1996

ANNUAL MEETING

NEW RESEARCH PROGRAM & ABSTRACTS

AMERICA'S MENTAL HEALTH

AMERICAN PSYCHIATRIC ASSOCIATION

ANNUAL MEETING ◆ MAY 4-9, 1996

NEW YORK, NEW YORK

PROGRAM
AND
ABSTRACTS ON NEW RESEARCH

IN SUMMARY FORM

149TH ANNUAL MEETING OF THE AMERICAN PSYCHIATRIC ASSOCIATION

NEW YORK, NY
May 4-9, 1996

SUBCOMMITTEE ON NEW RESEARCH OF THE SCIENTIFIC PROGRAM COMMITTEE

Leah J. Dickstein, M.D., *Chairperson*
Scientific Program Committee
New York, NY

Andrew E. Skodol, II, M.D., *Chairperson*
New Research Subcommittee
Washington, DC

Tana A. Grady, M.D.
Durham, NC

Marian I. Butterfield, M.D.
Durham, NC

Susan J. Fiester, M.D.
Chevy Chase, MD

149th Annual Meeting
New York, New York
May 4-9, 1996

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

May 4, 1996

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 1996 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 6, 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 OCD, substance abuse, geriatrics, and personality disorders. 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 7, at 9:00 a.m. is "Research Advances in Medicine," with special emphasis on basic mechanisms in pain and pain management, advances in understanding of basic mechanisms of genetics, and basic mechanisms in weight control. 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 alcohol and substance abuse disorders; and psychopharmacology (Tuesday); schizophrenia; and organic mental disorders (Wednesday); mood disorders; and personality 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 AIDS; child and adolescent psychiatry; infant and childhood, alcohol and substance abuse, personality disorders; violence, trauma and victimization; mood disorders; psychopharmacology; suicide; and eating disorders (Tuesday); organic mental disorders; biological psychiatry; brain imaging; consultation/liaison and emergency psychiatry; geriatric psychiatry; neurobiology; neuropsychiatry; genetics; schizophrenia; administrative psychiatry; community psychiatry and prevention; diagnostic issues; and cross-cultural and minority psychiatry (Wednesday); anxiety disorders; premenstrual dysphoric disorder; dissociative, sexual, sleep, somatoform, other psychiatric disorders; epidemiology; forensic psychiatry; psychiatric education; psychiatric rehabilitation; psychoimmunology; research issues; social psychiatry; stress; behavior and cognitive, group therapy; individual psychotherapy; treatment techniques and issues; computers; managed care and health care funding issues; and the Presidential Theme: America's Mental Health (Thursday).

The 48 oral/slide papers (including 12 Young Investigators) and 720 poster presentations (including 176 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,

Andrew E. Skodol

Andrew E. Skodol, II M.D.
Chairperson
New Research Subcommittee of the
Scientific Program Committee

Outside Reviewers for the New Research Program

Boris M. Astrachan, M.D.
Ross J. Baldessarini, M.D.
Carol A. Bernstein, M.D.
Wade H. Berrettini, M.D.
Dan G. Blazer, M.D.
Richard L. Borison, M.D.
Eric D. Caine, M.D.
Joshua Calhoun, M.D.
Gabrielle A. Carlson, M.D.
Paula J. Clayton, M.D.
C. Edward Coffey, M.D.
Joseph T. Coyle, M.D.
Jeffrey L. Cummings, M.D.
Glen C. Davis, M.D.
Mina K. Dulcan, M.D.
Michael A. Fauman, M.D.
Wayne S. Fenton, M.D.
Arnold J. Friedhoff, M.D.
Abby J. Fyer, M.D.
William M. Glazer, M.D.
Judith H. Gold, M.D.
Jack M. Gorman, M.D.
Igor Grant, M.D.
Katherine A. Halmi, M.D.
Dilip V. Jeste, M.D.
Donald F. Klein, M.D.
Joel E. Kleinman, M.D.
Donald S. Kornfeld, M.D.
Michael R. Liebowitz, M.D.
Markku I. Linnoila, M.D.
Robert W. McCarley, M.D.
Herbert Y. Meltzer, M.D.
Charles B. Nemeroff, M.D.
Charles P. O'Brien, M.D.
Robert M. Post, M.D.
William Z. Potter, M.D.
Frederic M. Quitkin, M.D.
Mark H. Rapaport, M.D.
Murray A. Raskind, M.D.
Stephen G. Rayport, M.D.
Charles F. Reynolds, M.D.
Elliott Richelson, M.D.
Peter P. Roy-Byrne, M.D.
Charles A. Shamoian, M.D.
Larry J. Siever, M.D.
Jonathan M. Silver, M.D.
Barbara Stanley, Ph.D.
Marvin Stein, M.D.
James J. Strain, M.D.
Kenneth J. Tardiff, M.D.
James W. Thompson, M.D.
Elisa G. Triffleman, M.D.
Gary J. Tucker, M.D.
Joe P. Tupin, 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.
Deborah A. Zarin, M.D.

AMERICAN PSYCHIATRIC ASSOCIATION
CONTINUING MEDICAL EDUCATION POLICY ON FULL DISCLOSURE

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 #
Abuzzahab, Sr., Faruk S.	Abbott Laboratories	NR710
Albright, Penny	Janssen Pharmaceutica and Research Foundation	NR375
Alderman, Jeffrey A.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR222
Amchin, Jess D.	Wyeth-Ayerst Laboratories	NR362
Ames, Donna	Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company; Otsuka; Sandoz Pharmaceuticals Corporation; Abbott Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Eli Lilly and Company; Hoechst-Roussell	NR578
Aronson, Stephen M.	Janssen Pharmaceutica and Research Foundation; SmithKline Beecham Pharmaceuticals; Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Wyeth-Ayerst Laboratories	NR493
Arvanitis, Lisa A.	Zeneca Pharmaceuticals	NR422
Beasley, Jr., Charles M.	Eli Lilly and Company	NR246
Belzie, Louis	Janssen Pharmaceutica and Research Foundation	NR214
Biondi, Franco	Synthelabo Spa Italy	NR660
Blum, Kenneth	NeuRecovery International	NR524, NR525
Bradford, L. DiAnne	Solvay Pharmaceuticals, Inc.	NR366
Burks, Emalie J.	Abbott Laboratories	NR332
Bymaster, Frank P.	Eli Lilly and Company	NR546
Chouinard, Guy	Janssen Pharmaceutica and Research Foundation	NR376
Chow, Eva W.C.	Sandoz Canada, Inc.	NR378
Clayton, Anita L.H.	SmithKline Beecham Pharmaceuticals; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Glaxo Wellcome	NR737, NR738
Cohen, Lee S.	Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR313, NR314
Cohn, Cal K.	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR369
Cookson, Ronald F.	Janssen Pharmaceutica and Research Foundation	NR761
Corrigan, Mark H.N.	Pharmacia & Upjohn Company	NR401
Crawford, Ann Marie	Eli Lilly and Company	NR723
Daniel, David G.	Abbott Laboratories	NR544
Davis, John M.	Janssen Pharmaceutica and Research Foundation; Wyeth-Ayerst Laboratories	NR382
DeQuardo, John R.	Janssen Pharmaceutica and Research Foundation; Sandoz Pharmaceuticals Corporation	NR625
Duncan, Alice F.	Janssen Pharmaceutica and Research Foundation	NR374
Dwight, Megan M.	Wyeth-Ayerst Laboratories; Pharmacia & Upjohn Company	NR165
Epperson, C. Neill	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR28
Fava, Maurizio	Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Synthe Labs; Roche Laboratories, a member of the Roche Group; SmithKline Beecham Pharmaceuticals; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Glaxo Wellcome;Wyeth-Ayerst Laboratories	NR415

Presenter	Manufacturer(s)	Final Program #
Feighner, John P.	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR370
Ferrando, Stephen J.	SmithKline Beecham Pharmaceuticals; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR205
Fox, Barbara S.	ImmuLogic Pharmaceutical Corporation	NR193
Frankenburg, Frances R.	Janssen Pharmaceutica and Research Foundation; Sandoz Pharmaceuticals Corporation; Abbott Laboratories	NR372
Frye, Mark A.	Abbott Laboratories	NR311, NR312
Ghaemi, S. Nassir	Janssen Pharmaceutica and Research Foundation	NR29, NR384
Glod, Carol A.	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR215
Goldstein, Jeffrey	Zeneca Pharmaceuticals	NR615
Goodnick, Paul J.	Glaxo Wellcome; Abbott Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Janssen Pharmaceutica and Research Foundation	NR323
Gorelick, David A.	Sandoz Pharmaceuticals Corporation	NR250, NR251, NR252
Greist, John H.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR759
Gutierrez-Esteinou, Rolando	Janssen Pharmaceutica and Research Foundation	NR385
Hantouche, Elie G.	Eli Lilly and Company	NR664
Hong, Walter W.	Zeneca Pharmaceuticals	NR589
Isaac, Michael T.	SmithKline Beecham Pharmaceuticals	NR319, NR320, NR321
Jacobsen, Frederick M.	Palisades Pharmaceuticals, Maker of Yolon	NR716
Joffe, Russell T.	Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Wyeth-Ayerst Laboratories; Abbott Laboratories	NR309
Keitner, Gabor I.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR316
Ketti, Paul A.	Manor Care Nursing Homes; Wyeth-Ayerst Laboratories	NR409
Kline, Neal A.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR689
Knutson, Brian	SmithKline Beecham Pharmaceuticals	NR98
Ko, Grant N.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR587
Kumar, Vinod	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR389
Lam, Yui Wing F.	Solvay Pharmaceuticals, Inc.	NR400
Lara-Munoz, Carmen	Pharmacia & Upjohn Company	NR344
Lawson, William B.	Zeneca Pharmaceuticals; Sandoz Pharmaceuticals Corporation	NR534
Lindenmayer, Jean-Pierre	Sandoz Pharmaceuticals Corporation; Janssen Pharmaceutica and Research Foundation	NR591
Luchins, Daniel J.	Janssen Pharmaceutica and Research Foundation	NR745
Marshall, Randall D.	SmithKline Beecham Pharmaceuticals	NR147
Miller, Norman S.	Dupont Pharma	NR223
Moroz, Georges	Hoffman LaRoche Inc.	NR694
Nabuisi, Azmi A.	Abbott Laboratories	NR566
Newhouse, Paul A.	Abbott Laboratories	NR488
Nierenberg, Andrew A.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Eli Lilly and Company; Wyeth-Ayerst Laboratories; Sandoz Pharmaceuticals Corporation; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR361
Patel, Bela	Eli Lilly and Company	NR617
Phillips, Katharine A.	Pharmacia & Upjohn Company; Solvay Pharmaceuticals, Inc.; Eli Lilly and Company; CoCensys, Inc.; SmithKline Beecham Pharmaceuticals; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR697, NR698, NR699
Piazza, Lisa A.	Astra/Merck Group, Division of Merck & Co.	NR354
Potkin, Steven G.	Abbott Laboratories	NR545
Preskorn, Sheldon H.	Abbott Laboratories; Astra/Merck Group, Division of Merck & Co.; Boots; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Glaxo Wellcome;Ciba Geigy Corporation, Pharmaceuticals Division; Eli Lilly and Company;Searle; Hoechst-Roussell; Hoffman LaRoche Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Phone-Poulenc; Sandoz Pharmaceuticals Corporation; SmithKline Beecham Pharmaceuticals; Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Company; Wyeth-Ayerst Laboratories; Lunbeck, National Psychopharmacology Laboratories	NR195
Rabkin, Judith G.	Pharmacia & Upjohn Company	NR203
Rasmussen, Kurt	Eli Lilly and Company	NR616
Reeves, Karen R.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR579

Presenter	Manufacturer(s)	Final Program #
Revicki, Dennis	Eli Lilly and Company	NR425
Ring, Barbara J.	Eli Lilly and Company	NR757
Rioux, Patrice	Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company	NR359
Rush, A. John	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Wyeth-Ayerst Laboratories; Eli Lilly and Company	NR517
Sachs, Gary S.	Roche Laboratories, a member of the Roche Group; Glaxo Wellcome; SmithKline Beecham Pharmaceuticals; Abbott Laboratories; Eli Lilly and Company	NR645, NR646, NR647
Satterlee, Winston G.	Eli Lilly and Company	NR603
Shapiro, Peter A.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	
Singh, Ashok N.	Janssen Pharmaceutica and Research Foundation	NR212
Stearns, Alan I.	Somerset Pharmaceuticals	NR621
Steiner, Martin	SmithKline Beecham Pharmaceuticals	NR200
Strain, James J.	CompuMed 1003	NR758
Street, Jamie S.	Eli Lilly and Company	NR604, NR605
Thompson, Jr., John W.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Janssen Pharmaceutica and Research Foundation	NR735
Tollefson, Gary D.	Eli Lilly and Company	NR547
Tran, Pierre V.	Eli Lilly and Company	NR607
Tucker, Phebe M.	SmithKline Beecham Pharmaceuticals	NR684
Valan, Michael N.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR483
Valenstein, Marcia T.	Roerig & Pratt Pharmaceuticals	NR763
van der Kolk, Bessel A.	Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR528
Van Kammen, Daniel P.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Abbott Laboratories	NR549
Ware, Michael R.	Dista; Glaxo Wellcome; Mead Johnson Pharmaceuticals, a Bristol-Myers Squibb Company; Organon Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Pharmacia & Upjohn Company; Wyeth-Ayerst Laboratories; Solvay Pharmaceuticals, Inc.; Eli Lilly and Company	NR676
Weissman, Myrna M.	Abbott Laboratories; Organon Inc.; Pharmacia & Upjohn Company	NR480
Wilner, Keith D.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR609, NR610, NR611
Wong, James Y.W.	Zeneca Pharmaceuticals	NR612
Zimbroff, Dan L.	Abbott Laboratories	NR543
Zimmer, Ben	Wyeth-Ayerst Laboratories	NR395

NEW RESEARCH

Monday, May 6, 1996, 9:00 a.m.-10:30 a.m.

New Research 1- Poster Session - Galleria, Level 4, Javits Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Marian I. Butterfield, M.D.

NR1 Evaluating the Relative Efficacy of Three Aversion Therapies Designed to Reduce Craving Among Male Cocaine Abusers
Patrick Bordnick, Ph.D., Ralph L. Elkins, Ph.D., T.E. Orr, Ph.D., Paul Walters, Ph.D., Bruce Thyer, Ph.D.

NR2 Outcomes of Depressed Male Alcoholics: Primary Versus Secondary Depression
Saeed A. Shah, M.D., Elizabeth J. Nickel, M.A., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Barry I. Liskow, M.D., Stephen D. Samuelson, M.D.

NR3 Common Physical Complaints As Predictors for Alcohol Abuse and Dependence in a Primary Care Women's Clinic
Tedra L. Anderson-Brown, M.D., Lori Bastian, M.D., Marian I. Butterfield, M.D., Malin Vollmer, B.A.

NR4 Factors Related to Alcohol Use Disorders
Sherrie A. Bieniek, M.D., Raymond L. Ownby, M.D., Alberto Penalver, M.D., Barbara J. Mason, Ph.D.

NR5 Opiate Withdrawal Using Dextromethorphan
Adam M. Bisaga, M.D., Philip Gianelli, M.D., Joseph Pugliese, M.D., Margo F. Spitzer, M.D., Ronald Brenner, M.D., Piotr Popik, M.D.

NR6 Violence, Prohibition and the War on Drugs: Is It Time for an Experiment in Detente?
Susan J. Boyd, M.D.

NR7 Psychotherapy During Opioid Detoxification
Philippe Cadilhac, M.D., Laurent Schmitt, M.D., Henri Sztulman, M.D., Pierre Moron, M.D., Max Reinert, M.D.

NR8 Attention Deficit and Substance Use Disorders
Chris L. Clure, M.D., Lee S. Cohen, M.D., Kathleen T. Brady, M.D., Michael Saladin, Ph.D., Laura M. Robertson, B.A., Margaret E. Rittenbury, M.D.

NR9 Naltrexone Decreases the Urge to Drink Alcohol
Dena Davidson, Ph.D., Robert M. Swift, M.D., Eric Fitz, B.Sc.

NR10 Stimulant Psychosis Symptoms and Clinical Course
Debra S. Harris, M.D., Steven L. Batki, M.D.

NR11 Reliability/Validation Study of the Cage Compared with the B-Mast and Discharge Diagnosis in Adult Psychiatric Inpatients
Jeffrey H. Hsu, B.S., Stephen B. Billick, M.D.

NR12 PRN Over the Counter Medication Use Among Substance Abusing Psychiatric Inpatients: A Pilot Study
Robert A. Karp, M.D., Jonathon D. Goldman, M.D., Paul E. Ruskin, M.D., Lisa B. Dixon, M.D.

NR13 Follow-Up Study of Persons Dually Diagnosed with Mental Illness and Substance Use Disorders
Scot McNary, M.A., Lisa B. Dixon, M.D., Anthony F. Lehman, M.D.

NR14 Social Phobia in Cocaine-Dependent Individuals
Hugh Myrick, M.D., Kathleen T. Brady, M.D.

NR15 Carbohydrate-Deficient Transferrin in Alcoholics
Richard Saini, M.D., Helen M. Pettinati, Ph.D., Ann E. Semwanga, B.A., Alexia L. Wolf, B.A., Alan Sharf, B.S.

NR16 Double Diagnosis of Schizophrenia and Chemical Abuse in a Public General Hospital in Spain
Natalia Sartorius, M.D., Guillermo Ponce, M.D., Isabel Herman, M.D., Pablo Del Pino, M.D., Enrique Ga Bernardo, M.D., Miguel A. Jimenez, M.D.

NR17 Coping Strategies in Patients with Substance Abuse
Himanshu P. Upadhyaya, M.D., Filomena Rebelo, Eugene Samoza, M.D., Juris P. Mezinski, Ph.D., Sue R. Dyrenforth, Ph.D.

NR18 Outcomes of Methadone-Maintained Pregnant Women
Janet D. Woolery, M.D., Manjiri M. Pansare, M.D., Lisa B. Dixon, M.D., Robert P. Schwartz, M.D.

NR19 Risk Factors for Depression in Patients with Coronary Artery Disease
Michael B. Gonzalez, B.S., Ted B. Snyderman, B.A., Jeffery T. Colket, B.S., Rebekka M. Arias, B.S., Christopher M. O'Connor, M.D., K. Ranga Krishnan, M.D.

NR20 Carbamazepine Versus Haloperidol for the Treatment of Acute Manic Episodes
Carlos A. Hernandez-Avila, M.D., Hector A. Ortega-Soto, M.D., Antonio Jasso, M.D., Cecilia A. Hasfura-Buenaga, Psic.

NR21 A Family Study of Seasonality in Seasonal and Nonseasonal Mood Disorders
Edwin M. Tam, M.D., Kerry Jang, Ph.D., Raymond W. Lam, M.D., Lakshmi N. Yatham, M.D., Judy M. Allen, M.D., Maria R. Corral, M.D., A.P. Zis, M.D.

NR22 Recidivism in Major Depressive Disorder
Michael E. Doyle, M.D., Lawrence A. Labbate, M.D.

NR23 Longitudinal Assessment of Quality of Life in Patients with Major Depression
Jeffrey M. Pyne, M.D., Robert M. Kaplan, M.D., Thomas L. Patterson, Ph.D.

NR24 Consumption of Alcohol, Nicotine and Caffeine Among Outpatients with Mood and Anxiety Disorders: Presentation and Impact on Treatment
John J. Worthington III, M.D., Maurizio Fava, M.D., Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Eliza T. McArdle, B.A., Jerrold F. Rosenbaum, M.D.

NR25 Lithium: Efficacy for Bipolar Depression Revisited
Claudia F. Baldassano, M.D., Gary S. Sachs, M.D., S. Nassir Ghaemi, M.D., Christina D. Demopulos, M.D., Christine J. Truman, B.A., Una Jain, B.A.

NR26 Treatment of Bipolar Mixed Mania with Levo-Thyroxine
Kiki D. Chang, M.D., Paul E. Keck, Jr., M.D.

NR27 Rapid Cycling Associated with Low Choline in the Basal Ganglia
Christina D. Demopulos, M.D., Perry F. Renshaw, M.D., Gary S. Sachs, M.D., B. Frederick, M.D., Beny Lafer, M.D., Andrew L. Stoll, M.D.

NR28 A Controlled Study of Antidepressant Treatment of Postpartum Depression
C. Neill Epperson, M.D., Christopher J. McDougle, M.D., Deborah Ward-O'Brien, M.S.N, Lawrence H. Price, M.D.

NR29 Insight in SAD: Results of a Treatment Trial
S. Nassir Ghaemi, M.D., Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christine J. Truman, B.A.

NR30 Dreams and Imaginary Activity in Depressed Patients
Raphael Glachetti, M.D., Laurent Schmitt, M.D., Maurice Bensoussan, M.D., Michel Escande, M.D., Sylvie Bourle, M.D., Marc Benatia, M.D.

NR31 Improved Self-Awareness Upon Resolution of Depression in Patients with SAD
Dina R. Hirshfeld, Ph.D., Mark A. Blais, Ph.D., Michael W. Otto, Ph.D., Una Jain, B.A., Christine J. Truman, B.A., Gary S. Sachs, M.D.

NR32 SAD and Personality Characteristics: Assessing Personality Traits of Pre-Treatment and Post-Treatment Phases of Seasonal Depression
Una Jain, B.A., Gary S. Sachs, M.D., Christine J. Truman, B.A., Mark A. Blais, Ph.D., Michael W. Otto, Ph.D., Dina R. Hirshfeld, Ph.D.

NR33 Nefazodone in Major Depression and Blood Levels
Cecilia M. Jorge, M.D., Paul J. Goodnick, M.D., C. Lindsay DeVane, Ph.D., Joseph Henry, M.D.

NR34 Diurnal Variation in CSF Serotonin Concentrations in Healthy Humans
Paul D. Kirwin, M.D., Christopher J. McDougle, M.D., George M. Anderson, Ph.D., George R. Heninger, M.D., James F. Leckman, M.D., Lawrence H. Price, M.D.

NR35 The Quantitative EEG in Major Depression: Before and After Treatment
Jun Soo Kwon, M.D., Tak Youn, M.D., Hee Yeon Jung, M.D.

NR36 Heterogeneity of Depressives' Attentional Deficits
Sophie Lemelin, B.Ps., Philippe Baruch, M.D., Annick Vincent, M.D., Pierre Vincent, M.D.

NR37 The Efficacy of a Passive Body Heating Procedure in Depressed Patients
John R. Meyers, M.D., Dale A. D'Mello, M.D., Anne M. Miller, D.O., Dominic V. Barberio, D.O., Donald Athearn, R.N., Neha Shah,

NR38 The Efficacy of a Warm Water Bath On Subjective Sleep Quality in Depressive Illness
Anne M. Miller, D.O., Dale A. D'Mello, M.D., John R. Meyers, M.D., Dominic V. Barberio, D.O., Donald Athearn, R.N., Neha Shah,

NR39 Attention Deficit in Psychotic Depression
Erik B. Nelson, M.D., Kenji Sax, Ph.D., Mark Setters, B.S., Stephen M. Strakowski, M.D.

NR40 Thyroid Indices in Mood Disordered Adolescent Inpatients
Rachael S. Nelson, M.D., Lawrence A. Labbate, M.D.

NR41 Atypical Depression: A Cluster Analysis
Heather A. Robertson, M.D., Raymond W. Lam, M.D., Justine N. Stewart, B.Sc., Lakshmi N. Yatham, M.D., Kathleeen A. McGarvey, M.D., Edwin M. Tam, M.D., A.P. Zis, M.D.

NR42 Thyroid Function in Adolescents with Mixed Versus Pure Mania
Cesar A. Soutullo, M.D., Kiki D. Chang, M.D., Sean P. Stanton, B.S., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Scott A. West, M.D.

NR43 Pattern of Illness Revisited: Duration of Depression in Bipolar Disorder
Christine J. Truman, B.A., Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christina D. Demopulos, M.D., Una Jain, B.A.

R44 Seasonality of Maniac Depressive Illness: 50 Years
Diane K. Whitney, M.D., Verinder Sharma, M.D., Karen Kueneman, B.A.

NR45 The Effects of Clomiphene Citrate on Mood: A Pilot Study
Katherine E. Williams, M.D., Regina K. Casper, M.D.

NR46 The Relationship of Shame in Depression Versus Mania
Sean P. Stanton, B.S., Paul Gilbert, Ph.D., Daniel R. Wilson, M.D., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D.

NR47 A Survey of Massachusetts Psychiatrists Regarding Antidepressant Maintenance Failure
Sarah E. Byrne, B.A., Anthony J. Rothschild, M.D.

NR48 Risperidone Treatment in Tardive Dystonia
Manuel M. Marquez, M.D., Inma O. Jodar, Ph.D.

NR49 Comparison of Extrapyramidal Syndrome with Haldol and Risperidol
Phillip W. Antunes, M.D., Cheryl Preece, M.S., Mary Marek, B.S., Jack D. Burke, Jr., M.D.

NR50 Use of SSRIs with Terfenadine and Astemizole
John Snuggs, M.D., Mary Marek, B.S., Cheryl Preece, M.S., Jack D. Burke, Jr., M.D.

NR51 Laboratory Monitoring in the Use of Lithium
Jonathan C. Lockhart, M.D., Mary Marek, B.S., Cheryl Preece, M.S., Jack D. Burke, Jr., M.D.

NR52 Pituitary Microadenoma, Risperidone and Clozapine
Rahim Shafa, M.D., Jayendra K. Patel, M.D., Anthony G. Kalinowski, Ph.D., Joseph J. Schildkraut, M.D., Alan I. Green, M.D.

NR53 Effect of Psychotropic Medication on Seizure Threshold and Duration in ECT
A. Chris Heath, M.D., Stephen H. Dinwiddie, M.D., Keith E. Isenberg, M.D., Michael R. Jarvis, M.D., Charles F. Zorumski, Jr., M.D.

NR54 Pharmacokinetics and Pharmacodynamics of Adinazolam
Kotra Ajir, M.D., Michael W. Smith, M.D., Keh-Ming Lin, M.D., Russell Poland, Ph.D., Joseph C. Fleishaker, Ph.D., James H. Chambers,

NR55 Olanzapine Versus Haloperidol in the Treatment of Schizophrenia
Douglas R. Dolnak, D.O., Kyungtak Minn, M.D., Mary Wieneke, Ph.D., Cheryl Watson, R.N., Scott Espinoza, RA-1

NR56 Clozapine Treatment Increases Serum Glutamate Compared to Conventional Neuroleptics
Anne E. Evins, M.D., Donald C. Goff, M.D., Edward Amico, M.Ed., Vivian Shih, M.D.

NR57 Use of ECT with Treatment-Resistant Depressed Patients: A Randomized Trial ECT Versus Paroxetine
Here W. Folkerts, M.D.

NR58 Designing GABA Receptor Subunit-Selective Agents: Toward "Better Benzodiazepines"
Rona T. Hu, M.D., Ruiyan Liu, Ph.D., Phil Skolnick, Ph.D., James M. Cook, Ph.D.

NR59 Nefazodone and Hypotension: Complication or Coincidence?
Roy J. Meland, D.O., Dale A. D'Mello, M.D., Sharon Ransom

NR60 Desmethylimipramine Induces Glucocorticoid Receptor Translocation In Vitro
Carmine M. Pariante, Bradley D. Pearce, Ph.D., Tracy L. Pisell, B.S., Andrew H. Miller, M.D.

NR61 New Treatments for SSRI-Induced Sexual Dysfunction
Carol A. Roeloffs, M.D., Barbara D. Bartlik, M.D., Helen S. Kaplan, M.D., Peter M. Kaplan, M.D., James Koscis, M.D.

NR62 Sertraline Modulation of Hemostatic Function
Brian P. Skop, M.D., Thomas Neuhauser, M.D., David L. McGlasson, M.S., Hilda A. Best, A.S.C.P.

NR63 Divalproex Sodium and Thrombocytopenia in a Psychiatric Population
Thomas J. Trannel, M.D., Iqbal Ahmed, M.D.

NR64 Risperidone in the Elderly
Carlos A. Zarate, Jr., M.D., Arthur Siegel, M.D., Ataru Nakamura, M.D., Mauricio Tohen, M.D., Tanya Cherkerzian, B.S., Ross J. Baldessarini, M.D.

NR65 Personality Disorders and OCD: A Meta and Citation Analysis
William T. Howard, M.D., Roger K. Blashfield, Ph.D., Wayne K. Goodman, M.D.

NR66 A Clinical Study of Rage Attacks and Episodic Dyscontrol in Children and Adolescents with Tourette's Syndrome
Kenneth S. Park, Cathy L. Budman, M.D., Ruth D. Bruun, M.D., Madelyn Olson, M.D., Robert Araujo, Ph.D., Hermann Davidovicz, Ph.D.

NR67 Quantitative EEG by Spectral Analysis in Children with ADHD
Bung Nyun Kim, M.D., Seong Woong Shin, M.D., Jun Soo Kwon, M.D., Soo Churl Cho, M.D.

NR68 Psychosocial Adjustment of Chronic Epileptic Children and Their Family in Korea
Bung Nyun Kim, M.D., Soo Churl Cho, M.D., Yong Seung Hwang, M.D.

NR69 Is Asthma a Predictor of Behavioral Dyscontrol?
Pe Shein Wynn, M.D., Lawrence E. Levy, M.D., Mohammed R. Khan, M.D., Catherine Karni, M.D.

NR70 Behavioral Side Effects of SSRIs in Children
Amanda N. Holmes, M.D., Mary Marek, B.S., Cheryl Preece, M.S., Jack D. Burke, Jr., M.D.

NR71 Placebo and Antidepressant Response in Children and Adults
Diana E. Robles, M.D., Carlos Blanco, M.D., Inmaculada Palanca, M.D., Madhurani S. Patkar, M.D., Inmaculada Gilaberte-Asin, M.D.

NR72 Clinical Features of Survivors of Sexual Abuse with PTSD and Comorbid BPD
Karen J. Rosen, M.D., Caron Zlotnick, Ph.D., Teri B. Pearlstein, M.D.

NR73 The Relationship Between Dissociation and Pain Insensitivity in Self- Mutilation
Karen J. Rosen, M.D., Caron Zlotnick, Ph.D., Teri B. Pearlstein, M.D.

NR74 Genetic Linkage Studies in Bipolar Disorder
Judith Badner, M.D.

NR75 Development of Chromosome 18 Markers to Aid in the Location of a More Restricted Region of Linkage Disequilibrium with Bipolar Disorder
Alan R. Sanders, M.D., Takeo Yoshikawa, M.D., Sevilla Detera-Wadleigh, Ph.D., Elliott S. Gershon, M.D.

NR76 Stress and Diet in Commodity Traders
Michael N. Kessler, B.A., Karin E. Kessler, M.S.

NR77 Lethality of Suicide Attempts in Adjustment Disorder Versus Major Depression
Alisa A. Devlin, M.D., Lisa B. Dixon, M.D., Lawrence A. Labbate, M.D.

NR78 A Taxonomy for Pregnancy and Perinatal Complications
Gwen L. Zornberg, M.D., Stephen L. Buka, Sc.D., Ming T. Tsuang, M.D.

NR79 Selective Attention in Pregnancy and Lactation
Yung-Mei Leong, SuZanne Chaves, B.S., Cheri Wiggs, Ph.D., Dana Plude, Ph.D., Margaret Altemus, M.D.

NR80 The Stability of Memories of Being Parented Over Ten Years
Lisa J.F. Miller, Ph.D., Virginia Warner, M.P.H., Priya Wickramaratne, Ph.D., Myrna M. Weissman, Ph.D.

NR81 Sertraline in the Treatment of Mixed Anxiety and Depression
Jose L. Carrasco, M.D., Marina Diaz-Marsa, M.D., Jose M. Montes, M.D., Jeronimo Saiz-Ruiz, M.D.

NR82 The Effect of Clinician Characteristics on the Performance of Case Management Activities in a Public Mental Health System
Alexander S. Young, M.D., Oscar Grusky, Ph.D., J. Greer Sullivan, M.D., Cynthia Webster, Ph.D., Deborah Podus, Ph.D.

NR83 Professional Courtesy, Current Attitudes and Practices
Harry T. Chingon, M.D., Linda B. Nahulu, M.D.

NR84 The Effect of Religious/Spiritual Beliefs on Psychological State and Coping in Women Presenting with Possible Breast Cancer
Catherine S. Riley, Ruth E. Johnson, M.D., Teresa A. Rummans, M.D., Laura L. Bloomquist, M.D., Peter C. Wollan, Ph.D., Michelle L. Taylor, Ph.D.

NR85 Prevalence of Adjustment Disorders Among Medical Students at a Caribbean Medical School University
Joseph V. Pergolizzi, Jr., M.D., Spencer Serras, David Sharma, M.D.

NR86 What Do Psychiatry Residency Applicants Want?
John C. Lindgren, M.D., R. David Ekstrom, M.S., Allan A. Maltbie, M.D., Susan G. Silva, Ph.D., Kristin A. Hardin, B.S., Robert N. Golden, M.D.

NR87 Prospective Study of Postpartum Blues
Ranna I. Parekh, M.D.

NEW RESEARCH

Monday, May 6, 1996, 1:00 p.m.-2:30 p.m.

New Research 2 - Oral/Slide Session - Room E6, Level 1, Javits Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

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

NR88	Chronic Major Depression Among HIV-Infected Drug Users Jeffrey Johnson, Ph.D., Judith G. Rabkin, Ph.D.	1:00 p.m.
NR89	One-Year Outcomes of Familial Male Alcoholics Sunil Chhibber, M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Barbara J. Powell, Ph.D., Jan L. Campbell, M.D., H. Mikel Thomas, M.D.	1:15 p.m.
NR90	Substance Abuse and Bipolar Disorder Carmen R. Blanco-Perez, B.S., Carlos Blanco, M.D., John A.R. Grimaldi, Jr., M.D., Carlos A. Rueda, M.D., Julia A. Mayo, Ph.D., Ralph A. O'Connell, M.D.	1:30 p.m.
NR91	SSRIs in Depression: A Meta-Analysis Carlos Blanco, M.D., Inmaculada Gilaberte-Asin, M.D., Inmaculada Palanca, M.D., Cletus S. Carvalho, M.D., Maria Becerril, J.B., Jesus Hernandez, M.D.	1:45 p.m.
NR92	Frontal Lobe Anatomy and Risperidone Response in Schizophrenia Sean W. Flynn, M.D., William G. Honer, M.D., Geoffrey N. Smith, Ph.D., G. William MacEwan, M.D., Siemion Altman, M.D., Lili C. Kopala, M.D.	2:00 p.m.
NR93	A Systematic Comparison of Personality Disorder Diagnoses in Patients with Social Phobia Versus OCD Sheila M. Seay, M.A., Teresa A. Pigott, M.D., Sue Pavelka, M.D., Billinda Dubert, M.S.N., Suzanne Bernstein, B.S., Eduina A. Martins, M.D.	2:15 p.m.

NEW RESEARCH

Monday, May 6, 1996, 1:00 p.m.-2:30 p.m.

New Research 3 – Oral/Slide Session – Room E17, Level 1, Javits Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

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

NR94	Seasonal Variation and Onset of Illness in Mixed Versus Pure Mania Sean P. Stanton, B.S., Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D., Stephen M. Strakowski, M.D., Kiki D. Chang, M.D., Cesar A. Soutullo, M.D.	1:00 p.m.
NR95	Sexual Dysfunction Induced by SSRIs CPT Jamie B. Grimes, M.D., Lawrence A. Labbate, M.D., Alan H. Hines, M.D.	1:15 p.m.
NR96	The Relationship of Adaptive Functioning to Neuropsychological Performance in Geriatric Psychiatry Patients Jovier D. Evans, Ph.D., Joshua C. Klapow, Ph.D., Barton W. Palmer, Ph.D., Jane S. Paulsen, Ph.D., Robert K. Heaton, Ph.D., Thomas L. Patterson, Ph.D., Dilip V. Jeste, M.D.	1:30 p.m.
NR97	The Prevalence of OCD in Bipolar Disorder Peter Braunig, M.D., Stephanie Kruger, M.D., Robert G. Cooke, M.D.	1:45 p.m.
NR98	Personality Effects of Paroxetine in Normal Humans Brian Knutson, Ph.D., Owen M. Wolkowitz, M.D., Victor I. Reus, M.D., Theresa Chan, B.A., Steven A. Cole, M.D., Elizabeth Moore, M.A., Francesca Manfredi, B.A., Jan I. Terpstra, M.D., Ronald Johnson, Ph.D.	2:00 p.m.
NR99	Gender Differences in Noradrenergic and Serotonergic Studies Ann M. Woo-Ming, M.D., Antonia S. New, M.D., Vivian Mitropoulou, M.A., Robert L. Trestman, M.D., Emil F. Coccaro, M.D., Larry J. Siever, M.D.	2:15 p.m.

NEW RESEARCH

Monday, May 6, 1996, 3:00 p.m.-5:00 p.m.

New Research 4 – Poster Session – Galleria, Level 4, Javits Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator.: Carol A. Bernstein, M.D.

NR100 Suicides Occurred in Buenos Aires During 1994
Gillermo J. Tortora, M.D., Alicia Sotelo Lago, M.D., Liliana Florio, Ph.D.

NR101 Neuropsychiatry and Clinical Evaluation and Infectology in Different Socioeconomic Level HIV-Infected Drug-Dependant Patients in Argentina
Guillermo J. Tortora, M.D., Adriana Portas, M.D., Juan Gonzalez Blanco, M.D., Oscar Garcia Messina, M.D., Liliana Florio, Ph.D.

NR102 Therapy Completion Rates in Patients Prescribed Isoniazid and SSRIs
Michael E. Doyle, M.D., Daniel W. Hicks, M.D., Naomi Aronson, M.D.

NR103 Recognition of Severe Depression and Suicidal Ideation in HIV-Infected Patients
Mark H. Halman, M.D., Ronald J. Heslegrave, Ph.D.

NR104 Congenital HIV: Effect of Knowledge of Diagnosis on Mood and Social Function
Cathy A. Mercaldi, M.D., John C. Markowitz, M.D., Ladd Spiegel, M.D.

NR105 Possible Alzheimer's Disease Resembles Probable Alzheimer's Disease with Respect to Clinical Features and Rate of Progression
Carmen M. Rodriguez, M.D., Steven Sevush, M.D.

NR106 A Cognitive-Behavioral Approach to Panic Attacks in Chronic Schizophrenia
Phyllis B. Arlow, D.S.W., Mary E. Moran, Ph.D., Paul C. Bermanzohn, M.D., Samuel G. Siris, M.D.

NR107 The Differential Effectiveness of Social Skills Training for Schizophrenia: Deficit Versus Nondeficit Negative Symptoms
Alex J. Kopelowicz, M.D., Robert P. Liberman, M.D., Roberto Zarate, M.A., Jim Mintz, Ph.D.

NR108 Effect of Patients Observing Their Videotaped Behavior
Stephanie A. Davidoff, M.D., Brent Forrester, M.D., S. Nassir Ghaemi, M.D., J. Alexander Bodkin, M.D.

NR109 Abnormal Parietal Lobe Asymmetry in Schizophrenia
Robert M. Donnino, B.A., Martha E. Shenton, Ph.D., Dan V. Iosifescu, M.D., Ota Hirokazu, M.D., Ronald Kikinis, M.D., Robert W. McCarley, M.D.

NR110 Medical Comorbidity and Psychotic Illness in an Outpatient Clinic Sample
Calvin J. Flowers, M.D., Lawrence S. Gross, M.D., Mina Tasic, M.D., George M. Simpson, M.D.

NR111 Positive and Negative Syndrome Scale Symptom Factors in Schizophrenia
Diane Fredrikson, William G. Honer, M.D., Peter F. Liddle, M.D., James M. Steiger, Ph.D., Lili C. Kopala, M.D., Siemion Altman, M.D.

NR112 Medical Illness in Relatives of Schizophrenics, Affective Disorders and Normal Controls
Janet E. Johnson, M.D., Elizabeth Squires-Wheeler, Ph.D., Simone A. Roberts, B.A., L. Erlenmeyer-Kimling, Ph.D.

NR113 The Effects of Risperidone Versus Haloperidol on Measures of Prefrontal Functioning in Treatment-Resistant Schizophrenia
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.

NR114 Trends and Patterns of Substance Use Amongst Schizophrenic Patients: A Ten-Year Study of Emergency Room Visits
Ashwin A. Patkar, M.D., Robert C. Alexander, M.D., Kenneth M. Certa, M.D., C. Boardman, Ph.D.

NR115 Referential Activity of Language in Schizophrenic Outpatients
Lisseth Rojas-Flores, M.A., Wilma Bucci, Ph.D., Lewis A. Opler, M.D., Jill R. Linder, M.D., Frank Cory, Psy.D.

NR116 No Association Between Null Allele at the Dopamine D4 Receptor and Schizophrenia
Walter G. Rooney, B.A., Anil K. Malhotra, M.D., David S. Goldman, M.D., Robert W. Buchanan, M.D., Alan F. Breier, M.D., David Pickar, M.D.

NR117 Clinical Predictors of Acute Risperidone Response in Elderly Patients with Schizophrenia and Schizoaffective Illnesses
Sean P. Stanton, B.S., Daniel R. Wilson, M.D., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Danielle L. Kizer, B.S., Tony M. Balistreri, B.S.

NR118 MRI Study of Auditory Memory in Schizophrenia
Alexander A. Stevens, Ph.D., Patricia Goldman-Rakic, Ph.D., John C. Gore, Ph.D., Bruce E. Wexler, M.D.

NR119 Neurological Soft Signs and Formal Thought Disorder in Schizophrenia
Raffaella Valigi Bjorck, M.D., Conny Nordin, M.D.

NR120 Medication Compliance and Self-Structure in Schizophrenia
Mary E. Witt, M.D., Stuart R. Schwartz, M.D., Michael Gara, Ph.D., Shula Minsky, Ph.D.

NR121 Hippocampal Synaptic Proteins in Schizophrenia
Clint E. Young, B.Sc., Kunimasa Arima, M.D., William S. Trimble, Ph.D., Peter Falkai, M.D., William G. Honer, M.D.

NR122 A Central Hypothesis for the Charles Bonnet Syndrome
Gil Lichtshein, M.D., Antony Fernandez, M.D., Lisa B. Dixon, M.D.

NR123 Sickness Behaviors As Manifestations of Immunoendocrine Dysregulation in Somatic and Psychologic Illness
Andrew N. Dentino, M.D.

NR124 Alcohol Abuse in An Inpatient Geriatric Psychiatry Unit
Edward W. Cowen, B.S., Paul A. Ketti, M.D.

NR125 Outcome of Psychiatric Hospitalization for Very Low-Functioning Demented Patients
Ayman Abdel Bakey, M.D., Mark E. Kunik, M.D., Victor Molinari, Ph.D., Claudia Orengo, M.D., Richard H. Workman, Jr., M.D., Joseph D. Hamilton, M.D.

NR126 Anxiety Sensitivity in Elderly Presenting to a Primary Care Clinic
William J. Apfeldorf, M.D., George F. Brady, M.A., M. Philip Luber, M.D., Barnett S. Meyers, M.D., Mary E. Charlson, M.D., George S. Alexopoulos, M.D.

NR127 Asystole Incidence in the Elderly Receiving ECT
Jeremy A. Burd, Paul A. Ketti, M.D.

NR128 Thyroid Screening in a Geriatric Psychiatry Unit
Craig S. Feaster, B.S., Paul A. Ketti, M.D.

NR129 Direct Assessment of Function in Older Schizophrenia Patients
Joshua C. Klapow, Ph.D., Jovier D. Evans, Ph.D., Thomas L. Patterson, Ph.D., Robert K. Heaton, Ph.D., Robert M. Kaplan, M.D., Dilip V. Jeste, M.D.

NR130 An Open-Label Study of Risperidone for the Treatment of Agitation in Dementia
Helen Lavretsky, M.D., David L. Sultzer, M.D.

NR131 Premorbid Personality of Dementia Patients and Caregiver Burden
Ziad H. Nahas, M.D., Victor Molinari, Ph.D., Mark E. Kunik, M.D.

NR132 Depression in Demented and Non-Demented Inpatients
Ziad H. Nahas, M.D., Claudia Orengo, M.D., Mark E. Kunik, M.D., Victor Molinari, Ph.D., Richard H. Workman, Jr., M.D.

NR133 Delusions of Theft Are Increased in Hispanic Patients with Alzheimer's Disease
Gloria Peruyera, B.A., Lauren Singleton, M.A., Steven Sevush, M.D.

NR134 MRI Correlates of Denial of Deficit in Alzheimer's Disease
Rene A. Poveda, M.D., Steven Sevush, M.D.

NR135 HIV High-Risk Behavior Identification in a Prison Population of India: A Pilot Survey
Piyal Sen, A.N. Choudhury, M.D., Ian Treasaden, M.B., Dhrubo J. Bagchi, D.P.M., K. K. Ghosh, M.B., K. D. Sen, D.P.M.

NR136 A Pilot Study to Evaluate a Simple Screening Test for Depression in Elderly
Piyal Sen, Elaine Arnold, M.B., Brian M. Kaveman, M.B., D. McCrea, F.R.C.P.

