edema with pruritic erythematous rash leading to scaly eruptions. The rash and hematological abnormalities resolved within three weeks with symptomatic therapy. Although multiple drugs complicate the clinical picture, the time course suggests an adverse reaction most likely due to CBZ. The notable feature in our patient was marked edema with severe eosinophilia. As eosinophil mediators have a role in the development of cutaneous edema, it may be relevant that the peripheral blood eosinophilia in our patient was greater than in most previously reported studies.

We integrate our findings with the current literature and discuss possible pathophysiologic mechanisms and monitoring strategies involved in these syndromes.

NR498 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

In Vivo Receptor Occupancy in Rat Brain By Novel and Reference Antipsychotic Drugs

A. Schotte, Janssen Research Foundat., Turnhoutseweg 30, Beerse, Belgium; PFM Janssen, P. Bonaventure, Philippe Lemmens, Ph.D., J.E. Leysen

Summary:

Numerous studies have shown that central dopamine-mediated systems have a key role in producing psychotic symptoms and that increased D_2-receptor occupancy and blockade are associated with increased extrapyramidal symptoms (EPS). Whereas conventional antipsychotics strongly antagonize dopamine and usually cause EPS, novel agents such as risperidone and clozapine change the balance between serotonin and dopamine and reduce both positive and negative symptoms of schizophrenia with a low incidence of EPS. The in vivo receptor occupancy of risperidone in rat brain was compared with that of clozapine, several conventional antipsychotics, and various new antipsychotics under development including olanzapine, sertindole, and seroquel. As shown by ex vivo autoradiography, a key difference between risperidone and the other compounds was risperidone's more gradual occupancy of D_2 receptors with increasing doses. Since it is now believed that positive symptoms of schizophrenia respond even at low rates of D_2 occupancy, low doses of risperidone may reduce positive symptoms with less risk of EPS than that posed by the comparison compounds.

NR499 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Anxiety and Depression Symptoms Control in Oncology: A Double-Blind Placebo Controlled Study Assessing the Effectiveness of Fluoxetine

Darius Razavi, M.D., Medico-Psychiatry, Hopital St. Pierre, Rue Haute 322, Brussels 1000, Belgium; Jean-Francois Allilaire, M.D.

Summary:

Objective: Although a high prevalence of adjustment disorders with anxious and depressive mood and major depressive disorders has been reported in oncology, little has been done to study the effectiveness of antidepressants for controlling anxiety/depression.

Method: A double-blind, placebo-controlled study was therefore designed to assess the effectiveness of 20 mg fluoxetine. Of 115 cancer patients who met entry levels of distress, 45 were randomized to a fluoxetine arm (FA) and 46 to a placebo arm (PA) after a one-week placebo period scheduled to exclude placebo responders. Montgomery and Asberg Depression Scale (MADRS), Hamilton Anxiety Scale (HAS), Hospital Anxiety and Depression Scale (HADS), Revised Symptom Checklist (SCL90-R), and Spitzer Quality of Life Index (SQOLI) were chosen to assess fluoxetine efficacy.

Results: Compared to the PA, patients in the FA showed a significantly higher decrease of SCL90-R mean total score after five weeks ($p = 0.02$) and no statistically significant higher decrease of HADS mean score. No difference between the two arms was found in observer reports assessments (MADRS, HAS, SQOLI). Significantly more drop-outs were observed in the FA ($N = 15$) compared to the PA ($N = 7$) ($p = 0.04$), although frequencies of side effects were not significantly different in the two arms.

Conclusions: Compared to cancer patients receiving placebo, patients receiving fluoxetine showed a significantly higher decrease of their psychological distress symptoms without significant increase of discomfort related to side effects of the drug. Although studies are needed to improve the efficacy reported here, physicians may already consider the adjunct of fluoxetine to psychological support in order to control anxiety and depression of cancer patients.

NR500 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Adverse Effects of Two Long-Acting Depot Antipsychotic Drugs

A. S. Shooka, M.B., Box 26441 Adliya, Manama, Bahrain; M.K. Al Haddad, V. Mathur

Summary:

A comparison of the adverse effects of the depot preparations of flupenthixol decanoate and fluphenazine decanoate was conducted in 100 chronic schizophrenic patients attending the outpatient department at the Psychiatric Hospital, Bahrain.

Although akathisia, parkinsonism, weight gain, and endocrine effects were seen in a large number of cases, there was no statistically significant difference in their incidence between the two groups. Furthermore, there was no difference in the efficacy of the two preparations studied.

We observed abnormal hair loss in 42 cases—22 on flupenthixol decanoate and 20 on fluphenazine decanoate. This previously unreported side effect is probably due to these long-acting antipsychotic drugs.

NR501 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Controlled Study of Attitude Change Towards ECT

Jagannathan Srinivasaraghavan, M.D., Psychiatry, University of Rochester, 300 Crittenden Boulevard, Rochester NY 14642; Pat Alfano, Ph.D., Richard Abrams, M.D.

Summary:

To our knowledge, this is the first controlled study of first-year medical students' change in attitude toward ECT.

Method: Thirty-six first-year medical students attending a regularly scheduled lecture on ECT answered two questionnaires of ten statements each. The first questionnaire, answered before the lecture, had students rate their attitude either on ECT (CMS-ECT), ($n = 18$, pre-post ECT Group) or anti-depressant medication and psychotherapy (CMS-Dep), ($n = 18$, pre-post Control Group). The second questionnaire, answered after the lecture, was the identical ECT questionnaire (CMS-ECT), ($n = 36$). Statements 1-9, analyzed together, asked students to rate their attitude on a scale of 1 (strongly agree) to 5 (strongly disagree). Statement 10, analyzed separately, asked students to show on a line marked 0 (most negative) to 100 (most positive), where they would place their feelings about ECT as a treatment modality.

Results: As predicted, positive attitude changes occurred when the ECT group was compared, pre-post, on questions 1-9, $t(17) = -3.7$, $p < .001$, and question 10, $t(17) = -3.62$, $p < .001$. Also, as predicted, the post-control group had a more favorable attitude toward ECT than the pre-ECT group on questions 1-9, $t(34) = -1.93$, $p < .05$, and question 10, $t(34) = -4.54$, $p < .001$.

*Conclusion:*This controlled study demonstrates how improved knowledge about ECT elicits positive attitude change toward ECT.

NR502 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Treatment of Compulsive Buying with Fluvoxamine

Donald W. Black, M.D., Psychiatry Administration, Univ of Iowa Hospital, 200 Hawkins Dr 2887 JPP, Iowa City IA 52242-1057; Janelle M. Gabel, R.N.

Summary:

Compulsive buying is characterized by a preoccupation with shopping and spending, which leads to impairment in social/occupational functioning, or to financial/legal difficulties.

Eight healthy, non-depressed subjects (seven women, one man) meeting the criteria of McElroy, et al., and having a score ≥2 SD from the mean on the Compulsive Buying Scale (CBS) were enrolled in an open-label treatment study testing the effectiveness of fluvoxamine in the treatment of compulsive buying. Baseline assessments include the CBS and the Yale-Brown Obsessive-Compulsive Scale—Shopping Version (YBOCS-SV), which is a modification of the original instrument used to assess cognitive and behavior components of compulsive buying. Following a one week single-blind placebo washout, patients were given fluvoxamine for eight weeks using a flexible dosing schedule. Improvement was assessed with the YBOCS-SV, three Clinical Global Impression (CGI) ratings, and the patient's self-report.

The patients' mean (SD) age was 42.1 (9.9); age of illness onset was 21.1 (8.2). Their mean (SD) fluvoxamine dose at week 9 was 186 (62.7) mgs. No patient improved during the washout. The mean (SD) YBOCS-SV at baseline was 21.3 (2.7). The mean (SD) score fell to 4.7 (2.8) by week 9 (paired t-test, $t = 11.8$, $df = 6$, $P < .0001$). The mean (SD) physicians CGI rating fell from 2.6 (0.9) to 1.0 (0) (paired t-test, $t = 4.8$, $df = 6$, $P = .003$) Three patients responded to drug during the initial week of treatment and all had responded by week 5 (i.e., had ≥50% reduction in their YBOCS-SV score).

The study suggests that fluvoxamine is a potentially effective treatment for compulsive buyers, and that improvement can be readily assessed in clinical trials.

NR503 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Serotonergic Responsivity in Compulsive Personality

Dan J. Stein, M.B., Psychiatry, Univ of Stellenbosch, P.O. Box 19063, Tygerberg 7505, South Africa; Robert L. Trestman, M.D., Emil F. Coccaro, M.D., Vivian Mitropoulou, M.A., Eric Hollander, M.D., Larry J. Siever, M.D.

Summary:

While impulsive and compulsive disorders may appear to lie at opposite ends of a phenomenological and neurobiological spectrum, there is also increasing evidence for their overlap. In particular, both impulsive and compulsive disorders may be characterized by dysregulation of harm assessment and serotonergic dysfunction. In this study, we compared serotonergic function, as assessed by prolactin response to fenfluramine, in male personality disorder patients with compulsive personality disorders (CPD) and other personality disorders (OPD). The two groups did not differ in age, depression, suicide history, or comorbid borderline personality disorder. However, CPD patients had significantly greater impulsive-aggressive scores than OPD patients and significantly blunted prolactin responses compared with OPD patients and normal controls. In the combined patient group, total CPD traits correlated positively with impulsive-aggression score, and inversely with prolactin response. These results support the hypothesis that impulsive and compulsive symptoms do not simply lie at polar ends of a phenomenological and neurobiological spectrum, but rather have a complex intersection.

NR504 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Metabolic Rates in Brodmann Areas in Alzheimer's Disease

Dan J. Stein, M.B., Psychiatry, Univ of Stellenbosch, P.O. Box 19063, Tygerberg 7505, South Africa; Monte S. Buchsbaum, M.D., Benjamin V. Segal, M.D.

Summary:

Neuropathological studies of Alzheimer's disease have found that certain cytoarchitectural regions consistently demonstrate pathology, while others are typically spared. Functional brain imaging studies have also shown selective decreases in glucose metabolic rates, but have focused on whole brain lobes or on arbitrary geometrically derived regions. In this study, we report the use of a template of Brodmann areas, derived from a whole brain histological section atlas, to analyze position emission tomography data in Alzheimer's disease. Patients with Alzheimer's disease had lowest glucose metabolic rate in temporal-limbic lobe and proisocortex, higher rates in frontal and primary association and primary nonassociation cortex, and relative sparing of parietal and occipital lobes and of granular and sensory cortex. These findings overlap with neuropathological studies of neurofibrillar tangles in Alzheimer's disease, and are consistent with the observation that vulnerability of cortices in the illness is greater in areas that are in closer synaptic contact with limbic areas.

NR505 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

CSF Cholecystokin Dynamics in the Human

Thomas D. Geracioti, Jr., M.D., Dept of Psych, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Wendell E. Nicholson, David N. Orth, M.D., Nosa N. Ekhator, M.S., Peter T. Loosen, M.D.

Summary:

Very little is known about the physiologic significance of the gut-brain hormone cholecystokinin (CCK) in the human central nervous system, although the hormone has been hypothesized to be involved in the regulation of both appetite and anxiety. We continuously collected lumbar cerebrospinal fluid (CSF) via indwelling subarachnoid catheters in ten normal volunteers, ten patients with major depression, and five abstinent alcoholic subjects, while fasting and after eating. Five other healthy subjects were fasted throughout the experiment. We quantified CSF immunoreactive CCK (IR-CCK) and glucose concentrations at 10 min intervals from 1100 to 1700 h. No difference in CSF IR-CCK concentration, half-life, or rhythm was observed between normal volunteers and either depressed or alcoholic patients. Fasting CSF IR-CCK concentrations were 1.3 ± 0.18, 1.3 ± 0.21 and 1.2 ± 0.21 fmol/ml (mean ± SEM) in normal volunteers, depressed patients, and alcoholic patients, respectively. After eating, CSF IR-CCK concentrations rose to 1.5 ± 0.21, 1.5 ± 0.24 and 1.4 ± 0.26 fmol/ml, respectively. Normal volunteers who did not eat had similar basal CSF IR-CCK concentrations (1.1 ± 0.1 fmol/ml) which similarly rose to 1.4 ± 0.13 fmol/ml during the sampling interval. In contrast, CSF glucose concentrations rose only in the subjects who ate, beginning to rise after about one h and remaining elevated for at least three h after eating. These data suggest the existence of a diurnal rhythm of IR-CCK release into CSF, as opposed to a response to feeding. The disappearance half-time of CCK in human CSF is less than 13 min. The rapid intra-individual concentration transients in CSF IR-CCK concentration observed suggest pulsatile release of CCK into and rapid removal from CSF. Thus, it is likely that the IR-CCK measured in lumbar CSF is principally derived from spinal cord and does not reflect possible changes in hypothalamic IR-CCK after eating. Finally, gel filtration chromatography confirmed that IR-CCK in human CSF is heterogeneous, but, in contrast to previous studies, we found that the majority of activity is associated with a peptide(s) whose molecular weight is 1660 daltons, corresponding in size to CCK-12 (CCK-[22-33]).

NR506 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Sulfotransferase Activity in Different Psychiatric Disorders

Donatella Marazziti, M.D., Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy; Lionella Palego, Ph.D., Alfredo Batistini, Ph.D., Chiara Mazzanti, Ph.D., Stefano Silvestri, M.D., Giovanni B. Cassano, M.D.

Summary:

Two forms of sulfotransferases (STs) are present in platelets, as they are in the central nervous system: one which acts preferentially on monoamine substrates, and another which prefers phenols and phenolic compounds. Although principal catabolic pathways of neurotransmitters are those catalyzed by monoamine oxidases and by catechol-O-methyl transferases, it is conceivable that a change in ST activity, although representing a minor degradative pathway, might affect the fine balance existing between different neurotransmitters and might have a role in the pathophysiology of some psychiatric symptoms.

The aim of our study was to measure and compare platelet ST activity in patients affected by different psychiatric disorders and in healthy controls.

The results showed that the activity of both the two forms of ST was significantly higher in 30 patients with obsessive compulsive disorder and in 15 manic patients than in 20 healthy volunteers or in patients with other psychiatric disorders. By contrast, normal values were found in 12 unipolar depressives and 12 dysthymic patients and lower values in 20 patients with migraine.

It thus seems that different neuropsychiatric disorders produce different changes in the activity of STs.

NR507 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Tryptophan Hydroxylase and Impulse Aggression

Yoram Yovell, M.D., Psychiatry, Mt. Sinai Sch of Med., 1 Gustave Levy Pl. Box 1230, New York NY 10029; Joel Gelernter, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., J. Erdos, M.D., Larry J. Siever, M.D.

Summary:

Decreased serotonergic activity, measured by a reduced prolactin response to fenfluramine and reduced prolactin response to fenfluramine and reduced cerebrospinal (CSF) 5-hydroxyindoleacetic acid (5-HIAA), has been associated with impulsive aggression in personality disorder patients (Coccaro et al., 1989; Siever and Trestman, 1993). A biallelic polymorphism in the tryptophan hydroxylase (TPH) gene, the first step in the biosynthesis of serotonin, has been identified using the single-strand conformational polymorphism method. The "L" TPH allele has been associated with lower 5-HIAA concentrations and a history of suicide attempts in a cohort of extremely impulsive Finnish alcoholics (Nielsen et al., 1994). No association between severity of impulsivity and genotype has been found in this cohort. However, an association between the "L" allele and impulsive aggression may be revealed by assessing a more heterogeneous clinical sample. We therefore assessed TPH genotype and impulsive aggression, using the Buss-Durkee Hostility Inventory (BDHI), in a sample of 40 Caucasian personality disorder patients. Twenty-one male patients with the "LL" genotype had significantly higher total BDHI scores (45.3 $\pm$ 9.8) compared to males with the "UL" or "UU" genotypes (32.9 $\pm$ 13.5; $t = 2.38$, $df = 19$; $p < .03$) and scored significantly higher on the BDHI irritability subscale. As in previous studies, the BDHI assault plus irritability subscales correlated negatively with the prolactin response to fenfluramine ($r = -.70$, $n = 16$, $p < .01$) in the 16 patients who had the fenfluramine challenge; patients with "LL" genotype demonstrated a nonsignificantly lower prolactin response to fenfluramine compared to those with "UL" or "UU" genotypes (9.36 $\pm$ 5.0 vs. 12.0 $\pm$ 10.5; $n = 17$; $t = .67$; $df = 15$; p = ns). Females with the "LL" genotype did not demonstrate higher BDHI scores or a blunted prolactin response to fenfluramine. These findings suggest that in male personality disorder patients impulsive aggression may be linked to TPH genotype.

NR508 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Effect of Repetitive Transcranial Magnetic Stimulation on Mood, Anxiety and Obsessive Compulsive Symptoms in OCD

Benjamin D. Greenberg, M.D., NIMH NIH Clinical Center, Room 3D41, 9000 Rockville Pike Bldg 10, Bethesda MD 20892; Mark S. George, M.D., Juliet Dearing, B.S., Jonathan Benjamin, M.D., Margaret Altemus, M.D., Barbara Karp, M.D., Eric S. Wassermann, M.D., Mark Hallett, M.D., Dennis L. Murphy, M.D.

Summary:

Background: Prefrontal mechanisms may be involved in the pathophysiology of obsessive compulsive disorder (OCD), and more generally in the expression of both normal and pathological mood states. Preliminary findings suggest that rTMS of prefrontal regions affects mood in healthy volunteers. We used this noninvasive technique to examine possible prefrontal involvement in OCD symptomatology.

Methods: We administered rTMS to six OCD patients. Stimulation was at 80% of motor threshold, at 20 Hz for 2 seconds once per minute over 20 minutes. Right orbital frontal, left orbital frontal, and occipital regions were stimulated on separate days, two to three days apart, in random order.

Results: Subjects ($n = 6$) tolerated rTMS without complications. Most reported overall symptom improvement after each of the two prefrontal stimulation sessions. Reductions in anxiety, obsessions, and compulsive urges were more common after right orbital frontal stimulation, and improved mood was reported more after left orbital frontal stimulation. These changes ranged from mild to moderate, lasting about one day after each prefrontal session.

Conclusions: rTMS may alter OC symptoms and mood in OCD patients. If confirmed, these preliminary results suggest rTMS may be a useful probe of brain regions possibly involved in the pathophysiology of this disorder.

NR509 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Three-Year Cohort Study of Seasonal Variation in Platelet Serotonin Uptake

Stephen D. Samuelson, M.D., Psych Serv 116A, Kansas City VA, 4801 E Linwood Blvd, Kansas City MO 64128; Jan L. Campbell, M.D., William F. Gabrielli, Jr., M.D.

Summary:

Description: Platelet serotonin uptake has been proposed as a model of neuronal serotonin uptake. Investigators have reported seasonal variation in platelet 5HT uptake and we have previously reported evidence of seasonal variation in a cohort study over one year, but with considerable interindividual variability. We hypothesized that to confirm physiological seasonal variability, a pattern of 5HT uptake should be consistent from year to year. We therefore studied a cohort of subjects over a three-year period.

Method: Subjects ($N = 8$) were without medical or psychiatric illness, medication free, and were studied between 8:00 and 9:00 a.m. at approximately monthly intervals for 36 months. Platelet 5HT uptake was performed by the method of Tuomisto and Tukainen (1).

Results: Data were grouped into the usual four seasons for each year, graphs were constructed displaying annual patterns, and findings were compared both within and between subjects. Inspection of the data do not support a consistent pattern of 5HT uptake from year to year within individuals and no correlation can be demonstrated over the three-year period. The data do not support a physiological seasonal variation in platelet 5HT uptake. It should be noted that all subjects were male, and these conclusions may not apply to females.

(Supported by Veterans Administration Research Service Merit Review Award)

NR510 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Effects of Renal Factors on Plasma and Urinary HVA

Farooq Amin, M.D., Psychiatry, Houston VAMC, 2002 Holcombe Blvd. RM 6C-316, Houston TX 77030; Thomas Kahn, M.D., Peter Knott, Ph.D., Michael Davidson, M.D.

Summary:

Background: The major dopamine metabolite homovanillic acid (HVA) in plasma and urine is frequently measured to assess dopamine metabolism in clinical studies of psychiatric disorders. Variations in HVA measurements are generally assumed to reflect changes in brain dopamine metabolism although a number of unrelated factors could also influence HVA measurements, including the renal excretion of HVA that has not been systematically investigated. For example, changes in urine pH or urine flow rate can theoretically influence renal handling of HVA and hence plasma or urinary HVA measurements, but these questions have never been studied.

Methods: Nine healthy volunteers were studied on four separate days. All subjects were determined to be physically healthy and free of major psychiatric disorders. Prior to each study day, subjects observed a low monoamine diet for 72 hours, fasted overnight for 14 hours, avoided strenuous activity and smoking on study

mornings, and arrived at the medical center at 8:15 a.m. An i.v. line was set up at 8:45 a.m. and blood samples were taken at 9:00 a.m. and 2:00 p.m. All urine excreted during this period was also collected. Day-1 was the control day. On Day-2 a base load (sodium bicarbonate) was infused to alkalinize urine, on Day-3 a salt load (sodium chloride) was infused, and on Day-4 a water load was infused to increase urine flow rate.

Results and Conclusions: Plasma HVA declined between 9:00 a.m. and 2:00 p.m. on all days, consistent with its diurnal variation. However, this decline of plasma HVA was not significantly different between the control day and any other day. Plasma HVA did not correlate with the urine flow rate. The urinary HVA data will also be presented. Preliminary results show that urinary HVA excretion was significantly positively correlated with the urine flow rate, raising the possibility that the urine flow rate should be taken into account when using urinary HVA measurements in clinical studies. On the other hand, plasma HVA data suggest that physiological variations in urinary pH, urine flow rate, and water and salt intake may not significantly affect plasma HVA concentrations and that these factors probably do not need to be controlled when using plasma HVA measurements in clinical studies.

NR511 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Personality in Temporal Lobe Disease

Gregory P. Lee, Ph.D., Psychiatry, Med. Col. of Georgia, 1120 15th Street, Augusta GA 30912; David W. Loring, Ph.D., Jason R. Newell, Ph.D., Susan L. Haverstock, M.D.

Summary:

There is continuing debate about whether or not lateralized temporal lobe seizure foci predispose patients to specific types of personality characteristics. Unfortunately, investigation of these issues has been hampered by many methodological difficulties, most importantly, sample selection biases and inadequate methods of psychological measurement. We addressed these problems by restricting our investigation to complex partial seizure patients who had verified epileptic foci confined to either the left or right temporal lobe using an objective personality inventory. Forty patients with unilateral (20 left, 20 right) temporal lobe epilepsy were compared using the Millon Clinical Multiaxial Inventory (MCMI). Left temporal lobe epileptics (TLEs) obtained higher scores than right TLEs on introverted-withdrawn personality scales while right TLEs tended to endorse the more extroverted-assertive scales. Despite these tendencies, the only statistically significant results were that left TLEs achieved higher scores on the Schizotypal-Schizoid, Psychotic Thinking-Schizophrenia, and Psychotic Depression scales than right TLEs. Results are supportive of a differential association of introversion with left, and extroversion with right, temporal lobe disease and a link between left temporal lobe disease and schizotypal personality characteristics.

NR512 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Effects of Light Therapy on Melatonin Production in Winter Depressives and Normal Controls

Saeeduddin Ahmed, M.D., Psychiatry, Oregon Hlth Sci. Univ., 3181 SW Sam Jackson Park Road, Portland OR 97201; Alfred J. Lewy, M.D., Robert L. Sack, M.D., Vance K. Bauer, M.A.

Summary:

The pattern of endogenous melatonin production and effects of light therapy were studied in 49 patients with winter depression and 49 controls. Recruitment methods have been described previously (Sack et al., 1990). Prior to the study, the dim light melatonin onset (DLMO) was determined for each subject and then sleep was held constant. After one week, 25 patients and 24 controls were administered 2500 lux white light therapy at 6-8 a.m. for two weeks, and after a washout week, switched to evening light (7-9 p.m.) for two more weeks. Another 24 patients and 25 controls received light therapy in the reverse order. DLMOs and 24-hr urinary 6-hydroxy-melatonin production were assessed each week.

Compared to normals, patients' DLMOs were 32 min delayed prior to the study ($p = .02$), 21 min delayed at baseline (trend), and 25 min delayed after washout ($p = .02$). This study supports a phase delay for winter depression, although the magnitudes of patient/control differences are smaller than previously reported (Lewy et al., 1987; Sack et al., 1990). There may also be differences in intra- and inter-individual variability of the DLMO and differences in 24-hr urinary 6-hydroxy-melatonin production in patients vs. controls.

NR513 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

MRI Hippocampal Volumes in Chronic PTSD

Tamara V. Gurvits, M.D., VA Research Service, 228 Maple Street Second Floor, Manchester NH 03103; Martha E. Shenton, Ph.D., Hiroto Hokama, M.D., Hirokazu Ohta, M.D., Natasha B. Lasko, Ph.D., Roger K. Pitman, M.D.

Summary:

Objective: This study explored anatomic correlates of previously described (1) functional neurologic impairment in post-traumatic stress disorder (PTSD) and specifically attempted to replicate reported diminished hippocampal (HC) volume (2) in PTSD.

Method: Vietnam veterans with PTSD (P = 7) and non-PTSD, combat control (C = 7) subjects underwent magnetic resonance imaging (MRI) with volumetric analyses of hippocampus and other structures. Comparison MRI data were obtained from eight additional, non-veteran, normal (N = 8) subjects. All subjects were males without substance dependence/abuse during the preceding year.

Results: Left and right hippocampi were significantly reduced in the PTSD subjects compared with the two control groups, which did not differ significantly from each other. Mean volumes (in ml) (and SDs) were: left HC, P 3.2 (0.3), C 4.3 (0.3), N 4.4 (0.3), $F(2,19) = 29.0$, $p < .001$; right HC, P 3.2 (0.6), C 4.1 (0.4), N 4.6 (0.4), $F(2,19) = 14.3$, $p < .001$. There were no statistically significant group effects for intracranial cavity, whole brain, third and fourth ventricles, and amygdala (a neighboring structure hypothesized to be implicated in PTSD psychopathology). ANOVAs were reperformed on volumes expressed as percentages of intracranial cavity and whole brain; the hippocampal diminutions in the PTSD group remained significant at $p < .003$ or lower.

Conclusions: It is unclear whether reduced hippocampal volume represents a pre-trauma risk factor or an acquired phenomenon in patients with PTSD.

NR514 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Pergolide in the Treatment of Restless Legs Syndrome

Siong-Chi Lin, M.D., Department of Psychiatry, Mayo Clinic, 4500 Sab Pablo Rd, Jacksonville FL 32224; Joseph Kaplan, M.D., Charles Burger, M.D., Paul A. Fredrickson, M.D.

Summary:

Introduction: Primary disturbances in sleep can result in behavior manifestation mimicking psychiatric symptoms such as insomnia, hypersomnia, irritability, depressed mood, poor concentration, self-medication, substance abuse, deteriorating interpersonal and social relationship. Restless Legs Syndrome (RLS) is a common cause of insomnia with an estimated prevalence between 5%-15% of the general population.[1] Its clinical manifestations range from episodically mild disturbance of sleep onset or sleep mainte-

nance to profound insomnia and severely debilitating diurnal symptoms. Benzodiazepines, opioids or opiates, as well as dopaminergic agents have been reported as effective treatment agents for RLS.[2] Unfortunately tolerance and/or breakthrough are commonly seen with each medication group.

We report an open trial with a dopaminergic agent, pergolide, in patients with treatment-resistant restless legs syndrome.

Methodology: Seven consecutive patients evaluated at the Sleep Disorders Center, Mayo Clinic, Jacksonville who 1) fulfilled the criteria of chronic and severe RLS according to the Diagnostic and Coding Manual of the International Classification of Sleep Disorders,[1] except for the polysomnographic confirmation of the presence of leg movements prior to sleep onset, 2) were treatment failures with previous trials of benzodiazapines, opioids, or opiates, 3) were maintained on carbidopa/L-dopa combination at the time of evaluation, 4) had both active nocturnal and diurnal RLS. Once current medications were either tapered or discontinued, all patients were started on pergolide. Subjective reports were obtained prospectively beginning a week after initiation of pergolide.

Results: In dose range from 0.05mg to 1.0mg per day, all six patients received lasting and near total resolution of their nocturnal and diurnal RLS symptoms. Minimal side effects were observed but well tolerated in two patients.

Discussion: RLS is a chronic and debilitating disorder often with dysfunctional behavioral presentation requiring psychiatric evaluation or intervention. Unfortunately in a significant portion of patients with RLS, there is a paucity of effectively lasting treatment option. Our report presents a novel finding in the treatment of RLS. We propose that pergolide, a non-selective D_1 and D_2 agonist with a half life of about 24 hours, is an effective treatment agent for treatment resistant RLS.

NR515 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Visual Analogue Scale for Psychopharmacological Study: Its Reliability and Validity

Yan-Ping Zheng, M.D., Psychiatry, Research & Education Inst, 1124 W. Carson Street, Torrance CA 90502; Keh-Ming Lin, M.D.

Summary:

For the simultaneous measurement of suppressive and stimulative effects of psychotropics, the visual analogue scale for psychopharmacological study—a 12-item, self-report scale was developed. One hundred and ninteen normal volunteers were recruited in this scale developmental study. All subjects repeated the VAS-P as well as were conducted nurse rating of sedation before and during the single dose administration of imipramine. The VAS-P was found to have excellent reliability (Cronbach's alpha = 0.91) and reasonable concurrent validity (Pearson r = 0.24). Construct validity analysis was performed using principal component analysis, which yielded two factors: suppressive effect and stimulative effect. Most importantly, individual VAS-P factor and total score changes were significantly associated with imipramine AUC (Pearson rs = 0.16 for srppressive effect, 0.13 for stimulative effect, and 0.25 for VAS-P total score of drug effects, indicating that the VAS-P was biologically valid, sensitive, and useful for psychopharmacological studies.)