NR137 Age and Gender Correlate with Delusions of Theft in Alzheimer's Disease
Lauren Singleton, M.A., Gloria Peruyera, B.A., Steven Sevush, M.D.

NR138 Severity of Dementia Does Not Predict Code Status
Stacy L. Hoenstine, Paul A. Ketti, M.D.

NR139 MRI Analysis in Schizotypal Personality Disorder
Chandlee C. Dickey, M.D., Martha E. Shenton, Ph.D., Yoshio Hirayasu, M.D., Iris A. Fischer, B.A., Martina M. Vogimaier, Ph.D., Robert W. McCarley, M.D.

NR140 Medial Temporal and Frontal Changes in Schizophrenia: A Quantitative MRI Study
Stephan A. Frost, M.D., Johannes Schroeder, M.D., Ingo Gerdsen, M.D., Lothar Schad, Ph.D., Marco Essig, M.D., Klaus Baudendistel, Ph.D.

NR141 Impaired Frontal Eye Field Control in Schizophrenics with Smooth Pursuit Eye Movement Disorders
Ingo Gerdsen, M.D., Joerg Pinkert, M.D., Rolf Foetzsch, M.D., L. Oehme, M.D., U. Neumann, M.D., Otto Bach, Ph.D.

NR142 Motor Task Performance and Cerebral Activation: A Study with Functional MRI
Ingo Gerdsen, M.D., Johannes Schroeder, M.D., Klaus Baudendistel, Ph.D., Marco Essig, M.D., Stephan A. Frost, M.D., Lothar Schad, Ph.D.

NR143 Brain MRI Analysis in First-Episode Psychosis
Yoshio Hirayasu, M.D., Martha E. Shenton, Ph.D., Chandlee C. Dickey, M.D., Dean F. Salisbury, Ph.D., Robert W. McCarley, M.D.

NR144 Automated Study of Subcortical MRI Brain Volumes in Schizophrenia
Dan V. Iosifescu, M.D., Martha E. Shenton, Ph.D., Ronald Kikinis, M.D., Simon K. Warfield, B.S., Joachim Dengler, Ph.D., Robert W. McCarley, M.D.

NR145 The Effects of Age on Brain Metabolic Response to Acute Idazoxan in Healthy Women
Jennifer L. Schouten, B.A., Mark E. Schmidt, M.D., Roseanne Leakan, R.N., David S. Goldstein, M.D., William Z. Potter, M.D.

NR146 Image Averaging in Structural MRI Studies of Schizophrenia
Gita Vaid, M.D., Henry Rusinek, Ph.D., Todd Lafargue, M.D., Luigi Arena, M.D., Michael P. Sanfilipo, B.S., Adam Wolkin, M.D.

NR147 An Open Trial of Paroxentine in PTSD
Randall D. Marshall, M.D., Franklin R. Schneier, M.D., Michael R. Liebowitz, M.D., Linda Abbate, B.A., Brian A. Fallon, M.D., David Printz, M.D.

NR148 Comorbid Major Depression and OCD in Pregnancy and the Puerperium
Susan F. Diaz, M.D., Lee S. Cohen, M.D., Deborah A. Sichel, M.D., Laura M. Robertson, B.A., Jerrold F. Rosenbaum, M.D.

NR149 Pharmacotherapy During Pregnancy in Women with OCD
Lynn R. Grush, M.D., Deborah A. Sichel, M.D., Lee S. Cohen, M.D., Laura M. Robertson, B.A., Carol S. Birnbaum, M.D., Lisa S. Weinstock, M.D.

NR150 Premenstrual Dysphoric Disorder and Its Relationship to Schizophrenia Symptom Severity
Andiea Hedayat-Harris, Ph.D.

NR151 Disorders of Extreme Stress in Anxiety Disorder Patients
Kevin B. Handley, M.A., Juliana R. Lachenmeyer, Ph.D., Regina Ucello, Andrew Shack, M.A., David Pelcovitz, Ph.D., Fran Mandel,

NR152 Deficiencies of Categorical Boundaries in Phoneme Perception in Schizophrenia
Angel Cienfuegos, M.D., Daniel C. Javitt, M.D., Anne-Marie Shelley, Ph.D., L. March, Ph.D.

NR153 Psychiatric Disorders in PMS: Five-Year Follow-Up
Catherine A. Roca, M.D., Peter J. Schmidt, M.D., David R. Rubinow, M.D.

NR154 OCD in Pregnancy, the Puerperium and the Premenstruum: A Pilot Study
Katherine E. Williams, M.D., Lorin M. Koran, M.D.

NR155 Reduced EEG Coherence in Narcolepsy Measured with Computerized EEG Mapping Technique
Do-Un Jeong, M.D., Doo-Heum Park, M.D., Jun Soo Kwon, M.D., Tak Youn, M.D.

NR156 WITHDRAWN

NR157 Double-Blind Crossover Study of Mirtazapine, Amitriptyline and Placebo in Patient with Major Depression
Mark L. Catterson, M.D., Sheldon H. Preskorn, M.D.

NR158 Acute Cardiovascular and Noradrenergic Effects Following the Alpha-2 Antagonist Ethoxyidazoxan in Humans
Libby A. Jolkovsky, B.A., Mark E. Schmidt, M.D., Michael Henry, M.D., Hyung G. Kim, M.D., Bradley S. Folley, B.S., William Z. Potter, M.D.

NR159 Sleep Electroencephalography in Depressed Versus Adolescents: Reanalyses of Sleep Data Collected During Adolescence After Longitudinal Follow-Up
Susan I. Wolk, M.D., Jeremy D. Coplan, M.D., Raymond R. Goetz, Ph.D., Neal D. Ryan, M.D., Ronald E. Dahl, M.D., Myrna M. Weissman, Ph.D.

NR160 Sleep-Related Growth Hormone Secretion in Depressed Versus Normal Adolescents: Reanalysis of Biological Data Collected During Adolescence
Susan I. Wolk, M.D., Jeremy D. Coplan, M.D., Raymond R. Goetz, Ph.D., Neal D. Ryan, M.D., Ronald E. Dahl, M.D., Myrna M. Weissman, Ph.D.

NR161 Delirium Detection in Elderly Emergency Room Patients
Francois Rousseau, M.D., Michel Elie, M.D., Martin G. Cole, M.D., Francois J. Primeau, M.D., Jane McCusker, M.D., Francois Bellavance, Ph.D.

NR162 Psychiatric Emergency Services and Medical Comorbidity
Thomas A. Armistead, M.D., Kenneth M. Certa, M.D.

NR163 Substance Use by Seriously Mentally Ill Patients and Their Families
Laura T. Rachuba, B.A., Lisa B. Dixon, M.D., Anthony F. Lehman, M.D., Leticia Postrado, Ph.D.

NR164 Depression in General Medical Settings: Diagnostic Limitations of Non-Psychiatric Physicians
David B. Arciniegas, M.D., Thomas P. Beresford, M.D.

NR165 Quality of Life in Fibromyalgia Patients
Megan M. Dwight, M.D., Lesley M. Arnold, M.D., Megan G. Murray, M.A., Emily Park-Morris, B.A., Hadley O'Brien, M.S.H.P/A

NR166 Risk Factors for Postpartum Depressive Symptoms in an Urban Minority Population
Janine S. Mele, B.A., Rhilina Ghosh, B.A., Veronika Solt, M.D.

NR167 Attitudes and Beliefs About Mental Illness Among Caribbean Immigrants
Sonia L. Cole, M.D., Lisa B. Dixon, M.D.

NR168 Psychiatric Disorders in an Arctic Community
John M. Haggarty, M.D., Harold Merskey, M.D., Zach Cernovsky, Ph.D., Patricia Kermeen, M.Sc.

NR169 Ethnicity and Self-Injurious Behaviors
Antonio A. Menchaca, M.D., Harold W. Koenigsberg, M.D., Tatsuyuki Kakuma, Ph.D.

NR170 Elevated Plasma Chloride in Psychiatric Patients
Medhat Aziz-Esaak, M.D.

NR171 Predictive Validity of Axis III Physical Disorders
Javier E. Saavedra, M.D., Juan E. Mezzich, M.D., Ihsan M. Salloum, M.D., Levent Kirisci, Ph.D.

NR172 Clinical Factors Associated with Positive Neuroimaging Studies in Psychiatric Inpatients
Michael Golding, M.D., John H. Gilmore, M.D., Ann M. Kopanski, M.A., Susan G. Silva, Ph.D.

NR173 Screening for Psychiatric Disorders in Medical Outpatients: A Patient Acceptance Study
Joseph V. Penn, M.D., Mark Zimmerman, M.D., Jill I. Mattia, M.A.

NR174 Domains of Psychopathology: Is Schizophrenia Different From Other Psychoses?
Santhi S. Ratakonda, M.D., Xavier F. Amador, Ph.D., Jack M. Gorman, M.D.

NR175 Archives of General Psychiatry: A Prevalence Study of Trials 1956-1995
Irshad Ahmed, M.D., Clive E. Adams, M.B, Rochelle Selfas, Karla V. Soares, M.D.

NR176 Thyroid Function Tests in First-Episode Mania
Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D., Silvina B.L. Zarate, B.S.

NR177 A Family Study of First-Episode Psychoses/Mania
Carlos A. Zarate, Jr., M.D., Bruce M. Cohen, M.D., Mauricio Tohen, M.D., Jennifer Sahatjian, Silvina B.L. Zarate, B.S.

NR178 Competency to Consent to Hospitalization and SPECT Scans Findings in Schizophrenia
Carlos A. Rueda, M.D., Stephen B. Billick, M.D., Carlos Blanco, M.D., James J. Daly, M.D., Woodward Burgert, B.A.

NR179 Limbic System-Associated Membrane Protein in Human Brain: An Immunocytochemical Study
E.M. Kemether, M.D., William M. Byne, M.D.

NR180 Tardive Suppression of Dopamine Neurons in Substantia Nigra but not Ventral Tegmental Area Following Neuroleptic Administration
Anthony J. Levinson, M.A., Sarah Garside, M.D., Patricia I. Rosebush, M.D., Michael Mazurek, M.D.

NR181 Diurnal Variation in Vagolytic Response to Lorazepam in Normal Subjects
Leslie R. Vogel, M.D., Philip R. Muskin, M.D., Eric D. Collins, M.D., Eva Petkova, Ph.D., Richard P. Sloan, Ph.D.

NR182 Effects of Prefrontal Repetitive Transcranial Magnetic Stimulation (rTMS) on Mood and Anxiety in Healthy Volunteers: A Replication Study
Juliet E. Dearing, B.S., Mark S. George, M.D., Benjamin D. Greenberg, M.D., Eric M. Wassermann, M.D., Thomas E. Schlaepfer, M.D., Robert M. Post, M.D.

NR183 Auditory Event-Related Potentials in An Oddball Paradigm in Children with Tourette's Syndrome
M. Yanki Yazgan, M.D., Sennur Zaimoglu, M.D., Sacit Karamursel, M.D.

NR184 Dermatologic QA Screening in 50 Psychiatric Inpatients
Sandra O. De Jesus, M.S., Stephen B. Billick, M.D., Sandra M. Bruni, M.S.

NR185 Patients Subjective Illness Concepts About Chronic Schizophrenia: A Comparison of Views Seen by Patients and Psychiatrists in Office Practice
Bettina Ripke, M.A., Julia Schellong, M.D., Antje Triemer, M.A., Franco Glasner, M.A., Otto Bach, Ph.D.

NR186 Changes of Interleukin Levels in Serum of Schizophrenic Patients Before and After Haloperidol Treatment
Yong-Ku Kim, M.D., Min Soo Lee, M.D.

NR187 Epinephrine Increases Plasma Interleukin-6 in Major Depression
Gregory H. Pelton, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D.

NR188 Schizophrenia Research Subjects: Gender Differences
Patrick T. Dooley, M.A., Jayendra K. Patel, M.D., Anthony G. Kalinowski, Ph.D., Rahim Shafa, M.D., Carla M. Canuso, M.D., Alan I. Green, M.D.

NEW RESEARCH

Tuesday, May 7, 1996, 9:00 a.m.-10:30 a.m.

New Research 5 – Oral/Slide Session – Room E6, Level 1, Javits Center

ALCOHOL AND SUBSTANCE ABUSE DISORDERS

Chp.: Boris M. Astrachan, M.D.

NR189 Bupropion Plus Bromocriptine for Treatment of Cocaine Dependence — 9:00 a.m.
Ivan D. Montoya, M.D., David A. Gorelick, M.D., Kenzie L. Preston, Ph.D., Edward Cone, Ph.D., Richard B. Rothman, M.D.

NR190 Use of Alcohol Detox Protocol on a Medical Unit — 9:15 a.m.
Lisa R. Fenton, P.S.D., Judy Ebbets, M.S., Wayne S. Fenton, M.D.

NR191 Prior Abstinence and Post-Transplant Drinking: Six Months of Abstinence Does Not Predict Alcoholic Relapse — 9:30 a.m.
Thomas P. Beresford, M.D., Michael R. Lucey, M.D.

NR192 Double-Blind Fluoxetine in Depressed Alcoholics — 9:45 a.m.
Jack R. Cornelius, M.D., Ihsan M. Salloum, M.D., Joan G. Ehler, M.D., Patricia J. Jarrett, M.D., James Perel, Ph.D., Michael E. Thase, M.D.

NR193 Development of a Therapeutic Cocaine Vaccine — 10:00 a.m.
Barbara S. Fox, Ph.D., Kathleen M. Kantak, Ph.D., Thomas J. Briner, Ph.D., Mark A. Exley, Ph.D., Philip A. Swain, Ph.D.

NR194 Electrocardiographic Findings in Chronic Heavy Cocaine Abusers — 10:15 a.m.
Faiq A. Hameedi, M.D., Lynn C. Winther, M.D., Conor K. Farren, M.D., Rukhshinda R. Hameedi, M.D., Elinore F. McCance-Katz, M.D., Thomas R. Kosten, M.D.

NEW RESEARCH

Tuesday, May 7, 1996, 9:00 a.m.-10:30 a.m.

New Research 6 – Oral/Slide Session – Room E17, Level 1, Javits Center

PSYCHOPHARMACOLOGY

Chp.: Joshua H. Calhoun, M.D.

NR195 Pharmacokinetic and Pharmacodynamic Effects of Co-Administration of Nefazodone and Desipramine to Normal Volunteers — 9:00 a.m.
Sheldon H. Preskorn, M.D., Ryan D. Magnus, M.D., Dale Horst, Ph.D., Jane Rosenblum, Darlene Jody, M.D., John R. Ieni, Ph.D.

NR196 Optimal Target Dose of Imipramine in Panic Disorder with Agoraphobia — 9:15 a.m.
Matig R. Mavissakalian, M.D., James Perel, Ph.D.

NR197 Fluvoxamine in the Treatment of OCD in Children and Adolescents: A Multicenter, Double-Blind, Placebo-Controlled Trial — 9:30 a.m.
Mark A. Riddle, M.D., Pediatric OCD Research Group

NR198 Serotonergic Antidepressants in Obsessive Personality — 9:45 a.m.
Marc M. Ansseau, M.D.

NR199 Double-Blind, Controlled Comparison of Haloperidol and Pimozide in Children with Gilles de la Tourette's Syndrome — 10:00 a.m.
Floyd R. Sallee, M.D., Lori Nesbit, Pharm D., Cherry Jackson, Pharm D.

NR200 Predictors of Response to Paroxetine Therapy in the Treatment of Panic Disorder — 10:15 a.m.
Martin Steiner, Ph.D., Rosemary Oakes, M.S., David E. Wheadon, M.D., Ivan P. Gergel, M.D.

NEW RESEARCH

Tuesday, May 7, 1996, 12 noon-2:00 p.m.

New Research 7 – Poster Session – Galleria, Level 4, Javits Center

AIDS; CHILD/ADOLESCENT PSYCHIATRY; VIOLENCE, TRAUMA AND VICTIMIZATION; AND INFANT/CHILD, ALCOHOL/SUBSTANCE ABUSE, AND PERSONALITY DISORDERS

Moderator: Susan J. Flester, M.D.

NR201 Treating Depression in HIV-Positive Patients
John C. Markowitz, M.D., Baruch Fishman, Ph.D., James H. Kocsis, M.D., Lawrence B. Jacobsberg, M.D., Lisa A. Spielman, Ph.D., Samuel W. Perry III, M.D.

NR202 Mediators of Bereavement Distress in a Gay Man Sample
Vicki L. Gluhoski, Ph.D., Baruch Fishman, Ph.D., Samuel W. Perry III, M.D.

NR203 Depression, Viral Load and Other AIDS Illness Markers
Judith G. Rabkin, Ph.D., Stephen J. Ferrando, M.D., Baruch Fishman, Ph.D.

NR204 A Comparative Analysis of Standard and Alternative Antidepressants in the Treatment of HIV Patients
Glenn J. Wagner, Ph.D., Judith G. Rabkin, Ph.D., Richard Rabkin, M.D.

NR205 Somatic Symptoms, Depression and HIV Illness Markers
Stephen J. Ferrando, M.D., Judith G. Rabkin, Ph.D., Baruch Fishman, Ph.D.

NR206 Fatigue in Ambulatory AIDS Patients
William Breitbart, M.D., Margaret McDonald, M.S.W., Barry Rosenfeld, Ph.D., Steve Passik, Ph.D., Monique Kaim, Ph.D., Paulette Murphy, Psy.D.

NR207 Undertreatment of Pain in AIDS
William Breitbart, M.D., Steve Passik, Ph.D., Barry Rosenfeld, Ph.D., Margaret McDonald, M.S.W., Howard Thaler, Ph.D., Russell Portenoy, M.D.

NR208 Pain in Women with AIDS
William Breitbart, M.D., Margaret McDonald, M.S.W., Barry Rosenfeld, Ph.D., Steve Passik, Ph.D., Jaqueline Calle, B.A., Howard Thaler, Ph.D., Russell Portenoy, M.D.

NR209 Brief Cognitive Therapy After HIV Antibody Testing
Baruch Fishman, Ph.D., Samuel W. Perry III, M.D.

NR210 Stress-Associated Changes in Neuropsychological Functioning in HIV-1 Infection
Susan G. Silva, Ph.D., Eric D. Jackson, B.S., Jane Leserman, Ph.D., Robert A. Stern, Ph.D., Robert N. Golden, M.D., Dwight L. Evans, M.D.

NR211 Psychological Functioning and HIV Risk Behavior Among Substance Abusers with HIV Infection
Julie A. London, Ph.D., James L. Sorensen, Ph.D., Meridith Miller, B.A., Kevin Delucchi, Ph.D., James W. Dilley, M.D., Bonnie Schwartz, M.S.W.

NR212 Safety of Risperidone in Patients with HIV and AIDS
Ashok N. Singh, M.D., Jose Catalan, M.B.

NR213 Emotional Distress in Seropositive Patients Who Both Monitor or Blunt Information
Lara A. Warburton, M.S., Baruch Fishman, Ph.D., Judith G. Rabkin, Ph.D.

NR214 Risperidone for AIDS-Associated Dementia: A Case Series
Louis Belzie, M.D.

NR215 Gender Differences in Hyperactivity in Children
Carol A. Glod, Ph.D., Martin H. Teicher, M.D., Cynthia E. McGreenery, Matthew Ducsik, B.A., Carl M. Anderson, Ph.D., Ann Polcari, M.S.

NR216 Characteristics of Juvenile Delinquents Admitted to an Adolescent Psychiatric Inpatient Unit
Wun Jung Kim, M.D., Youngsik Lee, M.D., Michael P. Carey, Ph.D.

NR217 Olfaction in Tourette's Syndrome: ADHD and Controls
F. Xavier Castellanos, M.D., Nancy E. Harnett, Ph.D., William E. Klein, R.N., Margaret DeMayo, Judith L. Rapoport, M.D.

NR218 Predicting Unmet Service Needs for ADHD Among Children in Special Education: Who is at Risk?
Regina Bussing, M.D., Amy Perwien, B.A., Thomas Belin, Ph.D.

NR219 Clinical Characteristics and Treatment Courses of the Children with Selective Mutism
Kang-E M. Hong, M.D., Sun-Ju Chung, M.D.

NR220 Positive Cognition in Depressed Adolescents
John B. Jolly, Psy.D., Thomas A.M. Kramer, M.D., David C. Weisner, Ph.D., Jane H. Feldman, M.D.

NR221 Perinatal and Obstetric Events As Predictors of Onset of Tourette's Symptoms
Raul R. Silva, M.D., Lorraine Wolf, Ph.D., Dinohra M. Munoz, M.D., E. Steven Dummit III, M.D., Jim Kim

NR222 Sertraline Treatment in Children and Adolescents: Tolerability, Efficacy and Pharmacokinetics
Jeffrey A. Alderman, Ph.D., Robert Wolkow, M.D., Hugh F. Johnston, M.D., Murray H. Rosenthal, D.O., James M. Ferguson, M.D., Floyd R. Sallee, M.D., Jeffrey Blumer, M.D.

NR223 Drug and Alcohol Trends in Adolescents
Norman S. Miller, M.D., Mark S. Gold, M.D.

NR224 The Lack of Effect of Methylphenidate on the Growth Hormone Axis
Paz Toren, M.D., Aviva Silbergeld, M.Sc., Sofia Eldar, M.D., Nathaniel Laor, M.D., Ronit Weizman, M.D.

NR225 Cognitive Impulsivity in Adolescent Inpatients
David L. Pogge, Ph.D., Susan R. Borgaro, M.A., William Horan, B.A., Joel Lord, M.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D.

NR226 Pilot Trial of Risperidone in Children and Adolescents with Pervasive Developmental Disorder
Richard I. Perry, M.D., Caroly S. Pataki, M.D., Dinohra M. Munoz, M.D., Jorge L. Armenteros, M.D., Raul R. Silva, M.D.

NR227 Placebo Response and Hyperactivity in Aggressive Conduct Disorder
Richard P. Malone, M.D., Louisa Seraydarian, Ph.D., Mary A. Delaney, M.D., Krista A. Biesecker, B.A., James F. Luebbert, M.D., Amy B. Rowan, M.D.

NR228 Buspirone in Adolescents with Anxiety Disorders
Manuel P. Bouvard, Alain-Jean Braconnier, M.D., Catherine Dissoubray

NR229 Psychopathology in Incarcerated Youth
Andres J. Pumariega, M.D., D. Lanette Atkins, M.D., Larry Montgomery, M.D., Kenneth T. Rogers, D.O., W. Franklin Sease, Jr., B.S., Gary Jeffers

NR230 Services Utilization in Incarcerated Youth
Andres J. Pumariega, M.D., D. Lanette Atkins, M.D., Larry Montgomery, M.D., Susan Appenzeller, M.S.W., Robert Caesar, Ph.D., Donald Millus, B.S.

NR231 Self-Reported Pathology and Psychiatric Assessment Among Special Education Students in a School-Based Clinic
Spyros J. Monopolis, M.D., John Myhill, Ph.D., Peggy Caltrider, M.S.W., Patricia Cronin, M.S.W., Patrick Crouse, M.A.

NR232 Attachment and Drug Use in Detained Youth
Adrienne E.R. Sheldon-Keller, Ph.D., Randolph J. Canterbury, M.D., Elizabeth L. McGarvey, Ed.D., Dennis Waite, Ph.D.

NR233 Sport, Coping Strategies and Depression in Adolescence
Fabien Durif, M.D., Pierre Tap, Ph.D., Jean-Philippe Raynaud, M.D., Laurent Schmitt, M.D., Pierre Moron, M.D.

NR234 Pilot Project Examining the Effectiveness of an Intensive Day Program for Truant, Severely Disturbed Adolescents
Frederick J. Matzner, M.D., Matthew Silvan, Ph.D., Raul R. Silva, M.D., Joanne Weiner, Jacqueline Bendo, Murray Alpert, Ph.D.

NR235 Treatment of Childhood and Adolescent Depression with Sertraline: Possible Therapeutic Range of Plasma Concentration
Vincenzo F. DiNicola, M.D., Irvin Epstein, M.D., James Owen, Ph.D., Kevin Parker, Ph.D., Kelly Driver, B.Sc.

NR236 Characteristics of Korean Learning Disordered Children
Ji-Hae Kim, Ph.D., Young-Ran Lim, M.D., S. Peter Kim, M.D.

NR237 Predictors of Neuroleptic Response in Psychiatrically Hospitalized Children
Dinohra M. Munoz, M.D., Raul R. Silva, M.D., Murray Alpert, Ph.D., Daniel M. Medeiros, M.D., Lissa Lacher, Richard I. Perry, M.D.

NR238 Predictors of Length of Stay in Child Psychiatry Inpatient Hospitilization
Ilisse R. Perlmutter, M.D., Dean McKay, Ph.D., John D. O'Brien, M.D.

NR239 The Factorial Composition of Thought Disorder in Adolescence
David S. Medoff, Ph.D., David L. Pogge, Ph.D.

NR240 Cognitive Impulsivity in Adolescent Conduct Disorder
Susan R. Borgaro, M.A., David L. Pogge, Ph.D., William Horan, B.A., John Stokes, Ph.D., Joel Lord, M.A., Philip D. Harvey, Ph.D.

NR241 Zinc Deficiency in ADHD
Sofia Eldar, M.D., Paz Toren, M.D., Ben-Ami Sela, Ph.D., Leo Wolmer, M.A., Ronit Weizman, M.D., Nathaniel Laor, M.D.

NR242 Brain EEG Abnormalities in 300 Hospitalized Preadolescents
Noelle K. Gehm, B.S., Henry A. Nasrallah, M.D.

NR243 Depressive Symptoms in Adolescent Conduct Disorder
William Horan, B.A., David L. Pogge, Ph.D., Susan R. Borgaro, M.A., Joel Lord, M.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D.

NR244 Financial Efficacy of Treatment Foster Care for Emotionally Disturbed Children and Adolescents
Edwin J. Mikkelsen, M.D., Wayne J. Steik, Ph.D., Lynn Morton-Epps, M.E.D.

NR245 Family and Peer Influences in Adolescent Drug Use
Ramon U. Florenzano, M.D., Paulina Z. Pino, Ph.D., Milka D. Kaplan, M.Sc., Perla C. Ben Dov

NR246 Olanzapine: Molecule to Drug Candidate
Charles M. Beasley, Jr., M.D., Gary D. Tollefson, M.D., Pierre V. Tran, M.D., Winston G. Satterlee, M.D., Todd Sanger, Ph.D.

NR247 Multiple DWI Arrests in Minority Offenders
Hyung K. Lee, M.D., Ali Khadivi, Ph.D.

NR248 Factor Analysis of the Addiction Severity Index
Juris P. Mezinskis, Ph.D., Jennifer Lewis, B.S., Eugene C. Somoza, M.D., Sue R. Dyrenforth, Ph.D., Mark Cohen, Ph.D.

NR249 Harm Reduction As an Outcome of Methadone Maintenance Treatment of Geriatric Heroin Addicts
Chandresh Shah, M.D., David Highfill, M.A., Lena Simitian, Ph.D.

NR250 Bromocriptine for Treatment of Cocaine Abuse
David A. Gorelick, M.D., James L. Hill, Ph.D., Jeffery N. Wilkins, M.D.

NR251 Phenomenology of Inpatient Cocaine Withdrawal
David A. Gorelick, M.D., Robin Stauffer, R.N., Jon-Kar Zubieta, M.D., James J. Frost, M.D.

NR252 Plasma Butyrylcholinesterase Activity in Drug Abusers
David A. Gorelick, M.D., Gilberto Carmona, M.S., Raymond Woosley, M.D., Kenneth Dretchen, Ph.D., George Belendiuk, M.D., Nicholas Carriero, Ph.D.

NR253 Brazilian Medical Students: Alcohol and Drug Use
Florence Kerr-Correa, M.D., Artur G. Andrade, M.D., Ana Z. Bassit, Psy.

NR254 Alcohol Severity in Comorbidity Depressed Patients
Helen M. Pettinati, Ph.D., Richard Saini, M.D., Alexia L. Wolf, B.A., Ann E. Semwanga, B.A., Alan Sharf, B.S.

NR255 Perceived Need for Substance Abuse and Mental Illness Treatment Among Dually-Diagnosed Psychiatric Inpatients
Jill Rachbeisel, M.D., Lisa B. Dixon, M.D., Jean Gearon, Ph.D.

NR256 Reduced Blue Cone Electroretinogram in Cocaine Patients
Alec Roy, M.D., Monique Roy, M.D., John A. Williams, M.D., Larry Wineberger, Ph.D., David Smelson, Psy.D.

NR257 Why Do Alcoholics Get Depressed?
Alec Roy, M.D.

NR258 Oral Morphine Maintenance Program
Gabriela Forster, M.D., Gabriele Fischer, M.D., Karin Diamant, M.D., Corinna Schneider, M.D., Lukas Pezawas, M.D., Siegfried Kasper, M.D.

NR259 MRI Evidence of "Silent" Neurotoxicity in Cocaine Dependence
George Bartzokis, M.D., Mace Beckson, M.D., Darwood Hance, M.D., Walter Ling, M.D., Stephen R. Marder, M.D.

NR260 Clinical Effects of Repeated Cocaine and Alcohol Use
Elinore F. McCance-Katz, M.D., Thomas R. Kosten, M.D., Peter I. Jatlow, M.D.

NR261 Comorbidity in Adult Inpatient Drug Abusers
Carlos M. Grilo, Ph.D., Steve Martino, Ph.D., Daniel F. Becker, M.D., Martha L. Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR262 Personality Disorders in Adults: Gender Effects
Carlos M. Grilo, Ph.D., Daniel F. Becker, M.D., Martha L. Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR263 Pregnancy and Opiate Dependence
Corinna Schneider, M.D., Gabriele Fischer, M.D., Karin Diamant, M.D., Gabriela Forster, M.D., Lukas Pezawas, M.D., Siegfried Kasper, M.D.

NR264 Type-B Alcoholics Have Poorer Drinking-Related Outcomes with Fluoxetine Treatment
Henry R. Kranzler, M.D., Joseph A. Burleson, Ph.D., Joseph Brown, Ph.D., Thomas F. Babor, Ph.D.

NR265 Targeted Naltrexone in Combination with Coping Skills Training in Early Problem Drinkers
Henry R. Kranzler, M.D., Howard Tennen, Ph.D., Christopher Penta, M.A., Michael J. Bohn, M.D.

NR266 Cardiovascular Interactions of Cocaine with Antidepressants
Richard A. Nelson, M.D., David A. Gorelick, M.D., Gilberto Carmona, M.S., Robert Keenan, M.D., Lino Covi, M.D.

NR267 Safety of Depakote in Bipolar Patients with Comorbid Alcohol Abuse/ Dependence
Susan C. Sonne, Ph.D., Kathleen T. Brady, M.D.

NR268 Eriksonian Stages of Psychosocial Development, Defense Styles and Mood States in Alcoholics: Repeated Measures
Paul W. Ragan, M.D., Linda Doty, R.N., Nancy E. Harnett, Ph.D., Dell Wright, B.S.N., Sandy Birdsong, B.S.N., Chris Geyer, R.N.

NR269 A Study on Ego Defense Mechanisms of Alcohol Abuse Patients by Ewha Defense Mechanism Test in Korea
Kun Hoo Rhee, M.D.

NR270 Psychosocial and Pharmacological Treatments for Cocaine Abuse: A Review of Empirical Research
Joy M. Schmitz, Patrick Bordnick, Ph.D., Bruce Thyer, Ph.D., Donald M. Dougherty, Ph.D.

NR271 A Comparison of Three Months Versus Six Months of Outpatient Alcohol and Drug Treatment
Sheku G. Kamara, Ph.D.

NR272 Gamma Hydroxybutyric Acid for Detoxification Treatment of Opiate-Dependent Patients
Gabriele Fischer, M.D., Corinna Schneider, M.D., Karin Diamant, M.D., Richard Frey, M.D., Angela Heiden, M.D., Siegfried Kasper, M.D.

NR273 Methylphenidate Treatment of Cocaine-Abusing Adults with ADHD
Frances R. Levin, M.D., Suzette M. Evans, Ph.D., Helga Yuan, B.A., Madeline Rhum, M.A., Nicole D. Regent, B.A., Herbert D. Kleber, M.D.

NR274 Characteristic Features of Responders to Acupuncture Detoxification for Acute Heroin Withdrawal Symptoms
Joselito B. Domingo, M.D., Cheng-Jen Chen, M.D.

NR275 EEG Signs of Cocaine Dependence
Ronald I. Herning, Ph.D., David A. Gorelick, M.D., Xiaoyan Guo, M.D., Linda L. Weinhold, Ph.D., Jean L. Cadet, M.D.

NR276 EEG and Evoked Potentials in Chronic Cocaine Abuse
John J. Straumanis, Jr., M.D.

NR277 Medication Adherence in Bipolar Substance Abusers
Roger D. Weiss, M.D., Shelly F. Greenfield, M.D., Cathryn Hufford, B.A., Lisa M. Najavits, Ph.D., Mauricio Tohen, M.D., Jose Martinez-Raga, M.D.

NR278 Distribution of Substance-Abusing Inpatients Along a Stages-of-Behavioral Change Continuum
Eve J. Wiseman, M.D., Margaret J. Briggs, L.P.N.

NR279 Behaviorally Contingent Pharmacotherapy for Opioid Abusers: An Outpatient Randomized Clinical Trial
Van L. King, Jr., M.D., Robert K. Brooner, Ph.D., Michael Kidorf, Ph.D.

NR280 Serum Cholesterol and Impulsive Aggressive Behavior in Personality Disorder Patients
Carol F. Zale, M.D., Antonia S. New, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR281 Validity of DSM-III-R Personality Disorders in Adolescents: Results From Follow-Up Two Years After Hospitalization
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.

NR282 Internal Consistency of DSM-III-R Personality Disorders in Hospitalized Adolescents
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.

NR283 Effects of Amphetamine on Cognitive Impairment in Schizotypal Personality Disorder
Richelle M. Kirrane, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Barbara A. Cornblatt, Ph.D., Larry J. Siever, M.D.

NR284 A Polymorphism in Tryptophan Hydroxylase and Irritable Aggression in Personality Disorders
Antonia S. New, M.D., Joel Gelernter, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR285 Self-Reported Abuse and Biological Measures in Personality Disorders
Antonia S. New, M.D., Rachel Yehuda, Ph.D., Bonnie J. Steinberg, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Emil F. Coccaro, M.D., Larry J. Siever, M.D.

NR286 Learning and Memory in Schizotypal Personality Disorder
Martina M. Vogimaier, Ph.D., Larry J. Seidman, Ph.D., Dean F. Salisbury, Ph.D., Robert W. McCarley, M.D.

NR287 Myers-Briggs Type Indicator Relationships with the Million Clinical Multiaxial Inventory Version II
Eric R. Braverman, M.D., Doug Stone-Miller, M.A., Richard Holland, Ph.D., Don Johnson, Ph.D., Kenneth Blum, Ph.D.

NR288 The Tridimensional Personality Questionnaire in Older Spanish Adults: A Validity Study
Manuel Gurpegui, M.D., Juan J. Lopez-Castillo, M.D.

NR289 A Behavioral Comparison of Female Adolescent Inpatients With and Without BPD
Carol J. Roach, B.A., William L. Grapentine, M.D.

NR290 Psychopathology in Physically Abused Children and Adolescents
Alan J. Flisher, M.B., Rachel A. Kramer, D.Sc., Christina Hoven, Ph.D., Margarita Alegria, Ph.D., Hector R. Bird, M.D., Glorisa Canino, Ph.D., Stevan Greenwald, M.A., Robert E. Moore, Dr.PH

NR291 Psychological Correlates of Domestic Violence
Caron Zlotnick, Ph.D., Robert Kohn, M.D., Johan Peterson, B.A.

NR292 Affect Management Group for Survivors of Sexual Abuse with PTSD
Caron Zlotnick, Ph.D., M. Tracie Shea, Ph.D., Teri B. Pearlstein, M.D., Karen J. Rosen, M.D., Kate Mulrenin, Ph.D., Elizabeth B. Simpson, M.D.

NR293 Predictors and Correlates of Self-Mutilation During Hospital Stay
Caron Zlotnick, Ph.D., Teri B. Pearlstein, M.D., Elizabeth B. Simpson, M.D., Ellen Costello, Ph.D., Ann Begin, Ph.D.

NR294 Validity of Self-Reported Trauma in Adolescence
David P. Bernstein, Ph.D., Taruna Ahluvalia, B.A., David L. Pogge, Ph.D., Leonard Handelsman, M.D.

NR295 Bosnian Students in America: Trauma and Adjustment
Stevan M. Weine, M.D., Alma Dzubur Kulenovic, M.D., Natasha Desai

NR296 Trauma, PTSD and Axis II Disorders in Addicts: Patterns of Comorbidity
Elisa G. Triffleman, M.D.

NR297 Childhood Abuse and Subsequent Axes I-II Disorders
Lynn A. Lyons, M.S., Heather Z. Lyons, Carolyn M. Mazure, Ph.D., Bruce E. Wexler, M.D.

NR298 Adult Serotonergic Correlates of Childhood Abuse in Male Alcoholics and Cocaine Addicts
Leonard Handelsman, M.D., David P. Bernstein, Ph.D., Paul Rinaldi, Ph.D., Stevan Gabriel, Ph.D., Karen Holloway, M.D., Christopher Sturiano, A.B.

NR299 An Examination of Clinical and Personality Characteristics Among Couples with a History of Less Violent Abusive Interaction in a Military Population
Charles D. Magruder, M.D., Roslyn Tartaglione, M.A., Gary Southwell, Ph.D., Robert Mays, Ph.D.

NR300 Characteristics of Childhood Sexual Abuse and Adult Psychopathology
Jill Pettigrew, F.R.A., Joyce Burcham, Ph.D.

NR301 A Longitudinal Study of Clinical Outcome Indicators and Rating Scales in Chronic State Hospital Inpatients
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D.

NR302 PTSD in Spanish Policeman
Inmaculada Gilaberte-Asin, M.D., Enrique Baca, M.D., Asuncion Abril, M.D., Carlos Blanco, M.D., Alfonso Calve, M.D.

NEW RESEARCH

Tuesday, May 7, 1996, 3:00 p.m.-5:00 p.m.

New Research 8 – Poster Session – Galleria, Level 4, Javits Center

MOOD DISORDERS, PSYCHOPHARMACOLOGY, SUICIDE AND EATING DISORDERS

Moderator: Charles B. Nemeroff, M.D.

NR303 Psychiatric Comorbidity of Atypical Depression
Isabel Lagomasino, M.D.

NR304 The Contributions of Family Burden and Denial of Illness to Outpatient Service Use in Bipolar Affective Disorder
JoAnne Sirey, Ph.D.

NR305 Sociodemographic Predictors of Response to Antidepressant Treatment
Maya Spillmann, M.D.

NR306 Differences in Expressed Emotion of Spousal Versus Parental Caregivers in Bipolar Affective Disorder
John F. Clarkin, Ph.D.

NR307 Determinants of Family Burden in Male Versus Female Caregivers of Persons with Bipolar Affective Disorder
Deborah A. Perlick, Ph.D.

NR308 Outpatient Service Use As a Predictor of Psychiatric Hospitalization in Bipolar Illness
Deborah A. Perlick, Ph.D.

NR309 The Thyroid and Cognitive Therapy for Depression
Russell T. Joffe, M.D.

NR310 Degree of Assertiveness in Major Depression
Asha I. Parekh, M.D.

NR311 Gabapentin Does Not Alter Lithium Pharmacokinetics
Mark A. Frye, M.D.

NR312 The Increasing Use of Polypharmacy for Refractory Mood Disorders: Twenty-Five Years of Study
Mark A. Frye, M.D.

NR313 Postpartum Prophylaxis in Women with Histories of Major Depressive Disorders
Lee S. Cohen, M.D., Laura M. Robertson, B.A., Deborah A. Sichel, M.D., Carol S. Birnbaum, M.D., Lynn R. Grush, M.D., Lisa S. Weinstock, M.D.

NR314 Impact of Pregnancy on Risk for Relapse of Major Depressive Disorder
Lee S. Cohen, M.D., Laura M. Robertson, B.A., Deborah A. Sichel, M.D., Carol S. Birnbaum, M.D., Lynn R. Grush, M.D., Lisa S. Weinstock, M.D.

NR315 Deliberate SSRIs Added to Tricyclic Antidepressant: A Combination to Achieve Therapeutic Tricyclic Antidepressant Levels in Rapid Metabolizers
Robert P. Kraus, M.D., Paula Diaz, MRPharmS.

NR316 Family Functioning and Chronic Depression
Gabor I. Keitner, M.D., Christine E. Ryan, Ph.D., Ivan W. Miller, Ph.D., Martin B. Keller, M.D.

NR317 Pharmacotherapy and Psychotherapy Response in Atypical Depression: Findings From the NIMH Treatment of Depression Collaborative Research Program
Stuart M. Sotsky, M.D., Sam Simmens, Ph.D.

NR318 Safety and Tolerability of the Sustained-Release Formulation of Bupropion in Depression: Results of Three Clinical Trials
Edmund C. Settle, Jr., M.D., Stephen M. Stahl, M.D., Sharyn R. Batey, Pharm D., J. Andrew Johnston, Pharm D., John A. Ascher, M.D.

NR319 Serotonergic Autoreceptor Blockade in the Reduction of Antidepressant Latency: A Controlled Trial
Michael T. Isaac, M.D., Maria B. Tome, M.D., Rosaril Harte, M.D.

NR320 Cost-Benefit Analysis of a Novel Antidepressant Regime
Michael T. Isaac, M.D., Maria B. Tome, M.D.

NR321 Comparison of Serotonin Levels in Depression Treated by New and Standard Antidepressant Regimes
Michael T. Isaac, M.D., Maria B. Tome, M.D., Roy Sherwood, M.D., Paul Eldridge, Ph.D.

NR322 Depression: A Disorder of Coincidence Detection?
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.

NR323 Bupropion SR Response in Depression: Diagnosis and Biochemistry
Paul J. Goodnick, M.D., Roberto A. Dominguez, M.D., Yolanda M. Don, M.D., C. Lindsay DeVane, Ph.D., Charles L. Bowden, M.D., Joseph Henry, M.D.

NR324 Hyperactivation of the HPT Axis in Depression: New Evidence
Patricia R. Mourilhe, M.D., Peter E. Stokes, M.D., Alexandra I. Barsdorf, Herminia Ombid

NR325 Ten-Year Follow-Up of Chronic Depressives
Timothy I. Mueller, M.D., Martin B. Keller, M.D., Andrew C. Leon, Ph.D., David A. Solomon, M.D., M. Tracie Shea, Ph.D., Jean Endicott, Ph.D.

NR354 Gender Differences in Iatrogenic Sexual Dysfunction in Chronically Depressed Patients Treated with SSRI: A Pilot Study
Lisa A. Piazza, M.D., John C. Markowitz, M.D., James H. Kocsis, M.D., Andrew C. Leon, Ph.D., Laura Portera, B.A., Nina Miller, M.A.

NR355 ECT in Patients with Major Depressive Disorder and Low Cardiac Output
Liat Stern, M.D., Shmuel Hirschmann, M.D., Leon J. Grunhaus, M.D.

NR356 Bipolar Spectrum Disorder in Velo-Cardio-Facial Syndrome
Demitri F. Papolos, M.D., Sabine E. Veit, M.D., Sam S. Parsia, B.A., Gianni L. Faedda, M.D., R. Goldberg, M.S., Robert Shprintzen, Ph.D., Bernice Morrow, Ph.D., Raju Kucherpalati, Ph.D., Herbert M. Lachman, M.D.

NR357 A Simplified Accounting of Drug Accumulation
Conrad M. Swartz, M.D.

NR358 Effects of Double-Blind Treatment with Nefazodone or Sertraline on Re-Emergence of Sexual Dysfunction in Depressed Patients
James M. Ferguson, M.D., Ram K. Shrivastava, M.D., Stephen M. Stahl, M.D., James J. Hartford, M.D., Barbara Nape, R.N., Frances Borian, R.N.

NR359 A Double-Blind Comparison of Nefazodone and Fluoxetine in Depressed Patients
Patrice Rioux, M.D., Yves Kibleur, M.D., Olivier Frachon, Remy von Frenckell, Prof. Edouard Zarifian

NR360 Evaluation of Fluvoxamine in Social Phobia
C. Lindsay DeVane, Ph.D., Michael R. Ware, M.D., Naresh P. Emmanual, M.D., Olga Brawman-Minizer, M.D., R. Bruce Lydiard, M.D.

NR361 Four Week Nonresponse: Who Responds at Eight Weeks?
Andrew A. Nierenberg, M.D., Rosemarie Mulroy, B.A., Jonathan E. Alpert, M.D., John J. Worthington III, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR362 Effect of Venlafaxine Versus Fluoxetine on the Metabolism of Dextromethorphan
Jess D. Amchin, M.D., Larry Ereshefsky, Pharm D., William M. Zarycranski, Pharm D.

NR363 Chart Review: Family Physicians' Prescription of Antidepressants
Marijo B. Tamburrino, M.D., Rollin W. Nagel, M.A., Denis J. Lynch, Ph.D.