NR516 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

An Indirect Measure of Dopamine Sensitization by Serum Prolactin Levels in Humans

Matthew D. Wortman, B.S., Bio. Psych., University of Cincinnati, 231 Bethesda Avenue ML 559, Cincinnati OH 45267; Sean P. Stanton, B.S., Paul E. Keck, Jr., M.D., Scott A. West, M.D.

Summary:

Introduction: Behavioral and neuronal sensitization have been proposed as a model for the pathogenesis of substance abuse and bipolar disorder (Goodwin and Jamison 1989). The purpose of this experiment is to test the theory that repeated amphetamine administration can sensitize dopamine-induced suppression of prolactin in human serum.

Method: Two subjects were matched for age, gender, education, race, and socioeconomic status. The subjects were recruited as controls in the continuous CSF sampling study at the University of Cincinnati Medical Center. The subjects were placed on low monoamine diets five days prior to admission to the psychobiology unit. A baseline sample was taken(T_0) just prior to amphetamine (0.50 mg/kg) or placebo dosing at 12:00 p.m. and samples were collected on the hour for the following five hours(T_1-T_5) after challenge. The identical procedure was performed six weeks later. Plasma concentrations of PRL were measured using immunoassay (Technicon Immuno1 Prolactin method).

Results: The prolactin response of the volunteer receiving placebo showed typical fluctuations in PRL levels, whereas the subject receiving amphetamine showed an overall increase in PRL at week one and a robust increase in PRL at week six. Specifically, after amphetamine administration at week one, plasma PRL concentrations rose by three-fold from baseline to time four (T_4). After the second amphetamine administration, plasma PRL concentration rose to four-fold of baseline by time two (T_2).

Discussion: The preliminary data suggest a sensitized response of dopamine to amphetamine as measured through dopamine's inhibitory effect on prolactin. This is in support of a theory of sensitization such that amphetamine stimulates the release of dopamine from the pre-synaptic neuron to such an extent that DA stores are depleted. Once these stores are depleted, PRL levels rise due to a lack of DA inhibition. This pathway may occur in both responses to amphetamine; however, in the second challenge, PRL levels rise to robustly higher levels perhaps due to greater DA response (i.e. greater release and depletion) secondary to sensitization.

NR517 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Gender Difference and the Effect of Alpha-methyl-para-tyrosine on Prolactin and Melatonin Secretion

Ralf C. Zimmermann, M.D., Psychiatry, c/o Dr. L. Krahn, Mayo Clinic, Rochester MN 55904; Lois E. Krahn, M.D., George Klee, M.D., Peter Y. Lu, M.D., Steven J. Ory, M.D., Siong-chi Lin, M.D.

Summary:

Introduction: AMPT, an inhibitor of catecholamine synthesis, has been used as a neuroendocrine probe in psychiatric research. The purpose of the study is to determine 1) if ML secretion can be a candidate to characterize the inhibitory effect of AMPT on catecholamines, 2) if AMPT inhibition of PRL has the same gender dependent effect as on ML secretion, 3) if there is a post AMPT induced NE depletion mood change in normal subjects.

Methodology: In a randomized, double-blind study, five male and five female normal subjects received either AMPT or promethazine in a crossover design. Serial plasma PRL, ML, and concurrent 24-hr urinary 6-SM were measured. Possible mood and anxiety symptoms associated with catecholamines depletion were also serially assessed using HAM-D, POMS and HAM-A rating scales.

Results: AMPT significantly ($p < 0.05$) suppressed both DA mediated PRL secretion and NE mediated ML secretion. The extent of PRL suppression is gender dependent where as ML suppression is free of gender bias. High correlation exists between total ML secretion and urinary secretion of 6-SM post AMPT. There were no significant mood or anxiety symptoms after AMPT induced catecholamines depletion in normals.

Discussion: We propose that ML and 6-SM are reliable measures of AMPT induced changes in central catecholamine activities. Urinary 6-SM, due to its ease of collection and freedom from gender differences, in addition to PRL should be measured when applying the AMPT paradigm in future psychiatric research.

This project was supported by NARSAD Young Investigator Award to (RCZ) and by GCRC, Mayo Foundation, Grant (M01 RR585). Current Address of RCZ is: Section of Assisted Reproduction, Presbyterian Hospital, Columbia University, 630 West 168 Street, New York City, N.Y. 10032

NR518 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Factor Analysis MRI Brain Structure in Schizophrenia

Allen Y. Tien, M.D., Dept of Mental Hygiene Jo, Hopkins Sch of Public Hlt, 624 North Broadway, Baltimore MD 21205-1999; Thomas Schaepfer, M.D., Godfrey D. Pearlson, M.D., William W. Eaton, Ph.D., Patrick E. Barta, M.D., Elizabeth Aylward, Ph.D.

Summary:

Objective: Much evidence shows various regional structural brain abnormalities in schizophrenia, but the complexity and variability of the brain makes it difficult to determine how these regions are related. Statistical methods which estimate factors underlying patterns of covariance have not been widely used, but could be useful for analyzing such complex data.

Method: We applied exploratory and confirmatory factor analysis procedures to specific cortical and subcortical regional brain volume measures from MRI data in 60 normal and 44 schizophrenic subjects.

Results: Basal ganglia, heteromodal cortical gray, and medial temporal lobe factors were present in both the normal and the schizophrenia groups. The factor structure observed in the normal group showed a high degree of bilateral symmetry which is present but disrupted in the schizophrenia group. In the bilateral data, the disruption is most pronounced with medial and lateral temporal lobe structures including entorhinal cortex and anterior and posterior superior temporal gyri. There was a significant correlation between the basal ganglia factor and the heteromodal cortical gray factor in the normal group that was not present in the schizophrenia group. In the unilateral data, left posterior superior temporal gyrus did not load onto any factor in the schizophrenia group. Confirmatory factor analyses showed significant differences between the two groups in factor structure.

Conclusions: A number of specific brain regions are affected in schizophrenia, and structural relationships between groups of regions also are abnormal. The results suggest that heteromodal dorsolateral prefrontal and superior temporal cortical gray regions are structurally related, whereas inferior parietal cortical gray is less so. Finally, the results demonstrate the potential utility of latent structure methods such as factor analysis in study of complex relationships in neuropsychiatric data.

NR519 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Temporal Lobe Length and Age at Illness Onset in Schizophrenia

George Bartzokis, M.D., Psychiatry, UCLA, 300 UCLA Medical Plaza Ste2200, Los Angeles CA 90024; Keith Nuechterline, Ph.D., Kevin Laack, Kenneth Dery, B.A., Marguerite Calinan, B.A., Stephen R. Marder, M.D.

Summary:

Post-mortem data (Bogerts et al, 1991) suggest that temporal lobe length may be associated with age at illness onset. We used sagittal MRI images standardly acquired in reference to a coronal pilot image to obtain linear measurements of the left hemisphere in 38 male schizophrenic patients early in the course of their illness and 21 matched normal controls. In addition to temporal lobe and anterior temporal lobe (anterior to the anterior commissure), maximal brain and skull lengths were also measured.

Within the patient group, a significant association between temporal lobe length and age at onset of psychosis was observed ($r = .38$, $p = .018$). The same association was observed when the anterior part of the temporal lobe was measured separately ($r = 0.43$, $p = 0.0071$). These associations remained significant after controlling for brain and skull length. The reduction in temporal lobe length in patients relative to normal controls ($t = 1.94$, $p = 0.058$) was related to significant differences between groups in the global measures of brain ($t = -4.11$, $p = 0.0001$) and skull lengths ($t = -3.81$, $p = 0.0003$). However, even after controlling for skull length, the subgroup of schizophrenic patients with the earliest onset of illness (before age 23; $N = 16$) had shorter temporal lobes than the normal control group ($t = 2.65$, $df = 16$, $p = .012$).

The data suggest that temporal lobe length may be a useful variable in investigating the biological heterogeneity of schizophrenia and highlight important technical issues regarding current efforts to measure the volumes of temporal lobe structures.

NR520 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Dynamic Brain Mapping Findings in Children with ADHD

Atilla Turgay, M.D., Psychiatry, Scarborough General Hosp, 251 Queens Quay West #701, Toronto ON M5J 2N6, Canada; Edward Gordon, M.D., Martin Vigdor, Ph.D.

Summary:

The study sample consisted of 49 boys and 7 girls, age 7-17, who were consecutively admitted to the Green Chimneys in Brewster, New York, a long-term residential treatment facility with an average length of stay of two years or longer. All of the children were admitted to the facility because of the lack of satisfactory treatment response to medication and other psychosocial therapies. They all met the diagnostic criteria of DSM-III-R Axis I for ADHD and the NIMH criteria for chronicity. Only 21 out of 56 patients (38%) had ADHD alone. Thirty-five of the 56 children who received the diagnosis of ADHD (63%) had more than one additional DSM-III-R Axis disorder, four of the 56 children (7%) had ADHD and two more additional psychiatric diagnoses. The most common co-morbid disorders were conduct disorder and oppositional defiant disorder. EEG, QEEG, and DBM data collection was completed with International 10-20 electrode placements on the scalp and at least 30 minutes of artifact free EEG recordings. The database for age- and gender-matched, healthy comparison subjects were provided by New York Institute of Medical Research data pool collected from 700 healthy control subjects and 2,000 patients in the age range 5-92. In only 11 of the 56 patients (20%) EEG, QEEG, and DBM were found "normal." In 13 patients (23%), the findings were classified as "borderline" and in 32 patients (57%) the findings were identified as "pathological." The most common pathological findings were: general slowing of the electrophysiological activities, general paroxysmal activities, and temporal lobe pathology. Since 33 children (59%) were on psychoactive medication, and 23 (41%) were psychoactive drug free for at least two weeks prior to the recordings, the findings were also compared among these two groups to determine if the drug effects can explain the frequency and the nature of the borderline and pathological findings. There was no statistically significant differences in any of the findings among the children on medication as compared to the children who were off medication at the time of the study ($p > 0.05$). The pathological findings seemed to be associated with primary pathology in children with treatment resistant ADHD. The children with more than one psychiatric disor-

der showed more pathological findings than the ones who were suffering from ADHD alone ($p < 0.01$). High incidence of low voltage and slow wave activities especially in the frontal areas provided electrophysiological support for the PET studies detecting low oxygen and glucose distributions in these areas.

NR521 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

The Use of SPECT in Psychiatry

Prof. M.T. Abou-Saleh, Ph.D., Psychiatry, UAE Univ. EMHS, P.O. Box 17666, Alain, U.Arab Emirates

Summary:

The introduction of single photon emission computerized tomography (SPECT) has markedly enhanced the study of brain function. The author has carried out a series of studies in dementia, depressive illness, and most recently in schizophrenia in UK and UAE.

Study I: A comprehensive study of SPECT in 14 patients with Alzheimer's disease, 18 patients with major depression, and 12 normal subjects. The results showed high rates of hypoperfusion in Alzheimer's disease (93%) and depressive illness (44%) compared to normal subjects (17%).

Study II: A SPECT study of the effects of an anti-dementia drug in seven patients with dementia compared with a placebo group showed no significant changes in brain perfusion.

Study III: A study of a group of 30 schizophrenic patients studied while hallucinating and a group of 25 depressive patients investigated when ill and on recovery. The results are under analysis.

NR522 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A Functional MRI Study of Transient Sadness in Healthy Adult Women: Brain Activity Due to Mood Versus the Effort of Changing Mood

Priti I. Parekh, B.A., Mark S. George, M.D., Mark Willis, Francois Lalonde, Ph.D., Terence A. Ketter, M.D., Robert M. Post, M.D.

Summary:

Background: We have previously demonstrated with 0-15 PET that healthy women activate the anterior limbic system and the prefrontal cortex during transient self-induced sadness. To what extent these increases are due to being sad, versus trying to change one's mood and induce sadness remains to be determined. In view of the superior time resolution of echoplanar MRI (acquiring images every second), we have extended this PET paradigm to functional MRI (fMRI).

Methods: We imaged six healthy adult women volunteers during states of no emotion (neutral) and transient emotions (three episodes of sadness and three of happiness), as well as during the transition between these states (a time when they were instructed to remember past emotionally laden events and try and change their mood). Images were co-registered across runs and statistically significant changes in regional activity were determined using ANOVA and particle analysis and were mapped onto the patient's structural MRI.

Results: During the state of sadness compared to the neutral emotion, most subjects on most runs had statistically significant increased prefrontal and anterior limbic activity. During the transition from neutral to sadness, prefrontal, occipito-parietal and mid-temporal activity significantly increased.

Conclusions: Changing from a neutral to sad mood by remembering personal affect-laden events is associated with markedly increased prefrontal and temporal activity. During sadness, the prefrontal and anterior limbic areas continue to be hyperactive compared to baseline. Additionally, some areas appear uniquely activated during the transition period and not during the maintained emotional state. Further exploration of these regions that are uniquely activated during mood transitions may help advance understanding of pathological mood switches such as occurs in bipolar affective disorder.

NR523 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Regional EEG Changes During Guided Recollection of Bereavement

Eric Rubin, M.D., Biological Psychiatry, New York State Psych Inst, 722 W 168th Street Box 72, New York NY 10032-2603; Nina A. Sayer, M.A., James R. Moeller, Ph.D., Bruce M. Luber, Ph.D., Gary P. Katzman, B.S., Harold A. Sackeim, Ph.D.

Summary:

Objective: To study the cerebral pathways mediating induced dysphoria.

Method: Within-subject design. Healthy females (N = 18, age 25-38; negative psychiatric history) used guided imagery to recall an episode of bereavement. Before and after this procedure, as a control condition, subjects similarly recalled an affectively neutral interpersonal event.

Results: Recollection of bereavement evoked transient but marked dysphoria, with robust changes in mood self-report and in facial electromyography (EMG). ANOVA showed that in dysphoria, relative to control, EEG alpha was suppressed ($p < .05$) at selected frontal sites and elevated ($p < .05$) at parietal and bilateral posterior temporal sites. A regional covariance method identified functional networks in the EEG data. One major network displayed an anterior-posterior gradient of alpha power. This network appeared especially related to general arousal and to involvement in the imagery task. A different network emphasized left frontal, left parietal, and right posterior temporal regions. Activation of this network correlated with subjects' reported experience of dysphoria.

Conclusions: Guided recollection of bereavement alters mood, facial EMG, and regional brain activity. Covariance analysis of the EEG data indicates possible brain pathways regulating dysphoria. We are now applying these procedures to other functional brain imaging modalities.

NR524 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Cortical Surface Area Increased in Schizophrenia

Patrick E. Barta, M.D., Psychiatry, Johns Hopkins Hospital, 600 N. Wolfe Street Meyer3-166, Baltimore MD 21287

Summary:

Previous research suggest that schizophrenic patients have abnormal patterns of cerebral gyrification. These findings, and reports of increased sulcal prominence in schizophrenia, led to the hypothesis that cortical surface area would be increased when schizophrenic subjects were compared with unaffected subjects.

Twelve schizophrenic subjects (mean age 37, S.D. 5.7 years) and 11 unaffected subjects (mean age 34, S.D 9 years) were recruited into the study. All subjects were male, and the two groups did not differ in age ($t = -.72$, $p = .48$, d.f. = 17) or parental socioeconomic status measured by the Hollingshead scale (chi-squared = .8, d.f. = 2, $p = .67$).

Cortical surface area was estimated by the method of vertical sections [2], applied to MRI images which were digitally reconstructed in a direction which was parallel to the inferior-superior axis with a uniform random degree of rotation about this axis to assure unbiased estimates of surface area. The investigator was blind to subject's diagnosis at the time of surface area measurement.

Unaffected subjects' mean surface area (in cm^2) was 1276, S.D. = 152 while mean was 1405, S.D. = 200 for the schizophrenic

subjects. This difference was significant (t = 1.75, one-tailed p = .048 with 20 d.f.) These results should be interpreted with caution though since p = 0.09 for a two-tailed t test and the sample size was small.

This is the first description of an unbiased estimate of cortical surface area using MRI in any subject group. These results, coupled with previous results on cortical *volumes,* suggest a thinning of cerebral cortex in schizophrenia. Additional data will be available at the meeting.

NR525 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

SPECT Changes with Emotional Task in Schizophrenia

Miklos F. Losonczy, M.D., Psychiatry, FDR VA Hosp. Mt Sinai, P.O. Box 100, Montrose NY 10548; Ileana Berman, M.D., Cecile E. Sison, Ph.D., Clara Schaefer, Ph.D., Edward R. Allan, M.D., Murray Alpert, Ph.D.

Summary:

Introduction: Negative symptoms, such as emotional withdrawal, flat affect, and poor rapport, represent an important aspect of the schizophrenic pathology and predict a poor prognosis. Some reports suggest that negative symptoms may be related with decreased frontal and temporal metabolism. The purpose of this study is to determine the changes in the brain activity during a reading using Tc-99m HMPAO Single Photon Emission Computed Tomography (SPECT).

Methods: Fifteen male patients with DSM-III-R criteria for schizophrenia (mean age = 48) entered the study. All patients had to be in stable medical condition (e.g., no recent onset of cardiac disease, cerebral vascular accident, pneumonia, seizures, anemia). The patients were rated with a modified Flat Affect subscale of the Scale for the Assessment of Negative Symptoms (SANS), the Simpson Angus Scale for extrapyramidal symptoms, the Minimental Status Examination, and the Hamilton Depression Scale. The patients had two SPECT studies within three weeks of each other. During this interval the psychiatric medication was kept unchanged. The patients received 10 mCi of Tc-99m HMPAO for each SPECT evaluation. During the SPECT studies the patients had to read loudly an emotional or a neutral text for ten minutes after the administration of the HMPAO. To analyze the cortical activity we used an automated image processing. We looked at the regions of interest (ROIs) in the frontal area located one slice above the head of the caudate level and the temporal area located at the caudate level. The ROIs frontal/whole slice ratios and temporal/whole slice ratios were used for data analysis.

Results: There were no significant changes in the studied ROIs during the emotional compared to the neutral task. During the emotional reading, however, we noticed a direct correlation between the activity in the frontal area and the flat affect scores as measured by the SANS (r = 0.48, p = 0.03). Another finding was a direct correlation between the temporal and the frontal activity both during the neutral (r = 0.57, p = 0.01) and emotional (r = 0.74, p = 0.001) tasks.

Conclusions: Our findings suggest that the frontal and temporal activity in the schizophrenic patients we examined, did not change significantly during the emotional activation, but that the frontal and temporal lobe activities may be directly correlated. In addition, there may be a direct correlation between negative symptoms and higher frontal activity during the emotional activation. Controlled studies are necessary to verify our findings.

NR526 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Brain Glucose Metabolic Correlates of Extrapyramidal Syndrome

Benjamin V. Siegel, M.D., Psychiatry, Mt. Sinai Med. Center, 1 Gustave Levy Place Bx 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Daniel Truong, M.D.

Summary:

The neurobiology of extrapyramidal side effects (EPS) of neuroleptic medication is thought to involve the balance of dopaminergic and cholinergic activity in the striatum. The pathophysiology of tardive dyskinesia (TD) is somewhat more controversial, possibly involving upregulation of striatal dopamine receptors, neuronal cell damage via free radical mechanisms, and/or activity at GABA or serotonin receptors. The regional glucose metabolic correlates of EPS and TD have not been well studied. Nine schizophrenic patients (7 male, 2 female; mean ± SD age: 31 ± 7, mean ± SD BPRS score: 35 ± 6) had 18-fluoro-2-deoxyglucose positron emission tomographic (PET) scans while performing the degraded stimulus continuous performance test after a minimum four-week wash-out from neuroleptic medication. Regions of interest were identified with a stereotactic method. Modified AIMS were performed by a neurologist two weeks or less prior to the PET procedure. Global brain activity correlated with severity of parkinsonian symptoms (r = 0.73, df = 7, p < 0.05) and of tardive dyskinesia (r = 0.72, df = 7, p < 0.05), but not with severity of akathisia (r = 0.45, df = 7, NS) Severity of EPS and TD did not correlate with relative metabolism (regional metabolism divided by whole brain metabolism) in striatal, lateral frontal, or medial temporal regions. These findings suggest that EPS and TD are related to global cortical function and do not provide evidence for a frontal, striatal, and/or medial temporal limbic role.

NR527 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

[^{123}I]B-CIT SPECT Imaging Demonstrates Increased Striatal Dopamine Transporter Binding in Tourette's Syndrome

Robert T. Malison, M.D., Department of Psychiatry, Yale School of Medicine, 34 Park Street, New Haven CT 06519; Chistopher J. McDougle, M.D., Christopher Van Dyck, M.D., Lawrence Scahill, M.S.N., Ronald M. Baldwin, Ph.D., John P. Seibyl, M.D., Lawrence H. Price, M.D., James F. Leckman, M.D., Robert B. Innis, M.D.

Summary:

Objective: Based on post-mortem reports of increased striatal dopamine transporter (DAT) densities in Tourette's syndrome (TS), the authors used the radioiodinated phenyltropane analog, [^{123}I]β-CIT and single photon emission computed tomographic (SPECT) imaging to assess DAT levels *in vivo* in patients with the disorder.

Methods: Five TS subjects and five age- and gender-matched healthy controls received 10 mCi of [^{123}I]β-CIT and were scanned 24 hours later under conditions of equilibrium binding. V_3'' ([striatum—occipital]/occipital), a measure proportional to the binding potential (B_{max}/K_d), was used to estimate DAT levels.

Results: Results showed a 37 ± 30% (mean ± SD; range 6-79%; p = 0.02; one-tailed paired t-test) increase in V_3'', with all TS patients demonstrating elevations relative to their paired control (p = 0.03, paired sign test). Elevations in V_3'' did not derive from differences in non-specific (occipital) binding between TS and healthy control subjects (% injected dose = $1.6 \pm 0.3 \times 10^{-3}$ vs $1.7 \pm 0.8 \times 10^{-3}$ ml^{-1}; p = 0.65).

Conclusions: These findings corroborate post-mortem findings of increased DAT densities in TS, and support the hypothesis of a dysregulation in pre-synaptic dopamine neuronal function in TS.

NR528 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

A PET Study of Developmental Stuttering

Glyndon D. Riley, Ph.D., Psychiatry, University of CA Irvine, Room 163 Irvine Hall UCI, Irvine CA 92715; Gerald A. Maguire, M.D., Joseph C. Wu, M.D., Eric A. Klein, B.S.

Summary:

Objective: The first specific aim is to identify regional brain metabolic changes which are seen during the stuttering state and *not* seen during the *non*-stuttering state *within the same subjects* using positron emission tomographic ("PET") scans. The second specific aim is to identify regional brain metabolic differences between stutterers and normal controls using PET scans.

Method: FDG PET scanning was used to investigate the neural substrate of stuttering. Four patients with severe developmental stuttering themselves were studied while reading aloud to another person (stuttering condition) compared to their reading aloud in unison with someone else (nonstuttering condition). Stutterers were compared with four normal controls doing solo reading.

Results: Stutterers showed significant decreases in regional glucose metabolism in Broca's area, Wernicke's area, and frontal pole during their stuttering condition compared with themselves while not stuttering. These differences were also seen in the stuttering condition compared to normal controls. Significantly lower left caudate metabolism was seen in patients during both stuttering and nonstuttering conditions compared to normal controls.

Conclusion: Left caudate hypometabolism is a possible trait marker for stuttering. Reversible hypoactivity in the left language and higher order association areas may represent a state dependent circuit that can be increased during induced fluency.

NR529 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Catatonia in Dementia: Three SPECT Scans

Brendan T. Carroll, M.D., Dept of Psychiatry, Ohio State Univ Hosp, 1670 Upham Drive, Columbus OH 43210-1228; H. Ronald Clements, Jr., M.D., Douglas Scharre, M.D.

Summary:

The presence of catatonia has been associated with medical conditions such as tuberculosis, alcoholism, and syphilis since the first description of this syndrome by Karl Ludwig Kahlbaum in his monograph published in 1873. Catatonia due to general medical conditions occurred in 20% of patients with this syndrome presenting to a neurological unit.

Functional brain imaging of patients with catatonia is sparse. One report suggests that patients with schizophrenia and catatonic syndromes have left temporal hypoperfusion.

Functional brain imaging in patients with catatonia may be difficult due to the lack of static brain lesions in patients with psychiatric disorders that may revert to their pre-catatonic state with treatment. We wish to present three patients with catatonia that underwent SPECT scanning while exhibiting catatonic syndromes.

The three cases are characterized by catatonic signs, psychosis, functional decline, and EEG abnormalities. The diagnoses include: thalamic degeneration, senile dementia in a patient with a history of schizoaffective disorder, and presenile dementia. In all cases the SPECT was interpreted as normal.

These cases illustrate the fact that normal SPECT scans may occur in patients with dementia and patients with static lesions associated with catatonia.

NR530 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Effect of Comorbidity on the Cerebral Blood Flow of Obsessive Compulsive Patients

Jose L. Ayuso-Gutierrez, M.D., Psychiatry, Hospital San Carlos, Martin Lagos S/N, Madrid 28040, Spain; Maria I. Lopez-Ibor, M.D., Juan J. Lopez-Ibor, Jr., M.D., Jose A. Cabranes, M.D., Jose L. Ayuso-Mateos, M.D., Benedicto Crespo, M.D.

Summary:

Objective: The measurement of cerebral blood flow (rCBF) with single photon emission computer tomography (SPECT) is a useful tool for exploring the neurobiology of psychiatric disorders. In this study, we used such an approach to assess the comorbidity of obsessive compulsive disorder (OCD).

Method: Twenty-four unmedicated patients with OCD (DSM-III-R criteria) were scanned with technetium labeled HMPAO (Ceretec) on SPECT system. Of this total, 11 had pure OCD, six had OCD and major depression, five presented OCD and tic disorder, and two presented OCD, major depression and tic disorder.

Results: OCD patients with comorbid major depression had significantly ($p < 0.05$) decreased rCBF, compared with pure OCD patients, in the following brain regions: left basal ganglia, right basal ganglia, left frontal, right parietal, left parietal, right anterior cingulate, left anterior cingulate, left hippocampus, left orbital frontal, right orbital frontal, and right thalamus. Patients with OCD and tic disorder had significantly higher rCBF than OCD patients without tics in the following areas: left cingulum, left orbital frontal, right orbital frontal.

Conclusions: Marked differences in cerebral blood flow patterns were observed in the different groups of OCD patients, as classified by the presence of comorbid major depression and tic disorder.

NR531 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Acute Tryptophan Depletion in Adults with Autism

Christopher J. McDougle, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Susan T. Naylor, M.S.N., Donald J. Cohen, M.D., Geo Kevork Aghajanian, M.D., George R. Heninger, M.D., Lawrence H. Price, M.D.

Summary:

Serotonin (5-HT) function has been the subject of biological research in autistic disorder for the past 35 years. Recent findings suggest that brain 5-HT function may be reduced in some persons with autism. A controlled investigation of acute tryptophan (TRYP) depletion was completed in drug-free adults with autism to test this hypothesis.

Methods: Twenty adults with autistic disorder (DSM-III-R, ADI, ADOS criteria) (4 women, 16 men; 8 inpatients 12 outpatients; mean $\pm$ SD age = 30.5 $\pm$ 8.5 years, range 20 to 53 years) participated in the study. A double-blind, placebo-controlled, randomized crossover design was used. Patients received a 24-hr, 160 mg/day low-TRYP diet with (sham) or without TRYP supplementation, followed the next morning by an amino acid drink with (sham) or without 2.3 gms of TRYP. Behavioral and biochemical measures were obtained throughout the test period. Seventeen of 20 patients completed both test sessions.

Results: Acute TRYP depletion markedly decreased plasma free (69%) and total (86%) TRYP levels 5 hrs after the drink. Eleven of 17 patients (65%) who completed both test days demonstrated a significant global worsening of behavioral symptoms with acute TRYP depletion, whereas 0/17 showed any change following sham depletion ($P = .001$). Acute TRYP depletion led to a significant increase in whirling, flapping, pacing, banging and hitting self, rocking, and toe walking ($F = 2.69$, $df = 3,48$, $P < .05$), and patients were significantly less calm and happy and more anxious. Patients with Autism Behavior Checklist scores of >78 ($P = .005$) and with higher baseline levels of total plasma TRYP were more likely to show symptom exacerbation.

Conclusions: These results support the hypothesis that reduced central 5-HT function may contribute to the pathophysiology and symptom manifestation of some patients with autistic disorder.

NR532 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Seasonal Variation of Prolactin Response to m-CPP

Robert A. Grossman, M.D., Psychiatry, Mt. Sinai Medical Center, Box 1230 1 Gustave Levy Place, New York NY 10029; Lisa J. Cohen, Ph.D., Concetta Decaria, Ph.D., Jennifer Rosen, B.A., Eric Hollander, M.D.

Summary:

Measures of serotonin (5-HT) function have been found to show significant seasonal variation. Ratios of 5-HT to 5-HIAA suggest increased degradation of 5-HT with decreased photoperiod, and increased rate of change of 5-HT turnover(Δ-5-HT) in spring and fall.

Objective: To assess whether peak delta prolactin(Δ-prl) to m-chlorophenylpiperazine(m-CPP) challenge varies with respect to season/photoperiod/Δ-5-HT.

Subjects: 100 healthy subjects(52M/48F), off medications, participated in our IRB approved protocol. Subjects included 43 obsessive compulsive disorder(OCD), 18 personality disorder, 18 social phobics, and 21 normal controls.

Methods: Double-blind m-CPP(0.5 m/kg)/placebo p.o., RIA for prolactin.

Results: There was a significant overall effect of season on Δ-prl($F = 2.960$; $df = 3,96$; $p = .0358$), but no between group differences. Long vs short photoperiod did not significantly affect Δ-prl. Delta-prl was significantly greater in high(spring/fall), as compared to low(summer/winter) Δ-5-HT period for the entire sample($F = 8.417$; $df = 1$; $p = .0046$), and OCD patients($F = 5.227$; $df = 1$; $p = .0275$). There was a significant gender effect for the entire sample($F = 7.600$; $df = 1$; $p = .007$). Females had a significantly greater Δ-prl than males.

Conclusion: High(spring/fall) rate of change of 5-HT turnover, caused significantly greater Δ-prl response to m-CPP.

NR533 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Chronobiological Analysis of Prolactin in PTSD

Robert A. Grossman, M.D., Psychiatry, Mt. Sinai Medical Center, Box 1230 1 Gustave Levy Place, New York NY 10029; Rachel Yehuda, Ph.D., Martin H. Teicher, M.D., Robert A. Levengood, M.D., Robert L. Trestman, M.D., Larry J. Siever, M.D.

Summary:

Prolactin (PRL) secretion is thought to be at least partially influenced by circulating glucocorticoid levels. Moreover, we have reported that PRL suppression following dexamethasone (DEX) is greater in combat veterans with PTSD who also show an enhanced suppression of cortisol(C). More recently, using chronobiological modeling techniques, we observed a lower mean (mesor) plasma C in PTSD. In the present study, we assessed PRL levels every 30 minutes for a 24-hour period in the same combat veterans with low C in order to determine the relationship between C and PRL secretion. We hypothesized that due to attenuated ambient C levels, PRL levels would be increased in PTSD.

Subjects: 14 Viet Nam veterans with PTSD and 15 normal controls (NCS). All subjects were healthy and off medications for four weeks.

Method: IV inserted at 8:00 AM in fasted subjects.

Results: There was a negative correlation between the PRL mesor and the C mesor that was largely due to a significant difference between these two variables in the NCS ($r = .395$ $df = 28$ $p = .034$). The C mesor was significantly lower in the PTSD group($9.47 \mu g/dl \pm 1.9$ vs 7.69 ± 1.7 $t = 2.65$ $df = 28$ $p = .01$). The PRL mesor was 14% higher than in the NC, but this effect was not significantly different ($11.08 \pm 3.5 ng/ml$ vs 9.54 ± 2.6). There was a substantial association between the P mesor and the severity of PTSD as measured by the Mississippi Scale ($r = .51$ $df = 14$ $p = .05$).

Conclusion: HPA axis abnormalities in PTSD may affect other neuroendocrine parameters in PTSD.

NR534 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Apparent Homologues of the Rat's Sexually Dimorphic Nucleus of the Preoptic Area in the Human and Rhesus Monkey

William M. Byne, M.D., Psychiatry, Mt. Sinai School of Med., One Gustave Levy Pl. Box 1230, New York NY 10029

Summary:

Objectives: Three of the interstitial nuclei of the anterior hypothalamus (INAH) of the human have been identified as possible homologues of the sexually dimorphic nucleus of the preoptic area (SDN-POA) of the rat and have been conjectured to participate in putatively sexually dimorphic brain functions and/or sexual orientation. The objectives of this study were to determine which of the INAHs is the best candidate for homology with the SDN-POA, and to determine if apparent homologues of the INAHs are identifiable in the rhesus monkey.

Methods: Serial thionin stained sections through the hypothalamus were prepared from formalin fixed tissue obtained from 36 human autopsies, ten rhesus monkeys, and six rats. Hypothalamic nuclei were examined at the light microscopic level and compared among species with respect to cytoarchitectonic characteristics.

Results: In the human, INAH3, unlike INAH1 or INAH2, resembles the SDN-POA of the rat with respect to cellular characteristics and positional relationships with other hypothalamic structures. Structures apparently comparable to INAH1, INAH2, and INAH3 were identified in the rhesus.

Conclusions: INAH3 is the best candidate for homology with the SDN-POA. Identification of a possibly homologous nucleus in the rhesus monkey is significant in light of important differences between rodents and primates with respect to the functional organization and sexual differentiation of the hypothalamus.

NR535 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Detection of 3a-Hydroxysteroid Dehydrogenases in Human Adult and Fetal Brain

Sardana Belkin, B.S., Pediatrics, Cornell Medical, 525 East 68th St. RM LC-929, New York NY 10021; William M. Byne, M.D., Marilyn Khanna, Ph.D., Kui-Chi Cheng, Ph.D.

Summary:

Objective: 3α-hydroxysteroid dehydrogenase activity produces neuroactive tetrahydrosteroids that interact with the inhibitory gamma-aminobutyric acid receptor. This interaction leads to anxiolytic, analgesic, anticonvulsive, and anesthetic responses. The objective of the present research was to determine the distribution of type I (high affinity) and type II (low affinity) 3α-hydroxysteroid dehydrogenases in human adult and fetal tissues, including brain.

Methods: The distribution of 3α-hydroxysteroid dehydrogenases was determined in specimens from autopsied adult and second trimester fetal brain, heart, kidney, liver, and lung. Activity assay, immunoblotting, and reverse transcription-polymerase chain reaction (RT-PCR) were employed.

Results: Moderate levels of enzyme activity were found in cerebellum, cingulate cortex, frontal cortex, hypothalamus, and pons. Less activity was found in medulla, midbrain, occipital cortex, temporal cortex, olfactory bulb, and pituitary. Type II enzyme was expressed in the brain and peripheral tissues of the fetus and adult. Type I enzyme was expressed only in the adult liver.

Conclusions: As 3α-hydroxysteroid dehydrogenase is involved in the production of neuroactive steroids, its presence in the fetal

and adult brain may have significant implications with regard to normal and abnormal brain development and function.

NR536 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Chronic Antipsychotic Treatment Induces a Long-Lasting AP-1 Complex in the Rat Striatum

Patrick J. Rogue, M.D., LNMIC VPR 416, CNRS Centre Neuroch, 5 Rue Blai Pascal, Strasbourg 67084, France; Guy Vincendon, M.D.

Summary:

A single injection I.P. of haloperidol (2 mg/kg) produces a rapid and transient increase in c-*fos* and *jun* B mRNA in the dorsal striatum of the rat. These inductions are also found in the nucleus accumbens, and are specifically blocked by pretreatment with a specific D_2 agonist (1 mg/kg quinelorane). Using gel-shift assays, we studied the effect of haloperidol on the AP-1 binding activity of nuclear extracts from the striatum. A single acute injection (2 mg/kg) rapidly determines a significant increase in the AP-1 binding activity in both the dorsal and the ventral striatum. This induction is transient and returns to normal with 24 hours, and it is prevented by pretreatment with a specific D_2 agonist (1 mg/kg quinelorane).

The clinically relevant therapeutic effects of antipsychotic drugs are delayed. Thus, we further studied the effect of prolonged haloperidol administration (2 mg/kg for 15 days) on striatal IEG expression. Both c-*fos* and *jun* B induction were significantly desensitized, though not completely abolished. However, despite this down-regulation, AP-1 binding activity remained elevated at levels comparable to those seen after acute haloperidol administration. This increase persisted for at least four days following the last administration of haloperidol. Similar results were found in the dorsal and in the ventral striatum. This suggests that the composition of the AP-1 transcription factor complex is modified upon prolonged neuroleptic administration.

The significance of these results for the mode of action of antipsychotics will be discussed.

NR537 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Effects of Repeated Cocaine Administration on Sensory Inhibition in Rats: Preliminary Data

Nashaat N. Boutros, M.D., Dept of Psych, Ohio State Univ, 1670 Upham Drive, Columbus OH 43210-1252; Norman L. Uretsky, Ph.D., Jennifer J. Liu, Ronel Millana

Summary:

Objective: Repeated cocaine administration has been associated with the development of paranoid schizophrenia. Changes in sensory processing produced by cocaine may provide a useful animal model of this condition. In order to assess the reversibility of the changes in sensory habituation observed with cocaine administration, we determined the electrophysiological responses to the S1 and S2 paired (S1 and S2) stimuli and the S2/S1 ratio 9.

Methods: Twelve male Sprague Dawley rats (250-300 gm) were included in this study. A recording electrode was placed on the central cortical region and a reference electrode placed in the frontal sinus. Animals were injected with either cocaine (20 mg/kg, IP) or saline for five consecutive days, and their auditory evoked responses were recorded after each injection. Following the five injection days, the animals were left in their home cages for nine days. After the nine days, their evoked responses to the auditory clicks were recorded for two days but without the drug or saline injections.

Results: During the five days of injection, the S_1 amplitudes of cocaine-treated animals were significantly decreased compared to those from the animals treated with normal saline (df 1, $F = 4.713$, $p = 0.05$). This decrease in S_1 amplitude was not found nine days after the last exposure to cocaine. The S_2/S_1 ratio was significantly greater in cocaine-treated animals compared to control animals during the days in which the animals received drug or saline injections (df 1, $F = 6.727$, $p < 0.03$) (Fig. 1). However, in contrast to the S_1 amplitude, the S_2/S_1 ratios remained significantly elevated nine days after the injections were discontinued (df 1, $F = 6.122$, $p < 0.04$).

Discussion: Acute cocaine administration caused a significant decrease in S_1 amplitude, as well as a significant increase in the S_2/S_1 ratio, indicating a strong effect of cocaine on sensory habituation mechanisms. The effect of cocaine on S_1 response was short lived, as it was not. This is in contrast to the cocaine-induced increase in the S_2/S_1 attenuation ratio, which remained significantly elevated after nine days of no drug exposure. These findings are consistent with the hypothesis that cocaine affects S_1 amplitude and S_2/S_1 ratios through different neurotransmitter systems.

NR538 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Protocol for Neuroimmunologic Animal Models for Psychiatric Disease Based on Paraneoplastic Limbic Encephalopathy

John L. Black, M.D., Dept. of Psych/Psychology, Mayo Clinic, 200 First Street SW W11A, Rochester MN 55905-0001; Guy E. Griesmann, M.S., Mieko Oguro-Okano, Ph.D., Terry P. Snutch, Ph.D., Vanda A. Lennon, M.D.

Summary:

Objective: To develop neuroimmunologic animal models for psychiatric disease based on insights gained from paraneoplastic limbic encephalopathy associated with small cell lung carcinoma for which autoantibodies reactive with N and P/Q type calcium channels have been identified as a marker.

Method: A Lambda Zap ® II cDNA library prepared from size-fractionated RNAs of a small cell lung carcinoma was screened for neuronal calcium channel alpha-1 sequences of A, B, and D classes (P/Q, N and L channel subtypes). Identified candidate cDNAs were excised and rescued in phagemid form for further characterization.

Results: Overlapping oligonucleotides encoding segments of all three calcium channel alpha-1 subunits were isolated and have been partially sequenced. The next step will be to construct protein expression vectors appropriate for induction of autoimmunity in rodents.

Conclusions: The protocol described can be used to find specific genes when a short segment of the gene in question is available. Subsequently genes can be cloned into protein expression systems to produce products useful for investigating the neuroimmunologic basis of some psychiatric diseases.

Supported in part by NIH grant CA37343.

NR539 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Menstrual Cycle Effects on Measures of Cognitive Variables

Allan Tasman, M.D., Dept of Psych & Behav Sci, Univ of Louisville Sch Me, 500 S. Preston St. A-Bldg R216, Louisville KY 40292-0001; Anita C. Maiste, Ph.D., Theresa A. Hahn, B.S., Rajani Adiga

Summary:

Alterations in event related potentials (ERPs) have previously been correlated with a variety of psychiatric disease states and shown to be influenced by age, diurnal cycle, subject alertness, and gender. ERP studies involving women have, until recently, ignored possible effects of the menstrual cycle on ERP measurements. This study examines whether changes in ERP measure-

ments occur as a function of menstrual cycle phase, and if so, to what degree. It documents these relationships so that they may be accounted for in the planning of future studies involving women. Nineteen women, aged 20 to 39 years, were each studied for an entire menstrual cycle for changes in the P1, N1, P2, N2, and P3 components of a visual event related potential (VERP) and the I, II, III, IV, and V components of an auditory brain stem response evoked potential. Basal body temperature, performances on a cognitive task, empirical measures of mood, the onset of menses, and the luteinizing hormone surge were also monitored during this time. ERP sessions were categorized as ovulatory, premenstrual, or follicular based on the occurance of the first day of menses and the luteinizing hormone surge. Results will be presented demonstrating ERP and menstrual cycle phase correlations.

NR540 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Lithium and Neuroleptics in Combination: Is There Enhancement of Neurotoxicity Leading to Permanent Sequelae?

Stephen A. Goldman, M.D., CDER/OPD HFD-6, Food & Drug Administra., 5600 Fishers Lane 9B04 Parklawn, Rockville MD 20857

Summary:

Objective: Neurotoxicity in relation to concomitant lithium and neuroleptics has been an ongoing issue, with particular focus on the lithium-haloperidol combination. The object of this study is to examine whether use of lithium with neuroleptics enhances neurotoxicity leading to permanent sequelae.

Method: The FDA Spontaneous Reporting System database and extant literature were reviewed for lithium-neuroleptic neurotoxicity spectrum syndrome cases. Lithium alone, lithium/haloperidol and lithium/non-haloperidol neuroleptics groups, each paired for recovery and sequelae, were established. Factors including age, psychiatric diagnoses and lithium level in relation to reaction onset were tabulated.

Results: Statistical analysis included pairwise comparisons of lithium levels using the Wilcoxon Rank Sums procedure and logistic regression analysis. Lithium alone and lithium/non-haloperidol neuroleptics groups showed significant statistical differences in median lithium levels between recovery and sequelae pairs; the lithium/haloperidol pair did not. Lithium level was associated with sequelae development overall and within the lithium alone and lithium/non-haloperidol groups; no such association was found for the lithium/haloperidol group.

Conclusions: While database limitations, including lack of a denominator measuring medication exposure, must be considered, the lithium/haloperidol results are notable. These findings may suggest a possible impact of pharmacodynamic factors in the lithium/neuroleptic combination.

NR541 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Comparison of the CNS Pharmacology of Two Formulations of Bupropion: Sustained Release and Immediate Release

Virginia M. Boncek, B.A., Pharmacology, Burroughs Wellcome, 3030 Cornwallis Road, Res Triangle Park NC 27709; Barry R. Cooper, Ph.D., Frank E. Soroko, B.S., Bernard T. Kenney, B.S.

Summary:

Introduction: Bupropion SR (HCl, 2-hr sustained release) has been developed to improve the dosing regimen and lower the incidence of side effects.

Objective: Three experiments were done in mice to compare the CNS effects of bupropion SR and IR for 1) potency in a test that predicts antidepressant efficacy, 2) seizure induction at high doses, and 3) stimulation of locomotor activity.

Method: Potency: Test compound was injected, tetrabenazine was injected 30 min later, and the subjects were scored for antagonism of the sedation produced by tetrabenazine.

Seizure: Subjects were observed for up to four hr after injection for signs of seizure and lethality. Stimulation: Locomotion was measured in automated open field activity chambers for 90 min after injection.

Results: The 95% confidence limits of the calculated ED_{50}s for antagonism of tetrabenazine-induced sedation overlapped, indicating no difference in antidepressant potency. At 366 mg/kg p.o., SR produced a longer latency to seizure and induced seizure and death in fewer subjects than did IR. At the ED_{84} for tetrabenazine antagonism, IR increased locomotion more than SR over the first 30 minutes. After 30 minutes, locomotion counts for the two formulations did not differ.

Summary: Bupropion SR and IR were equipotent for antagonism of tetrabenazine-induced sedation. At higher doses, SR showed less seizure induction, mortality, and locomotor stimulation. Pharmacokinetic data from other studies suggest that the differences seen here between SR and IR are correlated with differences in plasma drug levels.

NR542 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Catatonia, Parkinsonism, Tardive Dyskinesia and Akathisia in a Chronically Hospitalized Psychiatric Population

George Bush, M.D., Psychiatry, Mass General Hosp. East, CNY-9, Charlestown MA 02129; Andrew Francis, M.D., Georgios Petrides, M.D.

Summary:

Objectives: The potential phenomenonological overlap between catatonia, parkinsonism, tardive dyskinesia, and akathisia was examined to determine if catatonia could be distinguished from and/or coexist with these motor disorders commonly seen in psychiatric patients.

Methods: Chronically hospitalized psychiatric inpatients (N = 42) with schizophrenia, catatonic type (295.2) were rated for catatonia, using the Bush-Francis Catatonia Rating Scale [BFCRS], parkinsonism using the Simpson-Angus Neurological Rating Scale, and four items from the Webster Rating Scale, dyskinesia using the Abnormal Involuntary Movements Scale [AIMS], and akathisia using the Hillside Akathisia Rating Scale.

Results: Of the 42 patients, 29 (69%) had catatonia per the BFCRS, 22 (52%) had parkinsonism, 21 (50%) had tardive dyskinesia, and three (7%) had akathisia. Catatonia was the sole diagnosis in nine (21%), with patients displaying a mean total BFCRS score of 10.8 (S.D. 4.1) and an average of 5.8 signs (S.D. 2.2). Catatonia coexisted with parkinsonism in five (12%), tardive dyskinesia in four (10%), and both parkinsonism and tardive dyskinesia in 10 (24%). Aside from rigidity, cross-sectional phenomenologic overlap between syndromes was minimal.

Conclusions: Catatonia was readily distinguishable from motor disorders commonly found in psychiatric patients. Catatonic phenomenology in a chronic psychiatric population is described.

NR543 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Psychopathology Associated with Intracranial Tumors

M. Beatriz Currier, M.D., 1925 Brickell Ave #D-1913, Miami FL 33129; Thania V. Quesada, M.D.

Summary:

Patients with intracranial neoplasms (ICN) may develop an array of mental status changes. Few studies, however, have addressed the presence of distinct psychiatric disorders among this population. The purpose of this study is to examine the most common requests for psychiatric consultation among adult patients with ICN, to determine the presence and frequency of co-morbid psychiatric disorders, and to assess the relationship between patients with ICN and psychiatric disorders by identifying demographic, psychosocial, neurological, and tumor variables significantly associated with these psychiatric disorders.

Retrospective review of 3,794 psychiatric consultations over a three-year period revealed 28 patients with ICN. Standard clinical interviews using DSM-III-R criteria confirmed psychiatric diagnoses. Neuroimaging and tissue biopsy confirmed tumor diagnoses. Thirteen patients had benign ICN, 15 patients had malignant ICN. Twenty were supratentorial, five were infratentorial, and three were both supratentorial and infratentorial.

Eighty-two percent (23/80) of the patients had current psychiatric diagnoses. Even though "rule-out depression" was the most common request, dementia and/or delirium were the most common diagnoses accounting for 41% of the diagnoses. Premorbid psychiatric history, neurological variables, tumor type, and topography were not significantly associated with a particular psychiatric diagnosis and did not differentiate patients at risk for psychiatric comorbidity.

NR544 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Subtle Neurological Deficits and Psychopathological Findings in a Group of Homeless and Non-Homeless Veterans

Gerard Romain, M.D., Psychiatry, University of Miami VAMC, 1201 NW 16th Street, Miami FL 33125; Richard Douyon, M.D., Paul A. Guzman, M.D., Sue Ireland, Ph.D., Lourdes M. Mendoza, M.D., Fernando J. Milanes, M.D.

Summary:

Homeless individuals face a complex array of biopsychosocial problems that serve as barriers to rehabilitation if not identified and specifically addressed.

Objective: the purpose of the present study was to evaluate the hypothesis that homeless relative to non-homeless individuals would display higher levels of psychopathology and neurological deficits, particularly among frontal lobe or "executive" functions.

Method: Acutely homeless (n = 18), chronically homeless (n = 15), and non-homeless subjects attending the psychiatry service of a metropolitan VA hospital were administered a battery of neurological and psychosocial measures. Exclusion criteria included past and present schizophrenic, manic, floridly psychotic, and demented symptomatology.

Results: our findings supported the study hypothesis. In comparison to non-homeless subjects, homeless individuals exhibited higher levels of prior criminal activity, hostility, family history of psychiatric illness, and neurological deficits, but lower levels depression. There were no differences with their levels of HIV-1 high risk behavior and substance abuse. Chronically homeless subjects exhibited greater depression but less criminal behavior than acutely homeless. A positive relationship between hostility and neurological soft signs was also observed among chronically homeless subjects.

Conclusion: these findings suggest that a substantial subset of homeless veterans suffer from "occult" neuropsychiatric deficits. Recommendations regarding psychopharmacological, biopsychosocial, and training interventions are provided.

NR545 Wednesday, May 24, 3:00 p.m.-5:00 p.m.

Laterality of Extrapyramidal Symptoms Related to Positive and Negative Symptoms of Schizophrenia

Dong Won Shin, M.D., Psychiatry, Yonsei University, C.P.O. Box 8044, Seoul 120, Korea; Sungkil Min, M.D.

Summary:

This study was designed to test a hypothesis that positive symptoms are related with the asymmetry in extrapyramidal symptoms caused by antipsychotic medication, while negative symptoms are not. Thirty schizophrenic patients were examined for evaluation of positive, negative symptom with PANSS, and extrapyramidal symptoms in right and left extremities after one and three weeks treatment with antipsychotic drugs. One week after neuroleptic medication, there were no correlations between positive or negative symptom scores and extrapyramidal symptom scores in each side of body.

Three weeks after neuroleptic medication, positive symptom scores were significantly correlated with the scores of the right side extrapy symptoms but not with those of the left side.

These findings suggest that negative symptoms of schizophrenia are related with the pathological process of both brain hemispheres while positive symptoms are related with asymmetrical pathological process in hemispheres.

NR546 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Utility of the Obsessive Compulsive Drinking Scale to Measure Outcome During and Alcoholism Treatment Trial

Raymond F. Anton, M.D., Inst of Psych, Med Univ of SC, 171 Ashley Ave, Charleston SC 29425; Darlene H. Moak, M.D., Patricia K. Latham, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to appreciate the need to measure alcohol craving more systematically during alcoholism treatment and research and that the Obsessive Compulsive Drinking Scale provides a tool to quantify changes in alcoholism improvement or relapse over time.

Summary:

Although alcohol "craving" is important to evaluate during alcoholism treatment, its definition and measurement have remained ambiguous. The Obsessive Compulsive Drinking Scale (OCDS), a reliable and valid self-rating scale that quantifies one aspect of craving involving alcohol thoughts and drinking behaviors, was evaluated for utility during a treatment trial for alcoholism.

Forty-one (29 male; 12 female) outpatients (age 45 ± 9 yrs.) who met DSM-III-R criteria for alcohol dependence were given the OCDS at baseline and weekly during a 12-week, double-blind treatment trial of naltrexone and cognitive behavioral therapy. Weekly alcohol intake was measured using the time-line follow-back method. The mean baseline OCDS score for all patients was 17 ± 5. During treatment, abstainers (N = 20) mean score decreased to 3 ± 2, slip drinkers (N = 13) scores decreased to 7 ± 3, while relapsers (N = 8) scores decreased to 11 ± 3. Repeated measures ANOVA showed that the OCDS scores differed between the drinking outcome groups over the 12-week trial ($p < .0001$).

These results support the utility of this easily administered (five minutes) self-rating scale in the measurement of one dimension of craving during alcoholism treatment and outcome research.

References:

1. Anton RF, Moak DH, Latham P: The Obessive Compulsive Drinking Scale: a self rated instrument for the quantification of

thoughts about alcohol and drinking behavior. *Alcoholism: Clinical and Experimental Research,* in press.

2. Modell JG, Glaser FB, Cyr L, Mountz JM: Obsessive and compulsive characteristics of craving for alcohol in alcohol abuse and dependence. *Alcoholism: Clinical and Experimental Research* 16:272–274, 1992.

NR547 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Drug Craving Versus Withdrawal Symptoms: Are They Different?

Juris Mezinskis, Ph.D., Psychology, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Eugene C. Somoza, M.D., Susan Dyrenforth, Ph.D., Mark Cohen, Ph.D., R. Jeffrey Goldsmith, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate whether drug graving can be reliably measured, and whether craving can be distinguished from other negative feelings.

Summary:

The goal of this study was to investigate whether drug craving can be reliably measured, and whether craving can be distinguished from other negative feelings. Previous studies have questioned whether craving is a distinct variable or just a term used by drug-dependent patients to describe negative feelings associated with drug withdrawal. A review of the literature identified eight symptoms associated with drug withdrawal (anxiety, depression, restlessness, anger, irritability, frustration, impatience, and poor concentration). Inpatients being treated in a 28-day hospital-based treatment program were asked to rate these eight negative states using a four-point scale. They used the same scale to quantify the intensity and frequency of their craving for drugs of abuse. Factor analysis of 5,867 daily ratings, made by a total of 376 patients yielded two distinct factors with eigenvalues >1. All eight negative states loaded on factor one (factor loadings >.70, which explained 53% of the total variance). All ratings for the intensity and frequency of drug craving loaded on the second factor (factor loadings >.70, which explained 15% of the total variance). Additional analysis for specific drugs of abuse (alcohol, cocaine, cannabis) consistently revealed two factors, one for negative feeling states and one for craving. The data suggest that drug craving is a distinct state, separate from mood. This finding has significant implications for treatment, i.e., craving and mood should be addressed separately.

References:

1. Weddington WW, et al: Changes in mood, craving, and sleep during short term abstinance reported by male cocaine addicts. *Arch Gen Psychiatry* 47:861–868.

2. Rankin H, Hodgson R, Stockwell T: The concept of craving and its measurement. *Behav Res and Therapy* 17:389–396, 1979.

NR548 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Distinguishing Eating Disorder Preoccupations and Ritual

Rosalind G. Hoffman, M.D., Psychiatry, NY Hospital Cornell, 21 Bloomingdale Road, White Plains NY 10605; Steven J. Romano, M.D., Suzanne Sunday, Ph.D., Katherine A. Halmi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that preoccupations and ritualistic behaviors are an integral aspect of patients with eating disorders and are clinically distinct from the ruminations and behaviors often encountered in patients with major depression.

Summary:

Comorbidity of major depression (MD) and the eating disorders, including anorexia nervosa and bulimia nervosa, has been well documented (1, 2). In order to show that the preoccupations and ritualistic behaviors observed in eating-disordered patients are clinically distinct from those depressive ruminations and behaviors encountered in patients with MD, the Yale-Brown-Cornell Eating Disorders Scale (YBC-EDS), a clinician-rated, semistructured interview to evaluate the presence and severity of eating disorder specific preoccupations and ritualistic behaviors, was administered to three study groups. The first included patients meeting DSM-IV criteria for a current eating disorder without a history of affective disorder; the second was comprised of patients meeting DSM-IV criteria for current major depression without a history of an eating disorder; and the third group were patients meeting criteria for both a current eating disorder and major depression. Analysis of variance was conducted, and mean scores and standard deviations were obtained for the following categories for each study group: preoccupations, rituals, a total score, motivation, and global severity. Whereas eating disorder patients had high scores on both preoccupations and rituals, none of the patients with MD exclusively had any eating disorder rituals, and only a few had minor eating disorder preoccupations. The YBC-EDS appears to be rating preoccupations and ritualistic behaviors specific for eating disorders and not depression. However, comorbid depression intensifies the core eating disorder preoccupations and rituals but does not affect the motivation score.

References:

1. Halmi, et al: Comorbidity of psychiatric diagnosis in anorexia nervosa. *Arch Gen Psych* 48:712–718, 1991.

2. Laessle R, Kittl S, Fichter M, et al: Major affective disorder in anorexia nervosa and bulimia. *Br J Psych* 151:785–789, 1987.

NR549 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Linkage Study of Chromosome 18 Marker Loci and Bipolar Disorder

Peter A. Rao, M.D., Medical Genetics, NYS Psych Inst, 722 W 168th St Box 58, New York NY 10032; James Knowles, M.D., Jean Endicott, Ph.D., Jurg Ott, Ph.D., T. Conrad Gilliam, Ph.D., Miron Baron, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand what a linkage study is; understand the different parametric and nonparametric methods for linkage testing; and understand the current status of molecular genetic studies of psychiatric, especially bipolar disorder.

Summary:

The etiology of bipolar disorder is explained in part by inheritance. Molecular genetic studies currently are aimed at identifying regions of the genome that contain disease genes for bipolar disorder using the positional cloning paradigm. Recently, Berrittini et al. (1994) reported preliminary evidence for linkage of bipolar disorder and markers in the pericentromeric region of chromosome 18. Our research group is one of several that are attempting to replicate and expand upon this finding. We have ascertained and collected a sample of 57 pedigrees segregating bipolar disorder, which contain a total of 1508 individuals, 793 of whom are affected with mood disorder. Of those affected, 532 have RDC diagnoses of definite or probable bipolar I, bipolar II with major depressive disorder, unipolar manic, schizoaffective (bipolar type),

recurrent schizoaffective (depressed type) or recurrent unipolar major depressive disorder ("intermediate diagnostic model"); and of these , 350 have bipolar I, bipolar II with MDD, unipolar manic, or schizoaffective (bipolar type) disorder ("narrow diagnostic model"). DNA from each individual has been genotyped at each of eight polymorphic dinucleotide-repeat marker loci using standard techniques (D18S47, D18S56, D18S44, D18S45, D18S53, D18S37, D18S453 and D18S62). Data are analyzed for linkage using the lod score, affected sib pair (ASP), and affected pedigree member (APM) methods.

Preliminary analysis of the first 19 pedigrees typed reveals largely negative lod scores (ranging from 0.345 to -24.1) for both recessive and dominant models and for both narrow and intermediate diagnostic models. While a few pedigrees individually have lod scores > 1 for several markers, there is no statistically significant heterogeneity among the 19 pedigrees. Testing for linkage using the APM method reveals preliminary evidence for linkage at only the $p < 0.01$ level of significance (max APM statistic = 2.5). We will present final analyses for all 57 pedigrees. In addition, we will discuss our results in the context of current linkage findings for bipolar disorder.

References:

1. Baron M, et al: A pedigree series for mapping disease genes in bipolar affective disorder. *Psychiatric Genetics* 4:43–55, 1994.

2. Berrittini WH, et al: Chromosome 18 DNA markers and manic-depressive illness: evidence for a susceptibility gene. *PNAS* 91:5918–5921, 1994.