NR364 Clozapine and Associated Diabetes Mellitus
Anand P. Popli, M.D., P. Eric Konicki, M.D., George J. Jurjus, M.D., Matthew A. Fuller, Pharm D., George E. Jaskiw, M.D., Luis G. Ramirez, M.D.

NR365 An Open Trial of Venlafaxine in BPD
Paul J. Markovitz, M.D., Susan C. Wagner, M.A.

NR366 Flesinoxan in the Treatment of Major Depressive Disorder: A Fixed Dose, Placebo-Controlled Trial
L. DiAnne Bradford, Ph.D.

NR367 Risperidone in Patients with Developmental Disabilities
Theodore W. Wasserman, M.D., Carla Prinsze, M.D.

NR368 Costs of Treatment with Risperidone and Clozapine
David Thompson, R.N.

NR369 A Double-Blind Comparison of Nefazodone and Sertraline in Highly Anxious Inpatients with Major Depression
Cal K. Cohn, M.D., John P. Feighner, M.D., Steven D. Targum, M.D., Stephen G. Thein, M.D.

NR370 A Double-Blind Trial of Nefazodone Versus Placebo in Depressed Inpatients
John P. Feighner, M.D., Mary E. Bennett, M.D., Douglas L. Roberts, Jr., M.D., M. Frances D'Amico, M.S., Kathleen O'Brien, M.S.

NR371 Efficacy of Nefazodone in Continuation Treatment of Depression
Alan D. Feiger, M.D., Robert D. Bielski, M.D., James D. Bremner, M.D., Jon F. Heiser, M.D., Madhukar H. Trivedi, M.D.

NR372 Clozapine and Change in Body Mass
Frances R. Frankenburg, M.D., Mary C. Zanarini, Ed.D., Judith Kando, Pharm D., Franca Centorrino, M.D.

NR373 Risperidone in Patients with Chronic Schizophrenia: Acute Responses and Effects on One-Year Hospitalization Rates
Michael Phillipp, M.D., Risperidone Study Group

NR374 Risperidone in Schizophrenia: Practical Issues
Alice F. Duncan, M.D., Risperidone Study Group

NR375 Health Care Resource Utilization and Costs Before and After Initiation of Risperidone Treatment for Schizophrenia in Saskatchewan
Penny Albright, Ph.D., Scott Livingstone, M.Sc., David L. Keegan, M.D., Satish Shrikhande, M.D., Jacques Le Lorier, M.D.,

NR376 Risperidone in the Outpatient Treatment of Chronic Schizophrenia: A Phase IV Multicenter Trial
Guy Chouinard, M.D., Alain Labelle, M.D., Linda Beauclair, M.D., Lili C. Kopala, M.D., Sunny Johnson, Kulbir I. Singh, M.D.

NR377 Long-Term Safety of Risperidone
Martin B. Brecher, M.D.

NR378 The Effects of Clozapine on Aggression: A Randomized-Controlled Study
Eva W.C. Chow, M.D., Himansu Desai, B.Sc., Alison S. Bury, M.A., Rochelle Roy, R.N., Anne S. Bassett, M.D., Evan J. Collins, M.D.

NR379 Depot Versus Oral Neuroleptic Usage in New York State
Leslie L. Citrome, M.D., Jerome Levine, M.D., Baerbel Allingham, M.S.

NR380 Tardive Dyskinesia, Clozapine and Treatment Response
Gregory W. Dalack, M.D., Lisa M. Becks, B.A., Gina Baslock, B.A., James H. Meador-Woodruff, M.D.

NR381 Repeated ECT in Major Depression: Acute Effects on CBF
Michael H. Wiegand, M.D., David L. Duncan, M.D., Abbas Alavi, M.D., Mark Stecuer, M.D., William A. Ball, M.D., Laszlo Gyulai, M.D.

NR382 Meta-Analysis of Treatment Outcome with Risperidone Versus Conventional Neuroleptics
John M. Davis, M.D., Philip G. Janicak, M.D.

NR383 Effects of Conventional and Atypical Antipsychotic Agents on Cognitive Function in Schizophrenia
Bernd Gallhofer, M.D.

NR384 Risperidone As an Adjunct Mood Stabilizer for Bipolar Disorder
S. Nassir Ghaemi, M.D., Gary S. Sachs, M.D.

NR385 Bioequivalence of Oral Solution and Tablets of Risperidone in Normal Male Subjects
Rolando Gutierrez-Esteinou, M.D.

NR386 Clozapine and Quality of Life in Schizophrenia
Marianne S. Goodman, M.D., James W. Hull, Ph.D., Kenneth G. Terkelsen, M.D., Thomas E. Smith, M.D., John F. Clarkin, Ph.D., Donna T. Anthony, M.D.

NR387 Risperidone in Geriatric Patients with Chronic Psychoses and Concurrent Medical Illnesses
Usha P. Joshi, M.D., Praful M. Joshi, M.D.

NR388 Use of ECT in California, Revisited: 1984-1990
Barry A. Kramer, M.D.

NR389 Plasma Levels of Sertraline and the Clinical Response in Geriatric Depression
Vinod Kumar, M.D., Vivian Garcia, B.A., David Loewenstein, Ph.D., Nita Kumar, M.D.

NR390 Efficacy of Clinical Management Versus Drug Treatment of Depression in General Practice
Ulrik F.R. Malt, M.D., Ole H. Robak, M.D., Olaf Bakke, M.D., Hans-Peter Madsbu, M.D., Mitchell Loeb, M.Sc., Trond Smedsrud, M.Sc.

NR391 Risperidone in the Treatment of Tourette's Syndrome
Michael R. Martinez, M.D., Paul J. Perry, Ph.D., Gary R. Gaffney, M.D., Samuel Kuperman, M.D.

NR392 Risperidone Treatment in an Academic State Hospital Setting: A Retrospective Study of Outcome
Arnaldo E. Negron, M.D., Eduardo A. Liederman, M.D., Mohan Parkadavil, M.D., Angel Cienfuegos, M.D., Daniel C. Javitt, M.D.

NR393 Is Nefazodone an Anticoagulant?
Meena Narayan, M.D., George M. Anderson, Ph.D., J. Craig Nelson, M.D.

NR394 Optimal Minimum Doses of Trifluoperazine in Acute Schizophrenia
Hector A. Ortega-Soto, M.D., Elizabeth Brunner, M.D., Rogelio Apiquian, M.D., Pilar de la Torre, B.A., Rosa E. Uiloa, M.D., Arturo Mendizabal, M.D.

NR395 Venlafaxine and Blood Pressure Change Spanning the Ages
Ben Zimmer, M.D., Ravi Kant, M.D., Debbie Zeiler, R.N., Mary Brilmyer, R.N.

NR396 Lithium Carbonate Therapy Is Not a Risk Factor for Osteoporosis
Elie Lepkifker, M.D., Theodor B. Rais, M.D., Iris Vered, M.D., Ohad Cohen, M.D., Rueben Ziv, M.D.

NR397 Electrical Dose and Seizure Threshold in Bifrontal, Bitemporal and Right Unilateral ECT: Relations to Clinical Outcome and Cognitive Effects
Nicholas J. Delva, M.D., James S. Lawson, Ph.D., Martin Rodenburg, M.D., Rita M. Kesteven, Ph.D., James Inglis, Ph.D., Dennis W. Lywood, B.Sc., John J. Waldron, M.B.

NR398 Atypical Neuroleptics Are Less Likely to Produce Hyponatremia
Deborah A. Widmer, M.A., Cecile E. Sison, Ph.D., Robert G. Stern, M.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D., Benedict J. Connolly, M.A.

NR399 Risperidone for Disturbed Behavior and Tardive Dyskinesia in Developmentally Disabled Adults
Barkat U. Khan, M.D., William M. Glazer, M.D.

NR400 In Vivo Comparison of CYP2D6 Inhibition Among SSRIs: Implications for Drug Therapy
Yui Wing F. Lam, Pharm.D., Larry Ereshefsky, Pharm D., Cara Riesenman, Pharm D., Joseph A. Simpson, M.D.

NR401 Can Panic Disorder Patients Treated with More Than Four Milligrams Per Day of Alprazolam Reduce Their Dose?
Mark H.N. Corrigan, M.D., Jeffrey M. Jonas, M.D., Therese Kitt, M.D., Susanna Goldstein, M.D., Ann S. Swiontek, Stephen M. Stahl, M.D.

NR402 Mood Measures in Normals Treated with Fluoxetine
Robert B. Pohl, M.D., Richard Balon, M.D., John Deluca, Ph.D., Jennifer Standish, B.A.

NR403 Melatonin for the Treatment of Sleep Disorders in Major Depression
Ornah T. Dolberg, M.D., Shmuel Hirschmann, M.D., Joseph Zohar, M.D., Leon J. Grunhaus, M.D.

NR404 Risk Factors Distinguishing Fatal and Non-Fatal Suicide Outcome
M. Beatriz Currier, M.D., Victoria Bustamante, M.S., Ana I. Fins, Ph.D., Sherrie L. Baehr, Psy.D.

NR405 Self-Mutilation: Serotonergic and Clinical Findings
Barbara Stanley, Ph.D., Ronald M. Winchel, M.D., Michael Stanley, Ph.D., J. John Mann, M.D.

NR406 Combined Behavioral and Medicinal Treatment of Insomnia
Milton Kramer, M.D., Boris Dashevsky, Ph.D.

NR407 Protective Factors Against Attempted Suicide
Kevin M. Malone, M.D., Gretchen L. Haas, Ph.D., Shuhua Li, Ph.D., J. John Mann, M.D.

NR408 Predictors of Suicidal Behavior and Lethality in BPD
Beth S. Brodsky, Ph.D., Kevin M. Malone, M.D., Steven P. Ellis, Ph.D., Rebecca A. Dulit, M.D., J. John Mann, M.D.

NR409 Rise in Major Depression and Youth Suicide Rates
Paul A. Ketti, M.D.

NR410 Comparison of Recent and Distant Suicide Attempters on Psychopathology and Social Support
Noelle Y.C. Yuen, M.D., Naleen N. Andrade, M.D., Linda B. Nahulu, M.D., George K. Makini, Jr., M.D., George P. Danko, Ph.D.

NR411 Death Without Warning: First Attempt Completed Suicides Versus Suicides with Prior Attempts
Sara E. Oppenheim, M.A., Kevin M. Malone, M.D., Thomas M. Kelly, A.C.S.W., J. John Mann, M.D.

NR412 Relationships Between Alexithymia and Psychological Traits Associated with Eating Disorders
Graeme J. Taylor, M.D., James D. Parker, Ph.D., Michael R. Bagby, Ph.D., Michael P. Bourke, M.B.

NR413 Fenfluramine and Phentermine in Obese Binge Eaters
Dean D. Krahn, M.D., Roy Blank, M.D., Richard Atkinson, M.D., Laura Olson, Ph.D.

NR414 Predictors of Bulimic Behaviors in College Women
Dean D. Krahn, M.D., Candace L. Kurth, Ph.D., Michael J. Bohn, M.D., Laura Olson, Ph.D., Edith Gomberg, Ph.D., Adam Drewnowski, Ph.D.

NR415 Eating Disorder Symptomatology in Major Depressive Disorder
Maurizio Fava, M.D., Melissa Abraham, B.A., Nancy E. McLean, B.A., Joel A. Pava, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D.

NR416 A Pilot Study of Paroxetine in the Treatment of Patients with Bulimia Nervosa
Teresa A. Pigott, M.D., Brent A. Sunderland, M.D., Lawrence Horn, M.D., Suzanne Bernstein, B.S., Billinda Dubbert, M.S.N., Virginia Smolka

NR417 The Effects of a High-Carbohydrate Diet on Serotonin Turnover and Mood in Obese Women
Dana L. Hirsch, B.A., H. Keith H. Brodie, M.D., Richard S. Surwit, Ph.D.

NR418 The Relationship Between Dietary Restraint, Exercise Dependence and Training Patterns
Julian P. Morrow, Ph.D., Jerry L. Johnson, Ph.D.

NR419 Eating Disorders in African-Americans
Xenia Johnson, M.D., William H. Carson, Jr., M.D.

NR420 Eating Behavior, Serotonin and Tryptophan Depletion
Barbara E. Wolfe, Ph.D., Eran D. Metzger, M.D., David C. Jimerson, M.D.

NEW RESEARCH

Wednesday, May 8, 1996, 9:00 a.m.-10:30 a.m.

New Research 9 – Oral/Slide Session – Room E6, Level 1, Javits Center

SCHIZOPHRENIA

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

NR421 Informed Consent in Schizophrenia Research — 9:00 a.m.
Debra A. Pinals, M.D., Anil K. Malhotra, M.D., Alan F. Breier, M.D., David Pickar, M.D.

NR422 Quetiapine, an Atypical Antipsychotic: Results From a Multiple Fixed Dose, Placebo-Controlled Study — 9:15 a.m.
Lisa A. Arvanitis, M.D., Barbara G. Miller, M.S.

NR423 Regional Shape and PET Analysis of Corpus Callosum in Patients with Schizophrenia and Schizotypal Personality Disorder — 9:30 a.m.
Jack E. Downhill, Jr., M.D., Tse-Chung Wei, Ph.D., M. Mehmet Haznadar, M.D., Jacqueline Spiegel-Cohen, M.S., Larry J. Siever, M.D., Monte S. Buchsbaum, M.D.

NR424 Anticipation in a Large Representative Sample of Schizophrenia — 9:45 a.m.
Anne S. Bassett, M.D., Janice Husted, Ph.D., William G. Honer, M.D., Susana B. Correia, Alison S. Bury, M.A., Joseph Berg, M.D.

NR425 Quality of Life Outcomes for Olanzapine and Haloperidol Treatment for Schizophrenia and Related Psychotic Disorders — 10:00 a.m.
Dennis Revicki, Ph.D., Laura A. Genduso, Rph, Susan L. Hamilton, M.S., Christophe Martin, M.D., Joe Rebiando, B.S., Pierre V. Tran, M.D.

NR426 Late-Life Schizophrenia in the United States and the United Kingdom — 10:15 a.m.
Philip D. Harvey, Ph.D., Noam Trieman, M.D., Michael Davidson, M.D., Julian Leff, M.D., Janel Lombardi, M.D., Peter Powchik, M.D.

NEW RESEARCH

Wednesday, May 8, 1996, 9:00 a.m.-10:30 a.m.

New Research 10 – Oral/Slide Session – Room E17, Level 1, Javits Center

ORGANIC MENTAL DISORDERS

Chp.: Michael A. Fauman, M.D.

NR427	Platelet Aggregation is Increased in Alzheimer's Disease Steven Sevush, M.D., Wenche Jy, Ph.D., Richard S. Mallia, B.A., Lawrence L. Horstman, Luciano Kolodny, M.D., Yeon S. Ahn, M.D.	9:00 a.m.
NR428	Depressed Mood and the Incidence of Alzheimer's Disease Davangere P. Devanand, M.D., Mary Sano, Ph.D., Ming-Xin Tang, Ph.D., Yaakov Stern, Ph.D., Richard Mayeux, M.D.	9:15 a.m.
NR429	The Cost of Delirium in the Surgical Patient Kathleen N. Franco, M.D., Joseph A. Locala, M.D., David Litaker, M.D., David L. Bronson, M.D., Ziad Tannous, M.D.	9:30 a.m.
NR430	Glucose Metabolic Rate in the Frontal and Temporal Lobes in Alzheimer's Disease Lina S. Shihabuddin, M.D., Leonart Abel, Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., N. Pandit, M.D., Deborah B. Marin, M.D.	9:45 a.m.
NR431	Apolipoprotein E Epsilon 4 Allele Vascular Disease and Dementia Deborah B. Marin, M.D., Richard C. Mohs, Ph.D., Lawrence Altstell, M.D., David M. Greenberg, M.D., Melinda S. Lantz, M.D., Kenneth L. Davis, M.D.	10:00 a.m.
NR432	Recognizing Risk for Postoperative Delirium Joseph A. Locala, M.D., Kathleen N. Franco, M.D., David Litaker, M.D., Ziad Tannous, M.D., David L. Bronson, M.D., Joy Frame, R.N.	10:15 a.m.

NEW RESEARCH

Wednesday, May 8, 1996, 12 noon-2:00 p.m.

New Research 11 – Poster Session – Galleria, Level 4, Javits Center

ORGANIC MENTAL DISORDERS; BIOLOGICAL, GERIATRIC, C/L AND EMERGENCY PSYCHIATRY; BRAIN IMAGING; NEUROBIOLOGY; NEUROPSYCHIATRY; AND GENETICS

Moderator: Mina K. Dulcan, M.D.

NR433 Impact of Interventions to Prevent Delirium
Martin G. Cole, M.D., Francois J. Primeau, M.D., Jane McCusker, M.D.

NR434 Environmental Strategies Are Instituted in Response to Behavioral Challenges in Patients with Delirium
David J. Meagher, M.D., Donal O'Hanlon, M.D., Edmond O'Mahony, M.D., Patricia Casey, M.D.

NR435 Focal Anatomic Substrates in Late-Life Depression
Anand Kumar, M.D., David S. Miller, M.D., Patricia Cowell, Ph.D., Warren Bilker, Ph.D., Jin Zhisong, M.S., Laura L. Swan, B.A.

NR436 The Role of Medications in the Developmental of Postoperative Delirium
Joseph A. Locala, M.D., David Litaker, M.D., Kathleen N. Franco, M.D., David L. Bronson, M.D.

NR437 Evaluation of a Risk Assessment System for Postoperative Delirium
Kathleen N. Franco, M.D., Joseph A. Locala, M.D., David Litaker, M.D., Joy Frame, R.N., David L. Bronson, M.D., Ziad Tannous, M.D.

NR438 Postpartum Psychiatric Morbidity
Rafia O.S. Ghubash, Ph.D., Prof. M.T. Abou-Saleh, Ph.D.

NR439 Duration of Delirium: A Prospective Study
Peter J. Manos, M.D., Rae Wu, M.D.

NR440 Valproate Treatment of Behavioral Disturbances Associated with Dementia
Meena Narayan, M.D., J. Craig Nelson, M.D.

NR441 Psychiatric Morbidity in Epilepsy: The Role of Anticonvulsants
Bettina Schmitz, M.D., Mary J. Robertson, M.A., Michael R. Trimble, M.D.

NR442 Neurologic Status in Combat and Sexual Abuse PTSD
Tamara V. Gurvits, M.D., Daphne Simeon, M.D., Mark W. Gilbertson, Ph.D., Alexandra C. Tarhan, Ph.D., Natasha B. Lasko, Ph.D., Roger K. Pitman, M.D.

NR443 SPEM Abnormalities in Gilles de la Tourette's Syndrome and OCD
Stefano Pallanti, M.D., Leonardo Quercioli, M.D., Gaetano Zaccara, M.D., Graziamo Armetoli, Ph.D.

NR444 Carbamazepine Induces Escape From Dexamethasone Suppression Across Mood Disorder Subtypes and Panic Disorder
Gabriela Cora-Locatelli, M.D., Mark A. Frye, M.D., Timothy A. Kimbrell, M.D., Kirk D. Denicoff, M.D., Terence A. Ketter, M.D., Robert M. Post, M.D.

NR445 Nerve Growth Factor Plasma Levels in Schizophrenic Patients: A Preliminary Study
Giuseppe Bersani, Angela Iannitelli, Paolo Maselli, Francesco Angelucci, Enrico Alleva, Luigi Aloe

NR446 Role of Serotonin Receptors in Alcoholism
Marc M. Ansseau, M.D., William Pitchot, M.D., Valerie Barbier, M.D.

NR447 Low Serum Cholesterol, Suicide and Serotonin
Marc M. Ansseau, M.D., Beatrice Hild, M.D., William Pitchot, M.D.

NR448 CSF Monoamine Metabolites and the Weather in Humans
Timothy D. Brewerton, M.D., Michael J. Norden, M.D., Richard J. Lewine, Ph.D., S. Craig Risch, M.D.

NR449 Neuroendocrine Profiles in Psychiatric Disorders: Markers of Diagnosis or of Syndromes?
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.

NR450 Clinical and Pathophysiologic Implications of Structural Brain Abnormalities in Schizophrenia
Todd Lafargue, M.D., Luigi Arena, M.D., Michael P. Sanfilipo, B.S., Eric D. Peselow, M.D., Henry Rusinek, Ph.D., Adam Wolkin, M.D.

NR451 Menstrual Cycle Changes in Laterality and Emotion
Alexandra A. Bowers, B.A., Margaret Altemus, M.D., Bruce E. Wexler, M.D.

NR452 Physostigmine and Cognition in Personality Disorder
Ann M. Callahan, M.D., Antonia S. New, M.D., Andrea Bergman, Ph.D., Vivian Mitropoulou, M.A., Barbara A. Cornblatt, Ph.D., Larry J. Siever, M.D.

NR453 Blockade of NMDA Receptor Modulates C-FOS Expression in Cortex and Limbic Regions
Andrea De Bartolomeis, M.D., Luigi Aloj, M.D., Giovanni Muscettola, M.D., David Pickar, M.D., Alan F. Breier, M.D.

NR454 Quantitative EEG Topographic Maps: Testing Individual Patient's Maps Against a Data Base
James S. Lawson, Ph.D., Susan J. Adams, M.D., Donald W. Brunet, M.D., Magarita Criollo, M.D., Howard Galin, M.A., Duncan J. MacCrimmon, M.D.

NR455 mRNA Expression of Serotonin Receptors in Lymphocytes
Donatella Marazziti, M.D., Irma Nardi, M.D., Massimo Pasqualetti, M.D., Lionella Palego, Ph.D., Alessandra Rossi, M.D.

NR456 Fenfluramine Versus Clomipramine Challenge
Linda M. Nicholas, M.D., David F. Naftolowitz, M.D., Amy D. Heine, M.S., R. David Ekstrom, M.S., Manuel E. Trancer, M.D., Robert N. Golden, M.D.

NR457 Diurnal Rhythm of CSF Neurohormones in Major Depression: Comparison with Healthy Volunteers and Effects of ECT
Mitchel A. Kling, M.D., Thomas D. Geracioti, Jr., M.D., Michael D. De Bellis, M.D., Samuel J. Listwak, B.S., Debbie Hu, M.S.W., E.H. Oldfield, M.D., Philip W. Gold, M.D.

NR458 Discrepancy in Imipramine and Paroxetine Bindings
Mihaly Arato, M.D., George Bagdy, Ph.D.,Deirde E.M. Cooke, M.D., Ilona Ozoroczy, M.B.

NR459 The Influence of ECT on Olfactory Memory
Pinkhas Sirota, M.D., Tanya Mosheva, M.D.

NR460 Proton MRSI in Schizophrenia
Raymond F. Deicken, M.D., Zhou Ling, M.D., Faith Corwin, M.A., Sophia Vinogradov, M.D., George Fein, Ph.D., Michael W. Weiner, M.D.

NR461 Drug Effect on Regional Proton MRS in Schizophrenia
Carolyn Heimberg, M.D., Richard A. Komoroski, Ph.D., William B. Lawson, M.D., David W. Cardwell, M.D., Craig N. Karson, M.D.

NR462 Anterior Paralimbic Hypometabolism in Patients with Unipolar Depression in Remission
Timothy A. Kimbrell, M.D., Terence A. Ketter, M.D., Mark S. George, M.D., Robyn M. Stein, M.D., Aimee Danielson, B.A., Robert M. Post, M.D.

NR463 Increased Basal Ganglia, Thalamic and Anterior Cingulate Glucose Metabolism in Women Compared to Men
Timothy A. Kimbrell, M.D., Terence A. Ketter, M.D., Mark Willis, Mark S. George, M.D., Paul J. Andreason, M.D., Robert M. Post, M.D.

NR464 Characteristics of White Matter in Late-Life Depression: Brain Volumes and Clinical Characteristics
Hillel T. Grossman, M.D., Eric D. Caine, M.D., Leena Ketonen, M.D., Christophe Cox, Ph.D., Heather Booth, M.S., Jeffrey M. Lyness, M.D.

NR465 Effects of Aging and Gender on Regional Brain Glucose Metabolism in Healthy Individuals
Erin A. Hazlett, Ph.D., Monte S. Buchsbaum, M.D., Richard C. Mohs, Ph.D., Lina S. Shihabuddin, M.D., Tina Ciaravolo, B.A., Jacqueline Spiegel-Cohen, M.S.

NR466 Thalamic Metabolic Rate in Schizophrenia
Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., M. Mehmet Haznedar, M.D., Tse-Chung Wei, Ph.D., Jacqueline Spiegel-Cohen, M.S.

NR467 Patterns of Connectivity Assessed by Metabolic Rate During a Memory Task in Humans: A PET Study
M. Mehmet Haznedar, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Melissa Biren, B.S., Tse-Chung Wei, Ph.D., Philip D. Harvey, Ph.D.

NR468 Anterior Cingulate Gyrus Volume in Autistic Disorder
M. Mehmet Haznedar, M.D., Monte S. Buchsbaum, M.D., Andrea Solimando, B.S., Michael Metzger, B.S., Tina Ciaravolo, B.A., Eric Hollander, M.D.

NR469 Reduced Basal Ganglia Volumes in Trichotillomania Measured Via Morphometric MRI
Richard L. O'Sullivan, M.D., Scott L. Rauch, M.D., Hans C. Breiter, M.D., Igor Grachev, M.D., Lee Baer, Ph.D., David Kennedy, Ph.D.

NR470 Visual Functional Abnormalities Occur in Striate and Peristriate Regions in Alzheimer's Disease Despite Relatives Pathological Sparing
Marc J. Mentis, M.D., Gene E. Alexander, Ph.D., Terri Strassburger, M.D., Pietro Pietrini, M.D., Jack S. Krasuski, M.D., Mark Schapiro, M.D.

NR471 Abnormal Brain Perfusion During Opioid Dependence: SPECT Imaging with TC-99M-HMPAO
Lukas Pezawas, M.D., Gabriele Fischer, M.D., Karin Diamant, M.D., Corinna Schneider, M.D., S. Schindler, M.D., Siegfried Kasper, M.D.

NR472 SPECT Correlates of Depressive Symptoms in Patients with Dementia of Alzheimer's Disease
Igor I. Galynker, M.D., Silviu M. Burcescu, M.D., J. Paul Teusink, M.D., Fukiat Ongseng, M.D., Howard Feinstone, M.D., Dragos Serseni, M.D., Eamon Dutta, M.D., Naomi Vilkas, B.A., Richard N. Rosenthal, M.D.

NR473 Structural Brain Changes in Chronic Cocaine and Heroin Abuse
Thomas E. Schlaepfer, M.D., Eric Lancaster, B.A., Patrick E. Barta, M.D., Godfrey D. Pearlson, M.D.

NR474 The Effects of ECT on Cerebral Glucose Metabolism
Mark E. Schmidt, M.D., Michael Henry, M.D., John A. Matochik, Ph.D., Bradley S. Folley, B.S., William Z. Potter, M.D.

NR475 EEG and Provoked Potential Brain Mapping in ADHD
Karl G. Sieg, M.D., Gary G. Gaffney, M.D., Kevin D. Schockley, M.S., Teri O'Donnell

NR476 MRI and SPECT in Very Early Alzheimer's Disease
Godfrey D. Pearlson, M.D., Thomas E. Schlaepfer, M.D., Patrick E. Barta, M.D.

NR477 Constant Observation in a General Medical Hospital
Michael Blumenfield, M.D., Jane Milazzo, R.N., Barbara Orlowski, Ph.D.

NR478 Jumping and Other Suicides in a General Hospital
Richard T. White, M.B., Robert J. Gribble, M.B., Melissa J. Corr, M.B., Matthew M. Large, M.B.

NR479 Psychiatric Illness in Medical Inpatients Increases Medical Re-Hospitalizations and Outpatient Visits at Four-Year Follow-Up
Stephen M. Saravay, M.D., Eliot Goldman, Ph.D., Susan Hirsch, A.C.S.W., Jonathan Schor,

NR480 WITHDRAWN

NR481 Health Complaints Attributed to Dental Amalgam: A Study of 99 Patients and 272 Comparison Subjects
Ulrik F.R. Malt, M.D., Per Nerdrum, Ph.D., Bjorn Oppedal, D.D.S., Roger Gunderson, M.D., Martin Holte, M.D., Jostein Lone, D.D.S.

NR482 Postpartum Depressive Symptoms Are Associated with Decreased Prevalence of Breastfeeding
Veronika Solt, M.D., Carmello Colon, M.S.W., Andrea K. Gondocs, M.D., Alec Roy, M.D.

NR483 Incidence of Delirium in Patients Referred by Primary Care Physicians for Evaluation of Depression
Michael N. Valan, M.D., Donald M. Hilty, M.D.

NR484 Relationship Between Dental Status and Dental Anxiety
Bogdan P. Radanov, M.D.

NR485 Alzheimer's Disease and Its Lewy Body Variant
Myron F. Weiner, M.D., Richard C. Risser, M.S., C. Munro Cullum, Ph.D., Charles White III, M.D., Roger N. Rosenberg, M.D., Sam Speciale, Ph.D.

NR486 Testosterone, Mood and Psychotropic Medication
Catherine L. Woodman, M.D., W. Rockwell Williams, P.A.

NR487 Delirium Risk Factors in the Elderly: A Meta-Analysis
Michel Elie, M.D., Martin G. Cole, M.D., Francois J. Primeau, M.D., Francois Bellavance, Ph.D.

NR488 Acute Administration of the Nicotinic Agonist ABT-418 Improve Learning in Alzheimer's Disease
Paul A. Newhouse, M.D., Alexandra Potter, B.S., June Corwin, Ph.D., Robert H. Lenox, M.D.

NR489 Estrogen Effects on Cognitive Impairment in Women
M. Martin Costa, Ph.D., Victor I. Reus, M.D., Owen M. Wolkowitz, M.D., Francesca Manfredi, B.A., Morton Lieberman, Ph.D.

NR490 Control-Related Intervention in the Treatment of Nursing Home Residents with Mild to Moderate Depression
Jules Rosen, Joan C. Rogers, Ph.D., Robert S. Marin, M.D., Avner Shahar, M.D.,Benoit H. Mulsant, M.D., Charles F. Reynolds III, M.D.

NR491 Personality and Disability in Geriatric Depression
Robert C. Abrams, M.D., Lisa A. Spielman, Ph.D., George S. Alexopoulos, M.D., Ellen J. Klausner, Ph.D.

NR492 Depression and PET Imaging in Alzheimer's Disease
David L. Sultzer, M.D., Jeffrey L. Cummings, M.D., Michael E. Mahler, M.D., M. Andrew Berisford, Ph.D., Mark A. Mandelkern, M.D., Charles H. Hinkin, Ph.D.

NR493 Risperidone in the Treatment of Elderly Psychiatric Patients
Stephen M. Aronson, M.D., Venkataramana S. Lingam, M.D., K.A. Hasanat, M.D.

NR494 Risk of Depression in Caregivers of Alzheimer's Disease Patients
Marc Cantillon, M.D., Dylan G. Harwood, M.A., William Barker, M.S., Marina Bravo, M.S.W., Deborah A. Hurwitz, M.S.W., Ranjan Duara, M.D.

NR495 The Clinical Presentation of Vascular Depression
George S. Alexopoulos, M.D., Barnett S. Meyers, M.D., Robert C. Young, M.D., Tatsuyuki Kakuma, Ph.D., Mary E. Charlson, M.D., David A. Silbersweig, M.D.

NR496 Life Review Group Therapy in Degenerative Dementia
Rhoda R. Frankel, M.A., Karen S. Carlisle, M.S.W., Rajiv P. Sharma, M.D., Lawrence W. Lazarus, M.D.

NR497 Efficacy of Clozapine Versus Chlorpromazine in Geriatric Schizophrenia
Evelyn M. Howanitz, M.D., Moris Pardo, M.D., Peter Litwin, M.D., Robert G. Stern, M.D., Kathleen M. Wainwright, R.N., Miklos F. Losonczy, M.D.

NR498 Telemedicine Evaluation of Geriatric Depression
Beverly N. Jones, M.D., Lyn Exum, M.A., Mary McFarlane, Ph.D.

NR499 Late-Life Depression, Vascular Diseases and Brainstem-Evoked Response Abnormalities
Balkrishna Kalayam, M.D., George S. Alexopoulos, M.D., Robert C. Young, M.D., David A. Silbersweig, M.D., Frank E. Musiek, Ph.D.

NR500 Geriatric Patients with Manic Only Episodes: Characterization of Unipolar Mania
Isabelle Paquette, M.D., Jean-Francois Ricard, M.D., Maryse Charron, M.D.,Carole Murphy, M.D., Rosita Punti, M.D., Claude Richer, M.D., Arthur Amyot, M.D., Michelle Rochon, M.D., Jacques Garant, M.D., Hugues Cormier, M.D.,Marie-Claire Baril, M.D., Luiza Dumitrescu, M.D.

NR501 Screening for Depression in Primary Care Elderly
Tamson K. Noel, M.S., Jeffrey M. Lyness, M.D., Christophe Cox, Ph.D., Deborah A. King, Ph.D., Yeates Conwell, M.D., Eric D. Caine, M.D.

NR502 Perceived Adequacy of Psychiatric Consultation and Expertise in Nursing Homes
William E. Reichman, M.D., Andrew C. Coyne, Ph.D., Soo Borson, M.D., Barry W. Rovner, M.D., Kenneth M. Sakauye, M.D., Paul R. Katz, M.D.

NR503 Putamen Volume and Age at Onset in Geriatric Mania
Robert C. Young, M.D., J. Phillipe Bocksberger, M.D., George S. Alexopoulos, M.D., Mony J. De Leon, Ed.D., Balu Kalayam, M.D., Charles Elkin, M.D.

NR504 Characterization of Geriatric Mania According to Age of Onset
Rosita Punti, M.D., Maryse Charron, M.D., Isabelle Paquette, M.D., Carole Murphy, M.D., Claude Richer, M.D., Jacques Garant, M.D., Arthur Amyot, M.D., Michelle Rochon, M.D., Marie-Claire Baril, M.D., Luiza Dumitrescu, M.D., Hugues Cormier, M.D.

NR505 Aging Effects on Motor and Cognitive Skill Learning
Charles Peretti, M.D., Jean M. Danion, M.D.

NR506 The Need to Change Laboratory Lithium Reference Ranges to Avoid Geriatric Iatrogenesis
Hilary T. Hanchuk, M.D., Galina Staroselsky, M.D.

NR507 The Comprehensive Observational Psychiatric Screening Assessment in Dementia: Nursing Home Application of a New Behavioral Scale
Hilary T. Hanchuk, M.D., Jessica M. Berlet, M.D., Robert Hamer, Ph.D., David Epstein, M.S., Anmolsingh Roopa

NR508 Reduced Frequency of Self-Reported Anticholinergic Side Effects to Nortriptyline in the Elderly
Nunzio Pomara, M.D., Hla Tun, M.D., Dennis Deptula, Ph.D., Rajkumar R. Singh, M.D., Feliciano B. Leviste II, M.D., Thomas B. Cooper, M.A.

NR509 MRI Brain Ventricular Volumes in Geriatric Depression
Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., Jian Hu, M.D., Manzar Ashtari, Ph.D., Peter M. Aupperle, M.D., Houwei Wu, M.D., Bernhard Bogerts, M.D., Simcha Pollack, Ph.D.

NR510 Plastic Cortical Changes As Indicators of Pain Memories in Phantom Limb Pain Patients
Wolfgang Larbig, M.D., Pedro Montoya, Ph.D., Herta Flor, Ph.D., Neils Birbaumer, Ph.D.

NR511 Comparison of the Human Interstitial Nuclei of the Anterior Hypothalamus with the Sexually Dimorphic Nucleus of the Preoptic Area of the Rat
William M. Byne, M.D., E.M. Kemether, M.D., Inna Markhasima, M.D.

NR512 Writes with the Right Hand, but Throws with the Left: An Indicator of Pathology in Males?
P.S.B. Sarma, M.D.

NR513 Psychiatric Disorders in Patients with Intracranial Neoplasm
Thania V. Quesada, M.D., M. Beatriz Currier, M.D., Florinda S. Calderon, M.D., Vijaya L. Uppu, M.D., Ana I. Fins, Ph.D.

NR514 Comparison of Patients with Suicidal Plans During the Acute or Chronic Post-Stroke Period
Yasuhiro Kishi, M.D., Robert G. Robinson, M.D., J. Todd Kosier, M.A.

NR515 Postconcussional Disorder: DSM-IV Criteria
Lawrence A. Labbate, M.D., Deborah L. Warden, M.D., Andres M. Salazar, M.D., Anthony D. Pridgen, B.S

NR516 Selective Attention, Illness Duration and Symptoms
Janet L. Tekell, M.D., J. Arturo Silva, M.D., Charles L. Bowden, M.D.

NR517 Comparative Effects of Nefazodone and Fluoxetine on Sleep in Outpatients with Major Depressive Disorders
A. John Rush, M.D., Christian Gillin, M.D., Roseanne Armitage, Ph.D., H. Moldofsky, M.D.

NR518 Apathy Syndrome After Head Injury and Treatment Outcomes
Ravi Kant, M.D.

NR519 Clinical Features of Recurrent Catatonia
Andrew J. Francis, Jr., M.D., Krishna Divadeenam, B.A., George Bush, M.D., Georgios Petrides, M.D.

NR520 Standardized Assessment of Psychiatric Symptom Severity Enhances the Prediction of Length of Stay on an Intensive Rehabilitation Unit
Cori Salvit, B.S., Christian Miner, Ph.D., Richard N. Rosenthal, M.D., Igor I. Galynker, M.D.

NR521 Maintenance ECT for Intractable Parkinson's Disease
Steven P. Wengel, M.D., William J. Burke, M.D., William H. Roccaforte, M.D., Ronald Pfeiffer, M.D., Stephen R. Paige, Ph.D.

NR522 Differential Retention of Emotional Material in Patients with Schizophrenia
Kirsten Fleming, Ph.D., Jeff Moenter, B.A., Rimal B. Bera, M.D., Dan Carreon, M.D., Steven G. Potkin, M.D.

NR523 Dopamine Receptor Gene Polymorphism in OCD
Humberto Nicolini, Beatriz Camarena, B.Sc., Francisco Paez, M.D., Karen Herrera, M.D., Juan Ramon De La Fuente, M.D.

NR524 Dopaminergic Genes and Personality Disorders
Kenneth Blum, Ph.D., Nancy L. Schnautz, M.D., Eric R. Braverman, M.D., Daniel Matthews, M.D., L. Fischer, B. Williamson, A. Eisenberg, M. Sherman, J. Seals, John G. Cull, Ph.D., W. Walsh, D.E. Comings, R. Wood, T.H. Chen

NR525 Brain Electrophysiological Abnormalities As a Function of the Dopamine D2 Receptor A1 Allele and Comorbid Substance Use Disorder
Kenneth Blum, Ph.D., Eric R. Braverman, M.D., John G. Cull, Ph.D., B. Brenner, J. Gill, Mark Zedar

NR526 Complex Segregation Analysis of Schizophrenia
Alda P. Ruiz, Mauricio Arcos, Rafael Blanco, Jaime Santander, M.D., Adriana San Martin

NR527 A Family Study of Dyslexia
Gail A. Edelsohn, M.D., Wade H. Berrettini, M.D., Eric Richardson, Rachel Lashever, B.A., Jodi Langfeld, B.A.

NR528 The Nature of Traumatic Memories Following Adult and Childhood Trauma
Bessel A. van der Kolk, M.D., Jennifer Burbridge, M.A., Joji Suzuki, B.A., Rita E. Fisler, Ed.M.

NR529 Depression As a Predictor of Return-to-Drinking Using Categorical Diagnosis and Symptom Scores
Shelly F. Greenfield, M.D., Roger D. Weiss, M.D., Lisa Bello, B.A., Jacqueline Michael, M.S.W., John Kelly, B.A., Larry Muenz, Ph.D.

NEW RESEARCH

Wednesday, May 8, 1996, 3:00 p.m.-5:00 p.m.

New Research 12 – Poster Session – Galleria, Level 4, Javits Center

SCHIZOPHRENIA; ADMINISTRATIVE AND CROSS-CULTURAL/MINORITY PSYCHIATRY; COMMUNITY PSYCHIATRY/PREVENTION; AND DIAGNOSTIC ISSUES

Moderator: Deborah A. Zarin, M.D.

NR530 P50 and Stimulus Change in Schizophrenia
Nashaat N. Boutros, M.D., Patricia Tueting, Ph.D.

NR531 Treatment Resistance in First-Episode Psychosis
Jane I. Edwards, M.A., Dana Maude, M.A., Patrick D. McGorry, Ph.D.

NR532 Cognitive Correlates of Specific Types of Communication Disturbances in Schizophrenia
Nancy M. Docherty, Ph.D., Ralph E. Hoffman, M.D., Keith A. Hawkins, P.S.D., Jaak Rakfeldt, Ph.D., Donald M. Quinlan, M.D., William H. Sledge, M.D.

NR533 Prepulse Inhibition, Habituation and Communication Disturbances in Schizophrenia
Nancy M. Docherty, Ph.D., Anthony Hebert, B.A.

NR534 Race and Substance Abuse in Schizophrenia
William B. Lawson, M.D.

NR535 Sources of Diagnostic Uncertainty Among Chronically Psychotic Cocaine Abusers
Andrew L. Shaner, M.D., Jody M. Racenstein, M.A., Lisa J. Roberts, M.A., Thad A. Eckman, Ph.D., John W. Tsuang, M.D., Douglas E. Tucker, M.D.

NR536 Clozapine in Tardive Dyskinesia
George J. Jurjus, M.D., P. Eric Konicki, M.D., Anand P. Popli, M.D., Ken Y. Kwon, M.D., George E. Jaskiw, M.D.

NR537 Neurologic Soft Signs in Schizophrenia
Jeong-Ho Chae, M.D., In-Ho Paik, M.D., Kyu-Hang Lee, M.D., Chung Kyoon Lee, M.D.

NR538 Neuroleptic Dosing in Asian and Hispanic Outpatient Schizophrenic Patients
John M. Herrera, Ph.D., John J. Sramek, Pharm.D., Sigfried Ruiz, M.D., Peter Chu, M.D.

NR539 Neuroleptic Dosing in Hispanic and Asian Inpatient Schizophrenic Patients
John M. Herrera, Ph.D., John J. Sramek, Pharm.D., Jasmine Collazo, M.D., Raymond Tam, M.D.

NR540 Predictors of Treatment Response and Outcome in First Episode Schizophrenia
Amy R. Koreen, M.D., Jeffrey A. Lieberman, M.D., Jose Alvir, D.P.H.

NR541 Psychosocial Outcome of a First-Episode: Schizophrenia Cohort Followed Up to Five Years
Julia A. Becker, M.D., Amy R. Koreen, M.D., Miranda H. Chakos, M.D., Stephen H. Geisler, M.D., Jose Alvir, D.P.H., Margaret Woerner, Ph.D., Jeffrey A. Lieberman, M.D.

NR542 The Prevalence and Severity of Acute Extrapyramidal Side Effects in Patients Treated with Clozapine, Risperidone or Conventional Antipsychotics
Carl H. Miller, M.D., Daniel S.G. Umbricht, M.D., Jeffrey A. Lieberman, M.D., Fritz Mohr, M.D., Wolfgang Fleischhacker, M.D.

NR543 The Efficacy and Safety of Three Doses of Sertindole Versus Three Doses of Haloperidol in Schizophrenic Patients
Dan L. Zimbroff, M.D., Randall J. Mack, B.S., Joanne Zborowski, B.S.N., David D. Morris, Ph.D., Terri B. Sebree, B.S., Bruce A. Wallin, M.D.

NR544 Two Open-Label, Long-Term Safety Studies of Sertindole
David G. Daniel, M.D., Peter J. Schmitz, M.S., Jerry A. Staser, B.A., Kathryn L. Holgate, B.S.C., Terri B. Sebree, B.S., Matthew W. Cravets, M.A.

NR545 Brain Imaging to Determine the Effects of Sertindole in Schizophrenic Patients
Steven G. Potkin, M.D., Joanne Zborowski, B.S.N., Joseph C. Wu, M.D., Randall J. Mack, B.S., Terri B. Sebree, B.S., Bruce A. Wallin, M.D.

NR546 Radioreceptor Binding Profile of Olanzapine
Frank P. Bymaster, M.S., David T. Wong, Ph.D., David L. Nelson, Ph.D., David O. Calligaro, Ph.D.

NR547 The Course of Primary and Secondary Negative Symptoms in a Controlled Trial with Olanzapine
Gary D. Tollefson, M.D., Todd Sanger, Ph.D., Charles M. Beasley, Jr., M.D.

NR548 Childhood-Onset Schizophrenia: A Double-Blind Clozapine Trial
Sanjiv Kumra, M.D., Leslie K. Jacobsen, M.D., Judith L. Rapoport, M.D.

NR549 Gamma Aminobutyric Acid and the Pathophysiology of Schizophrenia: A Neurodevelopmental Perspective
Daniel P. Van Kammen, M.D., Frederick Petty, M.D., Mary E. Kelley, M.S., Gerald L. Kramer, B.A., Jeffrey K. Yao, Ph.D., John A. Gurklis, Jr., M.D.

NR550 Spontaneous Dyskinesia and Psychiatric Disorders
Wayne S. Fenton, M.D., Crystal R. Blyler, Ph.D., Richard Jed Wyatt, M.D., Thomas H. McGlashan, M.D.

NR551 MRI of Brain Iron in Tardive Dyskinesia
George Bartzokis, M.D., Keith Nuechterlein, M.D., Stephen R. Marder, M.D., Mace Beckson, M.D., Jim Mintz, Ph.D., Kenneth Dery, B.A.

NR552 Performance on the Stroop Color Naming Test and Signal Detection Accuracy During Auditory P300 Paradigms in Schizophrenic Patients
Edward L. Merrin, M.D., Monica Quesada, B.A., Thomas C. Floyd, M.A., Raymond F. Deicken, M.D., Sophia Vinogradov, M.D.

NR553 Concurrent Use of Clozapine and Sodium Valproate in the Maintenance Therapy of Chronic Schizo-Affective Patients: A Retrospective Analysis
Michael J. Reinstein, M.D., Kathleen D. Colombo, R.N., Lynn Jones, R.N., Sangarapillai C. Mohan, M.D.

NR554 The Relationship Between Neuropsychological Performance and Psychopathology in Schizophrenia
Myung A. Lee, M.D., Herbert Y. Meltzer, M.D.

NR555 Empirical Evaluation of Alternative Models of Schizophrenic Symptoms
Leonard White, Ph.D., Lewis A. Opler, M.D., Jean-Pierre Lindenmayer, M.D., Morris Bell, Ph.D., Professor Sonia Dollfus, Carol Cayton, M.D.

NR556 Longitudinal Course of the Offspring of Schizophrenics: Neurological and Cognitive Functioning in the First Seven Years
Stephen L. Buka, Sc.D., Jill Goldstein, Ph.D., Larry J. Seidman, Ph.D., William S. Kremen, Ph.D., Daniel Koren, M.A., Lisa R. Denny, B.A., Ming T. Tsuang, M.D.

NR557 Sex and Negative Symptom Dimension in Relatives of Schizophrenic Probands
Farooq Amin, M.D., Jeremy M. Silverman, Ph.D., Christopher Smith, M.A., Dianna Densmore, M.S., Larry J. Siever, M.D.

NR558 Is Diurnal Variation in Plasma HVA Due to Its Renal Excretion?
Farooq Amin, M.D., Adriana E. Stroe, M.D., Aqeel Hashmi, M.D., Dianna Densmore, M.S., Thomas Kahn, M.D., Peter Knott, Ph.D.

NR559 Quality of Life in Schizophrenic Patients Treated with Risperidone
Jose L. Ayuso-Gutierrez, M.D., Demetrio Barcia, M.D., Maria L. Herraiz, M.D., Antonio F. Fernandez, M.D.

NR560 Dose Reduction in Schizophrenia
Scott Badgett, M.A., Robert J. Hitzemann, Ph.D., Gail Burr, R.N., Kathy Piscani, R.N., Ede Frecska, M.D., Jack Hirschowitz, M.D.

NR561 Quality of Life in Schizophrenic Outpatients
Julio Bobes, M.D., Maria P. Gonzalez, Ph.D., Manuel Bousono-Garcia, M.D., Laura A. Munoz, Micaela G-Quiros, M.D., David Wallace

NR562 Length of Psychiatric Hospitalization in Veterans With or Without Service Connected Pensions
Benedict J. Connolly, M.A., Cecile E. Sison, Ph.D., Robert G. Stern, M.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D., Deborah A. Widmer, M.A.

NR563 Cigarette Smoking and Psychiatric Illness: A VA Outpatient Survey
Gregory W. Dalack, M.D., Lisa M. Becks, B.A., Elisabeth Abrams, Michael Castine, Cynthia Pomerleau, Ph.D., James H. Meador-Woodruff, M.D.

NR564 Nicotine Withdrawal and Psychiatric Symptoms in Smokers with Schizophrenia
Gregory W. Dalack, M.D., Lisa M. Becks, B.A., Elizabeth M. Hill, Ph.D., Ovide Pomerleau, Ph.D., James H. Meador-Woodruff, M.D.

NR565 Rapid Dose Escalating Safety, Tolerability and Pharmacokinetic Study of Sertindole
Jerome F. Costa, M.D., Neal R. Cutler, M.D., Randall J. Mack, B.S., John J. Sramek, Pharm.D., Terri B. Sebree, B.S., Janet M. O'Neil, B.S.

NR566 Reduction of Hospital Days in Sertindole-Treated Patients: One-Year Findings
Azmi A. Nabulsi, M.D., Randall J. Mack, B.S., Terri B. Sebree, B.S., Laura F. Copeland, M.S., Kathryn L. Holgate, B.S.C., Bruce A. Wallin, M.D.

NR567 Co-Occurrence of Vulnerability Markers in Relatives of Schizophrenic Patients
Rosemary Toomey, Ph.D., Stephen V. Faraone, Ph.D., Larry J. Seidman, Ph.D., William S. Kremen, Ph.D., Michael J. Lyons, Ph.D., Ming T. Tsuang, M.D.

NR568 Neuropsychological Measures of Prefrontal Dysfunction in Schizophrenia
Larry J. Seidman, Ph.D., Marlene Oscar-Berman, Ph.D., Anthony G. Kalinowski, Ph.D., Olu Ajilore, B.S., William S. Kremen, Ph.D., Stephen V. Faraone, Ph.D., Ming T. Tsuang, M.D.

NR569 Symptom Instability and Fluphenazine Decanoate
Anthony G. Kalinowski, Ph.D., Mohammed Y. Alam, M.D., Jayendra K. Patel, M.D., Joseph J. Schildkraut, M.D., Alan I. Green, M.D.

NR570 The Orienting Response and Instrumental Functioning in Schizophrenia and Mania
David B. Schnur, M.D., Jamie L. Weinstein, M.S.W., Scott P. Smith, M.A., Faisal Siddiqui, M.D., Phone M. Win, M.D., Adam Smith, Ph.D.

NR571 Associated Psychiatric Syndromes in Schizophrenia
Paul C. Bermanzohn, M.D., Samuel G. Siris, M.D., Linda Porto, M.S.N.

NR572 A Profile of Obsessive-Compulsive Symptoms in Schizophrenia
Linda Porto, M.S.N., Paul C. Bermanzohn, M.D., Samuel G. Siris, M.D.

NR573 Sex Differences in Neuropsychological Function in Nonpsychotic Relatives of Schizophrenic Probands
William S. Kremen, Ph.D., Jill Goldstein, Ph.D., Larry J. Seidman, Ph.D., Rosemary Toomey, Ph.D., Michael J. Lyons, Ph.D., Ming T. Tsuang, M.D., Stephen V. Faraone, Ph.D.

NR574 Hypofrontality in Schizophrenia: Assessment During Metabolic and Cognitive Challenge
Igor Elman, M.D., Neil I. Weissenfeld, B.S., Caleb M. Adler, M.D., Christopher Bir, B.S., Kayleen Hadd, M.S.N., David Pickar, M.D., Alan F. Breier, M.D.

NR575 Expression of Serotonin Transporter in Schizophrenia
Boris P. Sokolov, Ivan A. Hernandez, M.S., Varham Haroutunian, Ph.D., Kenneth L. Davis, M.D.

NR576 Serial Changes of P300 and Plasma Catecholamine Metabolites in the Course of 8 Weeks Pharmacological Treatment of Schizophrenia
Shin-ichi Niwa, M.D., Satoshi Takeuchi, M.D.

NR577 Mini Mental State Examination Score Fluctuation in Chronic Psychiatric Inpatients
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D.

NR578 Informed Consent: Assessment of Comprehension
Donna Ames, M.D., William C. Wirshing, M.D., Stephen R. Marder, M.D., Alix B. Strough, B.S., Doreen Ross, Danielle Goldstein, B.A., Robert E. Benveniste, Joanna Pashdag, Sun S. Hwang, M.S., Peggy J. Bowman

NR579 The Efficacy and Safety of Two Fixed Doses of Ziprasidone in Schizophrenia
Karen R. Reeves, M.D.

NR580 Psychosocial Rehabilitation Affects Positive and Negative Symptoms of Chronic Schizophrenics
Mario Guazzelli, M.D., Antonio Ciapparelli, M.D., Alessio Dani, M.D., Loretta Giuntoli, Ph.D., Stefano Marchetti, M.D., Laura Palagini, M.D., Alberto Parrini, M.D., Pietro Pietrini, M.D., Simonetta Starnini, M.D.

NR581 Symptoms in Chronic Schizophrenic: The Oldest Old
Cynthia Blum, M.A., Philip D. Harvey, Ph.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

NR582 Family Burden of Chronic Psychotic Patients: An Italian Multicenter Study
Gabriella Belelli, Mirella Ruggeri, M.D., Diana De Ronchi, M.D., Prof. Vittoris Volterra

NR583 Tardive Dyskinesia in Older Outpatients
Lawrence A. Labbate, M.D., R. Gregory Lande, D.O., Franklin D. Jones, M.D.

NR584 Schizophrenia and Date of Birth in New York
Nigel M. Bark, M.D., Ilya Kerelevich, B.A.

NR585 The Efficacy and Safety of 28-Day Treatment with Ziprasidone in Schizophrenia
Edmund P. Harrigan, M.D.

NR586 Neuropsychophysiological 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.

NR587 Sustained Serotonin Receptor Occupancy of Ziprasidone Using PET Ligand 18F Setoperone in Healthy Volunteers
Grant N. Ko, M.D., Stephen A. Williams, Alan J. Fischman, Celena E. Drury, Pierre G. Etienne, Robert T. Rubin, M.D.

NR588 Cognitive Impairment and Negative Symptoms in Schizophrenia: Evidence for Diverse Patient Group
Paul Hartel, M.A., Serge M. Sevy, M.D., Seamus Oflaithbheartaigh, M.D., Philip D. Harvey, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

NR589 Quetiapine Does Not Differ From Placebo in the Incidence of Extrapyramidal Syndrome or Effect on Plasma Prolactin
Walter W. Hong, M.D., Lisa A. Arvanitis, M.D., Barbara G. Miller, M.S.

NR590 Immigration in the Use of Schizophrenia Research: A Study in Israel
Haim Y. Knobler, M.D., Wladislaw Fainstein, M.D., Yehuda Kuniavsky, M.D., Bella Hanin, Shmuel Maizel, M.D., Yaacov Lerner, M.D.

NR591 Clozapine Versus Risperidone in Treatment Refractory State Psychiatric Inpatients
Jean-Pierre Lindenmayer, M.D., Mohan Park, M.D., Adel Iskander, M.D., Nigel M. Bark, M.D., Robert M. Smith, M.D., Thomas B. Cooper, M.A.

NR592 Prefrontal Cortical Structure-Function Correlations in Schizophrenia
Todd Lencz, Ph.D., Robert M. Bilder, Ph.D., Manzar Ashtari, Ph.D., Houwei Wu, M.D., Jose Alvir, D.P.H., Jeffrey A. Lieberman, M.D.

NR593 Cognitive Correlates of Spatial Working Memory in Schizophrenia
James J. Levitt, M.D., Paul G. Nestor, Ph.D., Jay E. Allard, B.A., Maria E. Karapelou, Ed.M., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

NR594 Odor Discrimination Performance and Deficit Schizophrenia
Delores Malaspina, M.D., Fabien Tremeau, M.D., Scott Yale, M.S.W., Marleen Van Kammen, M.P.H., Xavier F. Amador, Ph.D., Jack M. Gorman, M.D.

NR595 Gender Differences in Schizophrenia
Ashok K. Malla, M.D., Ross M. Norman, Ph.D., Sandra Morrison-Stewart, Ph.D., Edward Helmes, Ph.D., Peter J. Williamson, M.D., Leonardo Cortese, M.D.

NR596 Intact Affective Preference for Familiar Stimuli Despite Impaired Recognition Memory in Schizophrenics
Ariane Marie, B.A., John D.E. Gabriel, Ph.D., Richard Shaw, M.D., Bonny R. Brown, M.A., Kaaren Hanson, M.A., Felicia Pratto, Ph.D., R.B. Zajonc, Ph.D.

NR597 The Effect of Ziprasidone on Steady-State Pharmacokinetics of a Combined Oral Contraceptive
Gray J. Muirhead, Philip R. Holt, Stuart Oliver, Jane Harness, Richard J. Anziano

NR598 A Role of Working Memory in Language Dysfunction in Schizophrenia
Margaret Niznikiewicz, Ph.D., Paul G. Nestor, Ph.D., Brian F. O'Donnell, Ph.D., Jay E. Allard, B.A., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D.

NR599 Neuropsychological Correlates in Schizophrenia
Ross M. Norman, Ph.D., Ashok K. Malla, M.D., Sandra Morrison-Stewart, Ph.D., Edward Helmes, Ph.D., Peter J. Williamson, M.D., Jill Thomas, B.Sc., Leonardo Cortese, M.D.

NR600 Amantadine Disrupts Prepulse Inhibition in Rats
Michael S. Rappaport, M.D., David P. Yells, Ph.D., Stephen R. Paige, Ph.D., Shelton Hendricks, Ph.D.

NR601 Cognitive Subtypes of Schizophrenia According to Verbal Fluency Performance
Philippe H. Robert, M.D., Sandrine Thauby, M.D., Isabelle Chaix, Ph.D., Valerie Migneco, M. Benoit, M.D., Guy Darcourt, M.D.

NR602 Age-Related Changes in Formal Thought Disorder in Chronic Schizophrenic Patients
Janel Lombardi, M.D., Philip D. Harvey, Ph.D., Martin Leibman, Ph.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Peter Powchick, Ph.D.

NR603 Olanzapine Versus Haloperidol: Results of a Large Multi-Center International Trial
Winston G. Satterlee, M.D., Charles M. Beasley, Jr., M.D., Pierre V. Tran, M.D., Roy N. Tamura, Ph.D., John A. Krueger, M.B.A., Gary D. Tollefson, M.D.

NR604 Comparison of Extrapyramidal Syndromes Between Olanzapine and Placebo in Schizophrenia
Jamie S. Street, M.D., Mary Anne Deliva, M.S., Roy N. Tamura, Ph.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.

NR605 Long-Term Treatment-Emergent Dyskinetic Symptoms in Patients Treated with Olanzapine and Haloperidol
Jamie S. Street, M.D., Roy N. Tamura, Ph.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.

NR606 Comparison of Weight Gain During Risperidone and Clozapine Treatment in Chronic Schizophrenia
Tung-Ping Su, M.D., Igor Elman, M.D., Anil K. Malhotra, M.D., Caleb M. Adler, M.D., David Pickar, M.D., Alan F. Breier, M.D.

NR607 Clinical Experience with Long-Term Continuation Treatment with Olanzapine
Pierre V. Tran, M.D., Mary Anne Deliva, M.S., Charles M. Beasley, Jr., M.D., Winston G. Satterlee, M.D., Lynne M. Cousins, B.A., Gary D. Tollefson, M.D.

NR608 Relationship of Specific Areas of Prefrontal Cortex to Temporal Lobe Abnormalities and Symptomatology in Schizophrenia
Cynthia G. Wible, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Ronald Kikinis, M.D., Ferenc Jolesz, M.D.

NR609 Anxiolytic Effects of Ziprasidone Compared with Diazepam and Placebo Prior to Dental Surgery
Keith D. Wilner, Ph.D., Richard J. Anziano, Arlene C. Johnson, Jeffrey J. Micell, Ph.D., James R. Fricke, D.D.S., Cynthia K. Titus, R.N.

NR610 The Effects of Ziprasidone on Steady-State Lithium Levels and Renal Clearance of Lithium
Keith D. Wilner, Ph.D., Richard J. Anziano, Thomas G. Tensfeldt, M.S., Shawn N. Pelletier, B.S., Glen Apseloff, M.D., Nicholas Gerber, M.B.

NR611 Single and Multiple Dose Pharmacokinetics of Ziprasidone in Healthy Males
Keith D. Wilner, Ph.D., Robert A. Hansen, M.S., Arlene C. Johnson, Jeffrey J. Micell, Ph.D., Glen Apseloff, M.D., Nicholas Gerber, M.B.

NR612 Multiple-Dose Pharmacokinetics of Quetiapine in Elderly Schizophrenic Patients
James Y.W. Wong, Ph.D., Barbara J. Ewing, Ph.D., George E. Jaskiw, M.D., Per T. Thyrum, M.D., Chiao Yeh, Ph.D.

NR613 Intensive Group Treatment for Low-Motivated Patients
Douglas M. Ziedonis, M.D., Leslie A. Harmon, B.S., Edna Arlin, M.S.W., Larry Davidson, Ph.D., Bryce Kasuba, B.A., Karen D'Avanzo, Ph.D.

NR614 Medications for Cocaine Abusing Schizophrenics
Douglas M. Ziedonis, M.D., Jennifer M. Camerato, B.A., Patricia A. Harris, A.S., Kimberlee J. Trudeau, B.A., Surita Rao, M.D., Thomas R. Kosten, M.D.

NR615 Pharmacology of Quetiapine: An Atypical Clozapine-Like Antipsychotic
Jeffrey Goldstein, Ph.D.

NR616 Electrophysiological Effects of Olanzapine, a Novel Atypical Antipsychotic, on A9 and A10 Dopamine Receptors
Kurt Rasmussen, Ph.D., Marsha E. Stockton, B.S.

NR617 Effect of Smoking and Gender on Population Pharmacokinetics of Olanzapine
Bela Patel, Ph.D., Darcie L. Kurtz, M.S., J. Thomas Callaghan, M.D., Charles M. Beasley, Jr., M.D., Richard F. Bergstrom, Ph.D.

NR618 An Event-Related Potential Study of Visual Spatial and Object Selection in Students and Schizophrenic Patients
Geoffrey F. Potts, Ph.D., Brian F. O'Donnell, Ph.D., Jay E. Allard, B.A., Robert W. McCarley, M.D.

NR619 Short-Term Visual Memory Deficits in Schizophrenia: Medication and Electrophysiological Correlates
Esther F. Rabinowicz, Ph.D., David R. Owen, Ph.D., Raymond A. Knight, Ph.D., Gerard E. Bruder, Ph.D., Craig Tenke, Ph.D., Jack M. Gorman, M.D.

NR620 Differential Frontal Deficits in Schizophrenia
Godehard Oepen, M.D., Edward Federman, Ph.D., Jeff Zareff, Charles Drebbing, Ph.D.

NR621 Selegiline for Negative Symptoms and Tardive Dyskinesia
Alan I. Stearns, M.D., Angelo Sambunaris, M.D., Ahmed M. Elkashef, M.D., Fuad Issa, M.D., Michael F. Egan, M.D., Richard Jed Wyatt, M.D.

NR622 Reduced Subcortical Brain Volumes in Nonpsychotic Siblings of Schizophrenic Patients
Ming T. Tsuang, M.D., Larry J. Seidman, Ph.D., Stephen V. Faraone, Ph.D., Jill Goldstein, Ph.D., Julie Goodman, Ph.D., Genichi Matsuda, M.D., William S. Kremen, Ph.D., David Kennedy, Ph.D., Nikos Makris, M.D., Verne S. Caviness, M.D.

NR623 Lack of Clinically Significant Abnormalities in MRIs of Older Patients with Schizophrenia and Related Psychoses
Laura L. Symonds, Ph.D., John M. Olichney, Terry Jernigan, Ph.D., Jody Corey-Bloom, M.D., Dilip V. Jeste, M.D.

NR624 The Predictors of Schizophrenia
Matti K. Isohanni, M.D., Paula Rantakallio, M.D., Peter Jones, M.C.R., Juha Moring, M.D., Jari Tiihonen, Ph.D., Antero Myhrman, Ph.D.

NR625 Landmark Neuroanatomy of Schizophrenia
John R. DeQuardo, M.D., Fred L. Brookstein, Ph.D., James A. Brunberg, M.D., Rajiv Tandon, M.D.

NR626 Quality of Life and the Chronically Mentally Ill: A Critical Examination of the Self-Report Methodology
Mark J. Atkinson, Ph.D., Henry T. Chuang, M.D.

NR627 Does Reprovision Benefit Elderly Psychiatric Patients?
Noam Trieman, M.D., Julian Leff, M.D., Walter Wills

NR628 Outcomes of Homeless Persons with Mental Illness and Substance Use Disorders
Lisa B. Dixon, M.D., Bruce Deforge, Ph.D., Elmer Kernan, M.S.W., Anthony F. Lehman, M.D.

NR629 An Ounce of Prevention: What Our Patients Don't Know?
Sharon G. Dott, M.D., David P. Walling, Ph.D.

NR630 Evaluating Models of Condom Use and Risky Sexual Behavior in Young Heterosexual Men
Michael C. Seto, M.A., Vernon L. Quinsey, Ph.D.

NR631 Gender Differences in Patients with Chronic Temporomandibular Disorder
Donald S. Ciccone, Ph.D., Nancy Just, Ph.D., Erin B. Bandilla, M.A., Richard A. Pertes, D.D.S.,

NR632 Neuropsychological Functioning Before and After Methylphenidate Treatment in Adults with ADD
Henry J. Riordan, Ph.D., Kevin E. Carroll, Ph.D., Laura A. Flashman, Ph.D., Andrew J. Saykin, Psy.D., Leighton Y. Huey, M.D.

NR633 Criteria for Separating Normality and Psychopathology
Massimo Biondi, M.D., Maria Caredda, M.D., Angelo Ricciardi, M.D.

NR634 Artificial Neural Network Improves Psychiatric Diagnosis
Yizhuang Zou, M.D., Yu-Cun Shen, M.D., Liang Shu, M.D., Feng Feng, M.D., Yixin Zhong, Ph.D., Ying Qu, M.D.

NR635 Negative Symptoms in a Major Depressive Disorder
Igor I. Galynker, M.D., Jun Cai, M.D.

NR636 Negative Symptoms Associated with Hypofrontality in Stroke Patients
Igor I. Galynker, M.D., Naomi Vilkas, B.A., Dragos Serseni, M.D., Eamon Dutta, M.D., Marias Focseneanu, M.D., Richard N. Rosenthal, M.D., Fukiat Ongseng, M.D., D. Howard Finestone, M.D.

NR637 Suicide by Self-Immolation and Ethnicity: An Epidemiological Study
Manohar K. Shetty, M.D., Thyagaraja Kumaran, M.D., David J. Lynn, M.D., Radha K. Kambanpati, M.D.

NR638 Ethnic Consonance As a Determinant of Treatment Adherence
Leon L. Bernhardt, M.D., Joanne Caring, M.D.

NR639 Course of Acute Affective Disorders in India
Alan S. Brown, M.D., Vijoy K. Varma, M.D., Savita Malhotra, Sarah A. Conover, M.P.H., Ezra S. Susser, M.D.

NR640 Ethnicity and Imipramine Responses
Dora C. Anderson, B.S.N., Michael W. Smith, M.D., Yan-Ping Zheng, M.D., Keh-Ming Lin, M.D., Russell Poland, Ph.D., Inocencia Nuccio, M.S.N.

NR641 Psychiatric Emergency Room Visits of Asian-Indians
Chitra M. Shenoy, M.D.

NR642 Differential Behavioral and Physiological Responses to Cholinergic Agonist Challenge Before and After Chronic Scopolamine Alzheimer's Disease
Ruth A. Dukoff, M.D., Marcel Bahro, M.D., Judy Friz, M.A., Karen Putnam, B.A., Anne Conway, M.A., Susan E. Molchan, M.D., Trey Sunderland, M.D.

NR643 A Review of Psychiatric Consultations for Mental Capacity in an Urban Teaching Hospital
Cheryl A. Kennedy, M.D., James M. Hill, Ph.D.

NR644 Stimulants for SSRIs-Induced Sexual Dysfunction
Barbara D. Bartlik, M.D., Peter M. Kaplan, M.D., Carol A. Roeloffs, M.D., James H. Kocsis, M.D., Carol A. Roeloffs, M.D., Richard A. Friedman, M.D., Alan J. Cohen, M.D.

NR645 GAD: Influence of Comorbid Bipolar Illness on the Age of Onset
Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christine J. Truman, B.A., Beny Lafer, M.D., Una Jain, B.A.

NR646 Comorbidity of ADHD with Early- and Late-Onset Bipolar Disorder
Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christine J. Truman, B.A., S. Nassir Ghaemi, M.D.

NR647 Low Energy Radio Waves for the Treatment of Anxiety: A Double-Blind Study
Gary S. Sachs, M.D., Boris Pasche, M.D., Beny Lafer, M.D., Alexandre Barbault, B.A., Claudia F. Baldassano, M.D., Jerrold F. Rosenbaum, M.D.

NR648 Prevalence of Depression During Hospitalization for Bone Marrow Transplantation: Effects of Diagnostic Criteria
Jesus Prieto, Jordi Blanch, Jorge Atala, Cristobal Gasto, Esteve Cirera

NR649 Psychiatric Morbidity in the Bone Marrow Transplantation Setting
Jesus Prieto, Jordi Blanch, Jorge Atala, Esteve Cirera, Cristobal Gasto

NEW RESEARCH

Thursday, May 9, 1996, 9:00 a.m.-10:30 a.m.

New Research 13 – Oral/Slide Session – Room E6, Level 1, Javits Center

MOOD DISORDERS

Chp.: C. Edward Coffey, M.D.

NR650 Mood Disorders in 3,372 Male Twin Pairs — 9:00 a.m.
Michael J. Lyons, Ph.D., Nong Lin, Ph.D., Seth Eisen, M.D., William True, Ph.D., Rosemary Toomey, Ph.D., Joanne Meyer, Ph.D., Stephen V. Faraone, Ph.D., Ming T. Tsuang, M.D.

NR651 Clinical Features of Bipolar Disorder Linked to Chromosome 18 — 9:15 a.m.
Francis J. McMahon, M.D.,Jianfeng Xu, M.D., Colin Stine, Ph.D., Sylvia G. Simpson, M.D., J. Raymond DePaulo, Jr., M.D.

NR652 Treatment of Pregnancy-Related Mood Disorders — 9:30 a.m.
Susanne I. Steinberg, M.D., Francois Bellavance, Ph.D.

NR653 PMS: Do Ovarian Steroids Modulate Mood? — 9:45 a.m.
Dianne E. Schechter, Ph.D., Tracey J. Strasser, B.A., Jean Endicott, Ph.D., Eva Petkova, Ph.D., John Nee, Ph.D.

NR654 HPT and HPA Axis Dysfunction in Depression: Dopaminergic, Noradrenergic and Serotoninergic Correlates — 10:00 a.m.
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.

NR655 Focal Neuroanatomic Correlates of Minor Depression — 10:15 a.m.
Anand Kumar, M.D., David S. Miller, M.D., Edward E. Schweizer, M.D., Jin Zhisong, M.S., Warren Bilker, Ph.D., Susan Romberg, R.N.

NEW RESEARCH

Thursday, May 9, 1996, 9:00 a.m.-10:30 a.m.

New Research 14 – Oral/Slide Session – Room E17, Level 1, Javits Center

DEPRESSION

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

NR656	Treatment of Major Depression After Acute Myocardial Infarction with Sertraline: A Preliminary Study Peter A. Shapiro, M.D., Alexander H. Glassman, M.D., Francois Lesperance, M.D., Christopher M. O'Conner, M.D., Brian Baker, M.B., Lidia Lidagoster, M.D., Wei Jiang, M.D., Paul Dorian, M.D.	9:00 a.m.
NR657	Effects of Acute and Chronic Paroxetine on Regional Brain Metabolism in Depression Sidney Kennedy, M.D., Franco J. Vaccarino, Ph.D., Sylvain Houle, M.D., Gregory M. Brown, M.D., Kenneth R. Evans, Ph.D.	9:15 a.m.
NR658	Identification and Treatment of Depression in Primary Care M. Philip Luber, M.D., George S. Alexopoulos, M.D., James Hollenberg, M.D., Mark Callahan, M.D., Mary E. Charlson, M.D.	9:30 a.m.
NR659	Prevalence of Subclinical Hypothyroidism in Depressed Patients with Normal Baseline TSH Robert P. Kraus, M.D., Elizabeth Phoenix, B.Sc.N., Merrill W. Edmonds, M.D., Ian R. Nicholson, Ph.D., Praful C. Chandarana, M.D.	9:45 a.m.
NR660	Low-Dose Amisulpride Versus Fluoxetine in 281 Dysthymic Patients: A Randomized Medium-Term (3 months), Double-Blind Study Franco Biondi, M.D., Gianluigi Casadet	10:00 a.m.
NR661	Two-Year Outcome of Anxious Depression in Late-Life Alastair J. Flint, M.B., Sandra L. Rifat, Ph.D.	10:15 a.m.

NEW RESEARCH

Thursday, May 9, 1996, 12 noon-2:00 p.m.

New Research 15 – Poster Session – Gallerla, Level 4, Javits Center

ANXIETY DISORDERS AND OTHER PSYCHIATRIC RESEARCH

Moderator: Tana A. Grady, M.D.

NR662 The Efficacy of Once-a-Week Fluoxetine Dosing in the Treatment of Panic Disorder
Naresh P. Emmanuel, M.D., Carolyn Cosby, R.N., Michael R. Ware, M.D., R. Bruce Lydiard, M.D.

NR663 The Benefit of Client-Centered Treatment on Panic and Agoraphobia Symptoms
Ludwig Teusch, D.R., Hildegard Boehme, Prof. Dr. Markus Gastpar

NR664 Gender-Mediated Clinical Features of OCD and Obsessive-Compulsive Syndrome: New Data From a Large French Clinical Sample
Elie G. Hantouche, M.D., Marc L. Bourgeois, M.D., Myriam Bouhassira, M.D., Sylvie Lancrenon, Ph.D.

NR665 Death Anxiety and Death Attitudes in Panic Disorder and GAD
Vladan Starcevic, M.D., Stephanie K. Fallon, M.D., Eberhard H. Uhlenhuth, M.D.

NR666 Personality Change After Treatment of Panic
Vladan Starcevic, M.D., Stephanie K. Fallon, M.D., Eberhard H. Uhlenhuth, M.D.

NR667 Evaluating Suffocation False Alarm Hypothesis of Panic Disorder
Hisanobu Kaiya, M.D., Matui Akira, M.D.

NR668 Parental Representations Predict Social Avoidance in Patients with Panic Disorder
Richard J. Maddock, M.D., Mark H. Townsend, M.D., James G. Barbee IV, M.D., Cameron S. Carter, M.D.

NR669 Screening for PTSD in Primary Care Samples: Prevalence and Patterns of Health Care Utilization, Psychosocial Functioning and Life Satisfaction
Sharon Younkin, Mark Zimmerman, M.D., Bruce Horowitz, M.D., Anne Moulton, M.D., Jill I. Mattia, M.A.

NR670 OCD: Gender Differences
Marijo B. Tamburrino, M.D., Kathleen N. Franco, M.D., Nancy B. Campbell, M.D., Cynthia L. Evans, M.D., Rachel E. Kaufman, M.D.

NR671 SSRIs Normalizes Noradrenergic Function in Panic
Jeremy D. Coplan, M.D., Laszlo A. Papp, M.D., Daniel S. Pine, M.D., Donald F. Klein, M.D., Jack M. Gorman, M.D.

NR672 Respiratory Challenges in Panic Disorder
Laszlo A. Papp, M.D., Jose Martinez, M.A., Jeremy D. Coplan, M.D., Randolph Cole, M.D., Donald F. Klein, M.D., Jack M. Gorman, M.D.

NR673 24-Hour Growth Hormone Pattern in Panic Disorder
George C. Curtis, M.D., James L. Abelson, M.D., Thomas W. Uhde, M.D.

NR674 Respiratory Irregularity in Panic Disorder
George C. Curtis, M.D., James L. Abelson, M.D., John G. Weg, M.D., Randolph M. Nesse, M.D.

NR675 Embarrassment About the First Panic Attack Predicts Agoraphobia in Panic Disorder Patients
Michaela Amering, M.D., Heinz Katschnig, M.D., Peter Berger, M.D., Johann Windhaber, M.D., Wolfgang Baischer, M.D., Karl Dantendorfer, M.D.

NR676 Self-Reported Sexual Dysfunctions in Anxiety Disorder Patients
Michael R. Ware, M.D., Naresh P. Emmanuel, M.D., Michael R. Johnson, M.D., Olga Brawman-Mintzer, M.D., Rebecca Kapp, R.N., R. Bruce Lydiard, M.D.

NR677 Symptom Profiles of Adult Versus Childhood OCD
Daniel J. Fischer, M.S.W., Joseph A. Himle, Ph.D., Gregory L. Hanna, M.D.

NR678 Episodic Dyspnea As a Marker for Panic Disorder and Asthma in Young Adults: Results of Pulmonary and Psychiatric Evaluations
Norman B. Schmidt, Ph.D., Jeffrey P. Staab, M.D., John E. Brown, Jr., David A. Holden, M.D., Margaret A. Koselka, B.A.

NR679 Panic Disorder: Heat As a Significance Stressor
Gregory M. Asnis, M.D., Iulia Dogaru, M.D., Galina Bass, M.D., Margaret L. Kaplan, Ph.D., Lata K. McGinn, Ph.D., Paresh Pandya, M.D.

NR680 Serum Cholesterol Levels in Patients with Anxiety Disorders: A Comparison with Normal Controls
Helmut Peter, M.D., Susanne Muller, Philipp Goebel, Iver E. Hand, M.D.

NR681 The Role of the Beta-Noradrenergic System in CCK-4-Induced Panic Symptoms
Jean-Michel Le Melledo, M.D., Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., Jean-Phillipe Boulenger, M.D., Roger J. Cadieux, M.D., Francois Bellavance, Ph.D.

NR682 Open Trial of Fluvoxamine for Combat PTSD
Charles R. Marmar, M.D., Frank B. Schoenfeld, M.D., Daniel S. Weiss, Ph.D.

NR683 Peritraumatic Dissociation in Rescue Workers
Charles R. Marmar, M.D., Daniel S. Weiss, Ph.D., Thomas J. Metzler, Ph.D.

NR684 Paroxetine Normalizes Heart Rate Variability in Panic Disorder
Phebe M. Tucker, M.D., Philip Adamson, M.D., Samuel E. Payne III, M.D., Audrey Chang, M.S., Alfretia Scarborough, M.P.H., Monica Bottoms, B.A., Lawrence A. Labbate, M.D., Heather McLean, M.S., Brian Conley, Ph.D.

NR685 Caffeine Anxiety and Depression in Outpatients
R. Gregory Lande, D.O.

NR686 The Effect of Aging on Cholecystokinin-Induced Panic
Alastair J. Flint, M.B., Jacques Bradwejn, M.D., Franco J. Vaccarino, Ph.D., Diana Koszycki, Ph.D.

NR687 The Relationship Between Acute Stress Disorder and Subsequent PTSD in Three Disaster Populations
Jeffrey P. Staab, M.D., Thomas A. Grieger, M.D., James E. McCarroll, Ph.D., George T. Brandt, M.D., Carol S. Fullerton, Ph.D., Robert J. Ursano, M.D.

NR688 Autonomic Reactivity of Panic Patients During Carbon Dioxide Inhalation Procedures
Alexander Bystritsky, M.D., Michelle G. Craske, Ph.D., Emanuel Maidenberg, Ph.D., Tanya Vapnik, R.N., David Shapiro, R.N.

NR689 Within Class Safety and Efficacy Comparison of Imipramine Versus Desipramine in Early PTSD Treatment
Neal A. Kline, M.D.

NR690 Lesopitron: A Bridging Study in Patients with GAD
Jerome F. Costa, M.D., John J. Sramek, Pharm.D., Neal R. Cutler, M.D., Gaston Marlon-Landais, M.D., Christof M. Jensen, M.S., Neil M. Kurtz, M.D., Ann T. Carrington, Ph.D.

NR691 A Comparison of CCK-4 Panickers and Non-Panickers
Diana Koszycki, Ph.D., Robert M. Zacharko, Ph.D., Jean-Michel Le Melledo, M.D., Jacques Bradwejn, M.D.

NR692 Twelve-Year Follow-Up of Treated Specific Phobia
Joshua Lipsitz, Ph.D., Salvatore Mannuzza, Ph.D., Donald F. Klein, M.D., Donald C. Ross, M.D., Cindy Aaronson, C.S.W., Abby J. Fyer, M.D.

NR693 Childhood ADHD in Adults with Anxiety Disorders
Catherine L. Mancini, M.D., Michael A. Van Ameringen, M.D., Steve Collins, M.D., Carol Wilson, M.Sc.

NR694 Clonazepam Efficacy in the Treatment of Panic Disorder: Results of a Multicenter Placebo-Controlled Trial
Georges Moroz, M.D.

NR695 Functional Impairment in Anxiety Disorders
Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Carol Wilson, M.Sc.

NR696 Haloperidol in the Treatment of Trichotillomania
Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D.

NR697 Parental Bonding in OCD and Body Dysmorphic Disorder
Katharine A. Phillips, M.D., Gail Steketee, Ph.D., Leslie Shapiro, M.S.W.

NR698 Reliability and Validity of the Body Dysmorphic Disorder: Yale-Brown Obsessive-Compulsive Scale
Katharine A. Phillips, M.D., Bonnie R. Aronowitz, Ph.D., Concetta De Caria, Ph.D., Eric Hollander, M.D., Steven A. Rasmussen, M.D.

NR699 Fluvoxamine in Body Dysmorphic Disorder
Katharine A. Phillips, M.D., Susan L. McElroy, M.D.

NR700 Autonomic Dysfunction in Comorbid Panic Disorder and Depression
Mark H. Townsend, M.D., Nancy B. Bologna, Ph.D., James G. Barbee IV, M.D.

NR701 PTSD and Existential Life Attitudes in Bone Marrow Transplantation Survivors
Suzanne M.J. Vickberg, B.A., William H. Redd, Ph.D., Meridith Smith, Ph.D., Katherine N. DuHamel, Ph.D., Esperanza Papadopoulous, M.D., Lisa N. Rosen, M.A.

NR702 A Twin Study of Gene Environment Interaction in GAD
Francis A. O'Neill, M.D., Kenneth S. Kendler, M.D.

NR703 Cytokine Production in OCD
Ronit Weizman, M.D., Nathaniel Laor, M.D., Yerachmiel Barber, M.D., Haggai Hermesh, M.D., Meir Djaldetti, M.D., Hanna Bessler, Ph.D.

NR704 Dream Content in OCD: A Semantic and Emotional Analysis in Comparison with Controls
Dr. Alain Sauteraud, Jean-Claude Menny, M.D., Pierre Philip, M.D., Franck Peyre, M.D., Jean-Marie Bonnin, M.D., Marc L. Bourgeois, M.D.

NR705 PMS: Does Ongoing Stress Modulate Its Severity?
Tracey J. Strasser, B.A., Dianne E. Schechter, Ph.D., Jean Endicott, Ph.D.

NR706 Association Between Appetite and Mood in PMS
Tara M. Singer, B.A., Dianne E. Schechter, Ph.D., Jean Endicott, Ph.D.

NR707 Diagnostic Status of Women Presenting to a PMS Clinic
Carol S. Birnbaum, M.D., Lee S. Cohen, M.D., Jennie W. Bailey, B.A.

NR708 The Relationship Between the Menstrual Distress Questionnaire and Aggressive Responding
Donald M. Dougherty, Ph.D., Patrick Bordnick, Ph.D.

NR709 Dissociation and Somatization in Psychiatrically Disturbed Adolescents with Traumatic Life Experiences
Romuald M. Brunner, M.D., Prof. Franz Resch, Peter Parzer, DiplPsyc., Eginhard Koch, M.D.

NR710 Serum Pemoline Levels in Adult ADD
Faruk S. Abuzzahab, Sr., M.D., J.M. Gillund, R.L. Zimmermann, Ph.D.

NR711 Depersonalization Measured by a Questionnaire
Dr. Nannet Buitelaar, Dr. Robert Ferdinand

NR712 The Effects of Methylenedioxymethamphetamine ("Ecstasy") on Human Sexual Function
Zvi Zemishlany, M.D., Dov Aizenberg, M.D., Abraham Weizman, M.D.

NR713 Imipramine Treatment for Retrograde Ejaculation Induced by Thioridazine
Dov Aizenberg, M.D., Roni Shiloh, M.D., Zvi Zemishlany, M.D., Abraham Weizman, M.D.

NR714 Retrospective Review of Psychotropic-Induced Sexual Dysfunction in Women
Angela P. Aldrich, Ph.D., Marcus D. Cook, Ph.D., Leslie Pedersen, M.D.

NR715 Treatment of Antidepressant-Induced Sexual Dysfunction with Ginkgo Biloba Extract
Alan J. Cohen, M.D.

NR716 A Double-Blind Placebo-Controlled Trial of Yohimbine for Treatment of SRI-Induced Sexual Dysfunction
Frederick M. Jacobsen, M.D., Lillian Comas-Diaz, Ph.D.

NR717 Sexual Dysfunction with SSRIs: A Comparitive Analysis
Angel L. Montejo, M.D., Gines Llorca, M.D., Juan A. Izquierdo, M.D., Work Group of Spain

NR718 The Effects of Short and Long Naps Among Narcoleptic, Sleep Deprived and Alert Subjects
Leon D. Rosenthal, M.D., Todd Helmus, B.A., Thomas Roth, Ph.D.

NR719 Epidemiology of Frequent Nightmares in Adults
Thomas C. Neylan, M.D., Charles R. Marmar, M.D., Thomas J. Metzler, Ph.D., Roger M.Y. Wu, M.D., Douglas F. Zatzick, M.D., Daniel S. Weiss, Ph.D.

NR720 Circadian Rest-Activity Rhythms in Demented/Nondemented Elders and Their Caregivers
Charles P. Pollak, M.D., Peter E. Stokes, M.D., Patricia R. Mourilhe, M.D.

NR721 Predictive Value of Alexithymia: A Prospective Study in Somatizing Patients
Michael Bach, M.D., Doris Bach, Ph.D.

NR722 Trichotillomania: Etiology, Phenomenology, Comorbidity and Treatment Recommendations
Iver E. Hand, M.D., Annette Neudecker, Ph.D., Nicole Monchau, Ph.D.

NR723 Olanzapine: Impact of An Atypical Antipsychotic Candidate on Prolactin Release
Ann Marie Crawford, Ph.D., Charles M. Beasley, Jr., M.D., Gary D. Tollefson, M.D.

NR724 Self-Report of Psychiatric Symptoms in Rotterdam
F.M. Baker, M.D., Lenore J. Launer, Ph.D., Marie M.B. Breteler, Ph.D., Albert Hofman, M.D.

NR725 Rehabilitation: The Black Chronically Mentally Ill
F.M. Baker, M.D., Judie Stokes, M.S.W., Orlando R. Davis, M.D.

NR726 Screening for Psychiatric Disorders in Primary Care
Jill I. Mattia, M.A., Mark Zimmerman, M.D., Bruce Horowitz, M.D.

NR727 Prevalence of Hepatitis-C Antibody Positivity in Vietnam Veterans with PTSD
M. Michele Murburg, M.D., Shirley Shultz, M.S.N., Susan A. Ballagh, M.D.

NR728 Chile: What Determines Primary Care Physicians Detection of Psychiatric Morbidity?
Ricardo Araya, M.D., Graciela Rojas, M.D., Julia Acuna, M.D.

NR729 Chile: World's Highest Psychiatric Morbidity Prevalence Rates in Primary Health Care
Ricardo Araya, M.D., Graciela Rojas, M.D., Julia Acuna, M.D.

NR730 Prevalence of Affective and Anxiety Disorders in Hungary
Erika Szadoczky, Janos Furedi, M.D., Ilona Fazekas

NR731 WITHDRAWN

NR732 Medication Refusal: The Vermont Experience
Sandra Steingard, M.D., John Pandiani, Ph.D., Andrew Zovistoski

NR733 Criminal Recidivism in the Mentally Ill
Victoria L. Harris, M.D., Thomas Koepsell, M.D.

NR734 Homicides and Psychiatric Disorders
Markku E.J. Eronen, M.D., Jari Tiihonen, Ph.D., Panu Hakola, Ph.D.

NR735 Risperidone for Treating Violence and Aggression in Forensic Hospital Patients
John W. Thompson, Jr., M.D.

NR736 Survey of How Education Decreased Sexual Harassment Among Medical Students
Rebeka Moscarello, M.D., Katalin J. Margittai, M.D., Miriam Rossi, M.D.

NR737 Resident Research Seminar: Program Description
Anita L.H. Clayton, M.D., Adrienne E.R. Keller, Ph.D.

NR738 Hormones and Premenstrual Dysphoric Disorder
Anita L.H. Clayton, M.D., Adrienne E.R. Keller, Ph.D., Catherine A. Leslie, M.D., William Evans, M.D.

NR739 Tobacco Smoking Assessments and Treatment Outcomes Within a Community Mental Health Center
Douglas M. Ziedonis, M.D., Patricia A. Harris, A.S., Brandt Patricza, Thomas R. Kosten, M.D., Surita Rao, M.D., Amal Tanagho, M.D.

NR740 Immunologic Measurements in PTSD
Scott N. Wilson, M.D.