NR550 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Enhanced Adrenocorticotropic Hormone Response to Metyrapone in PTSD

Rachel Yehuda, Ph.D., Psychiatry, Mt. Sinai School of Med, 116A 130 West Kingsbridge Road, Bronx NY 10468; Robert A. Levengood, M.D., Ling Song Guo, M.D., Skye A.C. Wilson, B.A.

Educational Objectives:

To have a deeper understanding of the multifaceted approach to elucidating hypothalamic-pituitary-adrenal-axis abnormalities in psychiatric disorders. The data here are definitive and provide a final test of the hypothesis of negative feedback inhibition in PTSD.

Summary:

We have previously hypothesized that individuals with posttraumatic stress disorder show an enhanced negative feedback inhibition of cortisol. This hypothesis stems from three separate observations: PTSD patients show lower cortisol levels; they show increased numbers of lymphocyte glucocorticoid receptors; and they show an exaggerated decrease in cortisol levels in response to dexamethasone. In the present study, we wished to further explore the nature of negative feedback inhibition in PTSD using the metyrapone stimulation test. Metyrapone blocks the synthesis of cortisol from its immediate precursor thereby allowing a transient "unmasking" of the pituitary and brain from the influences of negative feedback. Oral doses of metyrapone (2.5 g) were administered to 12 combat veterans with PTSD and eight normal controls at 10:00 a.m.

Metyrapone administration resulted in a significant decrease in cortisol levels in both groups (PTSD cortisol: 1.4 ± 1.5 ug/100 ml; control cortisol: 1.8 + 1.6 ug/100 ml). The peak plasma ACTH level in response to metyrapone was more than twice as large in the PTSD group (220.07 ug/100 ml) as in the control group (103.25 ug/100 ml). PTSD patients showed a 9.6-fold increase in ACTH levels on the metyrapone day (as compared to the ACTH levels obtained at the same time on the baseline day), whereas normal controls showed a 3.9-fold increase (which is within the normal endocrinological range) $T = 2.43$; $df = 18$; $p = .02$).

The data suggest that pituitary activity may be quite high in PTSD, perhaps as a result of CRF hypersecretion. However, because of an enhanced negative feedback regulation, ACTH levels may appear to be normal or low under basal conditions. The findings support the idea of an enhanced negative feedback inhibition in PTSD.

References:

1. Yehuda R, Southwick SM, Krystal JM, et al: Enhanced suppression of cortisol following dexamethasone administration in combat veterans with posttraumatic stress disorder and major depression disorder. *American Journal of Psychiatry 150:83–86, 1993.*

2. Yehuda R, Boisoneau D, Lowy MT, Giller EL: Dose-response changes in plasma cortisol and lymphocyte glucocorticoid receptors following dexamethasone administration in combat veterans with and without posttraumatic stress disorder. *Archives of General Psychiatry,* provisionally accepted.

NR551 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Severe Stress Predicts Early HIV Disease Progression

John M. Petitto, M.D., Dept of Psych, Univ of Fl Hlth Sciences, P.O. Box 100256, Gainesville FL 32610; Jane Leserman, Ph.D., Diane O. Perkins, M.D., Carole Murphy, M.D., David Gettes, James D. Folds, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize how life stress may impact on immunity and health.

Summary:

Although many investigations have documented changes in immune status in association with severe life stress and depression, there is a paucity of data indicating that such immune alterations are clinically significant. Using a longitudinal, prospective design, we are conducting studies to test the hypotheses that stressful life events and associated depressive symptoms are predictive cofactors of disease progression in HIV-infected gay men. Converging evidence using different disease endpoints and statistical analytic strategies showed that severe life event stress is associated with early HIV disease progression. Analysis over the first 42 months of this cohort study revealed that higher severe life stress increased the risk/odds of developing HIV disease progression by nearly four-fold.

This longitudinal, prospective study is the first to demonstrate that severe life stress predicts both the likelihood and severity of *early* HIV disease progression. Ongoing study of this cohort provides the opportunity to now assess systematically the effects of severe life stress and associated depressive symptoms on the later stages of HIV disease progression.

References:

1. Petitto JM, Folds JD, Ozer H, et al: Abnormal diurnal variation in circulating natural killer cell phenotypes and cytotoxic activity in major depression. *Am J Psychiatry* 149:694–696, 1992.

2. Stein M, Miller AH, Trestman RL: Depression, the immune system and health and illness. *Arch Gen Psychiatry* 48:171–177, 1991.

NR552 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Classifying Subtypes Among Depressed Inpatients

John W. Goethe, M.D., Research, Institute of Living, 400 Washington Street, Hartford CT 06106-3309; Bonnie L. Szarek, R.N.

Educational Objectives:

To discuss subtypes of depression; to compare the subtypes derived from factor analysis to the DSM classification of MDD; to discuss potential applications of these data to national health care policy and planning.

Summary:

Objective: To determine if DSM criteria for major depressive disorder (MDD), as applied in the routine clinical setting, define distinct subtypes among depressed inpatients.

Methods: Using a checklist based on DSM-III-R, the treating clinician recorded the presence/absence of each MDD criterion for consecutive admissions (n = 876) assigned this diagnosis. Data were analyzed using chi square, t-tests, and principal components factor analysis.

Results: Four distinct factors were identified (endogenous (I), atypical (II), suicide (III), and psychotic (IV)), explaining 33.4% of the variance (11.7%, 8.6, 7.2, and 6.0, respectively). The factors were validated via reanalysis of two randomly selected subsamples, and this procedure showed high between-group correlations (r = .97, .93, .88, and .75, respectively). Further analysis revealed that Factors I and III were associated with a greater number of prior hospitalizations ($p < .05$); Factor II was more common in females ($p < .05$), and Factors I and IV were associated with older age ($p < .01$).

Conclusions: These findings suggest that DSM criteria for MDD, as used in clinically practice, define distinct subtypes among severely ill inpatients. The factors derived are generally consistent with other research and may be useful in characterizing patient populations for health care policy and reimbursement purposes. Subsequent studies will evaluate the ability of these factors to predict outcome and resource utilization.

References:

1. Nelson JC, Charney DS: The symptoms of major depress illness. *Am J Psychiatry* 138:1–13, 1981.

2. Clark LA, Watson D: Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *J Abnorm Psychol* 100:316–336, 1991.

NR553 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Withdrawn

NR554 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Psychopathology in the Relatives of Seasonal Winter Depressives

David S. Schlager, M.D., SUNY at Stony Brook, HSC T10, Stony Brook NY 11794; Daniel N. Klein, Ph.D., Joseph E. Schwartz, Ph.D., Karen Kasch, M.S., Laura M. Klein, M.S.W.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize the familial clustering of seasonal winter depression and its implications for nosologic validity and pathophysiology of the disorder.

Summary:

A family study design was used to compare lifetime rates of mood and other Axis I disorders among 114 first-degree relatives of 24 probands with major depressive disorder-winter-seasonal type (SAD), 110 first-degree relatives of 23 probands with non-seasonal recurrent major depression (MD-NS), and 223 first-degree relatives of 44 normal controls (NC). All available relatives were directly administered the SCID, including supplementary questions for assessing seasonal mood variation, and the Seasonal Pattern Assessment Questionnaire (SPAQ). Logistic regression controlled for proband gender and comorbidity, and direct interview status, age, gender, and generation of the relative. Lifetime rates of major depressive disorder (MDD) and recurrent MDD, respectively, were 34% and 17% among relatives of SAD probands, 27% and 10% among MD-NS relatives, and 15% and 5% among NC relatives. Logistic regressions revealed significantly higher rates of mood disorders, of MDD, of recurrent MDD, and of MDD with treatment among the relatives of SAD probands compared with normals. In contrast, the relatives of SAD and MD-NS probands did not differ on rates of any Axis I disorder. In the subsample of relatives with seasonality data, SPAQ-defined rates of SAD were 13.8% and 2.4% among relatives of SAD and NC probands, respectively ($p < .09$). Findings support the validity of SAD as a major depressive disorder and provide some evidence for familial aggregation of seasonal mood disorder.

References:

1. Allen JM, Lam RW, Remick RA, et al: Depressive symptoms and family history in seasonal and non-seasonal mood disorders. *Am J Psychiatry* 150:443–448, 1993.

2. Klein DN, Ouimette PC, Kelly HS, et al: Test-retest reliability of team consensus best-estimate diagnoses of Axis I and II disorders in a family study. *Am J Psychiatry* 151:1043–1047, 1994.

NR555 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Disability and Depression Among High Utilization Primary Care Patients

David J. Katzelnick, M.D., Dean Foundation, 8000 Excelsion Dr Ste 203, Madison WI 53717; Kenneth A. Kobak, M.S.W., John H. Greist, M.D., James W. Jefferson, M.D.

Educational Objectives:

To recognize the high prevalence and under diagnosis of depression among high utilizers of medical services; to understand the impact of depression on disability in both high and non-high utilizers of medical services.

Summary:

Data were obtained on approximately 50,000 patients enrolled in the DeanCare HMO. Patients were identified as high utilizers (HU) if their total cost of service utilization (inpatient, outpatient, and medications) during both of the two most recent 12-month periods was at or above the median utilization for the entire HMO plus $1,400 (the estimated cost of treating depression in primary care for one year).

HU comprised 8.7% of the total HMO population and accounted for 37% of the total utilization. HU were significantly older (53.2 vs. 50.1 yrs, $t(947) = 3.11$, $p = .002$) and significantly more likely to be female (67% vs. 60%, $X^2(1) = 9.96$, $p = .002$) than non-high utilizers (NHU).

A survey containing 1) the eight-item depression screener from the Medical Outcomes Study (MOS) and 2) a modified version of the MOS short-form general health survey was sent to the HU from two primary care clinics (n = 786) and to an equal number of randomly selected NHU from these two sites.

A significantly greater percentage of HU screened positive for depression (29%) than NHU (17%), $X^2(1) = 21.72$, $p < .001$. Within the high utilizer group, depressed HU scored significantly worse than nondepressed HU on overall health ratings, $t(249) = 5.35$, $p < .001$, bodily pain $t(244) = 4.07$, $p < .001$, number of days missed work, $t(152) = 2.15$, $p < .04$, and degree of work impairment, $t(174) = 4.12$, $p < .001$. Thirty-two percent of the women HU were also depressed, compared with 25% of men, $X^2(1) = 2.78$, $p < .01$. No significant age differences were found.

Of patients screening positive for depression on the MOS, only 19% of HU and 5% of NHU had been diagnosed as depressed by their primary care physician. Rates of these MOS identified depressed patients receiving antidepressant medication were 40% for HU and 9% for NHU. Only 31% of these MOS depressed HU and 5% of MOS depressed NHU received treatment with adequate doses.

Higher utilization is associated with significantly increased rates of depression and poorer health and occupational functioning. Depression increases impairment over and above utilization status. Surprisingly, depression in NHU was virtually undetected and untreated. The majority of depressed HU also were not diagnosed or treated. Identification and treatment of these patients by primary care physicians could have a significant impact on disability and utilization. A follow-up study is being conducted to determine if treatment of these depressed HU will impact disability and utilization.

References:

1. Katon W, Von Korff M, Lin E, Bush T, Ormel J: Adequacy and duration of antidepressant treatment and care. *Medical Care* 30:67–75, 1992.

2. Von Korff M, Ormel J, Katon W, Lin EH: Disability and depression among high utilizers of health care: a longitudinal analysis. *Archives of General Psychiatry* 49:91–100, 1992.

NR556 Thursday, May 25, 9:00 a.m.-10:30 a.m.

Disability in Geriatric Depression

George S. Alexopoulos, M.D., Department of Psychiatry, NYH-WD, Cornell UMC, 21 Bloomingdale Road, White Plains NY 10605; Konstantina Vrontou, M.D., Barnett S. Meyers, M.D., Tatsuyuki Kakuma, Ph.D., Robert C. Young, M.D., Maria Feder, M.D.

Educational Objectives:

To recognize clinical factors associated with disability in geriatric depression. This knowledge will be useful in the clinical evaluation of elderly depressives and in the design of outcome studies.

Summary:

Objective: The Medical Outcomes Study reported that depressed patients have impairment in functioning and well-being comparable to or worse than that of patients with chronic major medical illnesses. In elderly community samples, depression was shown to cause disability either directly or by exacerbating disability due to other causes. In contrast, studies of clinical geriatric populations found no association between severity of depression and disability. This study sought to identify clinical characteristics of geriatric depression that contribute to disability and examine the determinants of patient-rated and interviewer-rated disability in geriatric depressives.

Design: The subjects were 81 elderly patients with major depression and chronic intermittent depressive disorder with Hamilton (HDRS) scores higher than 17. Subjects were excluded if they had acute or severe medical illnesses, long-established dementing disorders, cognitive impairment for longer than six months, or a Mini-Mental State Examination (MMSE) score below 12. Disability was assessed with the Philadelphia-Multilevel Assessment Instrument (MAI) according to subjects' reports on specific activities of daily living and instrumental activities. A global disability score was given by raters using a five-point operationally defined scale. Potential determinants of disability were also identified and rated. These were: age, gender, marital status, education, severity of depression (HDRS), age of depression onset, duration of depressive episode, cognitive impairment (Mattis DRS), medical burden (CIRS-G), social support, and physical environment.

Results: Stepwise, multiple regression using demographic and clinical characteristics as independent variables showed that patient-rated disability was best accounted for ($r^2 = 0.40$, $F = 12.67$, $P < 0.0001$) by a model consisting of age ($P < 0.0001$), severity of depression (HDRS) ($P < 0.0001$), medical burden ($P < 0.004$), and education ($P < 0.02$). Logistic regression showed that interviewer-rated disability was predicted (chi square: 22.5, df = 3, $P < 0.0001$) by a model consisting of medical burden ($P < 0.0008$), cognitive impairment (Mattis DRS) ($P < 0.015$), and late onset of depressive syndrome ($P < 0.05$).

Conclusions: High severity of depression contributes to patient-rated disability, while onset of depression in late life was associated with interviewer-rated disability; late-onset depressives often have cognitive impairment and high medical morbidity. Advanced age, low education, and medical morbidity were associated with self-rated disability, while cognitive impairment and medical burden were associated with interviewer-rated disability. Differences between self-rated and interviewer-rated disability may explain the discrepancies between epidemiologic and clinical literature. In addition, these findings raise the question of whether clinicians are more likely to focus on medical and cognitive problems as determinants of disability than on the depressive syndrome itself.

References:

1. Laukkanen M, Era P, Heikkinen E: Factors related to coping with physical and instrumental activities of daily living among people born in 1904–1923. *Int J Ger Psychiatry* 8:287–296, 1993.

2. Lyness JM, Caine ED, Conwell Y, et al.: Depressive symptoms, medical illness, and functional status in depressed psychiatric inpatients. *Am J Psychiatry* 150:960–995, 1993.

NR557 Thursday, May 25, 9:00 a.m.-10:30 a.m.

The Role of Pterins in Depression and the Effects of Antidepressive Therapy

Prof. M.T. Abou-Saleh, Ph.D., Psychiatry, UAE Univ. EMHS, P.O. Box 17666, Alain, U.Arab Emirates

Educational Objectives:

To have a better understanding of the metabolic disturbance in depression; to gain knowledge of the impact of treatment on processes that accompany the neurohormonal changes in depression.

Summary:

Urinary excretion of neopterins (N) and biopterins (B) was measured in 48 patients with depression before and after treatment with placebo, antidepressants, and electroconvulsive therapy (ECT) and in 26 healthy control subjects. Patients prior to and after treatment had significantly greater neopterin/biopterin (N:B) ratios than control subjects. There was a significant correlations between N:B ratios and severity of depression and plasma cortisol. As a raised N:B ratio implies failure to convert neopterin in biopterin, it is possible that reduced availability of tetrahydrobiopterin, the essential cofactor for the formation of noradrenaline, serotonin, and dopamine, may exert rate-limiting control over the synthesis of monoamines implicated in the pathogenesis of depressive illness.

References:

1. Anderson DN, Abou-Saleh MT, Collins J, et al: Pterin metabolism in depression: an extension of the amine hypothesis and possible marker of response to ECT. *Psychol Med* 22: 863–869, 1992.

2. Abou-Saleh MT, Anderson DN, Collins J, et al: The role of pterins in depression and the effects of antidepressive therapy. *Biological Psychiatry* (in press).

NR558 Thursday, May 25, 12 noon-2:00 p.m.

Pharmacologic Treatment for the Antisocial Personality Disordered Alcoholic: A Pilot Efficacy Study

Jan L. Campbell, M.D., Psychiatry Service, VA Hospital, 4801 Linwood Blvd, Kansas City MO 64128; Elizabeth C. Penick, Ph.D., H. Mikel Thomas, M.D., Barry I. Liskow, M.D., Barbara J. Powell, Ph.D., Elizabeth J. Nickel, M.A.

Summary:

In a recent double-blind, random-assignment, placebo-controlled study of the efficacy of two pharmacologic interventions (nortriptyline and bromocriptine) with men alcoholics subtyped according to the presence or absence of certain coexisting psychiatric syndromes (Powell, et al., in press, 1995), we reported that the subgroup of men alcoholics with comorbid antisocial personality disorder (ASP) appeared to benefit significantly from the antidepressant nortriptyline at the end of a six-month followup. This unexpected finding stimulated us to look more closely at the drinking and sociopersonal outcomes of this relatively small subgroup (N = 29) of hospitalized ASP alcoholics who had been extensively studied at intake into the study and systematically followed after discharge. We divided the ASP alcoholics into those who did (N = 15; 51.7%) and those who did not (N = 14; 48.3%) satisfy inclusive DSM-III-R criteria for a current mood or anxiety disorder within one month of hospitalization on a VAMC substance abuse unit. Despite the very small N's, a reanalysis of the data showed for most outcome measures that: (1) ASP alcoholics, with a *current* mood/anxiety disorder improved most with pharmacologic treatment, relative to placebo, and (2) ASP alcoholics with *no current* mood/anxiety disorder failed to respond differently to treatment over the six months. These results suggest a possible useful and inexpensive approach to the long-term management of a very difficult-to-treat subgroup of male substance abusers.

(Supported by NIAAA #R01-AA-0736; NIDA #DA-06954)

NR559 Thursday, May 25, 12 noon-2:00 p.m.

Effect of Carbamazepine and Desipramine on Treatment Retention and Urine Toxicology in Outpatient Crack Cocaine Abusers

Jan L. Campbell, M.D., Psychiatry Service, VA Hospital, 4801 Linwood Blvd, Kansas City MO 64128; H. Mikel Thomas, M.D., Barry I. Liskow, M.D., William Gabrieli, M.D., Elizabeth C. Penick, Ph.D., Louise J. Laster, B.A.

Summary:

Description: Craving for cocaine is associated with early treatment dropouts among cocaine-dependent patients. Desipramine and carbamazepine have been reported to reduce craving. We assessed the efficacy of carbamazepine (CBZ) and desipramine (DSI) compared to placebo (PL) in retaining cocaine abusing patients and reducing positive urine toxicology in an outpatient treatment program.

Method: Subjects (N = 146) were drawn from patients enrolled in outpatient drug treatment at a community mental health center and met criteria for cocaine dependence. Subjects were randomly assigned to DSI, CBZ, or PL for a minimum eight-week trial, which could be extended to maximum of six months. Subjects participated in 10 hours of group/individual treatment weekly. Observed urine samples were obtained weekly and analyzed for cocaine and five other drugs of abuse.

Results: Survival analysis at eight weeks, 16 weeks, and six months indicated no difference between either drug and placebo in retaining subjects in treatment or in percent positive urine toxicology.

Comment: Results are consistent with those reported by other investigators and suggest that neither carbamazepine nor desipramine is efficacious in reducing craving or enhancing treatment retention and abstinence from crack in a heterogeneous outpatient population of crack-cocaine dependent patients.

(Supported by NIDA #R18 DA-06954)

NR560 Thursday, May 25, 12 noon-2:00 p.m.

Disability Income, Cocaine Use and Repeated Hospitalization Among Schizophrenic Cocaine Abusers: A Government Sponsored Revolving Door?

Andrew L. Shaner, M.D., Psychiatry, VA Medical Center, 11301 Wilshire Blvd B151Z, Los Angeles CA 90073; Thad A. Eckman, Ph.D., Lisa J. Roberts, M.A., Jeffery N. Wilkins, M.D., Douglas E. Tucker, M.D., Jim Mintz, Ph.D.

Summary:

Many people with serious mental illness are also addicted to drugs and alcohol. This comorbidity creates problems for patients, clinicians, health care systems, and social service agencies. One problem is that disability income, which many of these individuals receive to provide support for necessities, may facilitate drug abuse. In this study we assessed the temporal patterns of cocaine use, symptom severity, and psychiatric hospitalization in a sample of schizophrenic patients receiving disability income. A total of 105 schizophrenics were evaluated at hospital admission. The subjects were severely mentally ill, chronically dependent, frequently homeless, and repeatedly admitted to psychiatric hospitals. Psychiatric symptom severity and urinary benzoylecgonine were measured weekly for 15 weeks. Cocaine use, psychiatric symptoms, and hospital admissions all peaked during the first week of the month, shortly after the arrival of disability income on the first day. Subjects spent nearly half their total income on illegal drugs. These findings suggest that disability income may facilitate cocaine use early in each month, resulting in depletion of funds needed for housing and food, exacerbation of psychiatric symptoms, psychiatric hospitalization, and a high rate of homelessness. Ironically, income intended to compensate for the disabling effects of severe mental illness may instead have the opposite effect.

NR561 Thursday, May 25, 12 noon-2:00 p.m.

Monetary Reinforcement of Cocaine Abstinence in Cocaine Dependent Schizophrenics

Andrew L. Shaner, M.D., Psychiatry, VA Medical Center, 11301 Wilshore Blvd B151Z, Los Angeles CA 90073; Thad A. Eckman, Ph.D., Lisa J. Roberts, M.A.

Summary:

Many schizophrenics abuse drugs and alcohol, creating problems for patients, clinicians, social service agencies, and health care systems. Contingency management has been used to modify behaviors in both schizophrenia and substance abuse. This study was designed to determine whether contingency management could reduce cocaine use by schizophrenics.

Two male outpatients met DSM-III-R criteria for schizophrenia and cocaine dependence. They were homeless, actively psychotic, and frequent cocaine users despite enrollment in a dual-diagnosis treatment program. This study used an ABA design with each phase lasting two months. Twice weekly, in all three phases, subjects provided a urine specimen and information about income and expenditures. Urine specimens were assayed for benzoylecgonine. During the intervention phase, subjects provided an additional daily urine specimen that was tested for cocaine using a rapid qualitative test. If this test was negative, they were paid $25.

Efficacy was evaluated by comparing measures of cocaine use across the three phases.

Expenditures for cocaine, proportion of tests positive for cocaine, and the mean concentration of cocaine were significantly lower during the intervention than during the other two phases. These results suggest that modest monetary reinforcement of abstinence may decrease cocaine use among cocaine-dependent schizophrenics.

NR562 Thursday, May 25, 12 noon-2:00 p.m.

Family Physician's Detection of Alcohol Disorders: Survey and Chart Review

Marijo B. Tamburrino, M.D., Psychiatry, Medical College Ohio, 3000 Arlington Avenue, Toledo OH 43699; Denis J. Lynch, Ph.D., Rollin W. Nagel, M.A., Charles B. Travis, M.D.

Summary:

The purpose of this study was to explore family physicians' recognition and treatment of alcohol disorders. Five hundred sixty-six patients waiting to see their physicians at an academic family practice center completed a screening on depression and lifestyle habits. Ninety-two percent agreed to complete the survey and allow a chart review. Two hundred seventy-two persons were then invited for follow-up on the Diagnostic Interview Schedule (DIS). Seventy-two percent (N = 195) of these patients agreed to the DIS interview and made up this study's sample. On the DIS, 9.2% (N = 18) received a lifetime diagnosis of alcohol disorder: alcohol abuse (N = 2), alcohol dependency (N = 16). Thirty-three percent (N = 8) of the alcohol disorders were diagnosed by the family physicians. An extensive chart review explored whether the physician may have been aware of the drinking problem, but did not formally diagnose it. Chart review yielded no additional awareness of alcohol disorders. Physicians were significantly more likely to detect the diagnosis of alcoholism in older males than in young males. Interventions consisted mostly of medications (three antidepressants, three minor tranquilizers), and verbal encouragement to reduce drinking. The authors suggest that low recognition of alcohol disorders stems from cognitive dissonance, patient denial, and lack of sufficient training in this area.

NR563 Thursday, May 25, 12 noon-2:00 p.m.

Depression Screening in Women: Racial Differences

Marijo B. Tamburrino, M.D., Psychiatry, Medical College Ohio, 3000 Arlington Avenue, Toledo OH 43699; Rollin W. Nagel, M.A., Denis J. Lynch, Ph.D.

Summary:

Women waiting to see family physicians at six Toledo family practice sites were invited to participate in a survey study. The survey consisted of an eight-item, self-report, depression screening instrument (M.O.S. Depression Inventory), and demographics including age, race, marital status, education, and employment. The purpose of this study was to explore whether there was differences in depression between African-American and white females in family practice settings. Eighty percent of the women approached for this study agreed to participate (N = 453 whites and 128 African-Americans). Significantly more African-American women (46.1%) than white women (33.8%) scored above the cut-off for depression on the MOS (X^2 = 6.01, df = 1, p < .014). African-American high school graduates had significantly higher depression scores than white graduates. For white women only, depression was inversely related to level of education. The authors speculate that higher education may be less financially rewarding for African-American women than for white women, and that more specific measures of socioeconomic status be explored to understand the greater incidence of depression among African-American females.

NR564 Thursday, May 25, 12 noon-2:00 p.m.

The Effect of Alcohol on Social Phobic Anxiety

Joseph A. Himle, M.S.W., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor MI 48109-0840; George C. Curtis, M.D., Elizabeth M. Hill, Ph.D., James L. Abelson, M.D., Randolph M. Nesse, M.D., Hedieh Haghighatgou, M.S.W.

Summary:

Previous research has demonstrated a greater than expected association between certain anxiety disorders and alcoholism. Social phobia has often been found to co-occur with alcohol problems. As a test of the effect of alcohol use on social phobic fear, 40 treatment-seeking social phobics were asked to give two short speeches. Twenty received a placebo alcohol drink prior to both speeches, and the other 20 subjects received placebo prior to the first speech followed by a moderate dose of alcohol before the second speech. Repeated measures analyses of variance yielded no significant differences in anxiety (subjective, cognitive, physiological) improvement from speech one to speech two between the alcohol and the placebo groups. However, a consistent trend in the direction of alcohol-reducing anxiety was observed. Family history of drinking problems and current or past drinking habits did not significantly alter the effect of alcohol on anxiety. The belief that one received alcohol was a more powerful predictor of improvement from speech one to speech two than the actual ingestion of alcohol. These results suggest that alcohol problems may be associated with social phobia because of the anxiety-reducing effect of alcohol or at least of the expectation that the beverage would relieve anxiety.

NR565 Thursday, May 25, 12:00 noon-2:00 p.m.

Substance Use Disorders in Schizophrenic, Schizoaffective and Bipolar Patients

Helene Vedoux, M.D., Psychiatry, University Bordeaux, 121 Rue De La Bechade, Bordeaux Cedex 33076, France; Michel Mury, M.D., Guy Besancon, M.D., Marc L. Bourgeois, M.D.

Summary:

Objective: The aim of the study was to assess the prevalence and the pattern of illicit drug use in bipolar (BP), schizoaffective (SA) patients.

Method: Drug use disorders were assessed using the CIDI in 92 consecutive DSM-III-R BP (n = 40), SZ (n = 38), and SA (n = 14) patients.

Results: In the total sample, the lifetime (LT) prevalence and the current (previous six months) prevalence for any substance abuse or dependence disorder was 25% and 14%, respectively. No significant difference was found between the three diagnostic groups, although higher LT (42.9%) and current (21.4%) prevalences were found in SAs. Age at onset of substance use was earlier than that of psychotic or mood symptoms in most patients. Patients with current drug use disorder were younger than those without, but other sociodemographic and clinical variables did not differ between these two groups. Whatever the diagnostic group, the most commonly used drug was cannabis, followed by opiates and cocaine.

Conclusions: These results confirm the high comorbidity of substance use in SZ and BP patients and outline the possible role of geographical environment in the pattern of drug choice. The high prevalence of drug use in SAs suggests that drug use might modify the clinical expression of a genetic liability to mood disorders.

NR566 Thursday, May 25, 12:00 noon-2:00 p.m.

The CNS Neurochemistry of Alcoholism

Thomas D. Geracioti, Jr., M.D., Dept of Psych, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Peter T. Loosen, M.D., Michael H. Ebert, M.D., Nosa N. Ekhator, M.S., Donna Burns, R.N., Wendell E. Nicholson, David N. Orth, M.D.

Summary:

Abnormalities in corticotropin-releasing hormone (CRH) secretion, noradrenergic neurotransmission, and serotonergic activity in the central nervous system (CNS) have all been hypothesized to exist in alcoholic patients, as have abnormalities in hypothalamic-pituitary-adrenal function. To test these hypotheses, we continuously sampled cerebrospinal fluid (CSF) from alcoholic patients after 38 to 124 days of abstinence and from normal volunteers via a flexible, indwelling, lumbar subarachnoid catheter and measured CRH, norepinephrine (NE), 3-methoxy-4-hydroxyphenylglycol (MHPG), tryptophan, and 5-hydroxyindoleacetic acid (5-HIAA) concentrations at 10 minute intervals, from 11:00 h through 17:00 h. The spinal canal catheter was inserted at approximately 08:00 h. Serial plasma ACTH, cortisol, and NE concentration were also measured. A mixed liquid meal was consumed at 13:00 h.