NR741 Serum Concentration and HPA Axis in Major Depressed Patients
So-Hyun Choi, M.D., Yong-Gu Kim, M.D., Kwang-Yoon Suh, M.D.

NR742 Phenotypic and Functional Changes of Immune Reactivity in Schizophrenia and Depression
Prof. M.T. Abou-Saleh, Ph.D., M. Shahin Allen, B.S., Yousreya Amin, M.D., M.L. Lukic, M.D.

NR743 AIDS Patients' Attitudes Toward Assisted Suicide and Euthanasia
Ramaswamy Viswanathan, M.D., Shanthi Thangam, M.D., Anwarul Ahad, M.D., Jonathan Moreno, Ph.D., Martin Kramer, M.D.

NR744 Stress and Depressive Symptoms Predict Immune Change in HIV
Jane Leserman, Ph.D., John M. Petitto, M.D., Diana O. Perkins, M.D., James D. Folds, Ph.D., Robert N. Golden, M.D., Dwight L. Evans, M.D.

NR745 Retrospective Study of Risperidone in Illinois Department of Mental Health Developmental Dissabilities
Daniel J. Luchins, M.D., Patricia Hanrahan, Ph.D., Randy Malan, R.Ph., John Harris

NR746 Satisfaction with Treatment Pilot Study
Adrienne E.R. Sheldon-Keller, Ph.D., Randolph J. Canterbury, M.D., Kimberly Largay, B.A.

NR747 Primary Care in Santiago, Chile: Mental Health and Psychosocial Problems
Maria G. Rojas, M.D., Rosemarie Fritsch, M.D., Isabel Gonzalez, M.D., Berta Diaz, S.A., Fernando Lolas, M.D.

NR748 Acute Stress Disorder in Newly Diagnosed Cancer Patients
Elizabeth L. McGarvey, Ed.D., Randolph J. Canterbury, M.D., Cheryl Koopman, Ph.D., Gail J. Clavet, Ph.D.

NR749 PTSD After a Building Collapse Accident in Korea
S. Peter Kim, M.D.

NR750 Rehabilitation Readiness Determination in Schizophrenia
Thomas E. Smith, M.D., Scott Trefny, M.A., James W. Hull, Ph.D.

NR751 Skills Training for Engagement in After Care: The Community Re-Entry Program
Thomas E. Smith, M.D., James W. Hull, Ph.D., Sally J. Mackain, Ph.D., Marianne S. Goodman, M.D., Donna T. Anthony, M.D., Mary K. Kentros, M.D.

NR752 Evaluating a Community Bereavement Support Group
Nancy C. Maruyama, M.D., James Willsey, M.Div., Elinor Collins, R.N.

NR753 Effects of Psychodynamic Therapy in Schizophrenic Patients
Prof. Vittoris Volterra, Diana De Ronchi, M.D., Gabriella Belelli, Mirella Ruggeri, M.D., Antonella Lunardi, M.D.

NR754 Testimony Psychotherapy in Bosnian Refugees: An Open Trial
Alma Dzubur Kulenovic, M.D., Stevan M. Weine, M.D., Ivan Pavkovik, M.D.

NR755 A Dose-Response Study of Acupuncture Detoxification for Acute Heroin Withdrawal Symptoms
Cheng-Jen Chen, M.D., Alexander Babayan, M.D.

NR756 Parameters Predicting Extended Full Leather Restraints
Jagannathan Srinivasaraghavan, M.D., Linda Kossow, M.S.N.

NR757 Prediction of Drug Interactions with Olanzapine Through the Use of In Vitro Methodologies
Barbara J. Ring, M.S., Shelly N. Binkley, B.S., Mark Van den Branden, John Catlow, B.S., Thomas J. Lindsay, M.S., Steven A. Wrighton, Ph.D.

NR758 Computer Documentation at the Patient's Side
James J. Strain, M.D., Jeffrey S. Hammer, M.D., George Fulop, M.D.

NR759 Computer-Assisted Behavior Therapy for OCD
John H. Greist, M.D., Lee Baer, Ph.D., Isaac M. Marks, M.D., Kenneth A. Kobak, M.S.W., Keith W. Wenzel, B.S., Susan L. Dotti, Ph.D.

NR760 Satisfaction As a System Performance Indicator in Persons with Schizophrenia
Barbara M. Rohland, M.D., Douglas R. Langbehn, M.D., James E. Rohrer, Ph.D.

NR761 Pharmacoeconomic Evaluation of Risperidone in Schizophrenia
Ronald F. Cookson, Ph.D., Julian F. Guest, Ph.D., Warren M. Hart, M.Sc.

NR762 Cognitive Impairment As a Predictor of Psychiatric Length of Stay
Zinoviy Gutkovich, M.D., Christian Miner, Ph.D., Jennifer Rosenblum, Sc.B., Igor I. Galynker, M.D.

NR763 Effectiveness of the PRIME-MD in the Primary Care Setting: A Clinical Trial with Three Levels of Support
Marcia T. Valenstein, M.D., Gregory W. Dalack, M.D., Sara R. Figueroa, M.D., Frederic C. Blow, Ph.D., Alan B. Douglass, M.D.

NR764 Screening for Psychiatric Disorders in Primary Care: Patient Acceptance Versus Physician Reluctance
Mark Zimmerman, M.D., Bruce Horowitz, M.D., Jill I. Mattia, M.A.

NR765 A Study of Family Stress and Service Needs at the Time of Psychiatric Hospitalization
Marilyn J. Wedenoja, M.S.W., David L. Neal, M.S.W.

NR766 Barriers to Equity in Mental Health Services Provision to Children and Adolescents
Alan J. Flisher, M.B., Rachel A. Kramer, D.Sc., Rene C. Grosser, Ph.D., Sherryl H. Goodman, Ph.D., Stevan Greenwald, M.A., Sarah M. Horowitz, Ph.D., William E. Narrow, M.D., Christina Hoven, Ph.D.

NR767 Patterns of Service Utilization and Correlates in a Psychiatric Outpatient Clinic
Barnett S. Meyers, M.D., JoAnne Sirey, Ph.D., Patrick Raue, Ph.D., Deborah A. Perlick, Ph.D., Tara Di Domenico, M.A., George S. Alexopoulos, M.D.

NR768 Daily Left Prefrontal Repetitive Transcranial Magnetic Stimulation in Outpatient Depression: Initial Results of a Double-Blind Placebo Controlled Crossover Trial
Mark S. George, M.D., Eric M. Wassermann, M.D., Wendol A. Williams, M.D., Timothy A. Kimbrell, M.D., John T. Little, M.D., Mark Hallett, M.D., Robert M. Post, M.D.

NR769 Stress of Kaukaroon College Nursing Students
Wanpen Wangwiwatjaroen, M.D.

NR1 Monday, May 6, 9:00 a.m.-10:30 a.m.

Evaluating the Relative Efficacy of Three Aversion Therapies Designed to Reduce Craving Among Male Cocaine Abusers

Patrick Bordnick, Ph.D., Psychiatry, University of Texas, 1300 Moursund, Houston TX 77030; Ralph L. Elkins, Ph.D., T.E. Orr, Ph.D., Paul Walters, Ph.D., Bruce Thyer, Ph.D.

Summary:

Objective: This investigation evaluated the use of aversion therapies to eliminate conditioned craving for cocaine in crack-cocaine-dependent subjects.

Methods: Subjects (N = 70) were cocaine-dependent veterans who were hospitalized on an inpatient substance abuse unit. Subjects were randomly assigned to one of three aversion therapy conditions or a relaxation condition. The aversion therapies included: chemical aversion (emetine hydrochloride), covert sensitization, and faradic aversion. Craving measurements were assessed pre and post for each of eight treatment sessions.

Results: Overall, the aversion therapies significantly reduced craving for crack cocaine. The number of sessions it took to reduce subjective craving by 50% was 0.3, 0.9, and 3.7 for emetine, faradic, and covert-sensitization, respectively. Chemical aversion treatment offered the fastest reduction in craving and was the most efficacious method for eliminating craving. At session 8, 100% (n = 16) of the subjects in the chemical aversion, 78% (14) of subjects in faradic, 87% (n = 13) of subjects in covert-sensitization, and 55% (n = 11) of subjects in the relaxation groups reported craving equal to zero.

Conclusions: These results provide initial evidence that aversion therapies are efficacious in reducing subjective craving in crack cocaine abusers.

NR2 Monday, May 6, 9:00 a.m.-10:30 a.m.

Outcomes of Depressed Male Alcoholics: Primary Versus Secondary Depression

Saeed A. Shah, M.D., Psychiatry, Kansas University Med Ctr, 3901 Rainbow Blvd., Kansas City KS 66160; Elizabeth J. Nickel, M.A., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Barry I. Liskow, M.D., Stephen D. Samuelson, M.D.

Summary:

In this one-year, prospective, naturalistic study of alcoholism we wanted to determine whether major depression beginning prior to alcoholism (primary depression) differed in any clinically significant ways from depression beginning after the onset of abusive drinking (secondary depression). From a large sample of 360 hospitalized VA alcoholic men who were extensively investigated at intake into the study and systematically evaluated one year later, we extracted a subsample of 97 (30%) who also satisfied inclusive DSM-III-R criteria for major depression. Forty-one subjects of the 97 were eliminated: 28 subjects with co-occurring antisocial personality disorder (ASP) and 13 subjects in which the temporal relationship between the mood and substance abuse disorder could not be clearly determined. Concomitant anxiety disorders (N = 12) were allowed to vary. The remaining 56 subjects were then divided into three subgroups for comparative purposes: (1) Primary Depressed Alcoholic (N = 23). Onset of Depression preceded onset of alcoholism by at least two years. (2) Concurrent Depressed Alcoholic (N = 13). Onset of Depression and Alcoholism within plus or minus one year of each other. (3) Secondary Depressed Alcoholic (N = 20). Onset of depression followed onset of alcoholism by at least two years. At intake into the study, virtually no differences were found. Family history of psychiatric disorder including alcoholism and depression, age of alcoholism onset, medical and social problems associated with drinking, number of positive depressive symptoms, treatment history, and psychiatric comobidity did not distinguish the three subgroups. One year later, only two of the 56 subjects were lost to follow up. Outcome measures including abstinence rates, drinking sequelae, treatments received, psychiatric severity and ratings of psychosocial functioning were comparable across all groups, although the entire sample improved significantly with respect to abusive drinking and its sequelae over the follow-up period. Our results question the clinical utility of distinguishing primary and secondary depression in non-ASP male alcoholics.

NR3 Monday, May 6, 9:00 a.m.-10:30 a.m.

Common Physical Complaints As Predictors for Alcohol Abuse and Dependence in a Primary Care Women's Clinic

Tedra L. Anderson-Brown, M.D., Psychiatry, Durham VAMC & Duke, 508 Fulton Street RM 166C, Durham NC 27710; Lori Bastian, M.D., Marian I. Butterfield, M.D., Malin Vollmer, B.A.

Summary:

Objective: To determine whether common physical complaints endorsed by women veterans are predictors for alcohol abuse/dependence.

Methods: 369 consecutive patients enrolled in the Durham VAMC women's primary care clinic from July 1994 to June 1995 were administered the PRIME-MD patient questionnaire (PQ). The PQ consists of 26 yes/no questions that screen for mental disorders, including substance abuse. This instrument has good specificity for detecting alcohol abuse. The PQ also evaluates 15 physical symptoms that constitute the majority of complaints endorsed in primary care settings.

Results: Overall, 12% (45) of the women were identified with probable diagnosis of alcohol abuse or dependence using the PQ. The following physical complaints were significant predictors of drinking problems: stomach pain (odds ratio (OR) 1.8, 95% CI = 1.0–3.4); pain/problems during sexual intercourse (OR 2.2, 95% CI = 1.1–4.5); menstrual pain/problems (OR 3.0, 95% CI = 1.6–5.6); and insomnia (OR 3.0, 95% CI = 1.6–5.6).

Conclusions: Women with alcohol abuse or dependence presenting to primary care clinics may be more likely to endorse specific physical complaints such as insomnia, stomach pain, and pain or problems during menstruation or sexual intercourse. Increased awareness of these physical symptoms may help improve identification of alcohol use problems and ultimately result in appropriate substance abuse treatment.

NR4 Monday, May 6, 9:00 a.m.-10:30 a.m.

Factors Related to Alcohol Use Disorders

Sherrie A. Bieniek, M.D., Psychiatry, University of Miami, 328 Majorca Avenue #5, Coral Gables FL 33134; Raymond L. Ownby, M.D., Alberto Penalver, M.D., Barbara J. Mason, Ph.D.

Summary:

Objective: To assess demographic and functional variables related to a diagnosis of alcohol use disorder (abuse or dependence) in older adult and elderly patients presenting to a psychiatric emergency room.

Method: A retrospective chart review was done for the period July 1, 1995 to September 30, 1995. All charts generated at the psychiatric emergency service of a large public hospital in the Southeast were reviewed, and those of patients older than 45 years were intensively reviewed. Demographic data, nursing assessment, and psychiatric evaluations were reviewed and key data extracted. Stepwise multiple regression was used to identify variables related to a final psychiatric diagnosis of alcohol abuse or alcohol dependence disorder. Follow-up chi-square analyses

assessed the significance of nominal items independent of the regression analysis.

Results: Over the 12-week period, 1,502 charts were generated and were then reviewed for this study. Of these, 171 were for persons older than 45 years, and of these, 47 (or 28%) received an alcohol use disorder diagnosis. Gender, a diagnosis of hypertension, and level of education were related to the diagnosis. Patient's expressions of anxiety and fears of harming themselves were also related, as were nurses' assessment of cooperativeness, concentration, and ability to follow directions. Chi-square analyses confirmed the significance of these variables.

Conclusion: Alcohol use disorders are common among older adult patients in a public psychiatric emergency service. Factors related to the diagnosis of an alcohol use disorder include male gender, the presence of hypertension, more years of education, and the presence of mood and cognitive symptoms. The frequency of these diagnoses underscores the importance of assessing for alcohol use among older patients in this setting.

NR5 Monday, May 6, 9:00 a.m.-10:30 a.m.

Opiate Withdrawal Using Dextromethorphan

Adam M. Bisaga, M.D., Psychiatry, North Shore Hospital, 400 Community Drive #4F, Manhasset NY 11033; Philip Gianelli, M.D., Joseph Pugliese, M.D., Margo F. Spitzer, M.D., Ronald Brenner, M.D., Piotr Popik, M.D.

Summary:

Animal studies suggest that N-methyl-D-aspartate (NMDA) antagonists from various classes can attenuate physical and motivational signs of opiate abstinence syndrome. We thus hypothesized that treatment with dextromethorphan (DM)—a noncompetitive NMDA antagonist—would diminish the signs, symptoms, and craving characteristic of abrupt withdrawal from opiates in human subjects with opioid dependence.

Presented here are preliminary data from an ongoing, open-label, pilot study. We have studied six consecutive patients diagnosed for opioid dependence with the structured Clinical Interview for DSM-III-R. Assessments were administered three times per day and included Subjective and Objective Opiate Withdrawal Scales, a craving analog scale, and physiological parameters. All subjects received 75 mg of DM five times a day.

Two of the patients requested a change to methadone during the second day of the trial because of physical discomfort. The remaining four patients had a complete decrease in withdrawal ratings and disappearance of craving by the fourth day of treatment.

These findings provide preliminary evidence that DM may be a useful alternative method to methadone for detoxification for opioid-dependent individuals. Furthermore it may offer possible advantages for decreasing length of treatment and reducing craving when compared with methadone. Double-blind, placebo-controlled clinical trials are now indicated to test this hypothesis directly.

NR6 Monday, May 6, 9:00 a.m.-10:30 a.m.

Violence, Prohibition and the War on Drugs: Is It Time for an Experiment in Detente?

Susan J. Boyd, Ph.D., Psychiatry, University of MD Med System, 6029 Majors Lane Apt 6, Columbia MD 21045

Summary:

Eighty years after the first narcotics legislation, the debate rages as to how to overcome drug abuse and drug-related violence. This paper examines Prohibition as an "experiment of nature" in drug-abuse prevention through drug prohibition.

Objective: To study empirically the effect of drug prohibition on addiction and violence.

Materials and Methods: Rates of cirrhosis deaths and deaths due to homicide before, during, and after Prohibition are compared. A similar study of narcotics enforcement since the early 1960s is made, correlating total drug-related arrests, drug-related deaths, and total and firearms homicides.

Results: Cirrhosis deaths decreased during Prohibition and rose again after (although not to previous rates). Homicide deaths clearly increased during Prohibition and decreased to previous levels after. In comparison, homicide rates from 1961 to 1989 rose in tandem with increasing drug-related arrests during that period. Drug-related death rates show no clear relationship with either drug arrests or with homicides. For both time periods, nonfirearm homicides remained constant, with firearm homicides accounting for the increase in total homicides.

Conclusion: While cirrhosis rates did decrease during Prohibition, they did not return to the same levels under post-Prohibition alcohol regulation. In comparison, increasing rates of drug enforcement seemed to have no consistent effect on drug-related death rates; thus, the public health benefit of the prohibition of drugs is questionable. Since homicide rates clearly increase during periods of increased drug prohibition and enforcement, the public health risk of increasing deaths due to homicide must be weighed against any expected benefit of such prohibition. These findings may argue for experimentation with decriminalization of drugs.

NR7 Monday, May 6, 9:00 a.m.-10:30 a.m.

Psychotherapy During Opioid Detoxification

Philippe Cadilhac, M.D., Psychiatric Hospital, Casselardit Purpan, Toulouse, France, 3105G; Laurent Schmitt, M.D., Henri Sztulman, M.D., Pierre Moron, M.D., Max Reinert, M.D.

Summary:

Objective: Detoxification is a critical time to obtain a therapeutic alliance. Although results of interpersonal psychotherapy (IPP) in opioid addicts remains controversial, it was used to improve participation in maintenance. IPP is assessed through patients' written texts about the following interpersonal problem areas : transition, interpersonal disputes and deficits, and grief.

Method: Five opioid hospitalized addicts following classical detoxification using α_2 agonist are compared with six opioid addicts identically treated plus IPP. IPP is administrated on a four-session basis through the eight to 10 days of hospitalization. Interviews at the beginning and the end are assessed using discourse data analysis. Only significant high chi_2 value are described about essential words.

Results: First interview is strickly oriented on addiction and facts such as: injection, heroin, smoke, to steal, to take. Last interview significantly differs on three dimensions: 1) understand addiction with words like: "explain," "know," "question." 2) painful perception of life: "punishment," "fear," "bad." 3) interpersonal links: "discuss," "talk," "relations." These dimensions are related to duration of hospitalization and there is a trend toward significance about the action of IPP.

Conclusion: Cognitive changes appear through interviews depending on direction of hospitalization. Further study on a larger group is needed to evaluate IPP.

NR8 Monday, May 6, 9:00 a.m.-10:30 a.m.

Attention Deficit and Substance Use Disorders

Chris L. Clure, M.D., Psychiatry, Med University of SC, 171 Ashley Avenue, Charleston SC 29425; Lee S. Cohen, M.D., Kathleen T. Brady, M.D., Michael Saladin, Ph.D., Laura M. Robertson, B.A., Margaret E. Rittenbury, M.D.

Summary:

While there has been much recent interest in the relationship between adult attention deficit hyperactivity disorder (ADHD) and substance use disorders, little has been reported about ADHD diagnostic subtypes, persistence of symptoms from childhood into adulthood, and substance of choice in substance-dependent individuals with ADHD.

Methods: In order to examine the prevalence and subtype of ADHD in a group of substance-dependent individuals divided by drug choice, 136 inpatients with a substance dependence diagnosis (cocaine vs. alcohol vs. cocaine/alcohol) were administered a structured interview for ADHD and a standard psychiatric interview for Axis I disorders.

Results: 32% met criteria for ADHD and 49% of those with childhood diagnosis continued to have clinically significant symptoms into adulthood. There were no significant differences in the percentage of ADHD between groups. Of ADHD subtypes, subjects with full diagnosis and inattentive type were significantly more likely to have symptoms continue into adulthood ($p \leq 0.05$) than were subjects with the hyperactive/impulsive subtype. Patients with cocaine use were more likely to have symptoms resolve by adulthood.

Conclusions: ADHD is prevalent in treatment-seeking substance abusers without differences in prevalence or subtype by drug choice. ADHD is more likely to persist into adulthood in substance-abusers than in the general population.

NR9 Monday, May 6, 9:00 a.m.-10:30 a.m.

Naltrexone Decreases the Urge to Drink Alcohol

Dena Davidson, Ph.D., Psychiatry, Brown University, 825 Chalkstone Avenue, Providence RI 02908; Robert M. Swift, M.D., Eric Fitz, B.Sc.

Summary:

Objective: We investigated the effects of the opiate antagonist naltrexone on alcohol drinking, urge to drink alcohol, and subjective measures of alcohol intoxication on social drinkers consuming alcohol *ad libitum* in a cocktail bar.

Method: 16 college-age men and women participated in a double-blind, within subjects, crossover study. Subjects were tested during each of three drug conditions--NTX, 50 mg/day p.o., inactive placebo, and no drug. Each drug condition lasted eight to 11 days. Subjects were tested in groups during three two-hour evening drinking sessions, separated by approximately two weeks.

Results: Naltrexone significantly increased latency (time in s) to first sip the first ($p < .05$) and second alcoholic beverages consumed ($p < .01$). End of session BACs were significantly lower when subjects were treated with NTX ($p < .05$). No differences were found on self-report urge to drink alcohol; however, urge was always lower during naltrexone. Subjects reported more aversive effects during naltrexone treatment, including fatigue and tension on the POMS ($p < .05$) prior to drinking and increased nausea ($p < .05$).

Conclusions: The increase in the latency to sip alcohol may reflect the capacity of naltrexone to block urge for alcohol. These data suggest that the effectiveness of naltrexone for reducing drinking behaviors of alcoholics may be partially due to anticraving properties of naltrexone.

NR10 Monday, May 6, 9:00 a.m.-10:30 a.m.

Stimulant Psychosis Symptoms and Clinical Course

Debra S. Harris, M.D., Psychiatry, UC San Francisco, 3180 18th Street, Ste. 205, San Francisco CA 94110; Steven L. Batki, M.D.

Summary:

Objective: To examine the relationship between symptom profile and acute clinical course in patients with stimulant-induced psychosis.

Methods: Nineteen patients admitted to a county psychiatric emergency service with psychosis believed to be caused by or exacerbated by amphetamine (9), cocaine (4), or both (6) were recruited for confirmation of DSM-IV diagnosis of amphetamine- or cocaine-induced psychotic disorder and evaluation of symptoms with the psychosis sections (B-C) of the Scheduled Clinical Interview for DSM-IV (SCID-IV) and Positive and Negative Symptom Scale (PANSS). Reported measures of stimulant use were obtained, and charts were reviewed for length of stay, seclusion and restraint, and total dose of neuroleptic given.

Results: PANSS positive symptom score was significantly positively correlated with number of hours in seclusion. Negative symptom score and general psychopathology score were significantly positively correlated with time hospitalized. General psychopathology score was significantly positively correlated with time hospitalized. General psychopathology score was significantly positively correlated with milligrams of neuroleptic received in chlorpromazine equivalents.

Conclusions: In this sample, symptom profile was associated with treatment interventions used and related to acute clinical course. Attention to presenting symptoms in patients admitted for stimulant-induced psychosis may help in treatment planning.

NR11 Monday, May 6, 9:00 a.m.-10:30 a.m.

Reliability/Validation Study of the Cage Compared with the B-Mast and Discharge Diagnosis in Adult Psychiatric Inpatients

Jeffrey H. Hsu, B.S., Psychiatry, NY Med College, 206 E 95th Street #18B, New York NY 10128; Stephen B. Billick, M.D.

Summary:

The CAGE has been a widely used screening test with relative good validity for identifying patients with alcohol abuse/dependance. Inter-rater reliability has not been established. The B-MAST has also been shown to have good validity and good reliability for screening for alcoholism, but is slightly longer and more time consuming. The objective of this study was to establish inter-rater reliability for the CAGE and compare the CAGE results with the B-MAST, both being compared to discharge diagnosis for adult psychiatric inpatients.

Methods: 50 adult psychiatric inpatients from the acute adult unit, the geriatric unit, and the MICA unit for dual diagnosis, were screened for alcoholism using the CAGE and the B-MAST. Demographics and discharge diagnoses were obtained. Ten patients were videotaped while the CAGE was administered by the medical student primary rater. Two additional raters (psychiatric resident and attending) blindly rated the videotape.

Results: Both the CAGE and the B-MAST showed high validity for identification of alcohol problems on screening. The CAGE had a very high inter-rater reliability. Both the CAGE and B-MAST had acceptable sensitivity and specificity.

Conclusion: The CAGE is a reliable, valid screening device for alcohol problems and has the advantage over the B-MAST of being quicker and easier to use for primary care settings.

NR12 Monday, May 6, 9:00 a.m.-10:30 a.m.

PRN Over the Counter Medication Use Among Substance Abusing Psychiatric Inpatients: A Pilot Study

Robert A. Karp, M.D., Psychiatry, University of Maryland, 500 W University Parkway #4T, Baltimore MD 21210; Jonathon D. Goldman, M.D., Paul E. Ruskin, M.D., Lisa B. Dixon, M.D.

Summary:

Objective: This study compared the use of over the counter (OTC) PRN medications by substance abusers and non-substance abusers on an inpatient psychiatric unit.

Method: We conducted a retrospective chart review of 54 psychiatric inpatients consecutively admitted during a two-month period to a midwest Veterans Administration hospital. Chart diagnoses of substance use disorders (current and past) as well as the number of PRN doses of acetaminophen, non-steroidal medications, Mylanta, and milk of magnesia were recorded. T-tests and contingency tests were utilized to determine if substance abusers received more PRN OTC medications.

Results: Two patients were excluded due to medical conditions. Abusers and non-abusers did not differ in age, race, and sex (mean age = 44, black = 38%, white = 62%, 100% men). Substance abusers received more doses of acetaminophen (5.92 (SD = 10.08) vs 0.69 (SD = 0.95), t = 4.25, df = 1, 50, $p < 0.5$) and more OTC medications overall (6.92 (SD = 11.58) vs 1.19 (SD = 1.28), t = 3.85, df = 1,50, $p < 0.6$) than non-abusers. Similar results were obtained when current abusers were excluded.

Conclusions: This study suggests that substance abusers may have an increased use of PRN OTC medications while on an inpatient psychiatric ward, possibly reflecting overutilization. The reasons for this finding and the relationship of this phenomenon to other treatment issues are unclear. Further research is necessary to confirm and extend these findings.

NR13 Monday, May 6, 9:00 a.m.-10:30 a.m.

Follow-Up Study of Persons Dually Diagnosed with Mental Illness and Substance Use Disorders

Scot McNary, M.A., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Lisa B. Dixon, M.D., Anthony F. Lehman, M.D.

Summary:

Objective: This study of the natural history of persons with substance use disorders and mental illness compares one-year outcomes of three groups: patients with psychoactive substance use disorders (PSUD) *and* independent mental disorder (IMD) (N = 71); PSUD *and* a PSUD-induced mental disorder (N = 38); and IMD and *no* PSUD (N = 59)

Methods: Baseline and one-year follow-up interviews of 168 consecutively admitted inpatients received the SCID for DSM-III-R, the Quality of Life Interview, and Brief Psychiatric Rating Scale, and the Addiction Severity Index.

Results: Patients with PSUD-induced mental disorders were more likely to have been rehospitalized on follow-up (58%) than the other groups (39% (IMD + PSUD), 31% (IMD only) $p < .05$). Patients with baseline IMDs were more likely to have an IMD at follow-up than patients with baseline PSUD-induced mental disorders (IMD + PSUD, 59% IMD only, 66%; PSUD-induced mental disorder, 33%, $p < .01$). However, no group differences were observed in the likelihood of any mental disorder, independent or PSUD-induced, at follow-up. One-year group differences in other variables were largely accounted for by baseline differences.

Conclusions: This study shows the extent to which persons with PSUD-induced mental disorders are high utilizers of hospital. This may reflect inadequate services for these persons. All groups appear to have consistent, but different, ongoing service needs.

NR14 Monday, May 6, 9:00 a.m.-10:30 a.m.

Social Phobia in Cocaine-Dependent Individuals

Hugh Myrick, M.D., Psychiatry, Med University of SC, 171 Ashley Avenue, Charleston SC 29425; Kathleen T. Brady, M.D.

Summary:

To explore the relationship between social phobia and cocaine dependence, 156 individuals entering a pharmacologic treatment trial for cocaine dependence were administered the Structured Clinical Interview for DSM III-R and several other standardized measures of psychopathology and substance use. Twenty-two individuals met DSM III-R criteria for social phobia and in all but one case the social phobia preceded the cocaine dependence. With the exception of marital status, there were no significant differences in demographics between the two groups. The social phobia group was compared with 22 age- and sex-matched controls. Cocaine dependent individuals with social phobia were more likely to experience cocaine paranoia ($p \leq 0.05$), to have greater incidence of polysubstance abuse the month prior to study entry ($p \leq 0.1$), and less 12-step attendance ($p \leq 0.05$). In regard to psychopathology, the individuals in the social phobia group were more likely to have another Axis I disorder ($p \leq 0.05$) and particularly another anxiety disorder ($p \leq 0.05$). Their HAM-D ($p \leq 0.0001$) and BDI ($p \leq 0.001$) scores were significantly higher and more suicidal ideation endorsed ($p \leq 0.05$). Treatment implications of these data will be discussed.

NR15 Monday, May 6, 9:00 a.m.-10:30 a.m.

Carbohydrate-Deficient Transferrin in Alcoholics

Richard Saini, M.D., Psychiatry, University of Penn, 3900 Chestnut Street, Philadelphia PA 19104; Helen M. Pettinati, Ph.D., Ann E. Semwanga, B.A., Alexia L. Wolf, B.A., Alan Sharf, B.S.,

Summary:

Objective: This study focused on the utility of the liver enzyme carbohydrate-deficient transferrin (CDT), in an alcohol dependent treatment-seeking population, as a marker of alcohol consumption and severity of alcohol dependence.

Methods: Blood serum samples were collected from 47 DSM-III-R alcohol dependent subjects (26 males and 21 females) and assayed for CDT and gamma-glutamyl transferase (GGT), another marker commonly utilized in alcoholics. Subjects were also administered the Addiction Severity Index (ASI) to obtain an alcohol composite score reflecting the severity of their alcohol dependence, and were assessed for alcohol consumption during the three months preceding the study.

Results: Mean CDT values were 24.4 units/liter(U/L) ($sd = 16.3$) for males and 21.2 U/L ($sd = 7.6$) for females. Using the laboratory supplied cut-off values of 17 U/L for males and 25 U/L for females, CDT was abnormal in 12 of 26 males (46%) and four of 21 females (19%). Mean levels of GGT were 141.5 U/L ($sd = 396.5$) for males and 99.7 U/L ($sd = 189.9$) for females. Using reference cut-off values of 85 U/L for males and 70 U/L for females, GGT was abnormal in eight of the 26 alcohol dependent males (31%) and six of the 21 alcohol dependent females (29%). Percentages of abnormal CDT values were dissimilar to those for GGT, and were uncorrelated ($r = -.08$, $df = 45$). CDT correlated significantly with the number of standard alcohol drinks consumed in the past month in male alcoholics (Pearson $r = .60$, $df = 24$; $p < .001$) but not in female alcoholics ($r = .08$, $df = 19$). CDT correlated significantly with the alcohol composite score of the Addiction Severity Index (ASI) for male alcoholics ($r = .54$, $df = 24$; $p < .01$) but not for female alcoholics ($r = -.09$, $df = 19$). In contrast, GGT did not correlate with alcohol consumption or ASI composite scores for either males or females.

Conclusions: Using the reference cut-off values, the majority of this treatment-seeking alcohol dependent population had normal CDT and GGT values at presentation for treatment. However in males, CDT values (but not GGT) correlated significantly not only with alcohol consumption but also with alcohol severity.

NR16 Monday, May 6, 9:00 a.m.-10:30 a.m.

Double Diagnosis of Schizophrenia and Chemical Abuse in a Public General Hospital in Spain

Natalia Sartorius, M.D., Psychiatry, Hospitaliz Octubre, Av Andalocia KM5, 4, Madrid 28041, Spain; Guillermo Ponce, M.D., Isabel Herman, M.D., Pablo Del Pino, M.D., Enrique, Ga Bernardo, M.D., Miguel A. Jimenez, M.D.

Summary:

Although in the United States mentally ill chemical-abusing patients have received considerable attention, in most European countries little attention has been paid to this population. This poster will present the prevalence of schizophrenic chemical-abusing patients in a public general hospital in Spain and will describe their clinical, social, and service-utilization profiles. The psychiatric records of all patients (N = 709) hospitalized in the psychiatric inpatient unit of a public general hospital in Madrid, Spain, from January 1991 through December 1994 were reviewed by a team of psychiatrists. A total of 106 patients (13, 4%) met the criteria for both substance use disorder and either an Axis I or an Axis II diagnosis. The most common diagnoses were personality disorder (52, 8%) and schizophrenia (29, 2%), Eighty percent abused alcohol, 60% abused cannabis, 25% abused heroin, 20% abused cocaine, and 74% abused multiple substances. Males were overrepresented (90%), as were single persons (85%), and the unemployed (90%). As a group, these patients consumed a disproportionate amount of mental resources. Data from schizophrenic patients are specially analyzed.

The prevalence of substance-abusing psychiatric patients in this public general hospital in Madrid, Spain, is substantial. Preliminary analyses indicate that the clinical and social profiles of these patients are comparable to those of the mentally ill, chemical-abusing population described in the U.S. literature.

NR17 Monday, May 6, 9:00 a.m.-10:30 a.m.

Coping Strategies in Patients with Substance Abuse

Himanshu P. Upadhyaya, M.D., Psychiatry, University of Cincinnati, 341A Shawnee Run, West Carrollton OH 45449; Filomena Rebelo, Eugene Samoza, M.D., Juris P. Mezinski, Ph.D., Susan R. Dyrenforth, Ph.D.

Summary:

The objective of this study was to identify coping strategies used by substance abusing patients. Our hypotheses were: (1) Substance abuse patients use **disengagement** as a coping strategy rather than **engagement**. (2) Patients with legal or employment problems are more likely to use disengagement. (3) Cocaine abusing patients are more likely to use disengagement than are alcohol abusing patients. The method consisted of giving the Coping Strategies Inventory (CSI, 40 question self-rating scale) to 392 patients enrolled in substance abuse treatment at the VA medical center, Cincinnati, Ohio. This measure has several scales, including summary scores for engagement vs. disengagement coping styles. The patients were also given the Addiction Severity Index (ASI), which is a structured interview measuring patient functioning in seven problem areas: medical, employment, alcohol, drug, legal, social, and psychiatric. The results showed that alcohol was the most frequent substance abuse problem (48.5%), followed by poly-drug use, including alcohol (17.8%). Poly-drug use without alcohol was third in frequency (12.5%), followed by cocaine use (12%). It should be noted that cocaine use occurred in both poly-drug categories. Analysis of the coping strategies data revealed no statistically significant difference between the mean engagement score and the mean disengagement score when collapsed across all drugs ($p > .05$). Hypothesis 1 was not supported. In addition, the correlation between engagement and disengagement scores was non significant ($r = .08, > .05$). It was concluded that engagement and disengagement scores are two different coping styles, but are not polar opposites on the same continuum. Therefore, further analyses were performed by dividing the patients into groups using a median split on engagement and disengagement scores. This yielded four groups: (1) high engagement-high disengagement, (2) high engagement-low disengagement, (3) low engagement-high disengagement, and (4) low engagement-low disengagement. A MANOVA was performed using these four groups as independent variables and the seven ASI problem areas as dependent variables. Rao's R was significant ($p < .0000001$), indicating there were differences between the four groups on the seven dependent variables. The Neuman-Keuls post hoc test was used to probe for these differences. It was found that the high engagement-low disengagement group was least likely to have medical, alcohol, drug, social, and psychiatric problems. However, there were no differences between the four groups on employment and legal problems. Therefore hypothesis 2 was not supported. The mean disengagement score for cocaine patients was higher than their engagement score ($p < .05$). Conversely, the mean disengagement score for alcohol patients was lower than their mean engagement score ($p < .05$). Therefore, hypothesis 3 was supported. In general, it was found that disengagement was more predictive of harm, than engagement was predictive of benefit. Perhaps this implies that clinicians should put more effort into identifying and eliminating maladaptive coping styles than on teaching adaptive behaviors which may already be present.

NR18 Monday, May 6, 9:00 a.m.-10:30 a.m.

Outcomes of Methadone-Maintained Pregnant Women

Janet D. Woolery, M.D., Psychiatry, University of Maryland, 645 West Redwood Avenue, Baltimore MD 21201; Manjiri M. Pansare, M.D., Lisa B. Dixon, M.D., Robert P. Schwartz, M.D.

Summary:

Objective: The purpose of this study is to examine the patient characteristics and treatment outcomes in heroin dependent pregnant women receiving treatment at a university-based methadone program.

Methods: We reviewed charts of all women referred to the clinic from July 1994 to July 1995 (N = 22) who completed the program or were referred for more intensive services. Demographic information, substance abuse history, urine toxicology screens, and obstetrical complication rates were examined.

Results: The women were a mean age of 28 years (SD 4.8) years, 86% black, 71% single; 56% did not complete high school, and 50% were living alone. A total of 42% of the patients used cocaine in addition to heroin at referral. Overall, 14 women had complications at delivery. The complication rate was associated with an increased percentage of positive urines (73% vs 25%, $p < .05$). More positive urines were significantly associated with living alone ($p < .05$); there was also a trend linking positive urines with cocaine use at admission ($p < .10$). Increased weeks of gestation at delivery was associated at the trend level with receipt of financial support from family ($p < .10$) as well as living with family or significant others ($p < .10$).

Conclusions: This study confirms that substance use in pregnancy is associated with increased complications, and suggests that women receiving financial and psychosocial support from families and others may have improved outcomes. More research is necessary to investigate the link between patient's social network, drug treatment, and obstetrical outcome.

NR19 Monday, May 6, 9:00 a.m.-10:30 a.m.

Risk Factors for Depression in Patients with Coronary Artery Disease

Michael B. Gonzalez, B.S., Psychiatry, Duke University Med Center, Box 3018, Durham NC 27710; Ted B. Snyderman, B.A., Jeffery T. Colket, B.S., Rebekka M. Arias, B.S., Christopher M. O'Connor, M.D., K. Ranga Krishnan, M.D.

Summary:

Objective: The adverse effects of depression on functioning and mortality in patients with coronary artery disease (CAD) have been well documented. The present study was designed to test the hypothesis that severity of medical illness and familial history of psychopathology constitute risk factors for major depressive episode (MDE) in the CAD patient.

Method: Ninety-nine patients with CAD received a psychiatric diagnostic interview in the inpatient setting at a tertiary care teaching hospital. Medical severity ratings and familial psychopathology history were also obtained.

Results: Twenty-three percent of the patient sample met DSM-IV criteria for MDE. CAD patients with MDE had significantly higher medical severity ratings and a higher prevalence of familial psychopathology. Specifically, family history of mental or nervous disorder, drug abuse, nerve-medicine use, and suicide were associated with MDE.

Conclusion: Given the repercussions of depression in CAD patients, it is clinically imperative that MDE be accurately diagnosed and properly treated. Unfortunately, the diagnosis of MDE is often confounded in the medically ill. Close attention to risk factors such as medical severity and familial history of psychopathology may facilitate recognition and substantiation of diagnosis of MDE in the CAD patient population.

NR20 Monday, May 6, 9:00 a.m.-10:30 a.m.

Carbamazepine Versus Haloperidol for the Treatment of Acute Manic Episodes

Carlos A. Hernandez-Avila, M.D., Psychiatry, Univ. Conn. Health Center, 10 Talcott Notch, East Wing, Farmington CT 06032; Hector A. Ortega-Soto, M.D., Antonio Jasso, M.D., Cecilia A. Hasfura-Buenaga, Psic.

Summary:

Objective: To compare the efficiency of carbamazepine (CBZ) and haloperidol (HAL) in the treatment of acute mania.

Method: We studied in a double-blind fashion, 20 inpatients with an acute manic episode, between 18 to 55 years old, free of psychotropic medication for the previous two weeks. Patients were assessed weekly with the Brief Psychiatric Rating Scale (BPRS) and the Bech and Rafaelsen Mania Assessment Scale (MAS) for five weeks. They were randomly assigned to CBZ or HAL. The initial dose was three identical capsules per day, each containing 200 mg of CBZ or 5 mg of HAL. The dose was increased by one capsule at the 4th and 7th day, and every subsequent weekly assessment, if an improvement > 25% in the MAS and BPRS scores was not found.

Results: 75% of the subjects were females, with a mean age of 35.3 +/- 11.1 years. Initially, the symptoms severity was similar in both groups (MAS: CBZ 30.7 +/- 3.3 vs. HAL 27.3 +/- 7.1; BPRS: CBZ 24.2 +/- 8 vs. HAL 20.45 +/- 6.8). A therapeutic response was found since the first week of treatment (improvement on MAS score: CBZ 34% vs HAL 43%), with no significant differences between groups (ANOVA: $F < 1$) and a significant effect of time ($p < 0.001$). The overall improvement on the MAS scores was 71% for the CBZ group and 67% for the HAL group, but there was a higher frequency of behavioral decontrol episodes in the CBZ group (50%) than in the HAL group (10%).

Conclusions: The acute antimanic effect of CBZ is similar to that of HAL and should be considered as an option in the management of patients with an acute manic episode.

NR21 Monday, May 6, 9:00 a.m.-10:30 a.m.

A Family Study of Seasonality in Seasonal and Nonseasonal Mood Disorders

Edwin M. Tam, M.D., Psychiatry, University of B.C., 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Kerry Jang, Ph.D., Raymond W. Lam, M.D., Lakshmi N. Yatham, M.D., Judy M. Allen, M.D., Maria R. Corral, M.D., A.P. Zis, M.D.,

Summary:

Objective: To explore the genetic component of seasonality and seasonal affective disorder (SAD).

Methods: SAD and nonSAD probands diagnosed by DSM-IV criteria were recruited from an outpatient mood disorders clinic. Consent was obtained to interview family members. First-degree relatives were interviewed by telephone with the Toronto Depression and Seasons Interview (TDSI), a structured interview that assesses seasonality and generates DSM-IV criteria for depression. The two groups were compared with regards to seasonality and the presence of SAD using t-test and chi-square test as appropriate.

Results: Preliminary results are based on 101 and 50 family members from 33 SAD and 15 nonSAD probands, respectively. Depression was endorsed by 31.8% of family members, while criteria for SAD were met in 3.31%. The average Global Seasonality Score (GSS) was 4.34. There was no significant difference in GSS between the two groups (SAD vs. nonSAD, 4.29 vs. 4.46, $p = .78$), and no significant difference in the rate of SAD (SAD vs. nonSAD, 3% vs. 4%, $p = 1.00$).

Conclusions: Families of SAD and nonSAD patients do not differ either in rates of seasonal affective disorder or in seasonality scores. These data do not support a major role of genetic transmission in SAD.

NR22 Monday, May 6, 9:00 a.m.-10:30 a.m.

Recidivism in Major Depressive Disorder

Michael E. Doyle, M.D., Psychiatry, Walter Reed VAMC, Borden Pavilion, Washington DC 20307; Lawrence A. Labbate, M.D.,

Summary:

Objective: While recidivism has been studied in psychotic disorders, little has specifically been done to determine what differences exist between patients admitted multiple times compared with those admitted once for major depressive disorder (MDD).

Method: The records of patients admitted with MDD to a large military medical center were reviewed during the years 1991–1995. Recidivists were the first 39 patients admitted three or more times during the period. The comparison sample were 32 patients admitted for the first time in 1993 without subsequent admission. Patients groups were compared for age, gender, comorbidity, and the presence of medical conditions contributing to their admission.

Results: Recidivists (17 male, 22 female; mean age 47) were older than patients admitted once (16 male, 17 female; mean age 37) ($t = 2.6$, $p = .01$). Recurrent MDD was more common in the recidivists ($X^2 = 12.3$, $p < 0.001$) than in patients admitted once. Recidivists were more likely to have a medical condition contributing to their admission ($X^2 = 6.2$, $p = 0.01$). There was a trend toward recidivists being more likely to have a diagnosed personality disorder ($X^2 = 3.6$, $p = 0.06$). For both groups comorbid Axis I disorders were common, but there were no statistically significant differences. The were no differences in sex or rates of substance abuse.

Conclusion: Recidivism for MDD in this sample seemed more related to the depressive illness and associated medical conditions than to comorbid Axis I or II conditions.

NR23 Monday, May 6, 9:00 a.m.-10:30 a.m.

Longitudinal Assessment of Quality of Life in Patients with Major Depression

Jeffrey M. Pyne, M.D., Psychiatry, UCSD, 9500 Gilman Drive MC 0603, San Diego CA 92093; Robert M. Kaplan, M.D., Thomas L. Patterson, Ph.D.,

Summary:

Objective: This study examines the relationship between a quality-of-life measure and depressive symptoms over a six-month period of time.

Method: 163 patients with primary major depressive disorder and 82 controls from the SDVAMC and surrounding community were followed over six-month period. Diagnoses were made by concensus using SCID criteria for DSM-III-R. In addition the DIS (Diagnostic Interview Schedule), IMED (Interval Medical), HDRS, BDI, and QWB (Quality of Well-Being) were collected at entry and six months.

Results: Patients were divided into three groups based on DIS criteria for current depression. The groups included those who were not depressed and remained not depressed (N-N), those who were not depressed and became depressed (N-D), and those who remained depressed (D-D). In a multiple regression analysis, using the QWB as the dependent variable and age, IMED as the independent variables, the difference between groups was statistically significant at both T1 (p less than 0.001) and T2 (p less than 0.001). These differences remained significant after controlling for IMED and age.

Conclusion: The QWB is sensitive over time to changing symptoms of depression in patients diagnosed with major depression. The advantages of the QWB are its use in cost/utility analyses, over 20 years of use in general medical settings, and its being based on a social preference weighting system. The use of the QWB in the area of public policy will be discussed.

NR24 Monday, May 6, 9:00 a.m.-10:30 a.m.

Consumption of Alcohol, Nicotine and Caffeine Among Outpatients with Mood and Anxiety Disorders: Presentation and Impact on Treatment

John J. Worthington III, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street, WACC 815, Boston MA 02114; Maurizio Fava, M.D., Mark H. Pollack, M.D., Michael W. Otto, Ph.D., Eliza T. McArdle, B.A., Jerrold F. Rosenbaum, M.D.,

Summary:

Background: The comorbidity of substance abuse with mood and anxiety disorders is an issue of critical clinical importance and increasing research efforts. However, there has been little attention to the impact of consumption of alcohol, nicotine, and caffeine in moderate amounts on the presentation and response to treatment of patients presenting with primary mood and anxiety disorders in general psychiatric practice.

Objective: In the present study we assessed these patterns of consumption, psychiatric comorbidity, and response to treatment in patients with mood and anxiety disorders.

Method: Eligible subjects were outpatients between the ages of 18 and 65 years participating in pharmacologic trials in the Clinical Psychopharmacology Unit of the Massachusetts General Hospital (MGH). Patients received diagnostic assessments using the Structured Clinical Interview for DSM-III-R-Patient Edition. A total of 94 patients from the Depression Research Program and 51 patients from the Anxiety Disorders Research Program were enrolled in this pilot study. Patients were assessed with the MGH Drug Consumption Questionnaire, the 21-item Hamilton Rating Scale for Anxiety, the 17-item Hamilton Rating Scale for Depression, and the Clinical Global Impression.

Results: Data collection in this pilot study is ongoing. Preliminary analyses show that 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 illness at baseline.

Conclusions: Delineation of the nature and impact of alcohol and other substance consumption on response to treatment will spur efforts to develop targeted pharmacologic and behavioral strategies to reduce use in psychiatric outpatients and improve treatment outcome.

NR25 Monday, May 6, 9:00 a.m.-10:30 a.m.

Lithium: Efficacy for Bipolar Depression Revisited

Claudia F. Baldassano, M.D., Psychiatry, Mass General Hospital, 50 Staniford Street, 4th Floor, Boston MA 02114; Gary S. Sachs, M.D., S. Nassir Ghaemi, M.D., Christina D. Demopulos, M.D., Christine J. Truman, B.A., Una Jain, B.A.,

Summary:

Objective: Double-blind controlled studies established lithium's effectiveness for both mania and depression. Since recent open studies have failed to detect lithium's antimanic efficacy, this review was undertaken to determine lithium's efficacy for bipolar depression.

Method: The MGH bipolar clinic database was searched for outpatients meeting DSM-IV criteria for bipolar disorder, depressed phase over a one-year period. Patients were excluded if they received lithium previously. Clinical Global Inventory-Improvement score (CGI-I) was assigned for outcome of treatment four weeks after starting lithium. The CGI-I was based on structured ratings made by the treating psychiatrist at each follow-up visit, which included assignment of a clinical status based on DSM-IV mood disorder criteria, clinical global impression (CGI), and global assessment of function.

Results: For the 24 eligible subjects, the mean improvement in the CGI-I was 2.46. Response to lithium was rated satisfactory or better in 58%, while 42% had poor response.

Conclusion: These results are in excellent agreement with results from double-blind controlled studies for bipolar depression. Given the risk of affective switch during treatment with standard antidepressant drugs, our results support lithium as the first-line treatment in bipolar depressed patients.

NR26 Monday, May 6, 9:00 a.m.-10:30 a.m.

Treatment of Bipolar Mixed Mania with Levo-Thyroxine

Kiki D. Chang, M.D., Psychiatry, Univ of Cincinnati, 231 Bethesda ML 559, Cincinnati OH 45267; Paul E. Keck, Jr., M.D.,

Summary:

Background: High rates of subclinical hypothyroidism in patients with rapid-cycling bipolar disorder have been reported (Bauer, et al., 1990). The addition of thyroxine to medication regimens of patients with rapid-cycling bipolar disorder has been reported to decrease the frequency of cycling (Bauer, et al., 1990). We have collected data that suggest a similar level of thyroid dysfunction among bipolar patients in mixed manic states, with an increase in the rate of overall hypothyroidism when compared with bipolar patients with pure mania (Chang, et al., in submission). These findings suggest that bipolar patients in a mixed state may benefit from thyroxine treatment as well. We report data on an open trial

of four patients with bipolar disorder in mixed states who were treated with levo-thyroxine.

Method: All four patients were adults with bipolar disorder who were displaying mixed mania. Each was treated with divalproex sodium with serum levels in the therapeutic range (50–120 ug/ml). TSH values ranged from 3.8–6.6 mU/L (normal .4–5.0 mU/L). None of the patients had prior exposure to lithium or known previous thyroid disease. Treatment was begun with L-thyroxine (Synthroid) after each patient experienced a partial response to divalproex sodium alone with a subsequent plateau in improvement. HAM-D and Young Mania Rating Scale (YMRS) assessments were performed before and after thyroxine treatment to assess severity of mixed mania in each patient.

Results: All four patients showed improvement in HAM-D and YMRS scores. Average improvement in scores, final doses of L-thyroxine, mean TSH, and treatment time course will all be presented.

Conclusions: L-thyroxine supplementation of divalproex sodium in patients with mixed mania partially responsive to the latter agent may convert partial to full therapeutic response.

NR27 Monday, May 6, 9:00 a.m.-10:30 a.m.

Rapid Cycling Associated with Low Choline in the Basal Ganglia

Christina D. Demopulos, M.D., Psychiatry, Mass General Hospital, ACC 815 15 Parkman Street, Boston MA 02114; Perry F. Renshaw, M.D., Gary S. Sachs, M.D., B. Frederick, M.D., Beny Lafer, M.D., Andrew L. Stoll, M.D.,

Summary:

Objective: Choline may play an important role in neurochemical processes relevant to mood regulation. High brain choline levels have been reported in association with depressed mood, and an open study reported rapid-cycling patients refractory to lithium improved when receiving choline. This pilot study was undertaken to test the hypothesis that bipolar patients with a history of rapid cycling (RC) would have a lower brain Choline:Creatine ratio as determined by proton magnetic resonance spectroscopy (MRS) than bipolar patients without a history of rapid cycling.

Methods: Investigators blind to the clinical diagnosis used proton MRS to determine the basal ganglia Choline:Creatine ratio (N = 25). RC subjects were matched for sex, age, and mood state with non-rapid-cycling patients, and mean Choline:Creatine ratios were compared using paired t-test.

Results: A trend was observed for a lower Choline:Creatine ratio in RC patients than in bipolar patients without a history of rapid cycling.

Conclusion: Although the results did not reach the $p < .05$ level of significance, brain Choline:Creatine ratios may be a useful way to subtype bipolar patients. Proton MRS may be a useful technique for diagnostic assessment.

NR28 Monday, May 6, 9:00 a.m.-10:30 a.m.

A Controlled Study of Antidepressant Treatment of Postpartum Depression

C. Neill Epperson, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Christopher J. McDougle, M.D., Deborah Ward-O'Brien, M.S.N., Lawrence H. Price, M.D.,

Summary:

Ten percent of childbearing women will develop depression after delivery. To date, there has been no published report of a double-blind, placebo-controlled study of antidepressant treatment in postpartum depression. The purpose of this ongoing study is further our knowledge of the phenomenology, neurobiology, and pharmacological treatment of major depression that has its onset within six months of childbirth.

Methods: Subjects were outpatients of the Yale Postpartum Mood Disorders Clinic and met DSM-IV criteria for major depression with onset of symptoms within the first six months of childbirth. After a one-to two-week placebo lead-in, women were randomized to sertraline (Zoloft) or placebo for six weeks. The main outcome measures for antidepressant response were the Hamilton Rating Scale for Depression and the Clinical Global Impression scale.

Results: Thus far, six of 14 women who have been screened have entered the study. The mean age $\pm$ S.D. of those enrolled is 29.1 $\pm$ 4.6 years. One woman, who was randomized to sertraline, was a "responder," while two others are still in the double-blind phase. Of the two women who decompensated while on placebo, both have subsequently "responded" to open-label sertraline. The sixth patient, who dropped out, was also on active sertraline and was improved at her last appointment.

Conclusions: Preliminary findings from this ongoing study indicate that sertraline may be efficacious in the treatment of postpartum depression. Detailed results including comorbid diagnoses, severity of depression, and personal and family psychiatric history will be presented.

NR29 Monday, May 6, 9:00 a.m.-10:30 a.m.

Insight in SAD: Results of a Treatment Trial

S. Nassir Ghaemi, M.D., Aff Dis Prog, Medical College of VA, Box 980710, Richmond VA 23298; Gary S. Sachs, M.D., Claudia F. Baldassano, M.D., Christine J. Truman, B.A.,

Summary:

Objective: Lack of insight is a major clinical problem in the treatment of psychotic and affective disorders. No studies of insight in seasonal affective disorder (SAD) have been reported.

Methods: 16 patients with SCID-diagnosed SAD but no other Axis I conditions were treated acutely with light therapy. Insight was measured with the Scale to Assess Unawareness of Mental Disorder (SUMD) as modified by the authors to assess self-report of insight into depressive symptoms. Increasing scores (1–5) indicated increasing unawareness of illness (i.e., less insight).

Results: SAD patients displayed a moderate amount of insight when depressed (mean SUMD score = 2.4). When recovered, they showed no significant change in insight into past depressive symptoms (mean SUMD score = 2.7). Insight into current depressive symptoms and Hamilton Depression Rating Scale scores (HDRS) displayed a modest correlation ($r = 0.43$, $p = 0.10$).

Conclusion: SAD patients possess a moderate amount of insight into depressive symptoms, which does not change after recovery, a result that agrees with studies of insight in psychosis and mania. Further, in SAD, increased severity of illness may be associated with increased insight into depressive symptoms, a result not suggested by previous studies of mania or psychosis.

NR30 Monday, May 6, 9:00 a.m.-10:30 a.m.

Dreams and Imaginary Activity in Depressed Patients

Raphael Giachetti, M.D., Psychiatric Hospital, Casselardit Purpan, Toulouse 31059, France; Laurent Schmitt, M.D., Maurice Bensoussan, M.D., Michel Escande, M.D., Sylvie Bourie, M.D., Marc Benatia, M.D.,

Summary:

Objective: Dream activity and diurnal equivalents: reverie, creativity, magical thought are compared between depressed subjects and controls. Recently, K. M. Beauchemin (1995) and Riemann et al., (1990) indicated that dream activity is dependant on mood state.

Method: 30 Unipolar hospitalized patients under antidepressants are compared with a sample of 307 subjects ranging from 18 to 80 years old. A questionnaire of 11 items is used, including items such as frequency of dreams, content of dreams, emotions linked with dreams, reverie, magical thought, creativity, and awareness of spatiotemporality. Items are rated using an analogic visual scale.

Results: Depressed patients reveal a significant decrease in imaginary activity ($P < 0.001$). Frequency of dreams ($P < 0.01$), content of dreams ($P < 0.01$) interest in dreams ($P < 0.1$), and questions about dreams ($P < 0.001$) are reduced in depressed. Facility to express feelings and interest about dreams are correleted. In both groups, women mention more frequent dreams than men (women: 70.9%; men: 56%); women are more interested by their dreams than men (women: 50.7%; men: 31%).

Conclusion: This study shows that dream and imagery are significantly impoverished in depressed patients.

NR31 Monday, May 6, 9:00 a.m.-10:30 a.m.

Improved Self-Awareness Upon Resolution of Depression in Patients with SAD

Dina R. Hirshfeld, Ph.D., Psychiatry, Mass General Hospital, 50 Staniford MGH Res, 4th Flr, Boston MA 02114; Mark A. Blais, Ph.D., Michael W. Otto, Ph.D., Una Jain, B.A., Christine J. Truman, B.A., Gary S. Sachs, M.D.,

Summary:

Objective: To examine whether insight about personality characteristics improves upon successful treatment among patients depressed with seasonal pattern.

Method: Fourteen patients depressed with seasonal pattern (by DSM-IV) and treated successfully with phototherapy (≤ 50% reduction in Hamilton Depression Scale) were assessed for personality characteristics and global self-perception of personality traits before and after treatment. Personality traits on "Big Five" factors were assessed via the NEO-PI-R inventory. Global self-perception of traits was assessed by asking subjects to rate themselves on the five dimensions on a visual analog scale. Self-awareness scores were generated by calculating the number of accurate matches between ratings of "high," "average," or "low" on the visual analog scale and the NEO for each of the five scales (range: 0–5).

Results: Wilcoxon rank tests revealed that subjects' self-ratings were more accurate after treatment ($z = -2.40$, $p = .017$). The mean (± SD) number of accurate matches before and after treatment were 1.5 (± 1.1) and 2.4 (± 1.2), respectively.

Conclusion: Results suggest that upon successful resolution of depression, patients with seasonal affective disorder reveal more accurate awareness of personality traits. Findings will be presented on an expanded sample.

NR32 Monday, May 6, 9:00 a.m.-10:30 a.m.

SAD and Personality Characteristics: Assessing Personality Traits of Pre-Treatment and Post-Treatment Phases of Seasonal Depression

Una Jain, B.A., Psychiatry, Mass General Hospital, 15 Parkman Street WACC 815, Boston MA 02114; Gary S. Sachs, M.D., Christine J. Truman, B.A., Mark A. Blais, Ph.D., Michael W. Otto, Ph.D., Dina R. Hirshfeld, Ph.D.,

Summary:

Objective: To evaluate the impact of depression on NEO personality-inventory scale scores.

Method: The NEO Personality-Inventory was administered to patients meeting DSM-IV criteria for depression with seasonal pattern. The NEO was readministered to patients who met recovery criteria after six weeks of phototherapy. The influence of change in depression status on each of the five NEO personality factors was evaluated using paired t-test.

Results: 18 patients entered the study. Results are reported for the 16 who met recovery criteria (Ham-D ≤ 8). With recovery significant decreases were observed in neuroticism (mean change = 11.857, p-value = .0112). Significant increases were observed in extraversion (mc = -5.143, p-value = .0182), agreeableness (mc = 4.857, p-value = .0199), and conscientiousness (mc = 3.643, p-value = .0373). Openness did not change significantly with recovery from depression (mc = -1.000, p-value = .6259).

Conclusion: These data suggest that neuroticism, extraversion, agreeableness, and conscientiousness may be influenced by the occurrence and recovery from a major depressive episode and therefore amenable to treatment. The NEO openness scale score may assess a trait less influenced by mood state.

NR33 Monday, May 6, 9:00 a.m.-10:30 a.m.

Nefazodone in Major Depression and Blood Levels

Cecilia M. Jorge, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue, Ste. 304A, Miami FL 33136; Paul J. Goodnick, M.D., C. Lindsay DeVane, Pharm.D., Joseph Henry, M.D.

Summary:

Nefazodone is a recently released antidepressant with combined presynaptic serotonin reuptake inhibition and postsynaptic S2 blocking activity. We have recently conducted an open 12-week study of up to 600 mg/day of nefazodone in six males and eight females with a mean age of 49.4 ± 10.7 years who met criteria for DSM-IV major depressive disorder. Ten completed the trial; four dropped out for a variety of reasons including spontaneous remission or overwhelming multiple somatic complaints after one to two doses as well as noncompliance to dosage schedule. The ten completers showed a mean improvement in HDRS from 22.4 ± 7.5 to 3.7 ± 2.8 (p. 0001) and in the BDI from 27.3 ± 7.7 to 6.5 ± 5.4 (p .0001). We collected end-of-study blood levels of nefazodone and its metabolites. Results relating response to blood levels will be presented at the meeting.

NR34 Monday, May 6, 9:00 a.m.-10:30 a.m.

Diurnal Variation in CSF Serotonin Concentrations in Healthy Humans

Paul D. Kirwin, M.D., Psychiatry, Yale University, 34 Park Street, 3rd Floor, New Haven CT 06508; Christopher J. McDougle, M.D., George M. Anderson, Ph.D., George R. Heninger, M.D., James F. Leckman, M.D., Lawrence H. Price, M.D.,

Summary:

The role of serotonin (5-HT) in the pathogenesis and treatment of depression continues to be the subject of extensive research. Previous studies examining central 5-HT functioning measured CSF levels of 5-hydroxyindoleacetic acid (5-HIAA) by using single or multiple lumbar punctures. Recently several groups have demonstrated the feasibility of continuous CSF sampling via an indwelling lumbar catheter.

Methods: Healthy volunteers, aged 21–34 years, underwent continuous CSF sampling. CSF was collected at a constant rate of 1 ml every 10 minutes over a 30-hour period, with levels of the 5-HT precursor and metabolite, tryptophan, and 5-HIAA, measured every 30 minutes.

Results: To date, four females have completed the study. Adverse side effects included mild headaches responsive to bedrest,

oral fluids, and Tylenol. CSF levels of 5-HIAA and tryptophan, and 5-HT related measures in blood and urine will be presented.

Conclusion: Previous studies have utilized pharmacologic probes and peripheral response measures to explore 5-HT dysfunction in depression. The continuous CSF sampling paradigm provides the opportunity to directly examine changes in brain 5-HT, over time, in response to centrally acting pharmacologic probes.

NR35 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Quantitative EEG in Major Depression: Before and After Treatment

Jun Soo Kwon, M.D., Psychiatry, Seoul National Univ Hospital, 28 Yongon-Dong Chongro-Gu, Seoul 110-744, Korea; Tak Youn, M.D., Hee Yeon Jung, M.D.,

Summary:

Objective: To compare bipolar absolute and relative power of quantitative electroencephalography (QEEG) between major depression and normal controls, and to find the changes of QEEG after clinical improvement.

Method: The QEEG of drug-free depressed patients was compared to sex- and age-matched controls using spectral analysis. The QEEG after clinical improvement was also analyzed. The subjects were 20 right-handed patients suffering from major depression (according to the DSM-III-R). All subjects were improved by six-week antidepressant treatment; their Hamilton Rating Scale for Depression (HRSD) scores were reduced more than 50% after clinical improvement. The Wilcoxon signed rank test and the stepwise discriminant analysis was performed.

Result: In depressed patients, bipolar absolute delta and theta powers in right hemisphere were increased significantly. By discriminant analysis, the absolute power of theta at P4-02, T3-T5, delta at F8-T4 served to discriminate and correctly classified 85% of the depressed group and 75% of the controls. Although symptoms were improved, there were no significant differences in QEEG before and after treatment. The abnormal QEEG features persisted.

Conclusion: It is suggested that right hemisphere plays an important role in major depression. Depressive symptoms and QEEG features are not changed at the same time. QEEG features of major depression appear to need more time to become normalized or they could be a trait marker.

NR36 Monday, May 6, 9:00 a.m.-10:30 a.m.

Heterogeneity of Depressives' Attentional Deficits

Sophie Lemelin, B.Ps., Psychiatry, Hop Enfant-Jesus, 1401 18ieme Rue, Quebec G1J 1Z4, Canada; Philippe Baruch, M.D., Annick Vincent, M.D., Pierre Vincent, M.D.,

Summary:

As proposed by several authors, a wide range of cognitive impairments depressives, including memory deficits, could be due to an attentional disturbance, but few studies have directly analyzed this attentional deficit. Performance on the Stroop Color-Word Test, a classical selective attention test, is impaired in depression. However, a Stroop deficit may reflect a specific distractor inhibition disturbance as well as a global reduction of attentional resources.

Objective: To specify the cognitive mechanism underlying the Stroop impairment of depressed patients in order to better understand the attentional deficit of these patients.

Method: Untreated age- and sex-matched major depressives (n = 33) and normal subjects (n = 30) were evaluated using a modified computerized Stroop test comprised of three tasks: to name the color of XXXXXs, of non-conflicting words (e.g. TABLE printed in green), and of conflicting color words (e.g. BLUE printed in green). It was hypothesized that, unlike color words, non-conflicting word distractors would disturb the color naming task only in the case of a primary distractor inhibition disturbance.

Results: The slow depressives and fast depressives, according to their color naming speed without distractors, were contrasted in order to distinguish depressives with and without clear signs of resource deficit. It was found that interference produced by non-conflicting words was greater in fast depressives than in either slow depressives or normal subjects, while interference caused by color words was dramatically stronger in slow depressives than in other groups.

Conclusions: Results suggested the existence of two different attentional deficit patterns in clinical depression: some depressives have a distractor inhibition disturbance while others are deficient in processing resources.

NR37 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Efficacy of a Passive Body Heating Procedure in Depressed Patients

John R. Meyers, M.D., Psychiatry, NY Hospital, 525 East 68th Street, New York NY 10021; Dale A. D'Mello, M.D., Anne M. Miller, D.O., Dominic V. Barberio, D.O., Donald Athearn, R.N., Neha Shah,

Summary:

Objective: Passive body heating procedures such as a warm bath have demonstrated efficacy in increasing the duration of slow wave sleep in normal healthy volunteers. The clinical relevance of similar procedures in depressive illness has not been previously substantiated.

Method: A prospective study of 45 patients with major depression on a psychiatric unit in a mid-Michigan general hospital, examined the effect of a single 30-minute warm water bath on subjective mood, using the Profile of Mood States (POMS) questionnaire.

Results: Substantial declines were observed on the tension-anxiety, depression-dejection, anger-hostility, and confusion-bewilderment scores.

Conclusion: A warm bath may serve as an effective, inexpensive, and practical adjunct in the management of patients with depressive illness.

NR38 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Efficacy of a Warm Water Bath On Subjective Sleep Quality in Depressive Illness

Anne M. Miller, D.O., Psychiatry, Michigan State University, West Fee Hall, East Lansing MI 48824; Dale A. D'Mello, M.D., John R. Meyers, M.D., Dominic V. Barberio, D.O., Donald Athearn, R.N., Neha Shah,

Summary:

Objective: A passive body heating procedure such as a warm water bath is known to increase the duration of slow wave sleep in normal subjects, but the effect on patients with severe depressive illness has not been previously demonstrated.

Method: A prospective study of 45 patients hospitalized with major depression examined the effect of a single 30-minute warm water bath taken two hours before bedtime on subsequent nocturnal sleep using a sleep questionnaire.

Results: The number of hours slept before and after the bath remained constant. However, there was a substantial decrease (15 minutes) in sleep latency ($T = 2.03$, $df = 39$, $p < 0.05$). A similar decrease was observed in the number of nocturnal awakenings ($T = 3.06$, $df = 41$, $p < 0.005$), suggesting an increase in

the depth of sleep. The patients also reported feeling more refreshed upon awakening the morning after the bath.

Conclusions: A warm water bath may serve as an effective, inexpensive, and practical adjunct in the management of patients with depression accompanied by insomnia.

NR39 Monday, May 6, 9:00 a.m.-10:30 a.m.

Attention Deficit in Psychotic Depression

Erik B. Nelson, M.D., Psychiatry, University of Cincinnati, 231 Bethesda Avenue, Cincinnati OH 45267; Kenji Sax, Ph.D., Mark Setters, B.S., Stephen M. Strakowski, M.D.,

Summary:

Objective: This study was designed to use the Continuous Performance Test (CPT) to measure attention in patients with major depression, psychotic depression, and schizophrenia in order to determine if patients with psychotic depression or non-psychotic depression have attention deficits similar to that found in schizophrenia.

Method: A total of 37 patients with major depression without psychosis, psychotic depression, or schizophrenia as diagnosed by the Structured Clinical Interview for DSM-III-R were recruited from inpatient and outpatient psychiatric facilities at the University of Cincinnati. Subjects completed the CPT and the Hamilton Depression Scale (Ham-D). CPT results and Ham-D scores were analyzed among the three diagnostic groups and a control group of 40 subjects using the Tukey (HSD) Test.

Results: There was a significant ($p \leq .05$) impairment in overall CPT performance in the group with psychotic depression and the group with schizophrenia. The group with non-psychotic depression and the control group performed equally on the CPT.

Conclusion: Although patients with major depression without psychosis often report difficulty concentrating, we did not find any impairment in core attentional functioning as measured by the CPT in this group. However, patients with psychotic depression and schizophrenia both showed significant impairment in attention. This suggests that impaired attention as measured by the CPT occurs in major depression only in the presence of psychosis.

NR40 Monday, May 6, 9:00 a.m.-10:30 a.m.

Thyroid Indices in Mood Disordered Adolescent Inpatients

Rachael S. Nelson, M.D., Psychiatry, Walter Reed AMC, Borden Pavilion, Washington DC 20307; Lawrence A. Labbate, M.D.,

Summary:

Objectives: 1) To determine the frequency of hyper- and hypothyroidism in adolescent inpatients with mood disorders, and 2) to determine if there are differences in basal thyroid hormone levels between mood disordered adolescents and adjustment disorder controls.

Method: Admission thyroid function tests of 49 consecutive adolescent inpatients with mood disorders (32 girls; 14 bipolar, manic, 35 major depression; mean age 15.5) who were admitted for the first time were evaluated. Those included did not have a substance abuse or eating disorder diagnosis, nor were they taking lithium, anticonvulsants, or antidepressants. These patients were compared with 23 consecutive inpatients (14 girls, mean age 17.2) diagnosed with adjustment disorder with the same exclusion criteria.

Results: Of the depressed patients, there were two patients with subclinical hyperthyroidism (low TSH, nl FT4), one with subclinical hypothyroidism (high TSH, nl FT4), and two with low FT4 and normal TSH. For the bipolar patients, two evidenced subclinical hypothyroidism, and one with low FT4 and nl TSH. For the adjustment disorder patients, there were two cases of subclinical hyperthyroidism. None of the mood disordered or adjustment disorder patients had overt hypo- or hyperthyroidism. There were no differences between groups when comparisons were made among values for TSH, FT4, or T4.

Conclusion: Clinically important thyroid abnormalities appear uncommon among adolescent inpatients with mood disorders. Testing may be reserved for refractory cases or when clinical suspicion is high for thyroid disease. We did not find differences in basal thyroid levels between groups as was previously reported, possibly because our controls were inpatients.

NR41 Monday, May 6, 9:00 a.m.-10:30 a.m.

Atypical Depression: A Cluster Analysis

Heather A. Robertson, M.D., Psychiatry, University of BC, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Raymond W. Lam, M.D., Justine N. Stewart, B.Sc., Lakshmi N. Yatham, M.D., Kathleen A. McGarvey, M.D., Edwin M. Tam, M.D., A.P. Zis, M.D.

Summary:

Objective: Our objective was to examine the interrelationships between DSM-IV atypical depressive symptoms using cluster analysis.

Method: 109 patients diagnosed with DSM-IV major depressive episodes were examined using the Atypical Depression Diagnostic Scale (ADDS), a semi-structured interview that rates mood reactivity, rejection sensitivity, and reverse vegetative symptoms (hypersomnia, hyperphagia, leaden paralysis). A heirarchical cluster analysis was conducted to determine cluster membership based on these symptoms.

Results: A five cluster solution maximized the differences between groups and symptoms. In these clusters, there appeared to be an association between rejection sensitivity and hyperphagia, but not hypersomnia or leaden paralysis. Mood reactivity was not always associated with the other atypical depressive symptoms. The largest cluster ($n = 51$) consisted of patients with moderate mood reactivity, low rejection sensitivity, and low reverse vegetative symptoms (melancholic pattern). There were two clusters with high reverse vegetative symptoms; one with high mood reactivity and rejection sensitivity ($n = 4$), and the other having low mood reactivity and rejection sensitivity ($n = 11$). The remaining two clusters differed primarily on the severity of the reverse vegetative symptoms.

Conclusions: As there was no clear relationship between mood reactivity, rejection sensitivity, and reverse vegetative symptoms, there may be diagnostic and clinical heterogeneity in the DSM-IV concept of atypical depression.

NR42 Monday, May 6, 9:00 a.m.-10:30 a.m.

Thyroid Function in Adolescents with Mixed Versus Pure Mania

Cesar A. Soutullo, M.D., Psychiatry, University of Cincinnati, 231 Bethesda Avenue ML0559, Cincinnati OH 45267; Kiki D. Chang, M.D., Sean P. Stanton, B.S., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Scott A. West, M.D.

Summary:

A number of previous studies have reported an association between subclinical hypothyroidism and mixed mania or rapid cycling in adults with bipolar disorder (Chang, et al., 1995). Studies indicate that mixed mania may represent a distinct clinical state separate from pure mania, with a poorer outcome and different response to pharmacological treatment (McElroy, et al., 1992). Sokolov, et al., have also reported abnormalities in thyroid function in adolescents with mood disorders similar to those found in adults

(Sokolov et al. 1994). In this study, we examined possible differences in thyroid function in adolescents with mixed versus pure mania and compared these findings with those of adults.

Method: The sample (N = 65) included bipolar patients admitted to the psychiatric wards at the University of Cincinnati Hospital. Patients were separated into two groups: adolescents, ages 12–18 (n = 29), and adults, ages 19–65 (n = 36). In each of these two groups, patients were further separated into mixed and pure mania by the Structured Interview for the DSM-III-R: adolescents with mixed mania (n = 16) or pure mania (n = 13) and adults with mixed mania (n = 11) or pure mania (n = 25). Plasma concentrations of TSH, T3, and T4 were measured in each group by immunoassay (Immunol, Technicon). Results comparing the two adult groups were previously reported (Chang, et al., 1995).

Results: The majority of the adolescent patients had thyroid hormone levels within the normal range. Grade II hypothyroidism was present in 12.5% of adolescents with mixed mania and 0% of adolescents with pure mania. However, there were no significant differences in plasma concentrations of TSH, T3, or T4 in adolescents with mixed mania compared with adolescents with pure mania. Furthermore, in comparing adolescents and adults with mixed mania we found no significant difference in plasma concentrations of TSH, T4, or T3. However, when comparing adolescents and adults with pure mania we found a significant difference in T4 levels (mean ± SD = 7.25 ± 1.08 vs. 8.64 ± 2.45, $p < .04$, respectively), but not in TSH or T3.

Conclusions: Similar rates of subclinical hypothyroidism were present in adolescents and adults with mixed mania (12.5% vs. 14%, respectively). However, although the adult population showed differences in thyroid function in mixed compared to pure mania, the adolescent group did not. These results suggest that the differences in thyroid function between mixed and pure mania may emerge at a later age.

NR43 Monday, May 6, 9:00 a.m.-10:30 a.m.

Pattern of Illness Revisited: Duration of Depression 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., Christina D. Demopulos, M.D., Una Jain, B.A.

Summary:

Previous studies suggest the pattern of depressive and manic phases within an episode of bipolar illness is predictive of response to lithium prophylaxis. The present study examined the influence of pattern of episode and other clinical variables (age of onset, treatment, and seasonality) on the duration of depressive episodes.

Methods: The affective episodes of 100 bipolar patients observed during two periods, of open naturalistic treatment were categorized into four episode types: monophasic, biphasic with initial mood elevation, biphasic with initial depression, and polyphasic. Duration of episodes was based on prospective assessments made by the treating psychiatrist at routine follow-up visits including the structured clinical interview for DSM II-R mood modules, Global Assessment of Functioning, Clinical Global Impression, and assignment of a clinical status.

Results: Episode duration and time until recovery varied between groups. Polyphasic episodes and continuous cycling episodes had a longer duration than monophasic episodes. Monophasic depressive episodes were longer than monophasic episodes of mania. Similarly, the duration of depression tended to exceed the duration of mood elevation associated with polyphasic episodes.

Conclusion: Improved knowledge of the natural course of bipolar illness may improve management of bipolar patients.

NR44 Monday, May 6, 9:00 a.m.-10:30 a.m.

Seasonality of Maniac Depressive Illness: 50 Years

Diane K. Whitney, M.D., Mood Disorder Unit, London Psych Hospital, 850 Highbury Avenue, London ON N6A 4H1, Canada; Verinder Sharma, M.D., Karen Kueneman, B.A.

Summary:

Objective: To investigate whether a seasonal pattern exists for admissions of manic-depressive illness at a provincial psychiatric hospital.

Method: A review of the case conference books was conducted to collect data for the decades 1920 to 1960. The admissions were divided according to season for each mood state (mania; depression, mixed).

Results: There were 1,482 admissions for mania, 1,493 for depression, and 552 for mixed states over the 50 years. Using chi square for analysis, no seasonal pattern of admissions for mania was evident. There was a preponderance of admissions for depression in spring and summer, but this did not reach statistical significance. For mixed states, there was a peak incidence of admissions in the summer ($x^2 = 15.43$, $p < .01$).

Conclusions: The findings in this study do not support the results of most studies that have shown a peak incidence for major depressive episodes in spring and autumn and for mania in summer. The authors believe that the peak incidence for summer admissions of mixed states is a unique finding that has not been previously reported.

NR45 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Effects of Clomiphene Citrate on Mood: A Pilot Study

Katherine E. Williams, M.D., Psychiatry, Stanford University, 401 Quarry Road, Stanford CA 94305; Regina K. Casper, M.D.

Summary:

Objectives: Clomiphene citrate, a nonsteroidal weak estrogen, is associated with significantly increased mid-cycle and mid-luteal estradiol levels. Women taking Clomiphene for infertility frequently complain of marked affective lability most pronounced during the luteal phase. In this pilot study we investigated whether Clomiphene is associated with significant changes in depression and anxiety and whether same-day mood symptoms correlate with same-day gonadal hormone levels.

Methods: Eleven female outpatients with unexplained infertility recruited from a university infertility clinic completed baseline BECK and POMS. These pre-treatment assessments were compared with scores at mid-cycle, mid-luteal, and late luteal phase, at which time estradiol and progesterone levels were also drawn. Women completed a 21-item daily rating form of mood symptoms as well.

Results: We found no significant changes in mood symptoms during Clomiphene treatment, and same-day hormone levels did not correlate with measures of anxiety or depression. We found a significant decrease in fatigue during the mid-luteal phase. Discussion: Our finding of significantly decreased fatigue during the mid-luteal phase when estradiol levels. The lack of statistically significant change in depression and anxiety despite significant hormone fluctuations in Clomiphene cycles supports the majority of studies in the literature which find no direct correlation between hormone levels and mood in female-specific mood disorders.

NR46 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Relationship of Shame in Depression Versus Mania

Sean P. Stanton, B.S., Psychiatry, University of Cincinnati, 231 Bethesda Avenue ML 559, Cincinnati OH 45267; Paul Gilbert,

Ph.D., Daniel R. Wilson, M.D., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D.

Summary:

Apart from their diagnostic criteria, as operationalized in DSM-IV or ICD-10, depression and mania have other interesting characteristics associated with submissive behavior, shame proneness, negative social comparison, and entrapment. These primitive self-concepts arising from social competition could play a fundamental role in the phylogeny of human self-esteem. (Gilbert, et al., 1994) Our hypothesis was depression would predict low self-appraisal and mania would predict high self-appraisal based on specific rating scales. A further hypothesis is that standardized ratings of shame and related mechanisms of self-appraisal may predict psychopharmacologic treatment response, i.e., depressed patients would lower in rating scale score while the manic patients would increase in the course of treatment.

Methods: Patients (N = 16) were evaluated using six scales: the Entrapment Scale (E2), the Other as Shamer Scale (OAS), the Defeat Scale (D scale), the Social Comparison Scale (SCS), and two submissive behavior scales (ACTS2P-M and ACTSM). Mania (N = 9) or depression (N = 7) was determined through Structured Clinical Interview for the DSM-III-R (SCID). The patients were evaluated on an inpatient unit as part of ongoing depression and mania protocols. The scales were evaluated blind to pharmacological treatment but unblind to diagnosis. The scales were totaled and variance was determined by wilcoxon signed rank test from SAS.

Results: The depressed patient showed a significantly higher mean entrapment (E2 total score: depressed 57.6 ± 8.9, mania 24.4 ± 15.8; $p < 0.001$), mean shame (OAS total score: depressed 70.9 ± 14.1, mania 42.4 ± 13.7; $p < 0.005$), mean defeat (D scale total score: depressed 50.8 ± 6.8, mania 19.6 ± 11.0; $p < 0.001$), mean submissive behavior (ACTSM total score: 35.8 ± 6.1, mania 20.7 ± 10.4; $p < 0.01$) when compared to the patients with mania. Mania showed higher results only when evaluating mean social comparison (social comparison total: depressed 41.7 ± 33.9, mania 128.3 ± 21.8; $p < 0.004$). The second submissive behavior scale (ACTS-2P-M: depressed 33.3 ± 3.3, mania 30.8 ± 5.7) showed no mean difference. The patients were matched by age, race, socioeconomic status, and education. There were 67% male patients with mania and 71% females with depression.

Conclusion: As predicted, patients with depression evidenced low self-appraisal on most of the scales: total entrapment (E2 57 ± 8.9), shame proneness (OAS 70.9 ± 14.1), social comparison (SCS 41 ± 33.9), defeat (D scale 50.8 ± 6.8), and submissive behavior (ACTSM 35.8 ± 6.1). The second submissive behavior scale showed equal findings (ACTS2P-M 33.3 ± 3.3-depressed and 30.8 ± 5.7-mania). Longitudinal data, including patterns of response to pharmacologic treatment are being collected which appear to support these empirical findings.

NR47 Monday, May 6, 9:00 a.m.-10:30 a.m.

A Survey of Massachusetts Psychiatrists Regarding Antidepressant Maintenance Failure

Sarah E. Byrne, B.A., S Belknap Bldg, McLean Hospital, 115 Mill Street, Belmont MA 02178; Anthony J. Rothschild, M.D.

Summary:

We surveyed 300 members of the Massachusetts Psychiatric Society who identified their specialties as psychopharmacology on affective disorders about their response to a fictional case in which a patient became depressed while on long-term antidepressant therapy. A total of 142 psychiatrists responded to the survey; 131 physicians (92%) said they had patients who became depressed while taking SSRIs after a period of good response. The proportion of their patients taking SSRIs who relapsed was estimated as 1% to 10% by 50 respondents (35%), 11% to 20% by 50 (35%), 21% to 30% by 25 (18%), and over 30% by 9 (6%). Eighty (56%) said that they saw no common characteristics in such patients, while 14 (10%) believe they are more often female. Six (4%) believe there is often Axis II comorbidity; other answers were less frequent.

If the fictional patient had been taking 20 mg of fluoxetine, 129 respondents would choose to increase the dose, nine to augment the medication with tricyclic antidepressants or lithium, and four to change to a different antidepressant. Similar responses were obtained for 100 mg sertraline (n = 126, 12, and 3, respectively), nortriptyline (n = 67, 45, and 26), and 40 mg fluoxetine (n = 80, 37, and 17).

NR48 Monday, May 6, 9:00 a.m.-10:30 a.m.

Risperidone Treatment in Tardive Dystonia

Manuel M. Marquez, M.D., Psychiatry, Mollet Hospital, Cristobal Colon 1, Barcelona Mollet 08100, Spain; Diego J. Palao, M.D., Inma O. Jodar, Ph.D.

Summary:

Introduction: Use of risperidone has not been reported for treatment of tardive dystonia, an uncommon and disabling syndrome. Two cases of schizophrenic patients with tardive dystonia were treated with risperidone are presented.

Case 1: Mr A, a 31-year-old schizophrenic patient, began to experience dystonic symptoms in his trunk and legs after being started on trifluperazine. The dystonia persisted for the following two years, and trifluperazine was then discontinued. A regimen of risperidone and trihexyphenidyl was initiated, and the dystonia gradually resolved over a period of six months.

Case 2: Mr B, a 21-year-old schizophrenic patient, developed dystonia in his neck (retrocolli), trunk, and limbs 10 months after a regimen of trifluperazine was initiated. Three months later, trifluperazine was discontinued, and tetrabenazine, clonidine, and trihexyphenidyl were added. He did not improve from the dystonia, and he subsequently experienced a psychotic exacerbation. He was started on risperidone, and he gradually recovered from the dystonic symptoms as well as from the psychotic relapse.

Conclusion: These two cases suggest that risperidone may be a safe and useful antipsychotic in schizophrenic patients with tardive dystonia.

NR49 Monday, May 6, 9:00 a.m.-10:30 a.m.

Comparison of Extrapyramidal Syndrome with Haldol and Risperidol

Phillip W. Antunes, M.D., Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Cheryl Preece, M.S., Mary Marek, B.S., Jack D. Burke, Jr., M.D.

Summary:

Objective: To study the frequency of extrapyramidal side effects (EPS) among psychiatric patients taking Haldol or Risperidol in a general clinical practice.

Methods: Electronic medical records with full-text search capabilities permitted review of all patients seen in the Scott and White department of psychiatry taking Haldol and/or Risperidol from January 1994 to September 1995. A total of 164 patients qualified for this study. Information was collected on demographics, follow-up, change in drug dose, occurrence of EPS, and the need for medication for EPS side effects.

Results: There are no statistically significant differences between the two groups with respect to demographics and weeks of follow-up. There are no statistically significant differences between the Haldol and Risperidol groups with respect to incidence of side effects ($p = 0.87$; 48% vs. 49%), use of medications or side effects

(p = 0.84; 18% vs. 19%), number of dosage changes (p = .011; 43% vs. 56%), or among incidence of drug change (p = 0.08; 12% vs. 3%).

Conclusion: Previous clinical studies using formal protocols and selected patients demonstrated that Risperidol at optimal doses (6 mg/day) is associated with much fewer EPS than Haldol. The findings from this study suggest that EPS may occur as often with Risperidol as with Haldol in general clinical practice. Further analyses examining the effects of dose on EPS and the effects of switching from one medication to another will be carried out. Additional comparative studies on the frequency of EPS with Risperidol versus conventional antipsychotics should be performed as more clinical experience with this medication is gained.

NR50 Monday, May 6, 9:00 a.m.-10:30 a.m.

Use of SSRIs with Terfenadine and Astemizole

John Snuggs, M.D., Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Mary Marek, B.S., Cheryl Preece, M.S., Jack D. Burke, Jr., M.D.

Summary:

Objective: SSRIs have been shown to inhibit several cytochrome P450 enzymes including cytochrome P450-3A4, which metabolizes the nonsedating antihistamines terfenadine and astemizole. The purpose of this project was to document side effects among psychiatric and internal medicine patients using SSRI antidepressants and the nonsedating antihistamines.

Methods: Electronic medical records for outpatients seen in the Scott and White psychiatry and community internal medicine departments taking SSRI antidepressants in conjunction with terfenadine and astemizole from November, 1993 to October, 1995 were considered eligible for review. A total of 41 charts were reviewed and included in the study. Six of the 41 patients were followed while on different combinations for a total of 47 cases.

Results: In three cases (6%), patients experienced heart palpitations or arrhythmias. These patients were on a combination of Prozac/Seldane, Prozac/Hismanal, and Zoloft/Seldane. In one case (2%), a patient experienced syncope while taking Paxil and Seldane. This patient was later switched to Prozac/Seldane and experienced heart palpitations.

Conclusion: The inhibition of cytochrome P450-3A4 by SSRI antidepressants may cause terfenadine and astemizole toxicity resulting in cardiac arrhythmias in a small group of patients taking SSRIs and these nonsedating antihistamines.

NR51 Monday, May 6, 9:00 a.m.-10:30 a.m.

Laboratory Monitoring in the Use of Lithium

Jonathan C. Lockhart, M.D., Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Mary Marek, B.S., Cheryl Preece, M.S., Jack D. Burke, Jr., M.D.

Summary:

Objective: The purpose of this study is to document compliance with published laboratory monitoring guidelines among patients prescribed lithium for psychiatric disorders.

Methods: Electronic medical records for all outpatients who were first prescribed lithium during 1994 in the Scott and White psychiatry department were considered eligible for review. A total of 48 charts were reviewed and included in the study. Information was collected on laboratory values measured both prior to and during treatment with lithium and compared to published recommendations.

Results: Less than 57% of the patients received recommended laboratory evaluation prior to initiation of lithium treatment when measures of thyroid function, renal function, CBC, glucose, and EKG were considered. Similarly, following initiation of lithium treatment, less than 61% of patients received minimum recommended frequency of these measures. Monitoring of lithium levels was significantly more consistent with recommendations.

Conclusion: The use of electronic medical records make it possible to efficiently examine various aspects of medical practice in the clinical setting. This chart review demonstrates the contrast between published recommendations and actual practice in the treatment of a group of patients using lithium. Future work needs to be conducted to ensure adequate laboratory testing in this patient population.