CSF CRH concentrations were lower in alcoholic patients than in normal volunteers (26 $\pm$ 15 vs. 60 $\pm$ 30 pg/ml, respectively, $p < 0.05$ by ANOVA), as were CSF NE levels (0.33 $\pm$ 0.09 vs 1.15 $\pm$ 0.51 pmol/ml, respectively, $p < 0.01$). Plasma NE and CSF MHPG levels were normal in the alcoholic patients. CSF tryptophan and 5-HIAA and plasma ACTH and cortisol concentrations did not differ between the groups. These studies extend our finding of reduced spinal canal CSF CRH concentrations in depressed patients to abstinent chronic alcoholics. The very low CSF NE levels observed in our alcoholic patients stand in contrast to the normal CSF NE concentrations we previously found in depressed patients, and to their own normal levels of plasma NE and CSF MHPG (which largely reflect peripheral NE metabolism). Whether the deficits in CSF NE and CRH concentrations are the cause or consequence of alcoholism or abstinence or are related to the positively reinforcing effect of alcohol in alcoholics remains to be determined.

NR567 Thursday, May 25, 12:00 noon-2:00 p.m.

Crack Dancing: Are There Permanent Neurotoxic Sequelae?

George Bartzokis, M.D., Psychiatry, UCLA, 300 UCLA Medical Plaza Ste 2200, Los Angeles CA 90024; Mace Beckson, M.D., Marguerite Callinan, B.A., Walter Ling, M.D., Stephen R. Marder, M.D.

Summary:

The prevalence of movement disorders in cocaine addicts is unknown and may be underappreciated. Daras et al (1994) report that addicts themselves have dubbed the choreoathetoid movements (CM) associated with crack binges as "crack dancing."

Fifteen male cocaine-dependent (DSM-IV criteria) inpatients were evaluated for CM with the Abnormal Involuntary Movement Scale (AIMS). Patients were excluded for a current or past DSM-IV diagnosis of dependence on other substances but were not excluded for abuse of other substances with the exception of amphetamines. A group of 10 matched normal controls who denied a history of drug dependence or abuse were also examined. Differences between patients and normal controls in CM severity approached significance in the nonfacial (limbs plus trunk) AIMS subscore ($t = 2.02$, $p = 0.055$). With abstinence, some decrease in the severity of CM was observed. However, in some patients, mild to moderate CM appeared to be permanent sequelae. Preliminary MRI evidence of both subtle and gross brain damage will also be presented.

Increased nonfacial CM may be a marker for psychostimulant-induced basal ganglia neurotoxicity. Quantifying clinical and MRI markers of neurotoxicity associated with psychostimulant dependence could be useful in evaluating the impact of neurotoxicity on medication trial outcomes, and may suggest novel medication development strategies.

NR568 Thursday, May 25, 12:00 noon-2:00 p.m.

Relative Contribution of Negative Emotions to the Severity of Substance Abuse Problems Experienced by Substance Abusers

Michael M. Chang, M.D., Psychiatry, Maui VA PCC, 35 Lunalilo Street Suite 102, Wailuku HI 96793

Summary:

This paper examined the contribution of negative emotions when abstinent familial alcoholism, childhood factors, positive response to substance use, and quantity-frequency of substance use to severity of substance abuse problems. The subjects were 300 consecutive admissions to the Honolulu VA Outpatient Substance Abuse Program. Eight percent had a substance abuse disorder and 92% had a dependence disorder according to DSM-III-R criteria. The ethnic distribution was 40% Caucasian, 9% black, 6% Hispanic, 11% Polynesian, and 24% Asian. A composite variable, Severity of Problems (SP), was computed as the sum of financial, interpersonal, legal, and physical problems caused by substance use. Multiple regression analyses using SP as the dependent variable showed that familial alcoholism variables could account for 23%, childhood factors for 29%, quantity-frequency of use for 36%, positive response to use for 52%, and negative emotions when abstinent for 75% of the variance in SP. When variables from all domains were used together in a stepwise method, the negative emotions accounted for 74.6% of the variance in SP and the other domains could account for only an additional 4%. These results suggest that among addicts, negative emotions when abstinent is the major determinant of SP, and that learning to deal with negative emotions when abstinent may be the active ingredient of most treatments.

NR569 Thursday, May 25, 12 noon-2:00 p.m.

Geriatric Trauma Patients and Alcohol Use

Mark G. Fuller, M.D., Dept of Psych, Medical College of PA, 11676 Perry Highway Ste 3101, Pittsburgh PA 15090; Mark Lovell, Ph.D., Daniel L. Diamond, M.D., Trevor R.P. Price, M.D., Ricard N. Townsend, M.D.

Summary:

Objectives: Researchers have reported conflicting results regarding the impact of alcohol use on injury severity in trauma patients. In order to discover why there is such a disparity in findings, we evaluated one segment of trauma admissions—geriatric patients.

Methods: All patients admitted to a tertiary care teaching hospital had demographic and clinical data entered into a computerized data base. This study was conducted by reviewing this data base for all patients ages 60 and older who were admitted to the trauma service and received a blood alcohol level (BAL) between January 1988 and December 1993. Injury severity of alcohol positive patients (BAL+) was compared with alcohol negative ones (BAL–) as defined by four measures (Injury Severity Score-ISS, discharge to home, length of stay, and mortality rate).

Results: 1134 geriatric trauma patients were admitted with a BAL during this six-year period and 14.1% were positive for alcohol. There were no differences in ISS, discharge to home, or length of stay between BAL+ and BAL– subjects. However, BAL+

patients had a 22.5% increase in mortality over BAL– ones (16.9% vs. 13.8%), which is statistically significant.

Conclusions: The authors conclude that the presence of alcohol in geriatric trauma patients does not appear to increase injury severity as measured by ISS, discharge to home, or length of stay, but does appear to decrease significantly the likelihood of surviving the accident. This finding highlights the importance of identifying elderly alcohol abusers in order to educate and intervene with them regarding the additional risks associated with alcohol use and trauma.

NR570 Thursday, May 25, 12 noon-2:00 p.m.

Contingency Contracting for Illicit Drug Use with Opioid Addicts in Methadone Treatment

Donald J. Tusel, M.D., Psychiatry 116F, VA Medical Center, 4150 Clement Street, San Francisco CA 94121-1598; Nancy A. Piotrowski, Ph.D., Patrick Reilly, Ph.D., Karen L. Sees, D.O., Peter Banys, M.D., Sharon M. Hall, Ph.D.

Summary:

This study examines the effect of positive contingencies in the treatment of heroin addiction. Data are presented on 102 subjects admitted into a six-month methadone treatment that provided for 80 mg methadone per day and enhanced psychosocial treatment. Urine samples were collected at random twice a week and were analyzed for six drugs of abuse; an alcometer test was also administered randomly once a week. At treatment entry, subjects were randomly assigned to a contingency (N = 51) or noncontingency (N = 51) contract condition during the first four months of treatment. Subjects in the contingency condition were able to earn increasing cash credits ($755 maximum) for submitting negative alcometer tests and urine samples demonstrating consistent avoidance of illicit drug use. On average, subjects were 40.6 years of age, primarily male (70.6%), single or separated (76.5%), and unemployed (73.5%). Caucasians were dominant in this sample (39%) followed by African-Americans (34%). In the six months prior to intake, the modal subject had used at least two substances of abuse in addition to heroin. There were no differences between the two groups demographically, in methadone dose, retention, or psychosocial treatment received. The intervention was minimally effective until the last month of the contracting period, when the subjects in the contingency group submitted significantly more *consecutively* clean urine and alcometer tests (2.9) compared with the noncontingency group (1.1)—$p < .007$, as well as more "clean" test (34% versus 17%)—$p < .03$.

We conclude from these results that contingency contracting may be a useful adjunct to treatment of heroin addicts who are also polysubstance abusers, although waiting to implement a contingency contract until after the patient is stabilized on methadone might be more appropriate in this difficult-to-treat population.

NR571 Thursday, May 25, 12 noon-2:00 p.m.

Nicotine Craving: A Comparison Between a New Objective Measure and Traditional Self-Report Measures

Neil Hartman, M.D., Psychopharmacology, WLA VAMC, T350 (691/B151D), Los Angeles CA 90073; Sidney Gold, M.D., Nicholas H. Caskey, Ph.D., Bernard M. Kim, B.S., Damian C. Madsen, B.A., Murray E. Jarvik, M.D.

Summary:

The nationwide trend toward smoke-free hospitals has created a situation in which severely impaired psychiatric patients, most of whom are heavy smokers, suffer severe nicotine withdrawal when confined on locked units. At last year's annual meeting (Hartman et al 1994) we reported that by weighing the filter from smoked cigarettes one could objectively and reliably measure nicotine craving in this population for whom the traditional self-report inventories are not applicable. We now report that in a group of higher functioning psychiatric inpatients, the filter-weight method is highly correlated with traditional self-report inventories.

After an enforced overnight abstinence, verified by carbon monoxide, 11 voluntary, consenting patients on an unlocked psychiatric unit at the West Los Angeles VAMC were allowed to smoke successive standard filtered cigarettes to satiety. The butt from the first cigarette of the day and that from the second, smoked a few minutes later, were collected, and the filters dissected and weighed. Two standard self-report scales of nicotine craving (an analog scale and the Shiffman-Jarvik inventory) were administered prior to the first cigarette and prior to the second. In every case the filter from the first (abstinent) cigarette weighed more than the second ($P = .002$, 2-tail t-test). One of the 11 subjects failed to report greater craving for the first cigarette on the analog scale. An additional patient (two of 11) failed to report greater craving for the first cigarette on the Schiffman-Jarvik. As a measure of nicotine craving in psychiatric patients, the reliability of the objective filter-weight method compares favorably with traditional subjective self-report methods.

NR572 Thursday, May 25, 12 noon-2:00 p.m.

Validity of the Adolescent Imaginary Urine Drug Screen: Association Between Attitude When Giving Urine and Test Results

Steven L. Jaffe, M.D., Psychiatry, Emory University, 6667 Vernon Woods Dr #B-20, Atlanta GA 30328-3282; Scott W. Henggeler, Ph.D., Roanne L. Jaffe, M.Ed., Susan G. Pickrel, M.D.

Summary:

Objective: Clinical impressions among professionals treating substance abuse in adolescents suggest a positive relationship between youth resistance to provide a urine for a drug screen and likelihood that it will be positive for illegal substances. This association called "the adolescent imaginary urine drug screen" has not been studied empirically.

Method: The validity of this association was studied in 46 consecutive participants in an ongoing clinical trial of an intensive home-based treatment approach with substance-abusing juvenile offenders. Research assistants rated levels of cooperation/resistance to providing a urine for a drug screen. This was correlated with the actual results of the urine drug screen.

Results: 30% of the youths tested positive for cannabinoids, which accounted for almost all positive urines. We found that 86% of the youths resistant to testing had positive urine drug screens, which contrasted significantly with the 21% who were cooperative with providing a urine who tested positive.

Conclusions: Substance-abusing delinquent youths being treated in a home-based program who were resistant to providing a urine for a drug screen had significantly positive urine results for cannabinoid use. Thus, the validity of the adolescent imaginary urine drug screen that a youth's resistant attitude predicts a positive urine was supported.

NR573 Thursday, May 25, 12 noon-2:00 p.m.

FDOPA Uptake Differences in Cocaine Addicts in Withdrawal and Normal Controls

Clifford B. Widmark, M.D., Psychiatry, Univ of Calif. Irvine, Room 163 Irvine Hall UCI, Irvine CA 92715; Joseph C. Wu, M.D., Eric A. Klein, B.S., Kate M. Bell, M.D.

Summary:

Objective: The objective of this project was to assess dopaminergic function in cocaine addicts during withdrawal from cocaine using PET study of FDOPA uptake.

Method: Seven cocaine-dependent subjects in acute withdrawal (<30 days since last use) were studied using FDOPA uptake. Inclusion criteria were a) DSM-III-R diagnostic criteria for active cocaine dependency, b) continuous use of cocaine for at least the prior six months with claimed cocaine use of at least "2 grams" a week (estimated cost of $200/week). PET studies were performed on an Neuroecat IV system with FWHM of 7.6mm in-plane. Each subject received 2.0–4.0 mCi of 6-FD. Twelve 10-minute scans were performed. FDOPA uptake was determined (Martin et al. (1989)). FDOPA uptake was graphically represented pixel by pixel.

Results: The normal controls have a significantly higher FDOPA uptake in the right anterior cingulate, right caudate, and right putamen compared with cocaine addicts in acute withdrawal.

Conclusions: There may be a chronic suppression of presynaptic dopamine activity as an adaptation to chronic dopamine exposure induced by habitual cocaine use, which may predispose addicts to cocaine craving.

NR574 Thursday, May 25, 12 noon-2:00 p.m.

High Frequency of Intense Dieting Among Abstinent Alcoholics Who Crave Sweets and Rich Foods

Michael J. Bohn, M.D., Dept of Psych B6/210, UW Hospitals, 600 Highland Ave, Madison WI 53792; Dean D. Krahn, M.D., Jack Husted, M.S.W., Beth A. Staehler, Ph.D.

Summary:

Objective: In animals, alcohol consumption increases following palatable food deprivation, and high preferences for sweets and fats are associated with high rates of self-administration of alcohol and other drugs. High rates of alcohol abuse and dependence have been found among bulimics. We sought to determine (a) the frequency of dieting and related appetitive disturbances among treated, abstinent alcoholics; (b) if preferences for sweet and rich food were affected by abstinence; and (c) if prior dieting history, the intensity of drinking urges, gender, or the duration of abstinence affected sweet/rich food craving among alcoholics.

Methods: 347 treated alcoholics (108 females) were evaluated using the dieting severity scale, and their preferences for sweets, ice cream, other foods, and alcohol were determined using psychometrically validated scales.

Results: Subjects reported high prevalence of dieting behaviors (0.6% probable bulimia; 10.3% at-risk, 13.4% severe, 27.8% intense, 33% casual, and only 13.7% nondieters). Dieting intensity was significantly greater for women than for men. With abstinence, craving for sweets and ice cream increased in over 30% of subjects, a rate significantly greater than that for salty foods, fruit, vegetables, or meat. Multiple regression analysis revealed that craving for sweet and rich foods was significantly and positively related to the intensity of drinking urges and pretreatment dieting intensity, but not abstinence duration or gender.

Conclusions: Noncasual dieting is common among both male and female alcoholics, whose urges to consume alcohol and sweet and rich foods are related. Data from an ongoing study will be presented regarding the effect of palatable food consumption on alcoholic relapses.

NR575 Thursday, May 25, 12 noon-2:00 p.m.

Changes in Drug Craving During Inpatient Chemical Dependence Treatment

Sue R. Dyrenforth, Psychology, DVA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Juris Mezinskis, Ph.D., Mark Cohen, Ph.D., R. Jeffrey Goldsmith, M.D., Eugene C. Somoza, M.D.

Summary:

Previous studies have shown that chemically dependent patients being treated in a supportive environment such as a residential program typically show a decrease in psychiatric symptomatology such as depression. The goal of this study was to compare changes in psychiatric symptomatology with changes in craving for various drugs of abuse. During their stay in a hospital-based treatment program, 376 patients used a four-point scale to make a total of 5,867 daily ratings of eight symptoms (anxiety, depression, restlessness, anger, irritability, frustration, impatience, and poor concentration) as well as rating the intensity for craving of up to four specific drugs. Correlations were used to analyze changes across the 28 days of inpatient treatment.

The correlation between the mean of the eight psychiatric symptoms and days of treatment showed a significant decrease in symptomatology ($r = -.11$, $p < .001$). Significant correlations were also found between days of treatment and a decrease in craving for specific drugs (alcohol, $r = -.17$, $p < .0001$; cocaine, $r = -.22$, $p < .0001$; opiates, $r = -.20$, $p < .01$; nicotine, $r = -.08$, $p < .01$). Craving for alcohol and cocaine decreased at a faster rate than the rate of decrease for psychiatric symptoms ($p < .01$). The absolute value of craving for nicotine (the only drug still used while in treatment) was significantly ($p < .01$) higher than craving for the other drugs of abuse. Continued high craving for drugs at the end of treatment was predicted by a higher psychiatric composite score on the Addiction Severity Index at the beginning of treatment. It is concluded that inpatient treatment significantly reduces drug craving, but that continued craving is associated with preexisting psychiatric symptomatology.

NR576 Thursday, May 25, 12 noon-2:00 p.m.

Brain Metabolism of Cocaine Abusers in Middle Abstinence

Kate M. Bell, M.D., Psychiatry, Long Beach VAMC, 5901 E. Seventh Street, Long Beach CA 90822; Clifford B. Widmark, M.D., Joseph C. Wu, M.D., Eric A. Klein, B.S., Lori LaCasse, B.S.

Summary:

Objective: This study examined changes in brain glucose metabolism in chronic cocaine abusers during the middle phase of abstinence. We hypothesized that cocaine abusers would show decreased 18-F-deoxyglucose metabolism.

Method: Positron emission tomographic (PET) brain images of 13 male, right-handed veterans on an inpatient, substance-abuse treatment ward meeting DSM-III-R criteria for cocaine dependence, in the middle phase of abstinence (last cocaine use >1 week but <30 days) were compared with those of 10 matched controls. Patients had abused >4 grams cocaine per week as the free base (crack) for >6 months in the last year. Patients were excluded if they had a current or past psychiatric illness other than cocaine dependence, a Hamilton Depression score >7, history of intravenous drug abuse, more than moderate use of alcohol, or dependence on any substance other than cocaine, nicotine or caffeine.

Results: Patients showed decreased absolute and relative brain metabolism in several areas; most prominent were left anterior cingulate gyrus ($p < .05$), left amygdala and extended amygdala ($p < .01$), and the region of the left nucleus accumbens ($p < .01$).

Conclusion: Cocaine abusers in middle abstinence show decreased brain metabolism in left limbic regions that may mediate drug craving.

NR577 Thursday, May 25, 12 noon-2:00 p.m.

The Prevalence of Substance Use Disorders in Applicants for Thoracic Organ Transplantation

Bradley M. Pechter, M.D., Psychiatry, University of Illinois, 912 S. Wood Street MC 913, Chicago IL 60612; Norman S. Miller, M.D., James P. Houck, M.D., Dina M. Hess, R.N.

Summary:

Objective: This study was undertaken to determine the prevalence rate of substance-abuse-related disorders in patients applying for thoracic organ transplants.

Method: Subjects were all consecutive applicants for heart or lung transplants at a large urban tertiary referral university medical center and were not preselected for the presence of psychiatric, substance use or other mental illness. Patients were screened in a prospective design using a structured clinical interview administered by one psychiatrist in consultation with a second psychiatrist. Diagnosis was by DSM-IV criteria.

Results: To date, 21 patients have been screened. Twelve had a lifetime diagnosis of substance abuse or dependence. Five admitted to active substance dependence, and seven were in remission. Ten patients met criteria for alcohol abuse or dependence. Ten patients met criteria for abuse or dependence for more than one substance.

Conclusions: There is a high incidence of substance use disorder, especially alcoholism, in patients applying for thoracic organ transplants. These findings should help guide transplant physicians in assessment of candidates and in establishing priorities for the allocation of scarce resources. The need for a transplant may provide excellent motivation for these patients to participate in substance-dependence treatment and recovery.

NR578 Thursday, May 25, 12 noon-2:00 p.m.

Survey of Sexually Transmitted Diseases in Drug Addiction

Vasant Dhopesh, M.D., Psychiatry, VA Medical Center Dept 11, University & Woodland Avenue, Philadelphia PA 19104; Carrie Lainfester, M.H.T.

Summary:

Background and Objective: It was our empirical observation that drug and alcohol abusing patients frequently engage in high-risk sexual behavior. The objective of the study was to document the prevalence of sexually transmitted diseases (STDs) in drug addicts and alcoholics in our inpatient substance abuse treatment unit.

Method: As a part of the routine admission history in our substance-abuse treatment unit, a questionnaire was administered to each patient on admission from January 1st to June 30th, 1994. Patients were questioned about sexual practices such as number of partners and condom use.

Results: All 157 patients were male and ranged in age from 27 to 70 mean 43.9 $\pm$ 7.08. 110 (71.9%) were African American, 35 (23%) were Caucasian, and 12 (8%) others. A total of 104 (66.2%) were IVDA; 80% were polysubstance abusers. Mean drug use ranged from six years to 23 years. History of gonorrhea was present in 72 (46%) and syphilis in 13 (8%). While 13 (8%) were known HIV positive at the time of admission, three others tested positive. Eighty-five (55%) had multiple heterosexual partners and 71 (46%) had mainly single partners. Of the 85 who had multiple sexual partners 74 (87%) occasionally or never used condoms. Out of these 74 who rarely used condoms, 49 (66%) were IVDA. History of syphilis and or gonorrhea was present in 77 (49% of the total); 48 of these (63%) had multiple partners; 42 (88%) rarely used condoms. Of 16 (10%) positive HIV, eight (50%) had multiple partners and 13 of these 16 (81%) seldom used condoms.

Conclusion: 1.) This study confirms the general observation that a large percentage of drug and alcohol abusing patients have history of sexually transmitted diseases. 2.) Three high-risk groups are identified: patients who have multiple partners, are IVDA, and seldom use condoms; patients with history of gonorrhea or syphilis, continue to have multiple sexual partners, and seldom use condom, and positive HIV patients who occasionally use condoms and have multiple sexual partners. 3.) Educational programs should focus on these high-risk groups to prevent the spread of sexually transmitted diseases and to help these patients keep from getting reinfected.

NR579 Thursday, May 25, 12 noon-2:00 p.m.

Frequency of Dieting in the Sixth Grade Predicts Alcohol and Cigarette Use in the Ninth Grade

Dean D. Krahn, M.D., Psychiatry, University of Wisconsin, 600 Highland Avenue, Madison WI 53792; Douglas Piper, Ph.D., Monica King, M.S., D. Paul Moberg, Ph.D., Laura Olson, M.A., Jiyuan Wu, Ph.D.

Summary:

Objective: Severity of dieting and binge eating is positively associated with frequency of alcohol and cigarette use in women. Since dieting starts before substance use, we hypothesized that dieting might predict alcohol use in adolescents.

Methods: Data from 1,852 ninth graders surveyed from grades six through nine in Healthy for Life, a middle-school health promotion program, were analyzed. The frequency of starting a diet in the past year assessed the severity of dieting. Students were classified as users/nonusers of alcohol.

Results: Dieting in sixth grade was significantly positively related to alcohol use in ninth grade (gamma = 0.166, $p < .00002$). Logistic regression using alcohol use/nonuse in ninth grade as the dependent variable and sixth grade measures of dieting frequency, anticipated use of alcohol and cigarettes, peer alcohol use, peer dieting, parental approval of alcohol use, and self-esteem measures showed that dieting frequency and anticipated use of alcohol and cigarettes were significant predictors of later drinking.

Conclusions: Dieting frequency predicted alcohol use three years later in adolescents. Dieting frequency was a more potent predictor of subsequent alcohol use than several factors frequently cited as risk factors. Potential mechanisms underlying this relationship and further analyses will be presented.

NR580 Thursday, May 25, 12 noon-2:00 p.m.

Violence in Substance Abusers

Mace Beckson, M.D., PO Box 84507, Los Angeles CA 90073; George Bartzokis, M.D., James Herzberg, B.A., Walter Ling, M.D.

Summary:

Substance abuse and violent behavior are frequently comorbid, particularly in cocaine users in urban areas (Lindenbaum et al, 1989, Murdoch et al, 1990). Using the Suicide and Aggression Survey (SAS) (Korn et al, 1992), we tested the hypothesis that violent behavior is more frequent in cocaine abusers than alcohol abusers. Pilot data were collected on 31 consecutive admissions to a VA inpatient alcohol and drug rehabilitation center. SAS data were analyzed from 18 "crack" cocaine dependent patients and nine alcohol dependent patients without other psychiatric comorbidity (DSM-IV criteria). Duration of substance use was significantly greater among alcoholics than cocaine addicts ($t = 6.71$, $p < .0001$). No differences in "Violence Risk" (VR) or "Lifetime History of Aggression" (LHOA) were found between the two groups. However, when the data were reanalyzed controlling for duration of use, cocaine addicts demonstrated greater mean

scores on VR (alc. = 5.50, coc. = 7.19) and LHOA (alc. = 7.52, coc. = 15.29) than alcoholics. These differences were not significant. Data from a larger cohort are being gathered and will be presented.

NR581 Thursday, May 25, 12 noon-2:00 p.m.

The Diagnosis and Treatment of Chronic Visual Disturbances Following LSD

Henry D. Abraham, M.D., Dept of Psych, New England Medical Center, 750 Washington St Box 1007, Boston MA 02111

Summary:

Hallucinogen persisting perceptual disorder (HPPD) is a long-standing disorder of perception following the use of hallucinogenic drugs, most commonly lysergic acid diethylamide. This report summarizes clinical experience with 60 patients with this disorder, and compares the sample to a matched comparison group of 60 substance abusers without HPPD. HPPD subjects were followed as long as 14 years and reported daily, continuous pseudohallucinations for as long as 26 years following LSD. Unique symptoms included an array of geometric pseudohallucinations, afterimagery, and false perceptions of movement and drug-acquired dyslexia. One symptom in particular, visual trails of moving objects, was 83.5% sensitive and 100% specific for HPPD, suggesting a pathognomic relationship to the diagnosis. The disorder appeared to be permanent. Severity of visual symptoms correlated strongly with LSD use, but not with life dose. Increased prevalences of comorbid psychiatric illnesses included depressive, panic, and alcohol use disorders, but not psychotic or seizure disorders. Three subjects committed suicide. No pharmacological treatment was effective for HPPD, though behavioral techniques for reducing CNS arousal and supportive therapy appeared helpful. Comorbid disorders appeared to respond to conventional pharmacotherapy and psychotherapy. Long-term treatment is indicated to reduce the morbidity and mortality of HPPD and its associated conditions.

NR582 Thursday, May 25, 12 noon-2:00 p.m.

Yohimbine Induces Withdrawal and Anxiety Symptoms, and Increased Acoustic Startle Response in Methadone Patients

Susan M. Stine, M.D., Psychiatry, VA Medical Center, 950 Campbell Avenue, New Haven CT 06516; John H. Krystal, M.D., Steven M. Southwick, M.D., Christian Grillon, Ph.D., Andrew Morgan, M.D., Dennis S. Charney, M.D.

Summary:

Brain noradrenergic systems mediate aspects of opiate withdrawal in humans, therefore yohimbine, an alpha$_2$ adrenergic antagonist, would be expected to increase opiate withdrawal symptoms. This double-blind, placebo-controlled study in eight patients receiving 50–80 mg of methadone daily, measured withdrawal symptoms, craving, and intent to use opiates; Panic Attack Symptoms Scale (PASS); physiological responses (HR and BP); and acoustic startle after yohimbine 0.4 mg/kg I.V.

Yohimbine produced elevation in objective and subjective withdrawal as well as elevation in PASS scores. Comparisons of peak responses on PASS individual symptoms revealed significant elevation in predominantly somatic symptoms as opposed to "fear" symptoms. These symptoms overlapped with symptoms that changed significantly in the withdrawal scales. Craving was also significantly elevated. Systolic blood pressure, diastolic blood pressure, and heart rate also showed significant increase after yohimbine. Startle response after yohimbine was statistically significant by repeated measures analysis of variance (ANOVA). Sixteen normal controls also showed elevation in PASS scores and in physiological measures after yohimbine. Methadone patients were observed to have a relative significant increase in fear-related symptoms such as "fear of death," "fear of going crazy," and "fear of losing control." Methadone subjects also had increased startle amplitude when compared with normal subjects (n = 12). These results emphasize the sensitivity of opiate-dependent patients to noradrenergic stimulation and also suggest a particular risk for initiation or exacerbation of comorbid anxiety symptoms in this population.

NR583 Thursday, May 25, 12 noon-2:00 p.m.

Psychological Symptoms and Fenfluramine Treatment of Cocaine Dependence

Steven L. Batki, M.D., Dept of Psych Ward 93, San Francisco General Hos, 1001 Potrero Avenue, San Francisco CA 94110; Mark Bradley, B.A., Mark D. Herbst, M.D., Tracey Jones, B.A., Michael Markman, B.A., Reese T. Jones, M.D.

Summary:

Objective: A controlled trial of fenfluramine 60 mg/day was conducted to determine its effectiveness in treating cocaine abuse in methadone maintenance (MMT) patients.

Method: Balanced group, double-blind, placebo-controlled, crossover design. Subjects received either fenfluramine (FEN) 60 mg/da or placebo (PLA) for a four-week period, then received placebo for a one-week, single-blind washout, and then underwent a double-blind crossover to FEN or PLA for a second four-week period. Subjects were the first 38 of an eventual 39 DSM-III-R secondary cocaine dependent MMT outpatients. Subjects were 63% female, 50% African American, 24% white, 21% Hispanic, 2.5% Native American and 2.5% Pacific Islander. A total of 87% were HIV positive; 33% had lifetime major depressive disorder; and 8% had current major depressive disorder, 17% had antisocial personality disorder. Measures of cocaine use included quantitative urine benzoylecgonine (BE) levels.

Results: Mean HamD score (n = 30) was 10.5 at intake; 5.7 for the four weeks on FEN; and 4.9 for the four weeks on PLA; 17 of 30 Ss had lower HamD Scores on FEN. Mean Beck Depression Score (n = 30 Ss) was 14.90 at intake, 7.0 on FEN, and 6.9 on PLA; 14 of 30 Ss had lower Beck Depression Scores on FEN. Mean HamA (n = 30 Ss) was at 12.2 intake, 5.2 on FEN and 4.9 on PLA; 14 of 30 Ss had lower HamA Scores on FEN. Mean Total Yale-Brown Obsessive Compulsive Scale Score (n = 30 Ss) was 19 at intake, 14 on FEN and 14 on PLA; 11 of 24 Ss had lower YBOCS Scores on FEN. One subject (2.5%) had to discontinue FEN prior to completion of the study due to side effects.