NR52 Monday, May 6, 9:00 a.m.-10:30 a.m.

Pituitary Microadenoma, Risperidone and Clozapine

Rahim Shafa, M.D., Psychiatry, Harvard Med School, Mass MHC, Brocton VAMC, 74 Fenwood Drive, Boston MA 02115; Jayendra K. Patel, M.D., Anthony G. Kalinowski, Ph.D., Joseph J. Schildkraut, M.D., Alan I. Green, M.D.

Summary:

Introduction: Typical neuroleptic drugs, which block dopamine D2 receptors, elevate serum prolactin (PRL) and have been reported to cause pituitary microadenomas to enlarge. Risperidone, although different in its side-effect profile from standard neuroleptics, also increases PRL. By contrast, the atypical neuroleptic clozapine, perhaps because of its weak D2 action and its ability to release dopamine in the tuberoinfundibular area, does not significantly increase serum PRL. We report here on PRL level and tumor size in a patient with a pituitary microadenoma during treatment first with risperidone and later with clozapine.

Method: A 30-year-old woman with schizoaffective disorder and an elevated PRL level was studied with an MRI while being treated with risperidone, valproate, and clonazepam. An oral contraceptive was added to treat amenorrhea. She then went through a three-month trial of an experimental neuroleptic, valproate, and clonazepam. After the trial, clozapine was begun, and valproate, clonazepam, and the oral contraceptive were continued. During clozapine treatment, PRL was reassessed and the MRI scans redone.

Results: During treatment with risperidone, the PRL was elevated (94 ng/ml; nl 3.3–26.7 ng/ml) and an enlarged pituitary microadenoma was seen on MRI. After six weeks of clozapine treatment, the PRL level was normal and the repeat MRI showed a substantial decrease in the size of the adenoma. The MRI images will be presented.

Conclusion: Since a number of variables could have influenced our findings (including the interim treatment period between risperidone and clozapine, as well as the use of an oral contraceptive), our findings must be interpreted with caution. However, it appears that in this patient with a pituitary microadenoma, her PRL level was elevated and the tumor was enlarged during risperidone treatment, while during treatment with clozapine, her PRL level was normal and the tumor was smaller in size. Thus, this case suggests that clozapine may be an appropriate neuroleptic for psychotic patients with PRL secreting pituitary microadenomas.

NR53 Monday, May 6, 9:00 a.m.-10:30 a.m.

Effect of Psychotropic Medication on Seizure Threshold and Duration in ECT

A. Chris Heath, M.D., Psychiatry, Southwestern University, 5323 Harry Hines Blvd., Dallas TX 75235; Stephen H. Dinwiddie, M.D., Keith E. Isenberg, M.D., Michael R. Jarvis, M.D., Charles F. Zorumski, Jr., M.D.

Summary:

Objectives: To examine the effect of administration of psychotropic medication on seizure threshold and seizure duration in patients treated with electroconvulsive therapy (ECT).

Method: Seizure threshold was estimated at first right unilateral (RUL) treatment on 470 patients. Stimulation was initiated at 25 mC and increased in increments of approximately 25 mC to 100 mC; further stimulation, if needed, was given at > 500 mC. Clinical data, including drugs prescribed in the 24 hours prior to first treatment, were obtained by retrospective chart review and analyzed with SAS.

Results: Treatment with benzodiazepines was associated with lower seizure threshold and a trend toward shorter seizure duration. No clear effect on seizure threshold was seen with tricyclic antidepressants, but a trend toward lower threshold was seen with fluoxetine; neither showed an effect on duration. Antipsychotic medications were not associated with change in seizure threshold or duration, but lithium was associated with decreased seizure threshold.

Conclusions: With few exceptions, psychotropic medications given prior to ECT lack substantial effect on seizure threshold or duration after allowing for effects of charge, age, and health status.

NR54 Monday, May 6, 9:00 a.m.-10:30 a.m.

Pharmacokinetics and Pharmacodynamics of Adinazolam

Kotra Ajir, M.D., Psychiatry, Rei Harbor-UCLA, 1124 Carson Street B4 South, Torrance CA 00509; Michael W. Smith, M.D., Keh-Ming Lin, M.D., Russell E. Poland, Ph.D., Joseph C. Fleishaker, Ph.D., James H. Chambers

Summary:

Pharmacokinetics and pharmacodynamics of adinazolam and N-demethyl adinazolam (NDMAD), its major metabolite, were compared in 39 healthy male volunteers (13 Asian, 12 Caucasian, and 14 African-American). Subjects were administered oral adinazolam mesylate SR tablets, parenteral (IV) adinazolam mesylate, IV NDMAD, oral placebo tablets, and IV sterile water (placebo) in a four-way crossover design. Venous blood samples were collected at specific time intervals after drug administration and assayed for adinazolam and NDMAD concentrations. Sedation was rated at the time of each blood draw according to the Nurse-Rated Sedation Scale, and the digit-symbol substitution test was administered to evaluate psychomotor performance. After IV administration of adinazolam, Asians manifested significantly higher concentrations (higher Cmax and larger AUC) of both adinazolam and NDMAD than their Caucasian and African-American counterparts and slower CL than Caucasians after IV administration of both adinazolam and NDMAD. Similarly, Asians manifested larger AUC and slower CL than both of the other ethnic groups after oral administration of adinazolam mesylate SR tablets; however, this difference did not achieve clinical significance. These results are in accordance with previous observations of differences in pharmacokinetics of medications between the three ethnic groups studied. In this study, pharmacodynamic differences were not noted between the three study groups. However other studies have demonstrated increased pharmacodynamic effects of adinazolam on African-American subjects.

NR55 Monday, May 6, 9:00 a.m.-10:30 a.m.

Olanzapine Versus Haloperidol in the Treatment of Schizophrenia

Douglas R. Dolnak, D.O., Research, NAPA State Hospital, 2100 Napa-Vallejo Hwy., Napa CA 94558; Kyungtak Minn, M.D., Mary Wieneke, Ph.D., Cheryl Watson, R.N., Scott Espinoza, RA-1

Summary:

Olanzapine is an antipsychotic agent with affinity for various receptors including dopamine D2, dopamine D1, cholinergic, muscarinic, and serotonin 5HT2. Preliminary clinical data suggest that this agent has a favorable efficacy profile and adverse event profile. In this double-blind study, 17 patients who met the DSM-III-R criteria for schizophrenia or schizoaffective disorder were administered both olanzapine or haloperidol in single doses of 5mg/day to 20mg/day. All patients who were randomized in the study had a minimum score of 18 on the Brief Psychiatric Rating Scale (BPRS), stable medical conditions, and were taking no concomitant psychotropics except benzodiazepines. Efficacy assessments were conducted using PANSS and CGI rating scales. Safety assessments were monitored using clinical laboratory tests and adverse physical symptoms.

The results of this study indicate no significant difference between haloperidol and olanzapine at four weeks of treatment with respect to BPRS and to positive and negative symptoms. At 12 weeks of treatment, the olanzapine group demonstrated no significant change in BPRS scores since baseline. The olanzapine group, however, had fewer extrapyramidal symptoms compared with the haloperidol group. With respect to extrapyramidal symptoms, the adverse event profile of olanzapine may be more favorable than typical antipsychotics.

NR56 Monday, May 6, 9:00 a.m.-10:30 a.m.

Clozapine Treatment Increases Serum Glutamate Compared to Conventional Neuroleptics

Anne E. Evins, M.D., Psychiatry, Mass General Hospital, 25 Staniford Street, Boston MA 02115; Donald C. Goff, M.D., Edward Amico, M.Ed., Vivian Shih, M.D.,

Summary:

In a previous study, our group found that patients treated with clozapine had significantly higher serum glutamate concentrations than patients treated with conventional neuroleptics. In addition, D-cycloserine, a partial agonist at the glycine modulatory site of the glutamatergic NMDA receptor, significantly improved negative symptoms when added to conventional neuroleptics and worsened negative symptoms when added to clozapine. Baseline glycine concentrations predicted response of negative symptoms with D-cycloserine. The aim of this study was to prospectively measure the effects of switching from conventional neuroleptics to clozapine on serum concentrations of glutamate, aspartate, and glycine and to examine correlative relationships between these amino acid concentrations and changes in clinical measures.

Method: After obtaining informed consent, blood was drawn from seven patients with schizophrenia (six male, one female, mean age 48 $\pm$ 4 years) while receiving conventional neuroleptics and again three to 18 months after switching to clozapine (mean dose 39 $\pm$ 61 mg), (mean duration clozapine treatment 8.4 $\pm$ 3.6 mos). Serum samples were stored at – 80°C until assays of glutamate, aspartate, and glycine were performed using a Beckman 6300 Amino Acid Analyzer quantitative ion exchange column. BPRS and SANS were performed at the time of phlebotomy.

Results: Serum glutamate concentrations were significantly higher in patients on clozapine (mean 71.1 $\pm$ 28.7 micromoles/1) than patients on conventional neuroleptics (mean 49.2 $\pm$ 27.0 micromoles/1) ($df = 5$, $t = 2.34$, $p = 0.03$, one tailed). The improvement in scores on the Negative Symptom Subscale of the BPRS correlated significantly with baseline serum glycine concentrations ($df = 5$, $r = 0.79$, $p = 0.03$), and, at a trend level, with glutamate ($df = 5$, $r = 0.67$, $p = 0.1$). Changes in the SANS scores did

not correlate significantly with amino acid levels, nor did serum concentrations of aspartate correlate with ratings of clinical symptoms.

Conclusions: This small, prospective study replicates our previous finding that clozapine treatment is associated with an elevation of serum glutamate levels and further supports the hypothesis that clozapine's effects upon amino acid concentrations may reflect activity at glutamatergic sites in the brain, which may contribute to clozapine's superior efficacy for negative symptoms of schizophrenia.

NR57 Monday, May 6, 9:00 a.m.-10:30 a.m.

Use of ECT with Treatment-Resistant Depressed Patients: A Randomized Trial ECT Versus Paroxetine

Here W. Folkerts, M.D., Clinic Muenster, Psychiatric University, Albert-Schweitzer Str 11, Muenser 48149, Germany

Summary:

Objective: Failure to respond to adequate pharmacological treatment for major depression now stands as the most common indication for the use of ECT. The putative advantages of ECT with respect to both speed and quality of response are clinically important issues, but surprisingly little research has examined the efficacy of ECT relative to newer antidepressant agents like the selective serotonin reuptake inhibitors (SSRI).

Methods: 39 subjects with major depression and with at least two failed antidepressant trials (mean 4.95 trials) were randomized to either paroxetine treatment (n = 18), or right unilateral (RUL) ECT (n = 21). Strength of pharmacological treatment trials was rated.

Results: ECT was consistently superior to paroxetine. Until the end of the study treatment (ECT two or three weeks; paroxetine four weeks) we found a reduction of the HAM-D score of 59.8% for the ECT group and of 29.5% for the paroxetine group ($p < 0.000$ paired t-test). In the ECT group 71.4% fulfilled the response criteria (decrease of total HAM-D by 50% or more). Following failure of paroxetine after four weeks, seven of 18 patients received RUL-ECT; all seven patients now fulfilled the response criteria. There were only weak correlations between medication resistance and ECT outcome.

Conclusions: The results of the study strongly suggest that ECT is superior to paroxetine in medication-resistant major depression with respect to both speed and quality of response.

NR58 Monday, May 6, 9:00 a.m.-10:30 a.m.

Designing GABA Receptor Subunit-Selective Agents: Toward "Better Benzodiazepines"

Rona T. Hu, M.D., Neuroscience, National Institute of Health, 4903 Edgemoor Lane #808, Bethesda MD 20814; Ruiyan Liu, Ph.D., Phil Skolnick, Ph.D., James M. Cook, Ph.D.,

Summary:

Objective: Benzodiazepines, barbiturates, and ethanol are commonly used $GABA_A$ receptor agonists. All have multiple clinical effects, including--in varying degrees--anxiolysis, sedation, anticonvulsant activity, amnesia, respiratory depression, ataxia, tolerance, and withdrawal. Designing drugs with fewer side effects is an obviously desireable goal. Developing insights about $GABA_A$ receptor subunits, their differential distribution in brain regions, and the affinities of different drugs offer great hope for more specific pharmacologic agents.

Method: $GABA_A$ receptors containing $\alpha 5$ subunits were targeted because of their narrow distribution in the brain. A series of novel imidazo-benzodiazepines, synthesized based on the prototype Ro15-4513, was tested in vitro and in vivo. In recombinant $GABA_A$ receptors, several of these compounds showed high affinity (0.4–5 nM) and up to 75-fold selectivity for $\alpha 5$-containing receptors. Binding studies in native rat hippocampal and cerebellar tissues confirmed an $\alpha 5$-selective profile. In mice, the compounds were potent convulsants, correlating with their affinity and inverse agonist activity.

Results: We report the first highly selective agents for $\alpha 5$-containing $GABA_A$ receptors.

Conclusions: The design of $\alpha 5$-selective agents paves the way for "better benzodiazepines" with narrower, targeted clinical profiles.

NR59 Monday, May 6, 9:00 a.m.-10:30 a.m.

Nefazodone and Hypotension: Complication or Coincidence?

Roy J. Meland, D.O., Psychiatry, Michigan State University, West Fee Hall, East Lansing MI 48824; Dale A. D'Mello, M.D., Sharon Ransom

Summary:

Objectives: Despite its wide therapeutic index and relatively innocuous side effect profile, in pre-marketing clinical trials, nefazodone was associated with a placebo-adjusted incidence of dizziness in 23% of patients. The present study examined the prevalence and clinical consequences of dizziness in a typical clinical setting.

Methods: A retrospective naturalistic review of 16 consecutive patients who received nefazodone on an inpatient psychiatric unit in a mid-Michigan general hospital examined clinical, demographic, and treatment variables.

Results: Fifty percent of the patients developed a hypotensive reaction (SBP < 90 mm Hg and/or fall in SBP < 20 mm Hg). The mean drop in systolic pressure was 21 mm Hg ($T = 6.07$, $df = 15$, $p < 0.001$).

Conclusion: Despite the subsequent difficulties encountered with dosage titration, nefazodone was found to be effective even at levels below the recommended starting dosage range. Nevertheless, initiation of nefazodone therapy may require closer scrutiny of blood pressure than initiation of alternative recently introduced antidepressants.

NR60 Monday, May 6, 9:00 a.m.-10:30 a.m.

Desmethylimipramine Induces Glucocorticoid Receptor Translocation In Vitro

Carmine M. Pariante, Psychiatry, Emory University Med School, 1639 Peirce Drive, Ste. 4000, Atlanta GA 30322; Bradley D. Pearce, Ph.D., Tracy L. Pisell, B.S., Andrew H. Miller, M.D.

Summary:

Objective: Antidepressants have been shown to up regulate type II glucocorticoid receptor expression in the brain leading to increased glucocorticoid-mediated negative feedback on the hypothalamic-pituitary-adrenal (HPA) axis. Therefore, antidepressants may normalize the hyperactive HPA axis found in a significant percentage of depressed patients through a direct effect of these drugs on glucocorticoid receptor number and/or function. To further examine the impact of antidepressants on glucocorticoid receptor function, we investigated whether in vitro treatment with the tricyclic antidepressant, desmethylimipramine (DMI), might influence glucocorticoid receptor activation, namely the translocation of the cytoplasmic glucocorticoid receptor from the cytoplasm to the nucleus (where it interacts with DNA to influence cell function).

Method: Mouse fibroblasts (L929 cells) were pretreated with DMI for 24 hours (0.1–10μM) and then incubated in the presence or absence of the synthetic glucocorticoid, dexamethasone (0.1–

10 nM), for 90 minutes. Glucocorticoid receptor translocation was evaluated by an immunostaining procedure which uses a fluorescent-labeled antibody to identify the cellular localization of the glucocorticoid receptor.

Results: DMI was found to increase glucocorticoid receptor translocation from the cytoplasm to the nucleus in the absence of dexamethasone and facilitated dexamethasone-induced glucocorticoid receptor translocation.

Conclusions: These data suggest that DMI may lead to glucocorticoid receptor activation via a glucocorticoid-independent pathway; an effect which could be involved in the mechanism of action of antidepressant drugs.

NR61 Monday, May 6, 9:00 a.m.-10:30 a.m.

New Treatments for SSRI-Induced Sexual Dysfunction

Carol A. Roeloffs, M.D., Payne Whitney Clinic, 425 East 61st, Penthouse Flr., New York NY 10021; Barbara D. Bartlik, M.D., Helen S. Kaplan, M.D., Peter M. Kaplan, M.D., James Koscis, M.D.

Summary:

Sexual dysfunction due to serotonin re-uptake inhibitors is common and can lead to noncompliance and relapse. The estimated proportion of people on SSRIs with decreased libido or orgasmic or erectile dysfunction has been estimated at up to 90%. Suggested treatments include yohimbine, amantadine, cyproheptadine, bupropion, and buspirone, but results have been mixed. Psychostimulants have been noted to enhance sexual functioning. This poster will present observations of 12 cases in which SSRI-induced sexual dysfunction was successfully treated with low dosages of methylphenidate or dexedrine (up to 15 mg and 10 mg, respectively). Ginseng, a Chinese root believed to have aphrodisiac properties, has also been observed to improve SSRI-induced sexual dysfunction in several cases. Double-blind controlled studies are currently underway.

NR62 Monday, May 6, 9:00 a.m.-10:30 a.m.

Sertraline Modulation of Hemostatic Function

Brian P. Skop, M.D., Psychiatry, Wilford Hall, 2200 Bergquist Drive, Ste. 1, Lackland AFB TX 78236; Thomas Neuhauser, M.D., David L. McGlasson, M.S., Hilda A. Best, A.S.C.P.

Summary:

Objective: The selective serotonin reuptake inhibitors (SSRIs) have been implicated in case reports to cause diminished hemostasis. This study attempted to determine whether individuals treated with the SSRI, sertraline, demonstrated alterations in hemostasis.

Method: Subjects being started on sertraline underwent measures of hemostatic function before initiating and after at least one week on the drug. Tests included platelet count, bleeding time, partial thromboplastin time, international normalized ratio, and platelet aggregation studies to adenosine diphosphate, epinephrine, collagen, and arachidonic acid. Individuals with a history of bleeding disorders or on hemostatic altering agents were excluded. Fourteen individuals entered, and 11 subjects completed the study.

Results: Hemostatic tests measured before compared with those measured after initiation of sertraline were not found to be statistically different. No subject experienced bleeding complications during the study.

Conclusions: While the sample size of this study is small, impaired coagulation and platelet aggregation does not appear to be a general consequence of standard dose sertraline therapy. Case reports of bleeding in individuals on SSRIs are likely idiosyncratic. Further investigation of individuals who develop hemostatic difficulties is indicated to identify risk factors for this complication.

NR63 Monday, May 6, 9:00 a.m.-10:30 a.m.

Divalproex Sodium and Thrombocytopenia in a Psychiatric Population

Thomas J. Trannel, M.D., Psychiatry, University of Hawaii, 1319 Punahou Street, 6th Flr, Honolulu HI 96826; Iqbal Ahmed, M.D.

Summary:

Objective: This study explored the occurrence of thrombocytopenia in a psychiatric population taking divalproex sodium.

Method: A chart review was conducted of 36 inpatients who were started on divalproex sodium over a period of 38 months (6/91–8/94). Psychiatric diagnoses/medications, valproic acid dosage/serum levels, and general medical conditions/medications known to cause thrombocytopenia were noted. Mean age was 53 years (range = 22 to 81 years). Baseline hematologic function (wbc, rbc, platelets) were sought and then serially reviewed. The incidence of thrombocytopenia (platelet count < 100,00/mm3) was recorded as well as the average change in platelet count over time.

Results: Patients showed a decrease in platelet count throughout treatment, and this decrease was most significant in the geriatric population. Nine patients (25%) had at least one recorded episode of thrombocytopenia. The incidence of thrombocytopenia was much greater in the geriatric portion of our population (54%, 7 of 13 patients) than those patients under age 63 (9%, 2 of 23 patients). Descriptive statistics, T tests, and Pearson correlation coefficients were used to analyze the data.

Conclusions: Thrombocytopenia may occur more frequently in a geriatric population taking divalproex sodium, and more frequent hematologic monitoring may be necessary in this population.

NR64 Monday, May 6, 9:00 a.m.-10:30 a.m.

Risperidone in the Elderly

Carlos A. Zarate, Jr., M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Arthur Siegel, M.D., Ataru Nakamura, M.D., Mauricio Tohen, M.D., Tanya Cherkerzian, B.S., Ross J. Baldessarini, M.D.

Summary:

This pharmacoepidemiologic study was undertaken to determine the safety and efficacy of risperidone in the elderly and to develop guidelines for its use.

Method: Charts of 122 patients consecutively admitted ℓ 65 years old receiving risperidone were reviewed. The dosing characteristics, adverse effects, and efficacy of risperidone were determined.

Results: One-third of patients had side effects, the most common being hypotension (28.7%), extrapyramidal symptoms (10.7%), and symptomatic orthostatic hypotension (9.8%). The mean dose of risperidone was 1.6 mg/day (and was $\leq$ 2 mg in 78% (95/122) of patients. Significant decreases in blood pressure occurred with risperidone treatment ($p = 0.0001$) and was common in patients with cardiovascular disease, or taking a selective serotonin-reuptake inhibitor (SSRI), or valproate ($p < 0.03$). Two patients had a cardiac arrest and one of them died. Risperidone was effective in 85% (92/108) of patients. Patients taking more than 2 mg/day of risperidone were not more likely to have a better response compared to those taking less than 2 mg/day.

Conclusions: When prescribed with caution, risperidone can be both efficacious and safely used in the elderly. Most patients may benefit from a lower dose and a more gradual titration of risperidone than currently recommended.

NR65 Monday, May 6, 9:00 a.m.-10:30 a.m.

Personality Disorders and OCD: A Meta and Citation Analysis

William T. Howard, M.D., Psychiatry, University of Florida, 1600 SW Archer Road, Gainesville FL 32610; Roger K. Blashfield, Ph.D., Wayne K. Goodman, M.D.

Summary:

A meta-analysis was conducted on 35 articles using the DSM-III or DSM-III-R classifications. These articles reported information on both obsessive compulsive disorder (OCD) and Axis II disorders. The results suggest that Cluster C disorders have the highest prevalence among patients diagnosed with OCD. However, these articles have found no specific link between OCD and compulsive personality disorder. With respect to treatment outcome, the presence of a comorbid personality disorder generally predicts poorer response. Successful treatment of OCD is accompanied by a significant reduction in the prevalence of comorbid Axis II disorders as diagnosed by standardized diagnostic instruments. Generally, the presence of a comorbid Axis II disorder correlates positively with a greater level of psychopathology among OCD patients.

A citation and co-citation analysis performed on the same articles has several implications. The results suggest that this topic is primarily of only recent interest. Foreign authors may be less likely to cite themselves when compared with their American counterparts and may be less likely to be cited by others as well. The co-citation results, when displayed in a sociogram, demonstrate clusters which suggest sociological patterns of authorship.

NR66 Monday, May 6, 9:00 a.m.-10:30 a.m.

A Clinical Study of Rage Attacks and Episodic Dyscontrol in Children and Adolescents with Tourette's Syndrome

Kenneth S. Park, Psychology, Harvard University, 93 Leverett Mail Center, Cambridge MA 02138; Cathy L. Budman, M.D., Ruth D. Bruun, M.D., Madelyn Olson, M.D., Robert Araujo, Ph.D., Hermann Davidovicz, Ph.D.

Summary:

This study sought to determine if there is a relationship between episodic dyscontrol with rage attacks and other conditions known to be associated with Tourette syndrome (TS). A pilot study of 12 children with TS who presented to the Movement Disorders Center with rage attacks and episodic dyscontrol showed in all cases that these patients met diagnostic criteria for comorbid obsessive-compulsive disorder (OCD) and for attention deficit/hyperactivity disorder (ADHD). Fifty-six clinically referred Tourette syndrome children (N = 56, ages 6–16) were assessed in joint parent-child diagnostic interviews. Comorbid rates of ADHD and OCD in TS children with rage attacks (N = 24) were significantly higher than in TS children without rage attacks (N = 32; $p < 0.05$). Comorbid oppositional defiant disorder (ODD) and conduct disorder (CD) were also highly correlated with comorbid rage attacks, while tic severity was decreased in TS children with rage attacks when compared with TS children without rage. These findings suggest the existence of a distinct group of TS cases that requires special treatment methods and further research in this underexplored area of psychiatry.

NR67 Monday, May 6, 9:00 a.m.-10:30 a.m.

Quantitative EEG by Spectral Analysis in Children with ADHD

Bung Nyun Kim, M.D., Psychiatry, Seoul National Univ Hospital, 28 Yongon-Dong, Chongro-Gu, Seoul 110-744, South Korea; Seong Woong Shin, M.D., Jun Soo Kwon, M.D., Soo Churl Cho, M.D.

Summary:

Objective: To test the hypothesis that children with ADHD may have specific findings on topographic EEG using spectral analysis compared to controls, and to find the developmental changes in the profiles of QEEG in ADHD patients.

Method: Through measuring EEG of 20 patients with pure ADHD and 20 normal children whose sex, age, and achievement were matched to patients in standardized environment, we obtained the absolute and relative power of QEEG. The data were statistically analyzed using the Wilcoxon rank sum test.

Results: In absolute and relative power, theta (4–8Hz) and delta (< 3Hz) powers were increased on generalized areas in ADHD patients compared to controls. Although the significant differences in patients were not focal, increased theta and delta power were more prominent in frontal and temporal regions. When we divided the patients and controls into two groups (one group > 108 months, the other ≤ 108 months), in the younger group the difference between controls and patients in QEEG was more prominent than that of the older group.

Conclusion: We confirmed QEEG abnormalities in pure ADHD patients, especially in frontal and temporal areas. Moreover, we found these abnormalities might be lessened as the patients get older. These results may be related to the phenomenon of natural clinical improvement in ADHD as a normal developmental process.

NR68 Monday, May 6, 9:00 a.m.-10:30 a.m.

Psychosocial Adjustment of Chronic Epileptic Children and Their Family in Korea

Bung Nyun Kim, M.D., Psychiatry, Seoul National Univ Hospital, 28 Yongon-Dong, Chongro-Gu, Seoul 110-744, South Korea; Soo Churl Cho, M.D., Yong Seung Hwang, M.D.

Summary:

Objective: To assess comprehensively the impact of chronic epilepsy on the psychological well-being and social adjustment of children with epilepsy and their families; and to find out the factors associated with poor adaptation.

Method: We applied the following scales and questionnaires to 45 idiopathic chronic epileptic children, their family members, and 40 normal controls whose age, sex, and school achievement were matched to patients. We used the following nine scales, which were standardized in Korea. *Parent rating scales*: Yale children's inventory, disruptive behavior disorder scale according to DSM-III-R, parent's attitude to epilepsy questionnaire, family environment scale, symptom check-list-90- revised, child behavior check-list. *Children's self rating scales*: Children's depression inventory, Spielberger's state-trait anxiety scale, Piers-Harris self-concept inventory. The T-test and X2-test were performed to analyze the data.

Results: According to T-test, the mean score of the patient group in the children's depression inventory and state-trait anxiety inventory were higher than controls and reached statistical significance ($p < 0.05$). Some mean scores of the patient group reached highly significant levels ($p < 0.01$) on the Yale children's inventory (academic function, fine motor), Pier-Harris self-concept inventory (happiness, popularity, behavior), disruptive behavior disorder scale (ADHD), symptom check-list 90-revised of family members (all subscales), child behavior check-list, and family environment scale (conflict). According to T-test, X2-test, some factors were found to contribute to the maladjustment of chronic epileptic children and family: family factors (low social class, high score on SCL-90, high conflict score in FES), epileptic factors (younger onset, longer duration of Tx, combination treatment, TLE), paternal

overanxious attitude toward epilepsy, and patients' own poor self-concept.

Discussion: We found the chronic epileptic children and family members were suffering from severe psycho-behavioral problems. The result of this study shows both the patients and family members requiring immediate intensive psychiatric intervention.

NR69 Monday, May 6, 9:00 a.m.-10:30 a.m.

Is Asthma a Predictor of Behavioral Dyscontrol?

Pe Shein Wynn, M.D., Psychiatry, NY Med College, Psychiatric Institute, Valhalla NY 10595; Lawrence E. Levy, M.D., Mohammed R. Khan, M.D., Catherine Karni, M.D.

Summary:

Objective: A history of bronchial asthma (BA) has frequently been noted in children and adolescent emergency psychiatric admissions. Many studies show that emotional factors exacerbate symptoms of BA, but no studies have evaluated the association between asthma and behavioral dyscontrol (BD - aggressive and disruptive behavior). This study looks at the association between BA and BD.

Method: In 1994, all 62 patients (age < 18) admitted with a history of BA were compared with a randomized, age, sex, and race-matched control group. Demographic variables, admitting diagnoses, medication history, alcohol/illicit drug use, and psychiatric symptoms upon admission were collected. Chi-sq tests and multivariate logistic regression analyses were used.

Results: No significant differences were found regarding age, type of education, living status, past history of violence, alcohol, and illicit drug use. A total of 60% of cases with BD had history of BA, versus 40% of the control group ($p < 0.001$). A history of BA was significantly associated with BD (Odd Ratio = 3.3, $p < 0.05$, 95% C.I. = 1.1 to 9.87), controlling for sex, race, concurrent psychiatric symptoms, diagnostic categories, and history of taking asthmatic medications.

Conclusions: Early interventions of asthmatic symptoms, proper use of asthmatic medications, and attention to comorbid emotional disorders are essential strategies to minimize development of behavioral problems.

NR70 Monday, May 6, 9:00 a.m.-10:30 a.m.

Behavioral Side Effects of SSRIs in Children

Amanda N. Holmes, M.D., Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Mary Marek, B.S., Cheryl Preece, M.S., Jack D. Burke, Jr., M.D.

Summary:

Objective: To document behavioral side effects among prepubertal children taking SSRI antidepressants.

Methods: Electronic medical records for outpatients seen in the Scott and White department of Psychiatry ages 12 years and younger taking SSRI antidepressants for the calendar year 1994 were considered eligible for review. A total of 18 charts were reviewed and included in the study. Information was collected on age, gender, indication for SSRI, medication chosen and dosage, comorbid psychiatric diagnoses, other medications in use, behavioral side effects and clinical management of side effects.

Results: Of the 18 subjects, 44% had no behavioral side effects. Breakdown of the remaining 56% is as follows: three subjects had transient exacerbations of existing behavioral problems (oppositionality and hyperactivity), with having increased baseline behavioral problems that responded to a decrease or discontinuation of the SSRI (impulsivity, aggression, encopresis, motor tics, risk-taking behaviors). The remaining two subjects were given new diagnoses of cyclothymia and chronic motor tic disorder after beginning treatment of SSRIs.

Conclusion: The information obtained in this study suggests SSRIs may exacerbate underlying behavioral problems such as ADHD and oppositional defiant disorder in prepubertal children and may uncover or exacerbate tic disorders and hypomania. Interestingly, most of these side effects were mild and transient, or responsive to dosage manipulation. In light of these results and the small sample size in this study, further research is being completed for similar subjects for the calendar year 1995 in order to clarify the above noted effects.

NR71 Monday, May 6, 9:00 a.m.-10:30 a.m.

Placebo and Antidepressant Response in Children and Adults

Diana E. Robles, M.D., Psychiatry, St. Vincent Hospital, 101 W 15th Street #4CS, New York NY 10011-6700; Carlos Blanco, M.D., Inmaculada Palanca, M.D., Madhurani S. Patkar, M.D., Inmaculada Gilaberte-Asin, M.D.

Summary:

Several double-blind trials and meta-analyses have shown that tricyclics are not superior to placebo in the treatment of child and adolescent depression. However, no research has been done as to whether this results from a lack of response to antidepressants or an unusually high response to placebo in children. We reviewed all the published placebo controlled trials of antidepressants in children (N = 13) and selected those that provided data on changes in scores of antidepressant scales following treatment (N = 4). We estimated effect size parameters for placebo and antidepressants separately, that reflected the rate improvement on those "treatments," and calculated weighted estimated for both conditions. We followed similar procedures with seven studies carried out in adults that reported changes in antidepressant scores after treatment with tricyclics or placebo, and compared the effect size estimates.

Results: Adult patients ($g = 1.196$, $v = .003$) respond significantly more than children ($g = 1.147$, $v = .831$) to antidepressant therapy ($x^2 = 6.58$, df = 1, $p < .05$), whereas children ($g = .937$, $v = 878$) do not respond significantly more than adults ($g = .855$, $v = .003$) to placebo ($x^2 = 3.64$, df = 1, $p > .05$).

Conclusion: The available evidence suggests that lack of differences in therapeutic response in children between tricyclics and placebo is due to low rates of response to antidepressants, and not to high rates of placebo response.

NR72 Monday, May 6, 9:00 a.m.-10:30 a.m.

Clinical Features of Survivors of Sexual Abuse with PTSD and Comorbid BPD

Karen J. Rosen, M.D., Psychiatry, Butler Hospital, 345 Blackstone Blvd., Providence RI 02906; Caron Zlotnick, Ph.D., Teri B. Pearlstein M.D.

Summary:

Recently, there has been controversy concerning whether post-traumatic stress disorder (PTSD) and borderline personality disorder (BPD) are separate disorders, especially among survivors of sexual abuse. The purpose of this study was to examine whether PTSD with comorbid BPD in survivors of sexual abuse is associated with a distinct cluster of clinical features.

Subjects were 71 female outpatients. Measures were: CAPS, the BPD subscale of the Personality Disorder Questionnaire (PDQ-R), Complicated PTSD Inventory, Childhood Trauma Questionnaire, Self-Injury Survey, and Dissociative Experience Survey (DES).

Subjects with PTSD and BPD (N = 41) reported more difficulty in regulating affect ($t = 2.13$, $p < .01$), more recent impulsive behavior ($t = 2.67$, $p = < .01$), higher levels of dissociation ($t =$

2.91, p < .01), and more PTSD symptoms of arousal (t = 3.13, p < .01) than subjects with PTSD (N = 30). There were no differences between the two groups in PTSD symptoms of reexperiencing (t = 0.14, p = ns), and avoidance (t = 1.59, p = ns).

Our findings suggest that a greater degree of affect dysregulation may distinguish childhood survivors of sexual abuse with PTSD and comorbid BPD from those with PTSD without BPD.

NR73 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Relationship Between Dissociation and Pain Insensitivity in Self-Mutilation

Karen J. Rosen, M.D., Psychiatry, Butler Hospital, 345 Blackstone Blvd., Providence RI 02906; Caron Zlotnick, Ph.D., Teri B. Pearlstein, M.D.

Summary:

Animal and human studies show that a decrease in pain sensitivity occurs after early traumatic experiences. The purpose of this study was to examine the relationship between dissociation and reports of pain insensitivity during self-mutilation. Subjects consisted of 67 female survivors of sexual abuse with post-traumatic stress disorder (PTSD) who had a history of self-mutilation. Measures were: Clinician-Administered PTSD Interview (CAPS), Attention Subscale of the Complicated PTSD Inventory, Dissociative Experiences Scale (DES), and Self-Injury Survey.

Self-mutilators insensitive to pain (N = 32) reported higher levels of dissociative symptoms of PTSD (t = 2.73, p < 0.01), more avoidance symptoms (t = 2.53, p = 0.01), and a higher degree of attention difficulties (t = 2.20, p < 0.05) than self-mutilators sensitive to pain (N = 35); there were no differences in demographic variables between the two groups. There were no differences between the two groups in PTSD symptoms of reexperiencing (t = 1.62, p = ns) and arousal (t = 1.69, p = ns). A logistic regression found that pain-insensitive self-mutilators were 3.89 times more likely to be high dissociaters (i.e. a DES score > 20) compared to pain-sensitive mutilators. This study shows that among self-mutilators with PTSD, pain insensitivity during self-mutilative acts is related to a cluster of symptoms associated with numbing experiences. Possibly, for subgroup of self-mutilators, numbing experiences facilitate the act of self-mutilation.

NR74 Monday, May 6, 9:00 a.m.-10:30 a.m.

Genetic Linkage Studies in Bipolar Disorder

Judith Badner, M.D., Neurogenetics, NIMH, Bldg. 10, 3N218, Bethesda MD 20892

Summary:

Objective: Evidence of linkage between bipolar disorder and a group of linked markers on chromosome 18 has been reported by Berrettini et al. (1994) and Stine et al. (1995). The goal of this study was to narrow down the region where the susceptibility gene may be located through association studies.

Method: 22 families, previously showing evidence of linkage between bipolar disorder and chromosome 18, were tested for evidence of association of marker alleles to disease using the transmission disequilibrium test (TDT) of Spielman et al. (1993). Seventeen markers within the hypothesized linkage region were tested.

Results: Under affection status model II (Schizoaffective, BP I, BP II, Recurrent Unipolar Depression affected), D18S53 showed evidence of transmission disequilibrium (nominal p < 0.05). A subset of 10 families was created by selecting those showing greatest evidence of linkage (lod > 1.0) at any marker within the linkage region. This subset of families showed some evidence favoring transmission disequilibrium to D18S53 (nominal p < 0.001) and the D18S62, D18S44, and D18S37 (nominal p < 0.05). For D18S53, one allele appears to be preferentially *not* transmitted to affected individuals (nominal p < 0.005). Two candidate loci in this region, a corticotropin receptor (ACTH-R) and the α subunit of a GTP binding protein, did not show evidence of transmission disequilibrium.

Conclusion: These results may possibly narrow the region of interest for linkage and provide a hypothesis for testing in other samples.

NR75 Monday, May 6, 9:00 a.m.-10:30 a.m.

Development of Chromosome 18 Markers to Aid in the Location of a More Restricted Region of Linkage Disequilibrium with Bipolar Disorder

Alan R. Sanders, M.D., Gene Mapping, NIMH-DIRP-CNG, Bldg 10, Room 3N-218, Bethesda MD 20892; Takeo Yoshikawa, M.D., Sevilla Detera-Wadleigh, Ph.D., Elliot S. Gershon, M.D.

Summary:

In 1994, linkage was found in an NIMH bipolar pedigree series to the pericentromeric region of chromosome 18, and in 1995 this was replicated by a collaborative group of investigators from Hopkins, Stanford, and Cold Spring Harbor. Within an approximately 40 MB region in which linkage could be detected, one marker (D18S53) was determined by the NIMH group to be in linkage disequilibrium by the transmission/disequilibrium test. Across families, one allele appeared to be consistently protective.

The present project aims to generate more genetic markers in the region to aid in replication of the disequilibrium finding and in location of a more restricted region of linkage disequilibrium. This would help with future attempts to identify positional candidate genes.

We selected three Yeast Artificial Chromosome (YAC) clones containing the region of D18S53 and used inter-*Alu*-PCR to amplify some of their unique sequences which were used to screen a chromosome 18 specific cosmid library. 184 positive clones were rearrayed and screened for microsatellite repeats. We miniprepared DNA from 30 positive clones and EcoRI fingerprinted them. From each of the 22 fingerprinting classes, one clone's microsatellite repeat containing fragments are being subcloned. Sequencing across the repeat will follow to allow generation of PCR primers. The first one we have found is a CA repeat containing marker. CEPH pedigrees will be used to analyze for the amount of polymorphism. Polymorphic markers will be used to genotype the 22 NIMH bipolar pedigree series to test the linkage disequilibrium hypothesis described above.

NR76 Monday, May 6, 9:00 a.m.-10:30 a.m.

Stress and Diet in Commodity Traders

Michael N. Kessler, B.A., School of Med, University of CT, 646 Bloomfield Avenue, Bloomfield CT 06002; Karin E. Kessler, M.S.

Summary:

Objective: Studies have shown a link between stress and health and diet and health. We propose that diet is a direct link between stress and health. To test this, we attempted to show that stress and diet are significantly correlated.

Method: For seven consecutive days 20 male commodity traders completed the Perceived Stress Scale (PSS) and a detailed food diary that allowed us to calculate the gram amount and percentage of daily calories coming from protein, carbohydrate, fat, and alcohol. Next, we calculated correlation coefficients for the PSS scores and the dietary variables.

Results: While there was no correlation between any dietary variable and stress, positive correlations were found between the day of the week and fat consumption and the day of the week

and alcohol consumption. A negative correlation was found between the day of the week and carbohydrate consumption. Additionally, a negative correlation was found between the day of the week and stress.

Conclusions: Various confounders may have prevented the direct correlation between stress and diet from reaching statistical significance. Nevertheless, our results fail to contravene the belief that stress and diet are directly related. Based on our results, further research is clearly warranted.

NR77 Monday, May 6, 9:00 a.m.-10:30 a.m.

Lethality of Suicide Attempts in Adjustment Disorder Versus Major Depression

Alisa A. Devlin, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Lisa B. Dixon, M.D., Lawrence A. Labbate, M.D.

Summary:

Objective: The purpose of this study was to compare the lethality of suicide attempts made by persons diagnosed with adjustment disorder (AD) to those made by persons with major depression (MD) in a hospitalized military population.

Methods: We reviewed the charts of consecutively admitted persons who had made a suicide attempt and were diagnosed with AD (N = 51) or MD (N = 30) in fiscal years 1992–4 at a military hospital. We obtained demographic and diagnostic information, as well as data to compute a risk-rescue ratio score indicative of lethality of suicide attempt. Analysis of variance and correlations were used to determine the association of lethality with patient clinical and demographic factors. Patients had a mean age of 28 (SD = 10) years, 64% Caucasian, 53% male, 31% currently married, and 73% were active duty.

Results: Persons with MD tended to have a higher lethality score than persons with AD ($p < .10$). Higher lethality was significantly associated with older age ($p < .01$), the presence of any comorbid diagnosis ($p < .02$), and male sex ($p < .02$). Persons with MD were more likely to have a comorbid diagnosis than persons with AD ($p < .02$). Higher lethality was not associated with past suicide attempts or past psychiatric treatment.

Discussion: This study supports the hypothesis that higher lethality of suicide attempts is associated with a diagnosis of major depression as well as with advanced age, gender, and psychiatric comorbidity. More knowledge about suicide risk and lethality is necessary to prevent suicide and treat persons at risk.

NR78 Monday, May 6, 9:00 a.m.-10:30 a.m.

A Taxonomy for Pregnancy and Perinatal Complications

Gwen L. Zornberg, M.D., Proctor House, McLean Hospital, 141 Westchester Road, Newton MA 02158-2521; Stephen L. Buka, Sc.D., Ming T. Tsuang, M.D.

Summary:

Objective: The authors analyze the evidence for pregnancy and perinatal complications (PPCs) as risk factors to justify a novel approach to study determinants of schizophrenia.

Method: The authors reviewed the literature to derive a classification system for PPCs.

Results: Evidence uncovered in their review of more than 400 articles or chapters supports the theory that PPCs represent contributors to schizophrenia. PPCs apparently serve as surrogates for neurodevelopmental factors that may contribute to schizophrenia by disrupting early brain development. The consequences of that disruption indicated by PPCs, however, depend on the category, timing, severity, and location, combined with genetic endowment. The authors describe a conceptual and empirical framework to systematically assess neurodevelopmental risk factors. Four major categories of early brain injury likely to predict schizophrenia are: cerebrovascular, infectious, toxic/metabolic, and genetic.

Conclusions: If we are to link PPC risk factors with pathology in schizophrenia, then a more cogent strategy is needed for epidemiologic research. First, create a more precise, standardized method of measuring neurodevelopmental effects (hitherto classified under the PPC umbrella term); second, promote linkage of prospective PPC data banks to enhance analytic precision; and third, identify and quantify these effects across varying levels of genetic risk in family studies.

NR79 Monday, May 6, 9:00 a.m.-10:30 a.m.

Selective Attention in Pregnancy and Lactation

Yung-Mei Leong, LCS Bldg 10, Rm 3D41, NIMH, 9000 Rockville Pike, Bethesda MD 20892; SuZanne Chaves, B.S., Cheri Wiggs, Ph.D., Dana Plude, Ph.D., Margaret Altemus, M.D.

Summary:

Women undergo large shifts in plasma hormone levels during pregnancy and lactation. Although two of these hormones, cortisol and oxytocin, have been linked to changes in memory and other cognitive functions, there has been little study of the effects of pregnancy and lactation on cognitive function. We administered a feature recognition task developed as a measure of selective attention to 47 women during the last six weeks of pregnancy and to 28 control women during the follicular phase of their menstrual cycles. In addition we administered the same test to a separate group of 30 postpartum women, 15 of whom were breast-feeding and 15 of whom were bottle-feeding their infants. There were no differences between pregnant women and controls or between breast-feeders and bottle-feeders in reaction time and error rate across the range of display size difficulty provided in the test. In summary, hormonal changes associated with pregnancy and lactation do not seem to impair cognitive function as measured by a test of selective attention.

NR80 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Stability of Memories of Being Parented Over Ten Years

Lisa J.F. Miller, Ph.D., Child & Adolescent, NYSPI/Columbia University, 722 W. 168th Street, Unit 14, New York NY 10032; Virginia Warner, M.P.H., Priya Wickramaratne, Ph.D., Myrna M. Weissman, Ph.D.