Conclusion: Fenfluramine appears to have minimal effects on psychological symptoms in cocaine-dependent MMT patients. Further work needs to be done to determine if FEN is associated with a significant reduction in cocaine use.

NR584 Thursday, May 25, 12 noon-2:00 p.m.

A Double-Blind Placebo Controlled Trial of Fluoxetine for Treatment of Cocaine Abuse

Hyung K. Lee, M.D., Psychiatry, Bronx-Lebanon Hospital, 1256 Franklin Avenue, Bronx NY 10456; Eliseo A. Go, M.D., John B. Osei-Tutu, M.D., Harvey Bluestone, M.D.

Summary:

Previous research studies have demonstrated that fluoxetine has pharmacological efficacy in reducing cocaine self-administration in rats and attenuating cocaine-abusing behavior in human subjects. The purpose of this study is to evaluate fluoxetine's effects on cocaine craving and abuse with a double-blind, placebo-controlled design.

Methadone maintenance treatment patients who consistently showed positive toxicology for cocaine, after giving informed con-

sent, were assigned to three groups; Group A-fluoxetine 20 mg per day, Group B-fluoxetine 40 mg per day, and Group C-placebo. The patients were evaluated with a cocaine-craving scale on a weekly basis during the eight-week trial in addition to weekly urine toxicology screenings. Point changes of the cocaine craving scale and the toxicology results were compared between the three groups.

Preliminary results indicate that approximately half of the Group B patients showed negative toxicology at least half of the times tested. While Group A showed greater reduction of cocaine craving compared with that of Group C, toxicology results showed no difference between the two groups. The placebo group patients showed a significantly higher drop-out rate than did active drug groups. The authors believe that fluoxetine is a useful adjunctive pharmacological agent in management of cocaine abuse.

NR585 Thursday, May 25, 12:00 noon-2:00 p.m.

A Multicenter Safety Study of Naltrexone As Adjunctive Pharmacotherapy for Individuals with Alcoholism

Robert S. Croop, M.D., Clinical R&D, Dupont Merck, Barley Mill Plaza P27/1260, Wilmington DE 19805; Dominic F. Labriola, Ph.D., Jill M. Wroblewski, M.S., Donald W. Nibbelink, M.D.

Summary:

A multicenter, open-label usage study was conducted at 40 alcohol treatment programs in the United States to collect additional information regarding the safety profile of naltrexone administration to individuals participating in alcohol treatment programs. Patient selection criteria were designed to enable enrollment of a representative population of individuals entering alcohol treatment programs. Opioids were the only concomitant medications that prevented an individual from entering the study.

The study collected safety data from 570 individuals with alcoholism who received naltrexone as adjunctive medication while participating in a wide range of alcohol treatment programs. Data describing patient selection, dosing, and medication compliance were also collected. The characteristics of the study population and the concomitant medications used during the study are representative of current treatment practices in the United States. The study population had a mean age of 38.9 years, was 74% male, and 81% Caucasian. Approximately 80% of the enrolled patients received at least one concomitant medication during the study. The most frequently reported new-onset adverse clinical events were nausea, headache, dizziness, and nervousness (WHOART preferred terminology).

The profiles of adverse clinical events and liver function tests observed during naltrexone administration were similar to those seen during treatment of opioid-dependent populations. The study results confirm the value of a usage study as part of the development of adjunctive medications for the treatment of chemical dependencies.

NR586 Thursday, May 25, 12 noon-2:00 p.m.

In Search of a Universal Drug Craving Scale

Eugene C. Somoza, M.D., Psychiatry, VA Medical Center, 3200 Vine Street, Cincinnati OH 45220; Susan Dyrenforth, Ph.D., R. Jeffrey Goldsmith, M.D., Juris Mezinskis, Ph.D., Mark Cohen, Ph.D.

Summary:

We have recently shown that drug craving is an independent feeling state that is not just a linear combination of withdrawal symptoms. Although there exists anecdotal evidence that some drugs can elicit more intense craving than others, this belief has not been confirmed by formal clinical studies. We addressed this issue by taking daily measures of the intensity and frequency of craving on every patient treated at a VA 28-day rehabilitation unit every work day over a 21-month period. Of the resulting 5,967 craving measures on 376 patients, a total of 3,238 (55.2%) indicated a craving for at least one drug, and 2,418 (41.2%) craved at least two drugs. When patients craved more than one substance it was possible to determine how the craving intensity for one drug compared with the other. The ratio of the craving for the first drug to the second is called the drug preference ratio (DPR). The resulting DPRs are: cocaine/alcohol = 1.81, opioids/cocaine = 1.32, and cocaine/marijuana = 18.4. From these DPRs a drug-craving scale was constructed. If the craving intensity for marijuana is given a value of 1.0 on this scale, those for alcohol, cocaine, and opioids are 10.2, 18.4, and 24.3, respectively. The significance of these results, as well as some explanations for the large craving differences between these commonly abused substances, will be discussed.

NR587 Thursday, May 25, 12 noon-2:00 p.m.

Alcoholism and Typology: Relationship to Age of Onset, Family History and Serum Cortisol

Conor K. Farren, M.D., Psychiatry, SATU, Yale University, 1 Long Wharf, New Haven CT 06511; Anthony W. Clarke, M.D., Timothy G. Dinan, M.D.

Summary:

We examined a group of inpatient and outpatient alcoholics, N = 48, in a private hospital in Ireland, in the post-alcohol withdrawal phase. We found that there were differences between groups of alcoholics when divided according to Cloninger's typology hypothesis and by the age of onset criteria of von Knorring. The type 2 early age of onset alcoholics (N = 23) had a significantly higher percentage of positive family histories of alcoholism, $p < 0.01$, a higher percentage of sociopathic traits, $p < 0.01$, and increased severity of alcoholism, $p < 0.05$, relative to the type 1 late age of onset alcoholics (N = 25). The family-history-positive alcoholics had a higher baseline 9am serum cortisol than the family-history-negative alcoholics, $p < 0.05$. We concluded that there is some validity to alcohol typology theory in relation to this relatively genetically homogeneous Irish population, and that age of onset is a useful defining criterion. We also concluded that the differences found in serum cortisol may indicate differences in HPA function between groups of alcoholics and were worthy of further investigation.

NR588 Thursday, May 25, 12 noon-2:00 p.m.

Primary Care at a Methadone Clinic

Chandresh Shah, M.D., Dept of Psych SVC (116), VA Outpatient Clinic, 351 E. Temple Street, Los Angeles CA 90012; Lena Simitian, Ph.D., Steven Chen, Ph.D.

Summary:

Health care reform initiative has emphasized the role of primary care (PC) in our health care delivery system. To study how PC can be integrated into specialized programs like methadone clinic (MC), we reviewed records of 87 randomly selected patients who have been enrolled into MC for at least 180 days. All but one were males with an average age of 51.22 ± 10.68 years. The population was 61% Hispanic, 17% white (W), 21% black (B), and 1% Oriental. The W received 46.00 ± 5.83 mg of methadone daily, while the B received 0.11 ± 11.65 mg ($p = .0004$). A total of 29% of patients also had major psychiatric diagnoses; 75% of patients were suffering from major medical problems, out of which 58% had more than one organ system involved. Those with medical problems were older ($p = .005$) (52.71 ± 10.28 years) and received higher ($p = .05$) doses of methadone (38.55 ± 10.78 mg). Thirty-

seven patients were referred to other services—23 to medicine, 18 to surgery, and six to psychiatry. Half of the patients were prescribed medications (other than methadone) and of those, more than half received prescriptions for drugs of more than one class. Laboratory, radiological, and cardiographic tests showed that older patients had more abnormal tests and received higher doses of methadone. Inner-city heroin addicts constitute a population that is hard to reach and difficult to treat. A methadone clinic provides an environment where they feel safe, comfortable, and welcome. By providing primary care in this setup, we have an opportunity to improve not only "quality of care" but also "quality of life."

NR589 Thursday, May 25, 12 noon-2:00 p.m.

Dual Activation of Dopamine and Serotonin Neurons As a Strategy for Substance Abuse Treatment

Michael H. Baumann, Ph.D., NIH, NIDA, ARC, CPRB, 4940 Eastern Avenue Bldg C 267, Baltimore MD 21224; P. Hitzig, Richard B. Rothman, M.D.

Summary:

Preliminary evidence suggests that combined administration of phentermine (PHEN) and fenfluramine (FEN) may be useful for treating cocaine abuse (*J. Substance Abuse Treatment* 11:273–275, 1994). In that study, we reported retrospective evaluations of six patients who received PHEN/FEN (30mg/40–80mg) for the treatment of cocaine dependence. With the first dose of medication, patients reported reduced cocaine craving, which was maintained throughout treatment. Furthermore, patients exhibited significant decreases in feelings of anxiety and depression as revealed by POMS and SCL-90 scores. To assess the neurochemical basis of PHEN/FEN action, we performed in vivo microdialysis studies in rat nucleus accumbens. Drugs were infused locally (1, 10, 100 μM) through the dialysis probe, and samples were analyzed for dopamine (DA) and serotonin (5-HT) by HPLC-EC. PHEN selectively increased DA at 1 μM but increased both transmitters at higher doses. FEN selectively increased 5-HT at all doses tested. The PHEN/FEN combination elevated extracellular DA and 5-HT concurrently to a similar degree.

Based on our data, we propose that dual activation of DA and 5-HT neurotransmission represents an effective strategy for substance abuse treatment. Double-blind, placebo-controlled clinical trials with PHEN/FEN should be carried out to test this hypothesis directly.

NR590 Thursday, May 25, 12 noon-2:00 p.m.

Multivariate Analysis of Addiction Treatment

Norman S. Miller, M.D., Dept of Psych, M/C 913 U of IL Chicago, 912 South Wood St, Chicago IL 60612; Fred G. Ninonuevo, Ph.D., Norman G. Hoffman, Ph.D.

Summary:

Background: A multisite, longitudinal study of patients undergoing outpatient alcohol and drug dependency treatment was conducted in private outpatient facilities, consisting of 2,029 subjects from 33 independent programs enrolled in a national addiction treatment outcomes registry.

Methods: We performed structured interviews upon admission, and consecutive structured interviews were conducted prospectively for treatment outcome at six- and 12-month follow-up.

Results: Multivariate analysis with stepwise multiple regression indicated that the relatively most powerful predictors of post-treatment alcohol/drug use were peer support group attendance and program continuing care involvement. Logistic regression yielded similar results in the prediction of abstinence versus relapse. Participation in posttreatment continuing care showed statistically significant reductions between pretreatment versus posttreatment in job absenteeism, inpatient hospitalizations, and arrest rates.

Conclusions: Posttreatment more than pretreatment factors may be decisive in influencing risk for relapse.

NR591 Thursday, May 25, 12 noon-2:00 p.m.

Pharmacotherapy and Psychotherapy for Obese Patients with Binge Eating Disorder

Michael J. Devlin, M.D., New York State Psych Inst, Box 116, 722 W 168th Street, New York NY 10032-2603; B. Timothy Walsh, M.D.

Summary:

Objective: Binge eating disorder (BED) is a newly recognized eating disorder characterized by episodic uncontrolled binge eating in the absence of methods of attempted compensation. Most patients with BED who present for treatment are overweight and thus suffer from a somatic disturbance (obesity), a behavioral disturbance (binge eating), and a psychological disturbance (distress related to eating/weight and comorbid depressive symptoms). We have developed a novel treatment approach which, by combining a medication treatment used for obesity with a psychotherapeutic treatment of established efficacy in the treatment of eating disorders, targets all of these aspects of the disorder.

Method: This is an open treatment study of 13 patients to date. Patients received a course of individual cognitive behavioral therapy (CBT) consisting of 20 to 32 sessions over four to seven months. In addition, patients were offered the option of a trial of the stimulant appetite suppressant phentermine combined with a serotonergic agent (fenfluramine or fluoxetine). Treatment is followed by a two-year follow-up period with assessment/booster sessions at one-month intervals.

Results: Results from this initial group of patients, including eight completers, four currently in treatment, and one dropout, are presented. Of the eight completers, five had opted for medication and were still taking it at the end of treatment. Seven of eight had completely stopped binge eating over the course of treatment. Patients lost an average of 21.0 ± 21.4 pounds (range 5.8–66.5). Mean Beck Depression Inventory score dropped from 17.5 ± 8.0 to 7.1 ± 5.8, Binge Eating Scale score from 29.2 ± 7.0 to 13.6 ± 6.3, and Body Shape Questionnaire score from 129.8 ± 19.4 to 83.8 ± 30.8. Follow-up data are currently being collected.

Conclusion: Preliminary results suggest that the combination of CBT and appetite suppressant medication is an effective acute intervention for obese patients with binge eating disorder.

NR592 Thursday, May 25, 12 noon-2:00 p.m.

Cholecystokinin Release and Gastric Emptying in Patients with Bulimia Nervosa

Michael J. Devlin, M.D., New York State Psych Inst, Box 116, 722 W 168th Street, New York NY 10032-2603; B. Timothy Walsh, M.D., Harry R. Kissileff, Ph.D., Rodger A. Liddle, M.D., Janet L. Guss

Summary:

Objective: Studies of eating behavior in patients with bulimia nervosa suggest that their characteristic binge eating may be related to a disturbance of satiety mechanisms. In light of this, we examined the postprandial release of cholecystokinin (CCK), a hormone which appears to be an important mediator of satiety, in patients with bulimia nervosa (BN), and controls. We expand on previously published data by examining CCK response over a range of meal sizes and by simultaneously measuring gastric emptying, a process which both affects and is affected by CCK releasing.

Method: Eight patients with BN and ten controls consumed three meals of radiolabelled Ensure Plus (200 g, 400 g, 600 g) on three separate mornings. Over the next hour, gastric emptying was measured via gamma scintigraphy while blood samples and ratings of hunger, fullness, and satiety were obtained every ten minutes. Seven patients were restudied following short-term (approximately one month) cessation of binge eating and purging.

Results: Random regression modeling revealed a significant group by meal interaction in postprandial CCK response (area under the curve): in controls, CCK release increased with increasing meal size, but in patients, CCK release was unresponsive to meal size. There was a significant overall group effect on peak CCK response and slope to peak, indicating that controls had a more rapidly increasing and higher peak CCK response than patients. Gastric emptying was significantly delayed in patients compared to controls. There were no significant pre-treatment vs. post-treatment differences in postprandial CCK release or in gastric emptying.

Conclusion: Patients with eating disorders display abnormalities in physiological satiety-regulating systems which may not resolve with short-term remission of symptoms.

NR593 Thursday, May 25, 12 noon-2:00 p.m.

Tryptophan Depletion Using Revised Amino Acid Mix

Barbara E. Wolfe, M.S.N., Psychiatry, Beth Israel Hospital, 330 Brookline Avenue, Boston MA 02215; Eran D. Metzger, M.D., David C. Jimerson, M.D.

Summary:

Objective: Acute tryptophan depletion (AD) challenge testing has been used to assess behavioral and physiological sensitivity to transient reduction in CNS serotonin synthesis. In AD testing, administration of a 100 g amino acid-containing drink decreases blood tryptophan (TRP) levels and the ratio TRP to large neutral amino acids (ΣLNAA), resulting in decreased transport of TRP into the CNS for serotonin synthesis. This pilot study examined whether, by using a modified amino acid mixture, commonly observed side effects of nausea and vomiting could be minimized for studies in eating disorder patients.

Method: Six healthy women and five women with current or remitted bulimia nervosa, all medication-free, were studied using a double-blind, randomized design. Following overnight fast on a research unit, subjects received a 31.5 g encapsulated TRP-free amino acid mixture, or lactose placebo.

Results: On the active study day, plasma TRP decreased by 79.6 ± 5.0% and TRP/ΣLNAA decreased by 94.2 ± 2.3% from baseline. Ratings of nausea and vomiting were minimal, and did not differ on active and placebo day. In a partially overlapping group of 12 subjects, plasma insulin levels obtained as a measure of metabolic response showed, as expected, small post-challenge increases on both study days.

Conclusion: This modified procedure for AD challenge resulted in substantial plasma TRP depletion with minimal side effects, and may be advantageous in studies of eating patterns and related behavioral responses.

NR594 Thursday, May 25, 12 noon-2:00 p.m.

Comparison of Impulsivity and Aggression in Women with Bulimia Nervosa and Women with Depression

Theodore E. Weltzin, M.D., Clinical Sci Ctr RmB6/250, 600 Highland Ave, Madison WI 53729; Gregory G. Kolden, Ph.D., Timothy J. Strauman, Ph.D., Jerry Halverson, B.A.

Summary:

We have recently reported that women with bulimia nervosa (BN) score higher than healthy volunteers on ratings of impulsive/aggression (Weltzin et al., in press). Over 50% of BN women also have a lifetime mood disorder. In order to determine if impulsivity in BN women can be accounted for by depressive severity we compared impulsive/aggression ratings of BN women to those of women without BN who had a current major depressive disorder (MDD).

Ten women with BN and ten women with MDD were studied. All women were between 18 and 45 years old. MDD women had no past or current eating disorder. All subjects completed the Beck Depression Inventory (BDI) and the Anger, Irritability and Anger Questionnaire (AIAQ), a self-report instrument of impulsive/aggression (Coccaro et al., 1991).

BN women were 26 years old plus or minus five years, compared to MDD women who were 32 years old, plus or minus eight years old ($p < .10$). There were no differences in scores on the BDI between groups (BN: 27 + 12 vs MDD: 26 + 6). BN women had significantly increased scores on the irritability (20.0 + 5.0 vs. 14.8 + 4.8, df 18; $t = 2.4$; $p < .05$) and a trend toward increased scores on labile anger (12.8 + 5.2 vs 7.5 + 6.4; df 18, $t = 2.0$; $p < .10$) and assault (28.3 + 10.2 vs 20.7 + 9.7; df 18; $t = 1.7$; $p < .10$) subscales of the AIAQ.

The finding that women with BN have increased scores on the AIAQ compared to women with comparable levels of depression who do not have an eating disorder suggests that factors other than depressive severity contribute to impulsivity in BN. Previous studies suggest reduced serotonin activity in BN (Jimerson et al., 1990). An increased tendency to act impulsively in BN is consistent with the hypothesis that a disturbance of serotonin activity may account for a number of symptoms in BN including overeating, depression, and impulsivity.

NR595 Thursday, May 25, 12 noon-2:00 p.m.

Accidental Injuries and Behavioral Problems Among United States Children in Three Ethnic Groups

Regina Bussing, M.D., Division of Child Psychia, Box 100234 UFHC, Gainesville FL 32610-0234; Edgardo J. Menvielle, M.D.

Summary:

Objective: Accidental injuries account for considerable morbidity and mortality in children, and represent a major public health concern in the U.S. This study investigates: 1) The incidence of accidental injuries among children with and without behavioral problems. 2) The role of ethnicity on the relationship between behavioral problems and risk for accidental injuries.

Methods: We studied annual incidence of accidental injury in 11,630 children ages five to 17 using the 1988 National Health Interview Survey. We explored the role of possible child (including three measures of behavioral problems), family, and environmental risk factors for accidents among three ethnic groups (white, black, and Hispanic) using stratified analysis as well as multivariate analytic models.

Results: Accident rates were higher in white children (17.9%) than in black (9.3%) or Hispanic children (9.3%) (P-0.01). The odds of accidental injury in children with severe behavior problems was 1.65 ($P = 0.001$) times greater than in children without behavior problems, after controlling for relevant sociodemographic characteristics. Ethnicity did not alter the relationship between behavior problems and increased injury rates.

Conclusions: This study confirms that children with behavior problems represent a significant risk group for accidental injuries among three ethnic groups in the U.S. Lower accident rates among the two minority groups may be the result of differential reporting. This study points out the need to implement prevention strategies specially targeted at children with behavioral disorders.

NR596 Thursday, May 25, 12 noon-2:00 p.m.

Chronic Health Conditions and Transition to Adulthood: Findings From a Chohort Study

Regina Bussing, M.D., Division of Child Psychia, Box 100234 UFHC, Gainesville FL 32610-0234; Hillevi M. Aro

Summary:

Objective: This study explored the impact of chronic health conditions in adolescence on eventual transitional paths and young adult functioning in a cohort of Finnish youths.

Methods: The study population was derived from a cohort of Finnish youths who had completed a survey in school at the age of 16 and were followed by postal questionnaire at age 22. The surveys included questions about health status, chronic conditions, personal characteristics (including self-esteem), health behavior, education, family background, and personal relationships. The short, 13-item Beck's Depression Inventory was used as a screening instrument for depression. Youths who had reported persistent chronic conditions at both ages 16 and 22 were compared to peers without any chronic health conditions, using two-way analysis of variance for continuous outcomes and logistic regression models for dichotomous outcomes, adjusting for socio-economic differences.

Results: Overall, no major negative impacts of chronic conditions emerged on psychological well-being (including measures of depression and self-esteem), educational pursuits, and social development. These findings indicate that in this cohort most adolescents with chronic condition had a successful transition to adulthood. Against our expectation, youths with chronic conditions had similar rates of nicotine and alcohol consumption as their healthy peers, even though both habits might exacerbate chronic health conditions.

NR597 Thursday, May 25, 12 noon-2:00 p.m.

Rapidly Alternating Multiple Schedules: A Practical Method of Functional Assessment

Kathleen M. Zanolli, HDFL, Kansas University, 4001 Dole, Lawrence KS 66045; Julie Daggett, M.A.

Summary:

Objective: To demonstrate the utility of Rapidly Alternating Multiple Schedules (RAMS) for functional assessment. Current methods are time consuming and are available only in specialized inpatient or clinic settings, diminishing their ecological validity and usefulness for many clients.

Method: The RAMS is a series of one-minute components in which the hypothesized reinforcer is applied, alternated with components in which the reinforcer is not applied, with no break between components. Two adults fill the role of the S+ and S–. The RAMS was compared with lengthier descriptive and experimental analyzed. In Study 1, the adaptive behavior of a typical four-year-old girl was analyzed in a preschool. In Study 2, the aggression and disruption of a six-year-old boy with mental retardation was analyzed in an inpatient rehabilitation setting.

Results: The RAMS yielded the same results as the lengthy descriptive and experimental analyses, and provide more comparisons between experimental and control conditions in less time.

Conclusions: The RAMS provides time-efficient and effective direct assessment of variables that maintain behavior. The flexibility and ease of administration could permit functional assessment in school, clinic, and home settings, making the treatment benefits of functional assessment available to more clients than is currently possible.

NR598 Thursday, May 25, 12 noon-2:00 p.m.

Olfactory Thresholds in Boys with Tourette's Syndrome and ADHD

F. Xavier Castellanos, M.D., Child Psychiatry, NIMH, 10 Center Drive MSC 1600, Bethesda MD 20892; Nancy E. Harnett, Ph.D., William E. Klein, M.S.E.E.

Summary:

Though Tourette's syndrome (TS) has generally been considered a disorder of motor control, recent work has focused on associated sensory phenomena such as premonitory urges. Smelling tics are common in TS and many patients claim to have extraordinarily sensitive olfaction, particularly to noxious odors. As part of a larger study of boys (ages 8–16) comorbid for attention deficit hyperactivity disorder (ADHD) and TS, we assessed olfactory thresholds in ADHD boys (n = 8) and in boys with ADHD and a comorbid tic disorder (n = 10) using a triple-blind method (Olfacto-Labs, El Cerrito, CA). The groups did not differ in age, psychotropic use, or degree of ADHD symptomatology.

While the groups did not differ significantly in detection of the floral scent carbinol, the ADHD + TS patients had a significantly lower detection threshold to a component of sweat, (*E*)-3-methyl-2-hexenoic acid (Mann-Whitney U, 2-tailed p = .03).

This is the first demonstration that tic disorder patients differ in olfactory sensitivity. Extension of these results to medication-free patients and to normals are underway. Increased olfactory sensitivity may be an important phenotypic marker in tic disorders such as Tourette's syndrome.

NR599 Thursday, May 25, 12 noon-2:00 p.m.

Psychopharmacologic Intervention Patterns in Children and Adolescents

Ilisse R. Perlmutter, M.D., Psychiatry, Mt. Sinai, 178 E 80th Street #26-F, New York NY 10021-0450; Raul R. Silva, M.D., Hollis A. Boggs, B.S.

Summary:

Introduction: There is increasing attention directed at the pharmacological treatment of psychiatric disorders in children and adolescents. Assessment of prescribing practices has focused primarily on adults. The focus of this report is to identify variables that impact on the decision to recommend psychopharmacological intervention.

Methods: Sample selection was based on all consecutive psychiatric evaluations during a six-month interval in a pediatric consultation/liaison outpatient facility. Fourteen variables were collected from the charts to determine the unique relationship between them and the decision to recommend a psychopharmacologic intervention. In assessing the relationships that existed Pearson correlational matrices were initially performed. In order to control for confounding variables the information was entered into a multiple regression analysis (MRA).

Subjects: This sample consisted of 50 patients (37 males, 13 females), with ages ranging from 2.8 to 17 years (mean 9.3 ± 3.3).

Results: By correlational matrices the following variables were significantly or marginally significantly correlated: hyperactive symptoms (r = .64; p < .0001), number of psychiatric diagnoses (r = .40, p = .004), male gender (r = .39, p = .005), GAF in the past year (r = .26, p = .07), current GAF (r = –.23; p = .11), other therapeutic modalities (r = .22, p = .12), and conduct disorder (r = .27, p = .13). When the variables were assessed by means of a MRA only the hyperactive symptoms (p = .001) and psychotic symptoms (p = .006) were significantly correlated with the recommendation of medication initiation, while GAF in the past year demonstrated a small trend towards significance (p = .16), (F-ratio 14.335).

Discussion: Of striking interest was the fact that the presence of conduct disorder did not significantly correlate with a medication recommendation. Results will be further discussed at the presentation.

NR600 Thursday, May 25, 12 noon-2:00 p.m.

Predictors of Firesetting Children with Disruptive Disorders

Gabriel Kaplan, M.D., Psychiatry, New Jersey Medical, 991 Chimney Ridge Dr, Springfield NJ 07081-3701; Haftan Eckholdt, M.A.

Summary:

Objective: Children who set fires are frequently diagnosed with disruptive disorders. However, there are no established predictors in this diagnostic group that enable clinicians to assess potential for firesetting. This prospective controlled study examined whether differences existed between firesetters and non-firesetters in a group of conduct disordered children.

Method: Fifty-seven outpatients and parents consented to participate. There were 46 males and 11 females. Mean age was 10.58 years. Subjects were assigned either to a firesetters (N = 39) or non-firesetters (N = 18) group. Subjects were interviewed with the Diagnostic Interview Schedule for Children, Child Behavior Checklist (CBCL), Children's Firesetting Interview, Firesetting Risk Interview, and Coping Scale for Children and Youth. Data from these structured interviews yielded study variables. Differences between the firesetter and non-firesetter groups were analyzed for each variable.

Results: A regression analysis determined that some study variables predicted membership in the firesetters group: curiosity about fire, involvement in fire activities, knowledge of things that burn, fire safety skills, complaints about fire behavior, frequency of mild punishment, CBCL social competence, and CBCL somatic complaints.

Conclusion: A first step in establishing predictors of firesetting was achieved in that clinically measurable characteristics that differentiated firesetters from non-firesetters were found.

NR601 Thursday, May 25, 12 noon-2:00 p.m.

Impulsive Cognitive Style and Outcome in Adolescents

David L. Pogge, Ph.D., Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; John Stokes, Ph.D., Joel Lord, M.A., Philip D. Harvey, Ph.D., William Horan, M.A., Anne Lloyd, M.A.

Summary:

Cognitive impairment is a predictor of a poor outcome in adult psychotic disorders, but has received little research attention in adolescent psychiatric patients. Recent studies have indicated that impulsivity, including attentional impairments (CPT errors of commission) and observer rated behaviors, are associated cross-sectionally with conduct disorders and antisocial tendencies in children and adolescents. In this study, 200 adolescent (age range 13–17) psychiatric inpatients were examined with a battery of cognitive and attentional measures, as well as with psychometric measures of psychiatric symptoms (MMPI) and antisocial tendencies (Psychopathy Check List; PCL). Six months after discharge they were contacted and evaluated for the severity of symptomatology and level of functioning. Four different outcomes were identified: Good outcome; rehospitalization; continued residential treatment; or runaway. Of the first 64 cases followed up, 29 had a good outcome, 23 had been rehospitalized, six had continuous treatment, and six had run away. None of the cognitive or psychometric measures was able to identify bad outcomes as a group, but the subjects who ran away after discharge had a clear profile of psychometric and attentional characteristics. Runaways made over twice as many dual-task CPT errors of commission ($p < .001$), had significantly higher scores on the PCL ($p < .001$), and had significantly more frequent MMPI 4–9 profiles ($p < .01$). All three of these indicators independently ($p < .05$) entered a discriminant function equation which significantly ($p < .001$) discriminated the groups and classified the runaways at a level that was 60% greater than chance. Psychiatric diagnosis and substance abuse did not predict outcome. These data suggest that impulsive tendencies are strongly associated with a specific type of negative outcome in adolescent inpatients, running away, and that both psychometric and attentional measures independently assess this dimension. In addition, our preliminary results suggest that the tendency toward rehospitalization is not predicted by cognitive impairment in adolescents.

NR602 Thursday, May 25, 12 noon-2:00 p.m.

Selective Mutism in Preschool Children: Anxiety As a Primary Associated Feature

Dorothy Young, M.S.W., Neuropsychiatry, Univ of South Carolina, P.O. Box 202, Columbia SC 29202; Harry H. Wright, M.D., Tami Leonhardt, Ph.D., Michael Cuccaro, Ph.D., Laureen J. Noll, M.D.

Summary:

Selective mutism, a disorder that interferes with educational achievement and social communication, is characterized by a consistent failure to speak in specific social situations despite speaking in other situations. This relatively rare (0.3 to 0.8 per 1000) disorder usually has an onset during the preschool years. Comorbid diagnoses and associated features are common. Children with this diagnosis have been described as excessively shy and anxious and as negative and oppositional. We reviewed the published cases (N = 90) of selective mutism for descriptions of anxiety and/or oppositionalism. Over 90% of the cases reported anxiety and 34% reported oppositionalism as an associated feature. The literature reports that most interventions have been ineffective. We report on an effective multimodal intervention approach for preschoolers that includes behavioral family, play, group, and psychopharmacological strategies. Outcome results (12 years later) on two children treated as preschoolers are presented. All of our studies anxiety as a primary feature of selective mutism in preschool children.

NR603 Thursday, May 25, 12 noon-2:00 p.m.

Predictors of Level of Suicidality in Children's Psychiatric Hospitalization

Dinohra M. Munoz, M.D., Psychiatry, NYU Medical School, 20 Knickerbocker Road, Tenafly NJ 07670; Raul R. Silva, M.D., Richard I. Perry, M.D., Valerie Mnuchin, B.S.

Summary:

Introduction: The seriousness of suicidal ideation and gestures in children is often difficult to assess. Despite the fact that actual suicidal completers are uncommon before the age of 12, follow-up studies indicate that childhood suicide attempters go on to attempt suicide approximately twice a year. Additionally, in approximately 30% of certain samples the subsequent suicide attempts were deemed serious. We wished to determine if any of the factors previously described in the literature were useful in predicting level of suicidality in our sample.

Subjects: Sample consisted of 153 children (121 males, 32 females) consecutively admitted to an inpatient psychiatry unit. Their ages ranged from 2.1 to 11.6 years (mean 7.7 ± 2.6).

Methods: In reviewing the literature we identified 11 variables that may be related to level of suicidality in children. A multiple

regression analysis was used to determine if the above scales could predict level of suicidality.

Results: The results of the multiple regression analysis revealed that from the original 11 variables, only five significantly predicted level of suicidality. Male gender significantly predicted higher levels of suicidality ($p = .03$) as did full-scale IQ ($p = .04$) and Child Welfare Agency involvement ($p = .002$). The presence of conduct disorder ($p < .0001$) and attention deficit hyperactivity disorder ($p = .007$) were both negatively related to level of suicidality.

Discussion: In addition to the above results our findings confirm those of other authors who described that neither socioeconomic status nor aggression differentiated psychiatric controls from adolescents with suicidal behavior. We will further expound on our findings at the meeting.

NR604 Thursday, May 25, 12 noon-2:00 p.m.

Correlates of Antidepressant Responsive ADHD

Stephen G. Hayes, M.D., Medicine, University of South Calif, 2810 E. Del Mar B1 #4, Pasadena CA 91107

Summary:

There is some controversy regarding choice of class of psychopharmacological agent in the treatment of ADHD, and evidence that both stimulants and the so-called antidepressants are effective. No clear clinical criteria have been described heretofore which discriminate between good responders to either class of agents. In this study, 28 patients were divided into stimulant-responsive and stimulant-nonresponsive/antidepressant responsive by medication trials, using the Abbreviated Conners Quotient (ACQ) as a measuring instrument. A variety of comorbid symptoms and historical factors were studied prospectively and then analyzed in order to clarify any differences between the groups. A history of separation anxiety, enuresis, and encopresis were found to predict failure to respond to stimulants, with subsequent positive response to antidepressant agents. Relevant theoretical issues and practical applications are discussed.

NR605 Thursday, May 25, 12 noon-2:00 p.m.

Selective Serotonin Reuptake Inhibitors in Children: Pulse and Blood Pressure Change

Nancy B. Campbell, M.D., Medical College of Ohio, 3000 Arlington Avenue, Toledo OH 43614-5802; Marijo B. Tamburrino, M.D., Kathleen N. Franco, M.D., Cynthia L. Evans, M.D., Amy Eisaman, Royal Stacy

Summary:

Use of antidepressants in children, although common, has not been researched significantly, especially in the area of side effects.

The purpose of this study is to explore the pulse and blood pressure changes secondary to antidepressants in hospitalized children. Subjects consisted of 55 children, (13 females and 42 males) age range from four to 12 years, (average age 8.82 years). Of these 56 children, 77% (or 22 children) on fluoxetine had orthostatic changes, while 83% of the 18 children on imipramine, 92% of 13 children on sertraline, both of the two children on paroxetine, and one of the children on bupropion had significant orthostatic changes. Sixty-eight percent (68%) had both orthostatic blood pressure and pulse changes. The majority of these occurred within the first three days of medication initiation, thus occurring at low doses; changes were also frequently noted immediately following dose increases. Rarely were the children symptomatic or did they complain of side effects. This study suggests that most antidepressants affect blood pressure and pulse of children orthostatically; monitoring of these parameters and establishment of guidelines may be beneficial.

NR606 Thursday, May 25, 12 noon-2:00 p.m.

The Origins of Child Abuse: New Theory and Research

Max Lesnik-Oberstein, M.D., JJ Viottastraat 32II, Amsterdam 1077JS, The Netherlands; Arend J. Koers, M.D., Leo Cohen, Ph.D.

Summary:

A revised version of the three-factor theory of child abuse is presented. We report on a research designed to test three main hypotheses (and 23 subhypotheses) derived from Factor I. The three main hypotheses are: 1) that psychologically abusive mothers have a high level of hostile feelings (Factor I); 2) that the high level of hostile feelings is associated with low marital coping skills, a negative childhood upbringing, a high level of stress, and a high level of strain; and 3) that maternal psychological child abuse is associated with low marital coping skills, a negative childhood upbringing, a high level of stress, and a high level of strain.

Forty-four psychologically abusive mothers were compared with 128 matched (for age and educational level) non-abusing mothers on a variety of objective measures.

The three hypotheses were supported, with the exception of the component of hypothesis 2 concerning the association between stress and maternal hostility.

The positive results are consistent with the three-factor theory.

References:

1. Parental hostility and its sources in psychologically abusive mothers: A test of the three-factor theory. Child Abuse and Neglect, *International J* vol 19. No 1, pp 33–49, January 1995.

2. Tzeng OCS, Jackson SW, Karlson HC, Praeger: see pp 19, 48–50, 58–62, 189, 193, 197–200, 228, 232, 280, 1991.

NR607 Thursday, May 25, 12 noon-2:00 p.m.

A New Measure for Assessing Trauma in Adolescents

David Bernstein, Ph.D., Psychiatry, Bronx VAMC, 130 W. Kingsbridge Road, Bronx NY 10468; David L. Pogge, Ph.D., Taruna Ahluvalia, B.A., Leonard Handelsman, M.D.

Summary:

Objective: Childhood maltreatment is a common but frequently under-reported problem among psychiatrically impaired adolescents. In this study, we examined the utility of a new maltreatment scale, the Childhood Trauma Questionnaire (CTQ), in a sample of adolescent psychiatric patients.

Method: 398 male and female adolescents (age = 12 to 17 years, mean $\pm$ s.d. = 14.9 $\pm$ 1.4 years) consecutively admitted to the inpatient service of a private psychiatric hospital were given the CTQ as part of a larger test battery. Patients' CTQ responses were compared to ratings of suspected sexual or physical abuse made at intake, based on all available data at that time.

Results: Principal components analysis of CTQ items yielded five rotated factors—emotional abuse, emotional neglect, sexual abuse, physical abuse, and physical neglect—closely replicating the factor structure obtained in an earlier study of adult patients (Bernstein et al., 1994). The internal consistency of the CTQ factors was extremely high (Cronbach's alpha = .81 to .95, median = .91). Adolescents' CTQ responses were highly convergent with clinical intake ratings of suspected sexual and physical abuse (sensitivity = 81.5% and 81.7%, respectively). In addition, the CTQ identified many new potential cases of abuse that may have escaped detection at intake.

Conclusions: These initial findings suggest that the CTQ is an effective tool for assessing trauma histories in an adolescent psychiatric setting.

NR608 Thursday, May 25, 12 noon-2:00 p.m.

A Pilot Study of Attitudes Toward Behavioral Emotional Problems, Psychopathology, and Social Desirability Among Special Education Students

Spyros J. Monopolis, M.D., Psychiatry, Woodbourne Center U Med, 8116 Bellona Avenue, Towson MD 21204-1958; John Myhill, Ph.D., Peggy Caltrider, M.S.W., Patricia Cronin, M.S.W., Patrick Crouse, M.A.

Summary:

Objective: Our goal was to study the relationships among attitudes regarding behavioral/emotional problems, self-reported psychopathology, psychiatric diagnoses, and social desirability among special education students in a school-based mental health clinic.

Method: Subjects (N = 33, age $\bar{X}$ = 13.3 years, 67% black, 100% male) were assessed through: standardized instruments—Youth Self Report YSR), Rotter's Social Desirability Scale; psychiatric interview; and a questionnaire—Attitudes Toward Behavioral/Emotional Problems. Data analysis consisted of X^2, linear logistic regression, ANOVA/ANCOVA, and correlation procedures. Social desirability was included as covariant.

Results: Statistically significant findings included: Youngsters who attributed their problems to external factors or internal processes reported psychopathology on most YSR dimensions. Students who perceived their family as the most important source of help were less withdrawn. Youths who said that the most significant kind of help was change of school manifested withdrawal and delinquency. Those who thought that family therapy would be most helpful presented somatic complaints. Students attributing their problems to external factors received diagnoses of conduct disorder or dysthymia. Additional analyses are in process focusing on the relevance of specific attitudes in regard to psychopathology.

Conclusions: The interrelationships among attitudes, self-reported psychopathology, and psychiatric diagnoses are complex in this sample of special education students. A strong convergence occurs among attitudes and psychopathology regardless of attribution of youngsters' behavioral/emotional problems to external factors or internal processes.

NR609 Thursday, May 25, 12 noon-2:00 p.m.

Risperidone in the Treatment of Children and Adolescents with Psychotic Illness: A Retrospective Review

Stephen Grcevich, M.D., Psychiatry, Case Western Research U., 8500 East Washington Street, Chagrin Falls OH 44023; Robert L. Findling, M.D., S. Charles Schulz, M.D., William A. Rowane II, M.D.

Summary:

Risperidone is a safe and effective antipsychotic agent in adult patients with psychotic disorders. Its characteristics, including its association with a low incidence of dystonic reactions and low risk of causing long-term movement disorders, such as tardive dyskinesia, suggest that it may be a potentially useful agent in the treatment of psychosis in children and adolescents. We conducted a retrospective review of 15 children and adolescents whose psychotic illnesses had been treated with risperidone. Diagnoses were established by one child and adolescent psychiatrist according to DSM-III-R criteria and confirmed by another. Improvement was assessed by means of the Brief Psychiatric Rating Scale and the Clinical Global Impression scale, based on chart reviews by two psychiatrists. Adverse events were recorded by means of an event checklist. Risperidone appears to have been an effective treatment agent for most of the patients. Detailed results will be presented and discussed.

NR610 Thursday, May 25, 12 noon-2:00 p.m.

Families and Homelessness in Mental Illness

Lisa B. Dixon, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Bette Stewart, B.A., Nancy Krauss, M.S.W., Jean Hyde, M.S., Ann L. Hackman, M.D., Anthony F. Lehman, M.D.

Summary:

Objectives: Little is known about the relationships between *homeless* persons with severe mental illness (SMI) and their families. We characterize: 1) the supports families provided to clients, and 2) the interventions families received from an assertive community treatment (ACT) team serving 67 SMI homeless persons as part of an experiment comparing ACT to standard services. ACT includes an Alliance for the Mentally Ill (AMI) member providing family outreach.

Methods: The medical director reviewed all cases using charts and staff interviews to determine the frequency and nature of clients' and treatment team's family contact.

Results: 78% of clients had contact with their family of origin (mothers (46%), siblings (39%)); 42% had at least *monthly* contact. Families provided material and/or emotional support to 58% of clients. ACT worked with families of 62% of clients. ACT achieved more contact with the family if the client was female ($p < .02$), younger ($p < .05$), and non-substance abusing ($p < .005$). Increased ACT family contact was also associated with the client having more permanent housing days ($p = .06$). The most common obstacles included clients' substance abuse, psychosis, geographic distance, and family's lack of knowledge.

Conclusions: Contrary to the perception that homeless individuals are isolated from family, most homeless clients had significant family contact. ACT, with the participation of a family outreach worker, established contact with most families. Gender, age, and substance abuse were predictive of success in establishing family contact. Obstacles to family interventions were similar to those found among domiciled SMI persons.

NR611 Thursday, May 25, 12 noon-2:00 p.m.

Medication Compliance of Programs of Assertive Community Treatment Patients

Lisa B. Dixon, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Peter Weiden, M.D., Anthony F. Lehman, M.D., Michael A. Torres, M.D.

Summary:

Objectives: Programs of Assertive Community Treatment (PACT) have reduced hospitalization for persons with severe mental illness (SMI). This may be mediated by enhanced medication compliance. We determined the medication compliance of 77 homeless persons with SMI receiving PACT services.

Methods: The prescribing psychiatrist rated patients' baseline and quarterly medication compliance for one year as part of a randomized trial comparing the PACT model to standard services for homeless persons. Patients who refused initial medication prescription or missed more than one consecutive week of medication during the interval were considered noncompliant.

Results: 49 (64%) of patients were *noncompliant* at referral. The noncompliance rate dropped to 34% after three months, and 26% at one year. Fifty percent of baseline noncompliers became compliant by three months. Compliance patterns were not associated with number of days in permanent shelter or clinical or demographic factors except symptomatology which was significantly higher in noncompliers.

Conclusions: The PACT model produced a significant enhancement of medication compliance in a group of homeless persons with SMI. However, only partial compliance was achieved; the high intensity of PACT seemed necessary to maintain the 60%

to 70% compliance rate. Although noncompliance was related to level of symptoms, it did not appear to be related to housing outcomes.

NR612 Thursday, May 25, 12 noon-2:00 p.m.

The Efficacy of Respite Care in Psychiatry

Jeffrey L. Peters, M.D., Psychiatry, VA Medical Center, Highland Drive, Pittsburgh PA 15206; George G. Dougherty Jr, M.D., Lisa Fitzsimmons, M.S.W., Joanne Karcher, R.N., Daniel P. van Kammen, M.D.

Summary:

Purpose: This data analysis examines the effect of a psychiatric respite care program on inpatient utilization in the seriously and chronically mentally ill.

Methods: Information on 64 consecutive participants (62 men, two women, mean age 49 ± 13.4 years) was available. By *DSM-III-R* criteria, 61% had chronic schizophrenia, 19% a mood disorder, 13% a chronic anxiety disorder (most often PTSD), and 7% an organic mental disorder. Each patient served as his or her own control. The total number of inpatient days during the year prior to respite care was compared to the total number of inpatient days after the addition of respite care to the treatment plans using a two-tailed paired t-test. This respite care program is described in the poster.

Results: There was a significant reduction in total number of inpatient days (5688 to 2358 days, t = –2.67, p less than 0.01). In this sample, 38% of patients needed acute admissions along with respite stays, and 55% of the sample spent less total time in the hospital.

Conclusions: Respite care may be a clinically effective and cost effective addition to the treatment plans of some patients.

NR613 Thursday, May 25, 12 noon-2:00 p.m.

Correlation of Family Physician Demographics with Psychiatric Referral Patterns

Gregory E. Shadid, M.D., Psychiatry, Mayo Clinic, 200 First Street SW, Rochester MN 55905; John Gastorf, Ph.D., Joyce A. Tinsley, M.D.

Summary:

Objective: The purpose of this study is to determine if family physician demographics are related to specific patterns of psychiatric referral.

Method: A questionnaire was developed from interviews with family practice and psychiatric faculty at the University of Oklahoma College of Medicine-Tulsa. It was pilot tested by the family practice residents at OUCMT before being mailed to the 744 members of the Oklahoma Academy of Family Physicians.

Results: Urban family physicians refer more for problems in daily living (coping, chronic pain, etc.) and consider psychopharmacology and their own time limitations as important considerations for referral. Their rural counterparts are less satisfied with availability of psychiatrist, feedback from psychiatrist, and outcome of psychiatric referral. Younger family physicians refer more often but are less satisfied with availability, feedback, and quality of care of psychiatric referral. Female family physicians refer more often and refer twice as often to other mental health professionals (psychologists, social workers, and psychiatric nurses). They also refer more for anxiety, spouse abuse, separation and divorce, recurrent pain, and inability to cope.

Conclusion: The results suggest that family physician demographics such as age, gender, and urban versus rural setting are significantly related to specific patterns of psychiatric referral.

NR614 Thursday, May 25, 12 noon-2:00 p.m.

Quality of Life: Exploring How Patients Change

Sharon G. Dott, M.D., Dept of Psychiatry, Route D-28, 301 University Blvd., Galveston TX 77555; David P. Walling, Ph.D.

Summary:

The development of novel pharmacotherapy and continued emphasis on psychosocial treatment has resulted in increasing concern with quality of life (QOL). The present study examines QOL, using the Quality of Life Enjoyment Scale (Q-LES-Q), in a population of individuals with severe mental illness.

Objective: The following research questions were explored: 1) Do subjects admitted to a psychiatric hospital differ in perceived QOL from those admitted to a residential treatment center? 2) Does subjective QOL improve during short-term treatment? 3) Are there differences by diagnostic category in perceived QOL?

Method: Subjects were assessed upon admission and discharge using the Q-LES-Q. In addition, demographic data were obtained. A total of 78 subjects participated.

Results: Comparison of Q-LES-Q admission scores revealed no significant between-group differences on admission. Pre/post test MANOVA's suggest both groups significantly improved in perceived QOL. Groups did differ on admission, when compared by diagnosis, with subjects with depressive disorders scoring lower on four scales. No discharge differences were noted.

Conclusion: In sum, this study suggests that QOL can be improved during short-term treatment. Factors likely contributing to the noted change include medication stabilization, 24-hour supervision, and structured activity programs. Future research ideas are also discussed.

NR615 Thursday, May 25, 12 noon-2:00 p.m.

Persons with Disabilities in Public Housing: Resident Preferences, Supports and Service Needs

Susan J. Boust, M.D., UNMC Dept of Psychiatry, 600 South 42nd Street, PO Box 985575, Omaha NE 68198-5575; Earl H. Faulkner, M.A.

Summary:

Providing housing and supports for people with psychiatric and/or physical disabilities is a major public policy and service challenge. The aim of this study was to survey a population of disabled persons living in public housing high-rise apartments. Using a questionnaire developed by the Creighton-Nebraska University Department of Psychiatry, 88 persons with chronic mental disabilities were surveyed in regard to: perceptions of current living situation, supports and services, costs and income, and psychiatric/medical history. Results indicate that these participants were generally satisfied with their residential setting and choose to remain in these public housing settings. In times of emotional crisis most residents used informal sources of support (i.e., family and friends) rather than mental health personnel, clergy, or housing authority personnel. Many of the participants indicated the need for better access to mental health personnel and services. Respondents reported that significant tension exists between disabled and elderly patients. In general, respondents did not feel that the solution to this "mixed population" challenges was segregation. Recommendations are given for addressing these "mixed population" challenges and for increasing community mental health involvement in public housing of disabled persons.

NR616 Thursday, May 25, 12 noon-2:00 p.m.

Psychiatric Care in Emilia-Romagna 1978–1994: A Soft Revolution

Angelo Fioritti, M.D., Serv. Salute Mentale, Viale Pepoli 5, Bologna 40123, Italy; Russo Lo, M.D., Giovanni de Girolamo, M.D.

Summary:

The Italian psychiatric reform has gained worldwide attention, yet only recently has a substantial amount of quantitative information become available to perform a reliable and in-depth evaluation of its state of implementation. The authors present data gathered through an in-depth census of public and private, in- and outpatient psychiatric services currently available and established after the Reform in Emilia-Romagna, a wealthy region with approximately four million inhabitants in Northern Italy.

Large mental hospitals, which represented the mainstream of psychiatric care before the reform and contained up to 5,000 residents, have been gradually phased down, and the number of residents has decreased to a low of about 500, mainly elderly patients. There are in the region 136 community mental health centers (an average of one such service per 28,820 population), 46 day hospital centers, 11 general hospital psychiatric units (175 beds), four university psychiatric clinics (104 beds), and 121 sheltered flats are in operation. Seven private psychiatric facilities (438 beds) are also located in the region. Overall there are 717 psychiatric beds in the region (0.18 per thousand population).

On the whole, the feasibility of the reform has been proved; however, a closer coordination of regional policy seems necessary, together with an increase of the shift of funding from mental hospitals to the new community services.

NR617 Thursday, May 25, 12 noon-2:00 p.m.

Depression in Asian-Americans

Sudhakar Madakasira, M.D., Dept. of Psychiatry, Univ. of MS Medical Cente, 2500 North State Street, Jackson MS 39216-4505

Summary:

Literature generally suggests that Asian Americans are reluctant to seek mental health services and shy away from mental health research. Research involving Asian Americans has also been limited to large cities. The purpose of our study was to survey the depressive symptoms and mental health histories of Asian Americans living in a small city. Another purpose was to assess the relationship of depressive symptoms to other mental health symptoms, level of acculturation, and life events. Depression was assessed by the Center for Epidemiological Studies—Depression Scale (CES-D), mental health symptoms by the Symptoms Check List—90 (SCL-90), acculturation by the Suinn–Lew Acculturation Scale, and life events by the Holmes–Rahe Life Events Scale. Of the 462 Asian Americans (Filipino, Korean, Chinese, and Indian) who were mailed the survey questionnaire, 93 (20%) responded. A majority were male (56%), married (69%), older than 30 years (63%) and college-educated (87%). Twenty-two (25%) met the threshold score ≥16 on the CES-D and were considered significantly depressed. When compared to the nondepressed group, more in the depressed group admitted needing help ($X^2 = 12.4$, $p < .0004$) but not seeking help ($X^2 = 0.7$, NS). The mean CES-D scores did not correlate with the mean acculturation scores but correlated with life events scores ($r = 0.32$, $p < .002$) and SCL-90 scores ($r = 0.79$, $p < .000$). These results suggest that Asian Americans are resistant to mental health research; one-fourth may be depressed but do not seek help; their depression may be associated with other mental health symptoms and increased life stresses. These results warrant an outreach and mental health campaign aimed at Asian Americans.

NR618 Thursday, May 25, 12 noon-2:00 p.m.

Emotional Disorders in Adolescent Refugees From Central America and South East Asia

Cecile Rousseau, M.D., Research, Douglas Hospital, 6875 La Salle Blvd., Verdun Quebec H4H 1R3, Canada; Anne Levensque, M.Sc.

Summary:

The aim of this poster is to compare the manifestation of emotional disorder among refugee adolescents from different cultures.

Symptoms were assessed in 158 refugee adolescents, aged 12 to 16, from Central America and South East Asia using Achenbach's Child Behaviour Checklist and Youth Self-Report.

The global level of symptoms reported by the adolescents themselves was similar for both groups and quite high if compared to a North American normative sample. However, the parents from South East Asia reported dramatically fewer symptoms in their children than Central American parents. In contrast to the more common North American symptom profile, both parents and adolescents in the two cultural groups reported more internalized than externalized symptoms.

Results suggest that there is a predominance of internalized symptoms in refugee adolescents of different cultures that could be linked to the acute stress that these children have experienced. The acknowledgment of these symptoms by the parents appears to be subject to cultural variations and possibly to denial and post-traumatic avoidance. Comparison of these results with those from a previous study involving a similar group of children aged eight to 12 suggests that there may be stability of these characteristics over different developmental stages.

NR619 Thursday, May 25, 12 noon-2:00 p.m.

An Approach to Engaging in Culturally Sensitive Research on Puerto Rican Youth

Odette Alarcon, M.D., Research Center, Wellesley College, 106 Central Street, Wellesley MA 02181; Sumru Erkut, Ph.D., Cynthia Garcia-Coll, Ph.D.

Summary:

This paper describes two longitudinal research projects as examples of culturally-sensitive research on Latino youth, and gives the results of the work accomplished during the first year. Both papers are grounded in a cultural-ecological approach. The adolescent study is a four-year longitudinal study of socio-emotional development of 300 Puerto Rican adolescents, the child project is a five-year longitudinal study of health and growth of 300 Puerto Rican school-aged children. Specific stress factors such as racism, prejudice, minority status, migration, ethnicity and color, and their influence on health and development are studied.

The first year was spent in translating and adapting existing instruments and creating new ones. In translating, the dual focus approach was used. Working with focus groups, a theoretical approach to measure acculturation as composed of behavior, preference, competence, and identity was developed. The new instruments developed and field tested are:

A. *Acculturation* a 29-item scale yielding a reliability of .94
B. *Family Functioning and Values,* a 30-item scale yielding a reliability of .84
C. *Receptivity of the Neighborhood* to Puerto Ricans
D. *Perceived Discrimination* which measures experienced and anticipated discrimination and their impact on health and development.
E. *Child Perception of Color* which measures the child's self-perception of skin color. This measure has been tested in Puerto Rico.

The adolescent project is financed by NICHD and the child project by the Bureau of Maternal and Child Health.

NR620 Thursday, May 25, 12 noon-2:00 p.m.

Development of a Scale to Measure Japanese-American Values and Attitudes

Neal Anzai, M.D., Psychiatry, University of Hawaii, 1319 Punahou Street 6th Floor, Honolulu HI 96826; Junji Takeshita, M.D., Leslie A. Matsukawa, M.D., Satoru Izutsu, Ph.D., Roger Hamada, Ph.D., Linda B. Nahulu, M.D.

Summary:

Objective: To develop and validate a questionnaire measuring Japanese identity, culture, beliefs, attitudes, and values in American high school students who are either of pure or part Japanese ancestry and to compare this to a non-Japanese population. This scale would be used to study ethnic differences in the expression of psychopathology.

Method: A review of the literature and "focus groups" of Japanese-Americans in Hawaii were used to identify potential Japanese values and attitudes that could be endorsed on a five-point scale. In November 1994, a 41-item questionnaire was administered to approximately 700 students (grades 9–12) at a public high school in a suburb of Honolulu, Hawaii.

Results: Of these 700 students, there were 237 with varying amounts of Japanese blood. They were compared to 112 non-Japanese students on their endorsement of Japanese attitudes. Statistical comparison by T-test showed significant differences ($p < 0.05$) between Japanese and non-Japanese on 23 of the 41 questions. Significance was especially high ($p < 0.005$) on 14 questions.

Conclusions: Several questions were able to elicit differences in values and attitudes between Japanese and non-Japanese high school students. This scale would be useful in future investigations studying the ethnic differences.

NR621 Thursday, May 25, 12 noon-2:00 p.m.

Childbearing Practices in Japan and Canada

Susanne I. Steinberg, M.D., Psychiatry, St Marys Hospital, 3830 Lacombe Ave, Montreal PQ H3T 1M5, Canada; Hiroma Kohzu, M.D., Sophie Mainville, B.N., Megumi Oba, Kimiyo Hayakawa, M.A., Francine Houle, R.N.

Summary:

Childbearing practices have important implications for individual development and the creation of functional societies. One hundred ninety-five women from four groups (French Canadians, English Canadians, Japanese in Montreal, Japanese in Tokyo) were administered a semi-structure interview in English, French, or Japanese (back translated when appropriate). Each subject was interviewed in her mother tongue by trained interviewers, who were matched for ethnicity and language and who recorded the replies verbatim. Quantitative and qualitative information were elicited, then coded differently and separately. Some results follow. Toilet training was expected to commence at a specific age more so by Japanese than Canadians (=.006). If the schedule was not respected, the Japanese in Montreal but not Tokyo tended to label the mother as incompetent ($p = .025$) or lazy ($p = .032$). Certain disciplinary measures were shared (discussion, scolding, and screaming). Others were more common in Canada than Japan: eliminating an activity ($p = .007$), time out ($p < .001$), rewards for good behavior ($p < .001$), setting an example ($p < .001$). The Japanese in Tokyo reported the least spanking ($p = .011$). The profile of communication strategies used by the Japanese in Montreal may interfere with intimacy: little open discussion, more forbidden topics, more misunderstandings, and reliance upon non-verbal messages. Styles of emotional sharing differed between the Canadians who hug, cry, joke more (<.001) and hit less ($p = .029$) than the Japanese. Gender issues are evident in education and career choice, parental roles in discipline and sex education, with variations between the two nationalities. Transcultural research using a combination of qualitative and quantitative methods identifies areas requiring social and health interventions for families.

NR622 Thursday, May 25, 12 noon-2:00 p.m.

Polypharmacy: A Problem of the Decade of the Nineties

Marion E. Wolf, M.D., Psychiatry, VA Medical Center, 3001 Green Bay Road, North Chicago IL 60064; Edward D. Bukowski, M.D., John Conran, M.D., Larisa Sirotovskaya, M.D., Valery Kagan, M.D., Aron D. Mosnaim, Ph.D.

Summary:

Health care delivery systems in the United States, both in the private and public sectors are being closely scrutinized. Consumers and health care providers are well aware of the costs of psychiatric illness. The economic burden of depression alone amounts to an annual expense of $44 millions. This expense compares with the cost of cardiovascular diseases and cancer. Preliminary observations suggest that psychiatrists may be responding to pressures to decrease the length of inpatient stay by practicing polypharmacy. In this study the clinical characteristics and treatments of 80 chronic psychiatric patients in 1984 were compared with those of 60 similar patients treated in the same institution in 1993. The results obtained showed that there was a significantly higher frequency of substance abuse in the 1993 population (40% vs 21%). Whereas alcoholism accounted for all the 1984 cases of substance abuse, mixed substance abuse was prevalent in 1993. In 1984, most patients were managed with one or two psychotropic drugs, and only 7% received an anticonvulsant agent. In 1993, polypharmacy was common: 60% received three or more psychotropic agents. The most frequent combinations included neuroleptics, lithium, and anticonvulsants. These findings suggest that the recent evident shift toward polypharmacy may reflect rising expectations of rapid and less extensive hospital level psychiatric treatment, selection pressures toward more complex and less responsive patients, and availability of a wider array of psychotropic agents.

NR623 Thursday, May 25, 12 noon-2:00 p.m.

Long-Term Disability Benefits for Chronic Fatigue Syndrome

Peter Manu, M.D., Director of Medical Serv., Hillside Hospital, 75-59 263rd Street, Glen Oaks NY 11004; Thomas J. Lane, M.D.

Summary:

Objective: To determine the quality of medical evaluations leading to long-term disability benefits (LTD) for chronic fatigue syndrome (CFS).

Method: Cross-sectional study of 89 patients (pts) receiving LTD from one of three large private insurance companies. Data collected investigated compliance with published CFS diagnostic criteria.

Results: The pts were predominantly non-Hispanic white (97%), middle age (mean 40.8 years, S.D. 9.1 years), female (90%), and previously employed in managerial or clerical jobs (82%). The pts had been receiving LTD benefits for an average of 33 months. Only 60% of pts had documentation of sufficient symptoms to fulfill the CFS criteria. Although 88% of pts had symptoms consistent with psychiatric disorders whose symptoms include fatigue

and 76% were receiving treatment with antidepressant drugs (usually low-dose tricyclic agents or serotonin re-uptake inhibitors), only 38% of pts had a psychiatric evaluation. Similarly, although all pts complained of cognitive deficits, neuropsychological testing was used to confirm these deficits in only 12% of pts. In contrast, laboratory tests which have no recognized value (antibody titers to the Epstein-Barr virus or human herpes virus 6) had been performed in 82% of cases. The majority (54%) of physicians recommending LTD believed that CFS is produced by immune dysfunctions or chronic viral infection.

Conclusion: The quality of medical evaluations resulting in LTD for presumed CFS appears poor due to inadequate diagnosis and treatment of psychiatric disorders.

NR624 Thursday, May 25, 12 noon-2:00 p.m.

Psychometric Properties of a Decision Support Tool

William M. Glazer, M.D., Yale University, 22 Linden Point Road, Stony Creek CT 06405; Geoffrey Gray, Ph.D.

Summary:

In response to the managed care movement of the 1980s, the medical profession has begun to define criteria for assigning patients to various levels of treatment in order to reduce or eliminate biases that may be unrelated to the medical necessity of that treatment. Without such criteria, psychiatric practitioners are vulnerable to skepticism of payers and policy makers attempting to reform the health care industry. We report psychometric properties of a decision-support scale designed to quantify the decision-making process for allocating psychiatric care. The authors developed a scale to evaluate the level of care needed for patients requiring psychiatric treatment in a health maintenance organization (HMO) setting. This study examines the validity of that scale by measuring inter-rater agreement among utilization reviewers from the HMO and between those reviewers and the clinicians who evaluated the patients daily. Agreement (kappa) among the five raters on dimensions of the scale ranged from .71 to .98. Kappas for agreement between the treatment intensity proposed by the reviewer/rater and used by the treating clinician were .41, .38, .40, .35, .36, and .39, respectively. The scale is reliable in the hands of trained personnel.

NR625 Thursday, May 25, 12 noon-2:00 p.m.

The Behavioral Health Care Outcomes Project: Part II. The 15 Minute Psychiatric Medication Visit

Robert Raskin, Ph.D., Director, Tulsa Inst. Behav. Sci., 1620 East 12th St., Tulsa OK 74120; Jill Novacek, Ph.D.

Summary:

As a result of deinstitutionalization and the onset of managed care, modern psychiatry is in the midst of a major paradigmatic shift. The psychiatrist as therapist is rapidly evolving into the psychiatrist as medication manager, and the 60 minute psychiatry session is giving way to the brief psychiatric visit. What will psychiatrists in the year 2,000 encounter when they enter a modern truncated psychiatric playing field in which they have 15 minutes to practice their craft?

This study examines the 15-minute psychiatric visits of 470 patients who have serious mental illness and are receiving treatment at a state-funded community mental health center. Following a standard 15-minute medication treatment review, 9 psychiatrists rated their patients on: patient familiarity, severity of 15 symptom problems, current medications, medication compliance and side-effect problems, medication effectiveness, and medication plan. In addition, psychiatrist ratings are compared with data on the same patients derived from case manager ratings and one-hour structured interviews with the patients themselves.

Results describe the most and least common symptoms observed and medications prescribed, the relationship between observed symptoms and medications prescribed, the prevalence of observed medication non-compliance, drug and alcohol use, and medication side-effect problems. Results also describe discrepancies between psychiatrist, case manager and patient perspectives on medication compliance, drug and alcohol problems, and medication side-effect issues.

NR626 Thursday, May 25, 12 noon-2:00 p.m.

Court Ordered ECT at Veterans Affairs Hospitals in Illinois

Jagannathan Srinivasaraghavan, M.D., Psychiatry, VA Medical Center, 400 Fort Hill Avenue, Canandaigua NY 14424; Atul R. Mahableshwarkar, M.D.

Summary:

In the state of Illinois section 2-110 of the Mental Health and Developmental Disabilities Code requires a guardian of an incompetent recipient to get approval of the court to provide informed consent for participation of the ward in ECT, if the guardian deems that such services are in the best interest of the ward. The Veterans Affairs hospital patients who were considered for court-ordered ECT from 1988 to 1994 from six VA hospitals in Illinois are the subjects of this study. A simple questionnaire identified six patients considered for ECT by Illinois courts during the period.

Results: All the patients were male, mean age 53.5 (range 25–75). Four were white and two black. They came from two hospitals and two judges from different counties approved ECT for all six cases. Average number of days taken from date of filing for guardianship to date of court approval was 28 days. One of the six patients received two courses of ECT. Average number of treatments per course was 12.14 (range 6–29). Three courses were followed by maintenance ECT. Three patients had major depression with psychotic features, two had bipolar affective disorder with psychotic features, and one had catatonia. Treatments resulted in complete remission or marked improvement equally.

Conclusion: While court-ordered ECT for incompetent patients is cumbersome, the courts in general approve ECT and the outcome is very good for the patients.

NR627 Thursday, May 25, 12 noon-2:00 p.m.

Appropriateness of Forensic Hospital Admissions

Toshiyuki Shibata, M.D., Psychiatry, University of Hawaii, 45-710 Keaahala Road, Kaneohe HI 96744; R. Andrew Schultz-Ross, M.D., Carole McLeod, M.A.

Summary:

Objective: The appropriateness of forensic admissions to a state hospital based on civil commitment criteria and need of hospital level care was investigated.

Method: Sixty-one patients admitted to a forensic admissions ward over a six-month period were evaluated for dangerousness, suicidality, and inability to care for self. Committability was evaluated based on the state's commitment statutes for civil admissions.

Results: Of the sixty-one patients admitted to the hospital by the criminal court, 38% did not meet civil commitment criteria. The majority of the patients had committed minor offenses and were admitted for pre-trial evaluations. The clinicians showed good inter-rater reliability for assessment of committability and psychopathology.

Conclusions: The majority of patients did not meet civil commitment criteria and many did not have the degree of psychopathology that would suggest that hospital level care was required for their evaluation and/or care. The results that forensic admissions are being over-utilized by the court, possibly due to the combina-

tion of strict civil commitment standards and comparatively lax criminal commitment laws. The use of these beds for these individuals could mean that more acutely ill patients are being denied hospitalization.

NR628 Thursday, May 25, 12 noon-2:00 p.m.

Patients' Attitudes Regarding Forced Medication

Lanna M. Moore-Duncan, M.D., 71 Oakwood Village #2, Flanders NJ 07836; William M. Greenberg, M.D., Rachel Herron, M.S.W.

Summary:

Objective: Forcible antipsychotic medication procedures are usually felt necessary, but potentially traumatically violating individuals' bodies and autonomy. We explored such objecting patients' subsequent attitudes toward their experience.

Method: Previous studies interviewed still-hospitalized patients, perhaps affecting their answers. We interviewed consecutive forcibly medicated (72-hour emergency or non-emergent "Rennie" procedures) English-speaking acute inpatients who received community discharges, via subsequent telephone contact, by a clinician not involved with their treatment.

Results: Of 65 such patients, seven were rapidly readmitted, three didn't recall the procedure, and 32 others were not locatable or refused the interview. Of the 28 interviewed, only 43% received any injections, the remainder accepted oral medication under duress. Sixty-one percent professed fear of side effects, 18% feared "addiction," and 18% didn't like others controlling them. Thirty-six percent recalled being angry, 14% embarrassed, 25% fearful, 36% helpless, but 21% relieved. Surprisingly, 61% retrospectively felt it was good they were coerced, 54% stating they were more likely to take it voluntarily in the future.

Conclusions: Other forcibly medicated patients had poorer outcomes; rapid readmission, discharge to a state hospital, etc.: those patients may have harbored more negative feelings. However, a substantial number of patients reachable in the community appeared to support having received forcible medication.

NR629 Thursday, May 25, 12 noon-2:00 p.m.

Mental Disorders and Homicidal Behavior

Markku E.J. Eronen, M.D., Forensic Psychiatry, University of Kuopio, Niuvanniemi Hospital, Kuopio 70240, Fin-Finland Europe; Jari Tiihonen, Ph.D., Panu Hakola, Ph.D.

Summary:

Background: The possible relationship between mental disorders and violent behavior has been a controversial issue in forensic psychiatry during last decades. The validity and reliability of psychiatric predictors of dangerousness have been brought seriously into question.

Objective: To present a new epidemiological method to estimate the risk of violent behavior among mentally disordered persons compared to the general population.

Method: In Finland, homicide solving percentage is exceptionally high (over 95%). Most of Finnish homicide offenders have gone through a comprehensive forensic psychiatric examination. We have studied data obtained from about 70% of the homicide offenders (n = 613) in the whole nation of Finland during an eight-year period.

Results: The risk of committing a homicide in Finland appears to be elevated by the factor of ten among schizophrenics, alcoholics, and men with a personality disorder. Corresponding figures among disordered women may be even higher but in women the overall minor occurance of violent behavior reduces the general reliability of these data.

NR630 Thursday, May 25, 12 noon-2:00 p.m.

Biological Predictors of PTSD Following Rape

Rachel Yehuda, Ph.D., Psychiatry, Mt. Sinai School of Med, 116A 130 West Kingsbridge Road, Bronx NY 10468; Heidi S. Resnick, Ph.D., Roger K. Pitman, M.D., David W. Foy, Ph.D.

Summary:

We have previously reported findings from a prospective examination of 37 women studied in the immediate aftermath of rape. The study demonstrated that women with a prior history of rape or aggravated physical assault showed a significantly attenuated cortisol response to the acute stress of rape compared to women without such a history. Furthermore, women with a prior history of assault were significantly more likely to have PTSD at a three-month follow-up evaluation. However, the cortisol response observed several hours post-rape did not predict PTSD at the three-month follow up. In the present study we examined a subset of this sample (n = 20) for whom plasma MHPG concentration was also assessed. MHPG levels following rape were significantly higher in the group that had sustained a greater rape stress (e.g., multiple perpetrators, threat with weapon, physical injury) compared to women in a lower rape stress group ($p < .02$). In addition to the previous predictors (i.e., rape history, rape severity, interaction of history and severity, and cortisol) MHPG and the ratio of cortisol/MHPG were included as predictors of PTSD in a logistic regression analysis. The analysis demonstrated that the cortisol/MHPG ratio in the immediate hours post-rape is substantially associated with subsequent development of PTSD, after controlling for the effects of the other predictors. However, this ratio is not, by itself, a significant predictor of PTSD. Thus, the prediction of PTSD in response to rape requires consideration of interrelations of PTSD with variables such as history, severity, and biological response at the time of the trauma, which are themselves interrelated.

NR631 Thursday, May 25, 12 noon-2:00 p.m.

Major Depression and Reproductive Function in Women

Joyce Meyers, M.D., Psychiatry, Mass General Hospital, WAC 815 15 Parkman Street, Boston MA 02114; Melissa Abraham, B.A., Joseph F. Borus, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Summary:

Objective: The goal of this study was to assess the rate of menstrual abnormalities and reproductively-associated mood disturbances across the life cycle in a population of women with a primary diagnosis of major depressive disorder (MDD) and to examine the effect of MDD on the prevalence of these abnormalities.

Methods: For the study 87 women (mean age 39.8 ± 11.6) who met criteria for MDD using the Structured Clinical Interview for DSM-III-R Patient Edition (SCID-P) were assessed for the presence of comorbid axis I disorders and then administered a physician-rated menstrual history questionnaire designed to evaluate the following parameters: age of menarche, menstrual cycle regularity, presence of dysmenorrhea, mood changes related to the menstrual cycle, pregnancy and menopause, pregnancy history, and symptoms related to menopause.

Results: This study population had a mean HAM-D-17 score of 19.8 ± 3.1 with a mean age of MDD onset of 23.0 ± 12.6 years, and with 30 subjects (31.9%) meeting criteria for "double depression." Fifty-seven subjects were premenopausal (65.5%), 14 were perimenopausal (16.1%), and 16 were postmenopausal (18.4%). Mean age of menarche was 12.6 ± 1.5. In the premenopausal group 17 (30.1%) reported irregular menstrual cycles, and 23 (41.1%) reported dysmenorrhea. Of the 41 women who had been

pregnant, 20 (48.8%) reported a history of post-partum blues. A positive trend was noted between earlier menarche and the presence of "double depression" ($p = .08$). A recent history of premenstrual symptoms was reported by 39 (68.4%) of the premenopausal subjects, and this correlated positively with an earlier onset of depression ($p < .0001$). No association was found between greater degree of psychiatric comorbidity and menstrual abnormalities.

Conclusions: In this population of women with a diagnosis of MDD, there was a significant incidence of menstrual abnormalities and depressive symptoms related to periods of reproductive hormonal change.

NR632 Thursday, May 25, 12 noon-2:00 p.m.

Gender and Age Differences in Hospitalization and Mortality in Patients with Epilepsy

Daniel P. Chapman, Ph.D., Aging Branch, Ctrs for Disease Controls, 4770 Buford Hwy NE MS K-51, Atlanta GA 30341; Russell Roegner, Ph.D., Elizabeth K. Lloyd, M.S., John R. Livengood, M.D.

Summary:

Epilepsy has been associated with increased rates of neuropsychiatric disorders and mortality relative to the general population. Previous assessments of hospitalization and mortality among patients with epilepsy have generally been limited to selected clinical samples or to defined catchment areas. This study presents national estimates of hospitalization and mortality, using data from the National Hospital Discharge Survey for 1988 to 1990 ($N = 294,782$ discharges) and records from 1986 to 1990 from the National Center for Health Statistics ($N = 8,064$ deaths). Patient age was stratified into three groups: ≤14 years, 15–64 years, and ≥65 years. Overall annual hospitalization rates per 10,000 U.S. citizens were similar among patients with the primary diagnosis of epilepsy ≤14 and 15–64 years (4.4 vs. 3.2, respectively), although annual mortality rate per 100,000 U.S. residents for epilepsy as the underlying cause of death was the lowest among the youngest age group and rose significantly with age (.14 vs. .65 vs. 1.6, respectively). While hospitalization rates were similar between men and women across all age strata, mortality rates for epilepsy were significantly higher among men than women in the two oldest age strata. As epilepsy is more frequently associated with mortality in men than women despite comparable rates of hospitalization, the increased rate of mortality among men may reflect gender and cohort differences in the diagnosis, course, and treatment of epilepsy and its neuropsychiatric sequelae.

NR633 Thursday, May 25, 12 noon-2:00 p.m.

The Current State of Psychiatric Care in Italy: An Overview

Giovanni de Girolamo, M.D., Mental Health Service, Via Pepoli 5, Bologna 40123, Italy; Angelo Fioritti, M.D.

Summary:

Abstract: The 'Italian experience' of providing psychiatric care with comprehensive and integrated psychiatric services while blocking admissions to mental hospitals needs evaluation on the basis of quantitative evidence. In this paper, up-to-date national statistics, based on a national survey carried out by the *'Italian Institute of Social Medicine'* (IISM), and local case-register data pertaining to this issue are reported. The latest estimate of the number of inpatients in the 83 mental hospitals of the country is 23,402 residents (0.41 per thousand population). There are in Italy 316 general hospital inpatient psychiatric units, comprising a total of 3,840 beds (0.06 per thousand population). The IISM survey has found that 1,369 community mental health centers, providing mainly outpatient care, are in operation—an average of one such service per 41,200 population. The number of day hospitals, halfway houses, and sheltered flats has steadily increased over the last few years, as well as the number of personnel. The available data show that there is still a marked regional variation in service provision. However, the evidence suggests that where adequate community psychiatric services have been provided, they function successfully without the availability of 'backup' from the mental hospitals.

NR634 Thursday, May 25, 12 noon-2:00 p.m.

Women Veterans in Inpatient Psychiatric Care

Sarz Maxwell, M.D., Psychiatry, Westside VAMC, 820 S. Damen Ave MP 116A, Chicago IL 60612; Janet K. Willer, Ph.D., Jeffrey G. Stovall, M.D., Sandra G. McRae, Ph.D., Linda S. Grossman, Ph.D., Rebecca Nelson, M.A.

Summary:

Objective: Increasing numbers of female veterans are eligible for treatment at Department of Veterans Affairs (VA) hospitals as more women enter the military. Yet little has been done to characterize them or their psychiatric needs. Treatment programs designed for a predominantly male population may not provide unique services needed by women. This study describes women hospitalized on a VA inpatient psychiatric unit, compared to a male group.

Method: Demographic, diagnostic, and treatment data were collected from medical records of 31 consecutively admitted female patients and 31 male patients admitted to an acute psychiatric unit of an urban VA hospital.

Results: There were minimal demographic differences. Diagnostically, men were more complex, with more substance abuse and PTSD. Among women, 49% had more than one discharge diagnosis, while 78% of the men had psychiatric comorbidities or dual diagnoses. Many treatment parameters, including length of stay, PRN medications, and manner of discharge, showed no significant gender differences.

Discussion: Despite prominent diagnostic differences, some important treatment variables did not differ between women and men. This raises the possibility that women's psychiatric morbidity is being underdiagnosed in the predominantly male context of VA hospitals. Given the increasing numbers of female veterans, VA psychiatric services may require alterations to serve the increasing number of women presenting for treatment.

NR635 Thursday, May 25, 12 noon-2:00 p.m.

Automated Patient Assessment to Improve Quality

James R. Westphal, M.D., Division of Research, Kaiser Permanente, 3505 Broadway, Oakland CA 94611; Martin Williams, Ph.D., Enid M. Hunkeler, M.A.

Summary:

Improving mental health care in health maintenance organizations is hampered by diagnostic and documentation variability, paper-based narrative charts, and little measurement of patient outcomes. We developed a system which gives clinicians data from validated instruments on patients before clinical interviews, measures psychiatric outcomes, and monitors clinic case-mix regarding demographics, functional status, personality disorder, and symptom severity. New psychiatric outpatients, 73.9% of whom were white, 62.4% of whom were female, and 35.8% with college degrees, received personality disorder, role function, and demographic questionnaires. Computer-generated reports compared responses of new patients to those of psychiatric and medical outpatient populations. The 18% of patients with major depressive disorder and the 7% with panic disorder received specialized ques-

tionnaires and were followed at three and six months after intake. Most clinicians used the reports frequently and found them helpful. Clinicians said the reports alerted them to areas that needed in-depth probing in the initial assessment interview. Criticisms focused on length of questionnaires, inadequate training, the possibility of too many false positives, and insufficient administrative support. While more research is needed to demonstrate the usefulness of outcomes management, this study advanced the goal of having clinical practice become a true learning environment.

NR636 Thursday, May 25, 12 noon-2:00 p.m.

Assessing Women for Mental Illness and Help Seeking Behavior in Primary Care

Marian I. Butterfield, M.D., Psychiatry, Durham VAMC & Duke, 508 Fulton Street, Durham NC 27705; Cedar Koons, M.S.W., Andrea Wilks, F.N.P., Lori Bastian, M.D.

Summary:

Objective: To assess women for mental illness and help seeking behavior in primary care. Despite the high prevalence of mental disorders in primary care, physicians often fail to diagnose these patients.

Method: To screen for mental illnesses, we administered the PRIME-MD questionnaire and offered mental health help to 220 veteran women clinic users.

Results: Mean age was 41.2 and 47% were black. Symptoms endorsed included: 35% depression, 33% anxiety, 13% alcohol abuse, 14% eating disorder, 81% somatoform, and 45% sexual trauma or harassment history. Those who wanted mental health help were significantly different from those who did not: Black 59% vs. 41% ($p = 0.01$), depression 54% vs. 26% ($p < 0.001$), anxiety 43% vs. 27% ($p = 0.014$), somatoform 93% vs. 75% ($p = 0.001$), and sexual trauma or harassment 54% vs. 38% ($p = 0.025$). In a logistic regression model, help-seeking behavior was associated with age <50 (adjusted odds ratio [AOR] = 2.68, confidence intervals [CI] = 1.02–7.04), depressive symptoms (AOR = 2.0, CI = 1.03–3.92), somatoform symptoms (AOR = 2.7, CI = 0.95–7.5), and panic symptoms (AOR = 3.3, CI = 1.13–9.58).

Conclusions: Many women suffering from mental illness seek treatment in the primary care setting. Younger women and those with depressive, panic, or somatoform symptoms were most likely to seek mental health help.

NR637 Thursday, May 25, 12 noon-2:00 p.m.

Genital Reflexes Elicited By Stimulation of Autonomic and Somatic Nerves in the Investigation of Diabetic Impotence

Ismet Karacan, M.D., Psychiatry, Baylor College of Med., One Baylor Plaza Ste 710D, Houston TX 77030; Yakup Sarica, M.D., Mehmet Karatas, M.D., Hacer Bozdemir, M.D., Constance A. Moore, M.D.

Summary:

To investigate neurogenic impotence in diabetics, 46 males, aged 23–67 years (mean:45.8), with erectile complaints were enrolled in this study. We recorded the bulbocavernosus reflex (genital reflex) elicited by stimulation of the autonomic nerves at the vesico-urethral junction and the pudendal nerve at the glans penis. The vesico-urethral junction was stimulated by a special foley catheter, and the bulbocavernosus reflex was recorded by needle electrode.

The results compared to normal values are the following: Bulbocavernosus reflex elicited by stimulation of visceral afferents was absent in 26%, and with protracted latency in 20% of cases; 46% of cases had abnormal bulbocavernosus reflex. Bulbocavernosus reflex elicited by stimulation of the pudendal nerve had protracted latency in 11% of cases. Age and duration of diabetes had no effect on the rate of abnormal bulbocavernosus reflex in any modality. Insulin dependency was correlated with abnormal bulbocavernosus reflex elicited by stimulation of autonomic nerves.

This study, which has been the largest series evaluated so far, indicates that recording of bulbocavernosus reflex to stimulation of autonomic nerves is a more sensitive and specific tool than bulbocavernosus reflex to somatic nerve stimulation evaluating sexual dysfunction. This new technique for autonomic nervous system evaluation contributes to early diagnosis of diabetic impotence, and aids in ruling out the autonomic nervous system involvement in suspected impotent patients.

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Obsessive-Compulsive Symptom Profile in Gilles De La Tourette Syndrome and OCD: A Phenomenological Study

Valsamma Eapen, M.B., Psychiatry, UAE University, Faculty of Med P.O. Box 17666, Al Ain, U.Arab Emirates; Mary Robertson, M.D.

Summary:

Objectives: To compare the obsessive compulsive (OC) symptom profile in individuals with preliminary obsessive compulsive disorder (OCD), and in Gilles de la Tourette syndrome (GTS) patients with associated obsessive compulsive behaviors (OCB).

Method: Sixteen patients each, fulfilling the DSM-III-R criteria for the two disorders were studied.

Results: The two groups showed significant phenomenological differences. Presence of sexual/violent themes for obsessions, fear of harming self/others, symmetry/"evening up" behaviors, doing things 'just right' and forced touching, significantly predicted the subject to be belonging to the GTS group. Similarly, obsessions involving concern for germ/contamination, and compulsions involving washing, cleaning, and measures to remove contaminants, predicted the OCD status. Furthermore, there were phenomenological differences between OCD probands with and without a positive family history; the former shared a similar profile to that of GTS.

Conclusion: Our findings of clinical heterogeneity in OC subjects suggest genetic heterogeneity, and may provide a much needed clue toward the genetics and pathogenesis of GTS and OCD, and the relationship between the two disorders. If replicated, this will help us to categorize OCD subjects into more homogeneous subgroups based on their symptom profile. Further research is indicated to establish whether these symptom clusters breed true in families.

NR639 Thursday, May 25, 12 noon-2:00 p.m.

Genomic Imprinting in Tourette Syndrome

Valsamma Eapen, M.B., Psychiatry, UAE University, Faculty of Med P.O. Box 17666, Al Ain, U.Arab Emirates; Mary Robertson, M.D., Jane O'Neil, M.B., Hugh Gurling, M.D.

Summary:

It has recently been recognized that genomic imprinting (differential expression of genetic material depending on the sex of the transmitting parent) influences the specific expressions of a number of heritable human disorders. To test this in Tourette syndrome (TS), 437 first-degree relatives ascertained through 57 probands were studied. Age at onset, age at diagnosis, and phenotypic expressions (defined as TS, chronic motor tics and obsessive compulsive behaviors) in the offspring of affected males were compared with that in the offspring of affected females. Of the 437 subjects, 16.7% demonstrated evidence of maternal transmission and 13.9% that of paternal transmission. Chi-square analysis (for

heterogeneity) of the different phenotypic expressions and sex of the transmitting parent failed to provide evidence of significant group differences. There were no significant differences when age at diagnosis was compared. However, the maternally transmitted offspring showed a significantly earlier age at onset. This may point to an age-dependent methylation of the putative TS gene(s), and the explanations vary from intrauterine environmental influences to different linkage groups. The findings suggest a need to re-examine family data separately for maternally and paternally transmitted cases in order to address this issue further. The implications for future research are discussed.

NR640 Thursday, May 25, 12 noon-2:00 p.m.

Alcohol and Drug Use Disorders in Adults with ADHD: Effect of Psychiatric Comorbidity

Timothy E. Wilens, M.D., Child Psychiatry, WACC 725, Mass General Hospital, Boston MA 02114; Joseph Biederman, M.D., Erik Nick, B.A., Stephen V. Faraone, Ph.D.

Summary:

Background: ADHD is an increasingly recognized clinical entity in adults associated with psychiatric comorbidity, underachievement, and psychosocial impairment. Likewise, ADHD and the psychoactive substance use disorders (PSUD) appear to be related. However, the relationship of ADHD to PSUD has been confounded by the presence of other psychiatric disorders occurring with ADHD. In this study, the relationship of ADHD and PSUD was evaluated with particular attention to comorbidity.

Methods: We studied 120 adults (mean age 39 years) with a clinical diagnosis of childhood-onset ADHD confirmed by structured interview. Findings were compared with 268 adult controls elicited from an ongoing family-genetic study of ADHD. Subjects were evaluated with a comprehensive battery of psychiatric, cognitive, and psychosocial assessments.

Results: There were 62 ADHD adults and 73 controls with PSUD. As expected, depressive, anxiety, and antisocial disorders were more frequently comorbid in the adult ADHD group vs control subjects irrespective of PSUD (all p's < 0.01). ADHD and control adults with drug or alcohol *abuse* were quantitatively different than those with drug or alcohol *dependence.* Although the occurrence of ADHD alone did confer risk for PSUD, the presence of bipolar disorder, agoraphobia, or conduct/antisocial disorders in the ADHD adult substantially increased the risk for PSUD. Of those with drug or alcohol dependence, ADHD adults had higher rates of multiple anxiety disorders than controls. There were no differences in cognitive testing results between groups. ADHD adults with PSUD were functioning significantly poorer than ADHD without PSUD or control adults with or without PSUD.

Conclusions: These results suggest that drug or alcohol dependence in the ADHD adult appears to be moderated by ADHD, and particularly by the presence of comorbid psychiatric disorders such as agoraphobia, antisocial, or bipolar disorders.

NR641 Thursday, May 25, 12 noon-2:00 p.m.

A Double-Blind Comparison of Desipramine and Placebo in Adults with ADHD: Preliminary Results

Timothy E. Wilens, M.D., Child Psychiatry, WACC 725, Mass General Hospital, Boston MA 02114; Jefferson B. Prince, M.D., Joseph Biederman, M.D., Thomas J. Spencer, M.D., Daniel A. Geller, M.D., Rebecca Warburton, B.A., Phoebe Moore, B.A., Colleen E. Linehan, B.A., David R. Schleifer, B.A.

Summary:

Background: Despite the increasing awareness of attention deficit hyperactivity disorder (ADHD) in adults, there is a paucity of data on its pharmacological treatment outside of the stimulants. To this end, we undertook a randomized, six-week, double-blind, placebo-controlled study of desipramine (DMI) for the treatment of adult ADHD.

Methods: ADHD adults were randomized to placebo or DMI titrated to 200 mg/day and rated on multiple measures biweekly for six weeks.

Results: To date, 28 subjects were entered into the study. The completers (N = 26) had a mean age (SD) of 38.2 ± 8.0 years, and 62% were males. The mean DMI dose was 189 ± 39.6 mg/day resulting in DMI serum levels of 87 ng/ml. DMI significantly reduced ADHD symptoms by week 6 compared to baseline ($p < 0.001$). Whereas there was a substantial reduction in the ADHD symptom checklist scores in adults treated with DMI (18.8 ± 9.5), there was little change in those receiving placebo (0.0 ± 4.1; $p < 0.0001$). Likewise, there was a marked difference between the number of subjects responding to DMI (90%) compared to placebo (0%, $p < 0.0001$) by the clinicians global assessment of improvement of ADHD.

Discussion: These preliminary data indicate that DMI may be a promising agent for adult ADHD.

AUTHOR INDEX

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American
Psychiatric
Association

1400 K STREET, N.W.
WASHINGTON, D.C. 20005

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