Summary:

Psychodynamic psychotherapy attempts to alleviate anxiety and distress by uncovering childhood memories, which often concern being parented. Although much skepticism surrounds the validity of these memories, and their validity is difficult to assess, to date little empirical research has focused on the stability over the life span of these memories. Using the Parental Bonding Instrument (PBI) we looked at the effects of age, sex, and clinical status on the stability of memories of parental affectionateless-controlling (Aff-Cnt) over 10 years across two generations in Weissman's sample offspring at high and low risk for depression.

Results from 91 families and 220 offspring between Time 1 and Time 10 show: 1) mothers and offspring had more stable memories of maternal Aff-Cnt than of paternal Aff-Cnt, 2) compared with offspring, mothers had more stable memories of parental Aff-Cnt, 3) compared with male offspring, female offspring had more stable memories of parental Aff-Cnt, and 4) compared with offspring under age 25, offspring over age 25 had more stable memories of parental Aff-Cnt. Of particular note was that compared with

mothers without Time 1 MDD, mothers with Time 1 MDD *had more* stable memories of parental Aff-Cnt. This effect held true but was only marginally significant when controlling for a change in clinical status between Time 1 and Time 10. Overall stability of memories of parental Aff-Cnt increased based upon increased age, female sex, and MDD, and memories of maternal Aff-Cnt were more stable than memories of paternal Aff-Cnt. There were no significant differences in report rate of parental Aff-Cnt when looking by age, sex, or generation. However, report rate of memories of parental Aff-Cnt was higher among mothers with MDD than among mothers without MDD.

Increased rate of report and increased stability of memories of parental Aff-Cnt in mothers with MDD compared to mothers without MDD is consistent with experimental findings (Blaney, 1986; MacLeod & Mathews, 1991; Singer & Salovey, 1991) which show depressed subjects exhibit better recall for negatively-valenced material such as cue words. However, that maternal change in clinical status between Time 1–Time 10 did not decrease stability of memories of parental Aff-Cnt *contradicts* experimental findings that show decreased stability for negatively-valenced material such as single words and nonsense words accompanying clinical improvement (Slife et al, 1984; Dobson & Shaw, 1987). This difference between our findings and experimental findings may be due to the difference in the importance of the negative memories being studied implying that specifically more important negative memories remain stable in depressives even when the depression lifts.

That mothers with MDD show greater stability of memories of parental Aff-Cnt may represent something about memory in depressives analogous to Depressive Realism (Abramson and Alloy, 1977), which posits a cognitive bias towards realism in individuals who are prone to depression. Alternatively, greater stability of memories of parental Aff-Cnt in mothers with MDD may simply reflect that mothers with MDD had parents whose parenting styles were affectionateless and controlling, making Aff-Cnt memories difficult to forget.

Nonetheless, that memories grow more stable with time, that being parented is remembered with greater stability by women than by men, and that depressed women compared with nondepressed women have relatively more stable memories of parental affectionateless-control restores some credibility to the use of memories in psychological treatment.

NR81 Monday, May 6, 9:00 a.m.-10:30 a.m.

Sertraline in the Treatment of Mixed Anxiety and Depression

Jose L. Carrasco, M.D., Psychiatry, Salamanca University, AVDA Campo Charro S/N, Salamanca 37007, Spain; Marina Diaz-Marsa, M.D., Jose M. Montes, M.D., Jeronimo Saiz-Ruiz, M.D.

Summary:

Almost 30% of patients presenting with symptoms of anxiety and depression do not fulfill the required criteria for anxiety and mood disorders included in DSM-IV. The 10th edition of the ICD has created a new category for the mixed anxiety and depression disorder (MAD) to classify these patients. A general therapeutic guide has not been approved as yet. However, some antidepressant drugs with anxiolytic action, like the SSRIs, might improve both set of symptoms.

To test the efficacy of SSRIs in the treatment of MAD, an open clinical trial of sertraline in this disorder (ICD-10 criteria) was made. Thirty-four patients (22 female and 12 male) were included. Therapeutic effects were rated with the Hamilton anxiety and depression scales, the Montgomery-Asberg depression scale, and the Clinical Global Impression (CGI) scale. Sertraline was administered in flexible doses from 50 to 200 mg daily.

Following treatment with sertraline (medium dose 68 mg day), a 55% reduction of anxiety scales and 60% of depression scales was found. Twenty-seven patients (78%) were responders (CGI 1 or 2) and seven were nonresponders. Therapeutic response was independent of anxiety and depression ratings before treatment.

Since independent sertraline has a safe pharmacological profile and lacks dependence potential, this drug might be an efficient therapeutic option for patients with mixed anxiety and depression symptoms.

NR82 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Effect of Clinician Characteristics on the Performance of Case Management Activities in a Public Mental Health System

Alexander S. Young, M.D., Psychiatry, UCLA, 300 UCLA Med Plaza, Ste 2325, Los Angeles CA 90024; Oscar Grusky, Ph.D., J. Greer Sullivan, M.D., Cynthia Webster, Ph.D., Deborah Podus, Ph.D.

Summary:

Objective: It is not known whether clinician characteristics are associated with performing key components of case management, and whether more costly professionals deliver higher quality care. We investigated whether the performance of three domains of clinical case management was related to clinician gender, ethnicity, years of experience, professional training, optimistic attitudes about patients, belief in efficacy of the activity, and caseload size.

Method: An instrument was developed to measure performance of family management, service linkage, and assertive outreach. Data were collected in a cross-sectional survey of all 86 case managers in a county mental health system.

Results: After controlling for severity of patient illness, multivariate regressions demonstrated that case managers who believed in the efficacy of a case management component performed more of it. The performance of service linkage and assertive outreach increased with years of experience until about 15 years, after which they decreased. Male case managers performed more assertive outreach. However, less assertive outreach was performed by nurses, psychologists, and case managers with larger caseloads.

Conclusions: There are substantial differences among types of clinicians in the components of case management they perform. Case management activity information could be used to focus scarce resources on interventions known to improve patient outcomes.

NR83 Monday, May 6, 9:00 a.m.-10:30 a.m.

Professional Courtesy, Current Attitudes and Practices

Harry T. Chingon, M.D., Child Psychiatry, University of Hawaii, PO Box 15078, Honolulu HI 96830-5078; Linda B. Nahulu, M.D.

Summary:

Background: Traditionally, physicians have provided professional courtesy to other physicians and their families. Recently, there have been drastic changes in the way medical care is paid for and the way physicians are compensated. The last published study on professional courtesy surveyed physicians in 1991 and had a 46% response rate. We did a small pilot study with the hypothesis that changes in medical reimbursement are altering the way professional courtesy is viewed.

Methods: A copy of the 20-question survey used in the 1991 study by Mark Levy, M.D. was obtained with permission. It was administered to nine child and adolescent psychiatrists practicing

in Honolulu, Hawaii, seven of whom returned completed questionnaires.

Results: Surprisingly, the results in this small pilot study were very similar to those of the 1991 nationwide study done more than four years earlier. Due to the small sample size, however, there is statistically poor reliability.

Conclusion: The 1991 study by Levy, et al. showed that there had been little change in physicians' attitudes and practices of professional courtesy since 1958. Our pilot study suggests that even in 1996, despite drastic changes in the way medical care is paid for, psychiatrists' attitudes and practices may have remained constant.

NR84 Monday, May 6, 9:00 a.m.-10:30 a.m.

The Effect of Religious/Spiritual Beliefs on Psychological State and Coping in Women Presenting with Possible Breast Cancer

Catherine S. Riley, Med School, Mayo Clinic, 200 1st Street, Rochester MN 55905; Ruth E. Johnson, M.D., Teresa A. Rummans, M.D., Laura L. Bloomquist, M.D., Peter C. Wollan, Ph.D., Michelle L. Taylor, Ph.D.

Summary:

Women with undiagnosed breast abnormalities experience a wide array of emotions and employ numerous coping mechanisms. Researchers discovered 85% of women studied believed religion helped them cope with breast cancer. We examined religious beliefs and affiliations in women with possible breast cancer to determine if beliefs influenced the coping mechanisms employed.

Methods: We surveyed 199 women referred to Mayo Breast Clinic for undiagnosed breast abnormalities for spiritual, emotional, cognitive, and physical state. Survey instruments included Systems of Belief Inventory (SBI), Religious Orientation Scale (ROS), Profile of Moods State (POMS), State Trait Anxiety Scale, COPE, Folstein Mini Mental State Exam, and Karnofsky score.

Results: Mean age of women surveyed was 54.4 years (range, 19–87). Specific religious affiliation was reported by 181 (91%). Belief in God was cited by 191 (96%) on SBI and was correlated with positive reinterpretation coping strategies ($p = .0011$) and *inversely* correlated with the use of alcohol and drugs ($p = .0050$) on COPE and with anger/hostility on POMS ($p = .0028$). A religious system of social support was also inversely correlated with alcohol and drug use ($p = .0087$). No significant correlations were noted between ROS and POMS.

Conclusion: Religious beliefs and social networks resulted in *less* maladaptive coping through anger/hostility and drug and alcohol use.

NR85 Monday, May 6, 9:00 a.m.-10:30 a.m.

Prevalence of Adjustment Disorders Among Medical Students at a Caribbean Medical School University

Joseph V. Pergolizzi, Jr., M.D., Psychiatry, Ross University Med c/o JVP, 8390 Tamar Drive, Columbia MD 21045; Spencer Serras, David Sharma, M.D.

Summary:

Objective: To screen for the prevalence of adjustment disorders and to rate psychosocial stressors that may be causative factors.

Methods: A survey by means of questionnaire which included a statement of confidentiality was conducted on students of Ross University School of Medicine in October 1993.

Results: One hundred and ninety-three students were screened. Seventy-two percent of all students were identified as positive for adjustment disorder. There was no significant gender difference in the results nor any significant difference between each semester. Separation from family and friends, educational demands, the grading system, and living conditions were found to be significant psychosocial stressors. Over 50% of the students suffering from adjustment disorders were also experiencing impairment in their academic performance. Five students of different semesters, three males and two females, were also experiencing suicidal thoughts.

Conclusion: The finding of high prevalence for adjustment disorders warrants the need for adequate student preparation and student supportive programs.

NR86 Monday, May 6, 9:00 a.m.-10:30 a.m.

What Do Psychiatry Residency Applicants Want?

John C. Lindgren, M.D., Psychiatry, University of NC, Medical School Wing B, CB#7160, Chapel Hill NC 27599; Robert D. Ekstrom, M.P.H., Allan A. Maltbie, M.D., Susan G. Silva, Ph.D., Kristin A. Hardin, B.S., Robert N. Golden, M.D.

Summary:

Objective: The purpose of this study is to determine what psychiatry residency applicants report to be the most important aspects of the interview day, the residency program, and psychiatry, in general.

Methods: Psychiatry residency applicants seeking positions for July 1996 at 22 programs were asked to complete an anonymous, standard questionnaire.

Results: 164 questionnaires have been analyzed to date in this ongoing study. For applicants completing more than one questionnaire, only data from the first are included in these analyses. From a list of 22 items, the most interesting or appealing aspect of psychiatry among the respondents is "large amount of patient contact," followed by "mood disorders," "biological psychiatry," and "providing continuity of care." Of the 13 listed characteristics of psychiatry residency programs, "department attitude, style, and atmosphere" is the most important/influential, followed by "resident morale" and "program reputation." The most important part of the interview day is the interview with the residency training director, and applicants prefer two to three additional interviews with both faculty and residents, as well as lunch with residents.

Conclusion: Psychiatry resident applicants have clear preferences about the interview day and the program, and specific interests within the field of psychiatry. They report relatively little concern regarding specific curricula, attractive call schedules, or good location, and are most interested in working in a pleasant, collegial environment which offers a large amount of patient contact.

NR87 Monday, May 6, 9:00 a.m.-10:30 a.m.

Prospective Study of Postpartum Blues

Ranna I. Parekh, M.D., Psychiatry, Mass General Hospital, 9 Fruit Street, Boston MA 02114; Lee Cohen, M.D., Laura Robertson, B.A.

Summary:

Postpartum blues are self-limited symptoms which occur within ten days of delivery followed by remission of symptoms. While the benign course of blues does not require treatment, the extent to which it may be a predictor of later postpartum mood disorder has not been adequately established.

Methods: This report describes the prospective course of postpartum blues assessed with the 28-item self-rated Kennerly Blues Questionnaire in 19 women with histories of major depression as part of a prospective longitudinal study of mood disorder during pregnancy and the postpartum period. Patients were also assessed with respect to the extent to which they met Pitt criteria for postpartum blues during the ten postpartum days.

Results: All women were noted to have family histories of a major depressive disorder. Twelve subjects met Pitt criteria for blues and nine of these had Kennerly scores of greater than 10/28. Women who met Pitt criteria and scored high on the Kennerly questionnaire tended also to meet criteria for a major depressive disorder (7/9) at postpartum three months compared to those who did not experience postpartum blues (2/7).

Conclusion: Postpartum blues may be a predictor for postpartum depression in women with histories of recurrent major depression.

NR88 Monday, May 6, 1:00 p.m.-2:30 p.m.

Chronic Major Depression Among HIV-Infected Drug Users

Jeffrey Johnson, Ph.D., Psychiatry, Columbia University, 722 W. 168th Street, New York NY 10032; Judith G. Rabkin, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how intravenous drug users with major depressive disorder and/or HIV infection are at substantial risk for chronic major depressive disorder.

Summary:

Objective: To investigate the three-year course of major depressive disorder (MDD) among intravenous drug users (IDUs) and to determine whether HIV infection increases the likelihood that IDUs will experience MDD.

Method: Structured psychiatric evaluations (SCID) were conducted every six months over a three-year period among 72 HIV seropositive and 70 seronegative IDUs.

Results: At baseline, 18% of HIV + IDUs and 17% of HIV- IDUs had current MDD. These rates did not increase over time in either group, despite declining CD4 cell counts in the former. However, baseline MDD strongly predicted future episodes of MDD: 36% of IDUs with vs. only 7% of those without baseline MDD subsequently had MDD on 3+ occasions (odds ratio (OR) = 7.7; $p < .0001$). In addition, 18% of HIV+ participants, but only 6% of HIV- participants, had chronic MDD (OR = 3.7; $p < .05$); 54% of participants with both baseline MDD and HIV infection suffered chronic MDD. Logistic regression analyses indicated that baseline MDD (adjusted OR = 8.37; $p < .001$) and HIV seropositivity (adjusted OR = 4.33; $p < .05$) were independently associated with elevated risk for chronic MDD after gender, drug use, ethnicity, income, and the presence of other psychiatric disorders were controlled statistically.

Conclusions: IDUs with MDD and/or HIV infection are at substantial risk for chronic MDD.

References:

1. Gala C, Pergami A, Catalan J, Durbano F, Musicco M, Riccio M, Baldeweg T, Invernizzi G: The psychological impact of HIV infection in gay men, drug users and heterosexuals: Controlled investigation. *Br J Psychiatry.* 1993;163:651–659.

2. Lipsitz JD, Williams JBW, Rabkin JG, Remien RH, Bradbury M, Sadr W, Goetz R, Sorrell S, Gorman JM: Psychopathology in male and female intravenous drug users with and without HIV infection. *Am J Psychiatry.* 1994;151:1662–1668.

NR89 Monday, May 6, 1:00 p.m.-2:30 p.m.

One-Year Outcomes of Familial Male Alcoholics

Sumil Chhibber, 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., Jan L. Campbell, M.D., H. Mikel Thomas, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how a family history positive with a family history negative compare and how the two groups differed in severely disabling problems.

Summary:

Retrospective studies comparing family history positive (FH+) with family history negative (FH-) alcoholics typically report that FH+ alcoholics show an earlier onset of problem drinking, a more severely disabling course, and greater psychiatric comorbidity in the probands and their close biological relatives. In this one-year, prospective study (N = 360) of consecutively admitted, hospitalized male alcoholics, 69 percent (N = 247) reported one or more first-degree relatives who drank abusively, while 31 percent (N = 113) denied alcoholism among any first-degree relatives. At intake into the study, we replicated the results of our previous investigation and that of others. We found, in comparison to the nonfamilial group, the familial alcoholics were: younger, reported more unemployment, began drinking at an earlier age, had an earlier age of alcoholism onset, and suffered a greater number of drinking-related sequelae. At intake into the study the FH+ group also reported more psychiatric illness among first-degree relatives and themselves satisfied inclusive diagnostic criteria for more lifetime psychiatric syndromes, namely drug abuse and antisocial personality disorder.

Three hundred nineteen (89%) patients participated in the one-year followup (five died). Expecting a poorer outcome for the FH+ alcoholics, we were surprised to find no differences between the two groups for most of the outcome measures. Abstinence rates, alcohol severity scores, ratings of psychosocial functioning and psychiatric severity measures were comparable for the FH+ and FH- alcoholics at follow up. The FH+ group received significantly more treatment during follow up (more medications and more weeks of out patient treatment) and reported fewer drinking days in the six months prior to the outcome evaluation. Is it possible that more intensive treatment served to offset the anticipated poorer prognosis for the familial alcoholic subgroup?

References:

1. Penick EC, Powell BJ, Bingham SF, Liskow BI, Miller NS and Read MR. (1987) A Comparative Study of Familial Alcoholism. *Journal of Studies on Alcohol*, 48:136–146.

2. Babor TF, Doinsky ZS, Meyer RE, Hesselbrock M, Hofmann M and Tennen H. (1992) Types of Alcoholics: Concurrent and Predictive Validity of Some Common Classification Schemes. *Br J Addictions*, 87:1415–1431.

NR90 Monday, May 6, 1:00 p.m.-2:30 p.m.

Substance Abuse and Bipolar Disorder

Carmen R. Blanco-Perez, B.S., Research, Hosp Ramon Y Cajal, Ctra De Colmenar KM 9100, Madrid 28034, Spain; Carlos Blanco, M.D., John A.R. Grimaldi, Jr., M.D., Carlos A. Rueda, M.D., Julia A. Mayo, Ph.D., Ralph A. O'Connell, M.D.

Educational Objectives:

1. Be able to recognize some characteristics that are frequently associated to substance abuse in patients with bipolar disorder.
2. Identify those characteristics and consider differential treatment plans for bipolar patients that are also substance abusers.

Summary:

Objective: To compare the characteristics of substance-abusing and non-substance-abusing bipolar patients.

Method: Patients enrolled in a long-term research project on the course of bipolar disorder were divided in two groups, depending on whether or not they were consuming psychoactive

substances (N = 136 and N = 178, respectively). Chi-square and t-tests were performed to compare the distribution of different in both groups. Logistic regression was used to estimate the odds ratio associated with the variables that were statistically different between both groups.

Results: Substance abuse was associated with male gender, child trauma, earlier onset of bipolar disorder, higher number of hospitalizations, lower social support, and higher frequency of attempted suicide. Bipolar patients with substance abuse were more likely to be on carbamazepine than the comparison group, and less likely to be on lithium.

Conclusion: Bipolar patients with substance abuse represent a specific group of bipolar patients with clinical differences that include onset, course, treatment, and prognosis of the disorder. Identification of those differences in patients with bipolar disorder will allow medical practitioners to recognize patients who may be at risk for substance abuse.

References:

1. O'Connell RA, Mayo JA, Flatow L, Cuthbertson B, O'Brien BE: Outcome of bipolar disorder on long-term treatment with lithium. *Br J Psychiatry* 1991;159:123–129.

2. Weiss RD, Mirin SM, Griffin ML: Methodological considerations in the diagnosis of coexisting psychiatric disorders in substance abusers. *Br J Addiction 1992; 87:179–187.*

NR91 Monday, May 6, 1:00 p.m.-2:30 p.m.

SSRIs in Depression: A Meta-Analysis

Carlos Blanco, M.D., Psychiatry, St. Vincent's Hospital, 101 West 15th Street, New York NY 10011; Inmaculada Gilaberte-Asin, M.D., Inmaculada Palanca, M.D., Cletus S. Carvalho, M.D., Maria Becerril, J.B., Jesus Hernandez, M.D.

Educational Objectives:

1. Be knowledgeable with the current literature on use of SSRI's in the treatment of major depression.
2. Recognize that the available evidence shows fluoxetine, sertraline and paroxetine to be equally effective in the treatment of depression.

Summary:

Objective: To compare the efficacy of the SSRI's in the treatment of major depression.

Method: MEDLINE search was used to identify all the published double-blind, placebo-controlled trials that included fluoxetine, paroxetine, or sertraline in the design (N = 35). After eliminating all identified duplicated reports, we performed a metanalysis of those that included enough data to calculate effect size statistics (N = 21). Studies were grouped by drug. Effect size estimates are reported using Pearson product moment correlation "r". The Q statistic was used to test for heterogeneity within and between the groups.

Results: Fluoxetine (r = .33), sertraline (r = .35), and paroxetine (r = .39) had similar effect size estimates. No heterogeneity was found in effect size parameters within the studies ($x^2 = 31.11$, df = 18, p > .05) or between them (= 2.14, df = 2, p > .05).

References:

1. Cooper H, Hetges LV: The Handbook of Research Synthesis. New York, Russell-Sage Foundation, 1994.

2. Kasper S, Heiden A: Do SSRIs differ in their antidepressant efficacy. Human Psychopharmacology, 10:S163–S172; 1995.

NR92 Monday, May 6, 1:00 p.m.-2:30 p.m.

Frontal Lobe Anatomy and Risperidone Response in Schizophrenia

Sean W. Flynn, M.D., University of British Columbia, 757 East 38th Avenue, Vancouver BC V5W 1H9, Canada; William G. Honer, M.D., Geoffrey N. Smith, Ph.D., G. William MacEwan, M.D., Siemion Altman, M.D., Lili C. Kopala, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be more informed about Poor clozapine response in schizophrenia related to cortical sulcal enlargement, but not to ventricular enlargement.

Summary:

Objective: Poor clozapine response in schizophrenia appears to be related to cortical sulcal enlargement, but not to ventricular enlargement. We studied the relationship between risperidone response and regional brain anatomy.

Method: Forty hospitalized patients (32 men, eight women, mean age 28, range 15–50), fulfilling DSM-III-R criteria for schizophrenia, underwent a trial of risperidone. CT scans were rated using a scale to assess CT regional cortical and ventricular anatomy in schizophrenia. Subjects were defined as responders (discharge CGI ≤ 4, Improvement score ≤ 2) or nonresponders. Analysis of variance, covaried for age, was used to compare the regional cortical and ventricular scores of responders with those of nonresponders.

Results: Poor response to risperidone was associated with increased frontal measures: the frontal horns ($p < 0.013$), the lateral frontal sulci ($p < 0.043$), and the medial frontal sulci ($p < 0.023$). In contrast, temporal cortical, lateral ventricle, and third ventricle measures were not related to poor response.

Conclusions: These findings suggest an association between poor response to risperidone and frontal anatomy. This may be somewhat different from findings observed with clozapine, where response appeared to be related to global cortical anatomy. Further work is needed to explore the relationship between anatomical changes and treatment response using more subtle indicators of psychopathology, such as the PANSS.

References:

1. Honer WG, Smith GN, Lapointe JS, MacEwan GW, Kopala L, Altman L, Altman S: Regional cortical anatomy and clozapine response in refractory schizophrenia. *Neuropsychopharmacology* 13:85–87, 1995.

2. Friedman L, Knutson L, Shurell M, Meltzer HY: Prefrontal sulcal prominence is inversely related to response to clozapine in schizophrenia. *Biol Psychiatry* 29:865–877, 1991.

NR93 Monday, May 6, 1:00 p.m.-2:30 p.m.

A Systematic Comparison of Personality Disorder Diagnoses in Patients with Social Phobia Versus OCD

Sheila M. Seay, M.A., Psychiatry, University of Texas, 18333 Egret Bay Blvd, Ste. 150, Houston TX 77058; Teresa A. Pigott, M.D., Sue Pavelka, M.D., Billinda Dubert, M.S.N., Suzanne Bernstein, B.S., Eduina A. Martins, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe that avoidant personality disorder and obsessive-compulsive personality disorder are the most common personality disorder diagnoses in both OCD and social phobia, and obsessive-compulsive personality disorder is more common in social phobia in comparison to OCD.

Summary:

Patients with obsessive-compulsive disorder (OCD) or social phobia (SP) often exhibit extreme harm/shame avoidance, altered risk assessment, and lack of novelty-seeking behavior. In order to investigate whether these features may contribute to an increased risk of certain personality disorder diagnoses, we administered the Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II) to 58 non-depressed subjects meeting DSM-III-R criteria for either SP (n = 29) or OCD (n = 29). The SP group (17 females, 12 males; mean age ± SEM, 42 ± 2 yrs; baseline Ham-D, 7 ± 1; baseline BSPS, 38 ± 2) and the age- and sex-matched OCD group (16 females, 13 males; mean age, 40 ± 2 yrs; baseline Ham-D, 9 ± 2; baseline YBOCS, 25 ± 3) were psychotropic medication-free (mean, 42 ± 3 days) at the time of SCID-II administration. In SP, the most common PD were avoidant (83%), OCPD (79%), borderline (42%), dependent (42%), paranoid (38%), and passive-aggressive (38%). The most common PD in OCD were obsessive-compulsive personality disorder (OCPD) (45%), followed by avoidant, borderline, and narcissistic (each 31%). There were significantly more Cluster C PDs than Cluster A or B in both groups. A diagnosis of avoidant and OC PD were significantly more frequent ($p < 0.05$) in the SP group in comparison to the OCD group. These results suggest that: a) avoidant PD and OCPD are the most common PD diagnoses in both OCD and SP and b) OCPD is more common in SP in comparison to OCD. These results suggest that there is substantial diagnostic overlap between OCD, SP, avoidant PD, and OCPD.

References:

1. Davidson J, Potts N, Richichi E, & et al.: (1991). The Brief Social Phobia Scale. *J Clin Psychiatry*, 52(11), 48–51.

2. Pigott TA, L'Heureux F, Dubbert B, et al. (1994). Obsessive-compulsive disorder: comorbid conditions. *J Clin Psychiatry*, 55(10), 15–27.

NR94 Monday, May 6, 1:00 p.m.-2:30 p.m.

Seasonal Variation and Onset of Illness in Mixed Versus Pure Mania

Sean P. Stanton, B.S., Psychiatry, University of Cincinnati, 231 Bethesda Avenue ML559, Cincinnati OH 45267; Susan L. McElroy, M.D., Paul E. Keck, Jr., M.D., Stephen M. Strakowski, M.D., Kiki D. Chang, M.D., Cesar A. Soutullo, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how first episode patients and patients with multiple pure manic admissions had a seasonal component.

Summary:

Seasonal trends have been described in the epidemiology of populations of patients with psychiatric disorders, and seasonal patterns are evident in the course of bipolar disorder in individual patients (Goodwin and Jamison, 1990). Episodes tend to cluster in the spring and fall, especially among those patients with annual recurrences (Wehr and Rosenthal, 1989). The incidence of mania has been reported to be higher in the summer months (Davies and Carney 1978, Davis and Carney, 1988) and depression has been associated with a late summer-early fall and late winter-early spring pattern (Goodwin and Jamison 1990). Seasonal variations have been linked to daily light exposure. A problem in past studies is that bipolar patients are included in the depressive samples (Goodwin and Jamison 1990). Also, a lack of standardization in diagnostic assessment from study to study makes comparisons between studies difficult (Goodwin and Jamison 1989). Furthermore, mixed mania has not been well studied with regard to seasonal variation. Mixed mania may represent a distinct clinical state separate from pure mania, with poorer outcome and different response to pharmacological treatment (McElroy, 1992). To our knowledge, no prospective studies have examined seasonal variation in patients with mixed bipolar disorder. In this study, we examined the effect of seasonality on the occurrence of episodes in patients with mixed verses pure mania.

Method: Bipolar patients were diagnosed with mixed (N = 64) and pure mania (N = 98) by the Structured Clinical Interview for the DSM-III-R (SCID). The onset of illness was also recorded for first episode (N = 92), as well as multiple episode (N = 70) patients. The sample consisted of patients recruited as part of the University of Cincinnati Mania and First Psychosis Projects. Demographic information was collected at admission and analyzed according to subgroup: pure mania-first episode (N = 56), pure mania-multiple episodes (N = 42), mixed mania-first episode (N = 36), and mixed mania-multiple episodes (N = 28). Seasonal variation was grouped into late winter-early spring, summer, late summer-early fall, and winter. The subgroups were analyzed according to the seasonal admission of patients.

Results: Patients diagnosed with having first episode-pure mania displayed a seasonal pattern. The majority of patients were admitted in late winter-early spring (34%) months. The late summer-early winter months (23%) showed a lower number of admissions, as did the winter months (25%). The lowest incidence was during the summer months (18%). Patients with multiple episodes of pure mania showed greatest occurrence in late summer-early fall (38%). In late winter-early spring months (29%) there was also a high incidence. Winter months (24%) showed less occurrence, and the summer months (9%) showed the least occurrence. First episode mixed mania showed no consistent pattern across the seasonal groups: late winter-early spring (25%), summer (25%), late summer-early fall (25%), and winter (25%). Patients with multiple admissions showed greatest concentration in the late summer-early fall (43%) months. Where as the late winter-early spring months (25%) showed another smaller peak with other seasonal groups having similar low rates of occurrence: summer months (18%) and winter months (14%).

Conclusions: First episode patients and patients with pure manic admissions had a seasonal component. Mixed mania had no seasonal variable in the first admission patients, but had a robust seasonal component in the multiple admission patients. Pure mania has been previously reported to be more prevalent in summer months (Posidonius, 4th century; Kraeplin, 1921; Davies and Carney, 1988). However, our results show a higher incidence in late winter-early summer and late summer-early fall. These results may be due to the inclusion of only pure and mixed patients or the use of structured interviews.

References:

1. Goodwin FK, Jamison KR: Sleep and Biological Rhythms. In: Goodwin FK, Jamison KR, eds. Manic Depressive Illness. New York, NY: Oxford University Press; 1990:562–571.

2. McElroy SL, Keck PE, Pope HG, Hudson JI, Faedda GL, Swann AC. (1992): Clinical and research implications of the diagnosis of dysphoric or mixed mania or hypomania. *Amer J Psychiatry*. 149:1633–1644.

NR95 Monday, May 6, 1:00 p.m.-2:30 p.m.

Sexual Dysfunction Induced by SSRIs

CPT Jamie B. Grimes, M.D., Psychiatry, Walter Reed Army Med Ctr, Borden Pavilion, Washington DC 20307-5001; Lawrence A. Labbate, M.D., Alan H. Hines, M.D.

Educational Objectives:

Participants should recognize the nature and time course of serotonin reuptake inhibitor induced sexual dysfunction.

Summary:

Objective: To determine the effect of serotonin reuptake inhibitors (SRIs) on sexual function over three months.

Method: Patients presenting to a psychiatric clinic were enrolled in a three-month prospective study of the effect of three SRIs [fluoxetine (N = 4), sertraline (N = 24), and paroxetine (N = 14)] on five aspects of sexual function: libido, erection/lubrication, orgasm quality, orgasm delay, and sexual frequency. Measurements were made at baseline and at each month on the five parameters by a 10cm visual analogue scale (VAS). The VAS endpoints were 0 for none or absent and 10 for normal for self.

Results: Sixty-two patients (mean age 37.9, SD = 11; 36 women; 55 Caucasian) entered, and to date 32 completed three months. Primary diagnoses were as follows: major depression N = 33; panic disorder N = 13; OCD N = 7; social phobia N = 9. On all parameters, depressed patients had lower baseline scores than anxious patients. Drugs selection was no different by diagnosis or baseline VAS scores. At month one, 62% of patients suffered orgasm delay; the VAS scale was lower ($t = 5.38$, $df = 42$, $p < 0.0001$). For women, the orgasm delay gradually improved over three months, but remained less on the VAS scale ($t = 2.2$, $p = 0.02$). For men, orgasm delay persisted through month three ($p = 0.003$). Orgasm delay persisted nearly unchanged over three months with sertraline and paroxetine ($p < 0.03$), but nearly returned to baseline with fluoxetine ($p = 0.30$). Three men (one each drug) reported orgasm delay helped premature ejaculation. For women lubrication decreased nonsignificantly over one month, and was nearly at baseline at three months ($p = 0.6$). Erection decreased significantly at month one, but by month three was only slightly less than baseline ($t = 1.5$, $p = 0.2$). On average, sexual frequency and libido did not significantly change over time. Orgasm quality decreased for both sexes at one month ($p < 0.001$) and did not fully recover by month three ($p < 0.02$). Sexual dysfunction change did not differ by diagnosis. Drugs were equally likely to be associated with a clinically significant problem at each time point.

Conclusion: The SRIs are commonly associated with sexual dysfunction. Orgasm delay and orgasm quality may not recover after three months, though erection and lubrication may decline and improve. Libido and sexual frequency may not change significantly with SRIs. SRI-induced sexual dysfunction seems independent of drug or diagnosis.

References:

1. Harrison WM, Rabkin KG, Erhardt AA, et al. Effects of antidepressant medication on sexual function: A controlled study. *J Clin Psychopharm* 1986;6:144–149.

2. Zajecka J, Fawcett F, Schaff M, Jeffries H, Guy C: The role of serotonin in sexual dysfunction: fluoxetine associated orgasm dysfunction. J Clin Psychiatry 1991:52:66–68.

NR96 Monday, May 6, 1:00 p.m.-2:30 p.m.

The Relationship of Adaptive Functioning to Neuropsychological Performance in Geriatric Psychiatry Patients

Jovier D. Evans, Ph.D., Psychiatry, VA Med Ctr, 3350 La Jolla Village Drive, San Diego CA 92104; Joshua C. Klapow, Ph.D., Barton W. Palmer, Ph.D., Jane S. Paulsen, Ph.D., Robert K. Heaton, Ph.D., Thomas L. Patterson, Ph.D., Dilip V. Jeste, M.D.

Summary:

Objective: The study was designed to determine the relative importance of cognitive and clinical measures in predicting functional abilities using the Direct Assessment of Functional Status (DAFS) Scale in a sample of geriatric psychiatry outpatients.

Methods: Subjects were 62 geriatric psychiatry outpatients with psychotic disorders (DSM-III-R diagnoses included 38 schizophrenia, five schizoaffective, and 19 psychotic mood disorder patients), and 31 normal comparison subjects, all over the age of 45. All subjects underwent a comprehensive neuropsychiatric evaluation, which included an expanded Halstead-Reitan Neuropsychological (NP) Test Battery and clinical ratings of psychopathology.

Results: Among patient groups, the DAFS was significantly correlated with age, education, duration of illness, and neuropsychological performance. Similar associations were noted among normals. Separate stepwise multiple regression analyses on the DAFS total score using both NP and clinical ratings as predictors indicated that NP performance was a significant predictor of functional ability (R^2 range .24–.54). Clinical ratings of symptoms were not significant predictors.

Discussion: Measures of NP functioning accounted for more variance in functional capacity than did psychiatric ratings of symptomatology. Results extend previous research by demonstrating the strong relationship between NP abilities and observed performance of daily living skills.

NR97 Monday, May 6, 1:00 p.m.-2:30 p.m.

The Prevalence of OCD in Bipolar Disorder

Peter Braunig, M.D., Psychiatry, Westfal Zentrum, Alexandrinenstr, Bochum 44791, Germany; Stephanie Kruger, M.D., Robert G. Cooke, M.D.

Educational Objectives:

1. Recognize the importance of comorbid conditions in bipolar disorder.
2. Diagnose OCD in bipolar disorder.
3. Consider different treatment strategies for this subgroup of patients with bipolar disorder.

Summary:

Objective: To determine the prevalence of obsessive-compulsive disorder (OCD) in subjects with bipolar disorder (BD) and its relationship to other comorbid psychiatric disorders in bipolar subjects with and without OCD.

Method: Subjects (n = 254) were euthymic patients with DSM-III-R BD type I and II in treatment in two tertiary treatment centers; the general psychiatry division of the Zentrum für Psychiatrie, associated with the University of Bochum, Germany (n = 123), and the Bipolar Clinic of the Clarke Institute of Psychiatry, affiliated with the University of Toronto, Canada (n = 131). Lifetime prevalences of OCD and other comorbid conditions were determined by structured interview. Differences were evaluated by chi-square analysis.

Results: Subjects with OCD (n = 16) were more likely than those without OCD to be male (68% vs. 37.4%, $X^2 = 6.17$, $df = 1$, $p = 0.013$), to have a diagnosis of BD type II (50% vs. 20.6%, $X^2 = 7.45$, $df = 1$, $p = 0.0006$), and a lifetime diagnosis of dysthymia (37.5% vs. 8.4, $X^2 = 13.8$ $df = 1$, $p = 0.0002$).

Conclusions: These findings suggest that BD type II, OCD, and dysthymia may tend to cluster together in some subjects with BD. The putative central role of serotonin in the pathophysiologic mechanisms underlying these clinical features is discussed.

References:

1. Strakowski SM, McElroy SL, Keck PW and West SA: The co-occurrence of mania with medical and other psychiatric disorders. *Int J Psychiatry in Medicine* 24:305–328, 1994.

2. Krüger S, Cooke RG, Hasey GM, Jorna T, Persad E: Comorbidity of obsessive-compulsive disorders in bipolar disorder. *J Aff Disorders* 34:117–120, 1995.

NR98 Monday, May 6, 1:00 p.m.-2:30 p.m.

Personality Effects of Paroxetine in Normal Humans

Brian Knutson, Ph.D., Psychology, Bowling Green State Univ., Bowling Green OH 43402; Owen M. Wolkowitz, M.D., Victor I. Reus, M.D., Theresa Chan, B.A., Steven A. Cole, M.D., Elizabeth Moore, M.A., Francesca Manfredi, B.A., Jan I. Terpstra, M.D., Ronald Johnson, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how serontonergic function in a dimension of human personality linked to to negative emotional experience.

Summary:

Serotonin-specific reuptake inhibitors (SSRIs) can effectively remediate depression, but the effects of these compounds on human personality have not received empirical analysis. We report here the first double-blind, placebo-controlled trial of SSRI effects on the personality of normal humans. We administered paroxetine (20 mg/day, p.o.) to 23 adults screened to exclude personal or familial history of psychopathology and placebo to 28 identically screened subjects, for four weeks in a randomized, double-blind protocol. All subjects completed personality assessments at baseline, one week into treatment, and four weeks into treatment. Each assessment included a blood draw and ratings of personality on standardized self-report measures. Paroxetine-treated subjects reported reduced Negative Affect ($p < 0.05$, PANAS; Watson, Clark & Tellegen, 1988) and Hostility ($p < 0.01$, BDHI; Buss & Durkee, 1957) at weeks one and four relative to controls. Other personality variables such as Positive Affect and Self-Esteem were not significantly affected. Further, reductions in Negative Affect and antisocial personality disorder symptomatology (DAPP; Livesley et al., 1993) were positively correlated with blood levels of paroxetine at week four ($p's < 0.05$). Covariance analyses indicated that changes in Negative Affect could account both for more focal shifts in Hostility and broader shifts in antisocial personality disorder symptomatology. These findings implicate serotonergic function in a dimension of human personality linked to negative emotional experience.

References:

1. Livesley WJ, Jang KL, Jackson DN, & Vernon PA: Genetic and environmental contributions to dimensions of personality disorder. American Journal of Psychiatry. 150(12), 1826–1831; 1993.

2. Watson D, Clark LA & Tellegen A: Development and validation of brief measures of positive and negative affect: The PANAS scales. Journal of Personality and Social Psychology, 54(6), 1063–1070; 1988.

NR99 Monday, May 6, 1:00 p.m.-2:30 p.m.

Gender Differences in Noradrenergic and Serotonergic Studies

Ann M. Woo-Ming, M.D., Psychiatry, Mt. Sinai Med Ctr, One Gustave Levy Place, New York NY 10029; Antonia S. New, M.D., Vivian Mitropoulou, M.A., Robert L. Trestman, M.D., Emil F. Coccaro, M.D., Larry J. Siever, M.D.

Educational Objectives:

The goal of this presentation is to familiarize the audience with the neurohormonal challenge studies used to study noradrenergic and serotonergic systems in mood and personality disorder patients. Data will then be presented describing the outcomes of these challenges in female patients, in comparison to what is historically known about male subjects.

Summary:

Previous studies of male patients have shown a blunted growth hormone (GH) response to clonidine to be associated with depression (Trestman, et al. 1992) and an increased GH response to be associated with irritability (Coccaro, et al. 1991). Studies have also shown a diminished prolactin response to fenfluramine (FEN) in males which is associated with suicidality in patients with major depression and personality disorders, and with impulsivity/aggression in patients with personality disorders. Female subjects have not been as extensively evaluated. To examine gender differences in these biological markers, the GH response to clonidine and prolactin response to FEN were assessed in female patients with major depression (MDD), borderline personality disorder (BPD), other personality disorders (OPD), and normals.

Results: GH response to IV clonidine, an index of postsynaptic alpha-adrenergic function, was measured in patients with primary diagnoses of MDD ($n = 19$; mean 7.2 ± 6.2), BPD ($n = 14$; mean 4.8 ± 5.3), OPD ($n = 15$, mean 3.1 ± 3.6), and normals ($n = 9$; mean 2.9 ± 3.3). Unlike our male subjects, our female subjects showed no differences in GH response related to diagnosis ($F = 1.3$, p = ns), and no relationship with either degree of depression (HAM-D) or irritability scores (Buss-Durkee Hostility Inventory: $r = -.07$, p = ns). Prolactin response (delta PRL) to fenfluramine was measured as an index of central 5HT function as previously reported (Coccaro, et al. 1989) in patients with primary diagnosis of MDD ($n = 14$, mean 21.4 ± 9.5), BPD ($n = 11$, mean 31.2 ± 22.8), OPD ($n = 20$, mean 26.6 ± 17.6), and controls ($n = 6$, mean 18.1 ± 12.8). Unlike men, women had higher delta PRL responses to FEN with no differences related to diagnosis ($F = .98$, p = ns) and no relationship with irritability or assault ($r = .30$, p = ns). Our preliminary data have shown a negative correlation between time of response to fluoxetine (defined as a decrease of > 6 points in the HAM-D compared to baseline score) and peak PRL level in male and female MDD patients ($r = -0.93$, $p < 0.001$, $n = 7$).

Implications: There appear to be gender differences in monoaminegic behavioral relationships that might have implications for gender differences in response time to antidepressant treatment.

References:

1. Coccaro EF, Siever LJ, Klar HM et al: Serotonergic studies in patients with affective and personality disorders. Archives of General Psychiatry, 1989, 46;587-599

2. McBride A, Tierney H, DeMeo M: Effects of age and gender on CNS serotonergic responsivity in normal adults. Biological Psychiatry, 1990, 27:1143-1145

NR100 Monday, May 6, 3:00 p.m.-5:00 p.m.

Suicides Occurred in Buenos Aires During 1994

Gillermo J. Tortora, M.D., Hospital Borda, Ituzaingo 1250 3A, Lanos Buenos Aires, Argentina; Alicia Sotelo Lago, M.D., Liliana Florio, Ph.D.

Summary:

There are various great enigmas in human life, suicide being one of them. Nobody really knows why a human being can kill himself.

Attempts to study this subject, through so-called psychological autopsies, were difficult because of reluctance to give details on the episode by the relatives, neighbors, or friends mainly due to shame, family situations, religious reproach and, especially, the fear of being denied insurance benefits. For this reason, this research is aimed at analyzing the epidemiological data that permit the evaluation of the death rates through the legal-medicine autopsies performed at the judicial morgue of the Body of Forensic Physicians of Buenos Aires, Argentina, during 1994. (N:3,094 autopsies). We determined the rates (N: 499 suicides) by age, sex, marital status, season, place, and mechanism employed.

Although the figures are highly reliable, we note the possibility of sub-recording as described in many epidemiological works on this issue. This is the case of so-called concealed suicides, i.e., suicides that could not be recorded as such as they were reported as accidents.

Based on the data obtained, our findings confirm the statistic trend that the epidemiological profile of committed suicide differs from the profile of attempted suicide, mainly in regard to sex (males 62.72%; females 37.28%), age (67.5%, majority of 40 years), and method (males: fire guns:48.80; females jumping: 34.40%).

NR101 Monday, May 6, 3:00 p.m.-5:00 p.m.

Neuropsychiatry and Clinical Evaluation and Infectology in Different Socioeconomic Level HIV-Infected Drug-Dependant Patients in Argentina

Guillermo J. Tortora, M.D., Hospital Borda, Ituzaingo 1250 3A, Lanos Buenos Aires, Argentina; Adriana Portas, M.D., Juan Gonzalez Blanco, M.D., Oscar Garcia Messina, M.D., Liliana Florio, Ph.D.,

Summary:

Purpose: Determining a) epidemiology in population by analyzing clinical virological, and immunological patterns, predictable value. b) neuropsychological evaluation; c) psychic condition; d) drug used, beginning age, types, addiction levels, importance of legal values, and e) evaluation of antirretrovirals.

Materials and Methods: Two groups of drug-dependant populations were analyzed in two different centers: Center A. the Jose T. Borda Hospital is a gratuitous public hospital, and a hospital where criminals were confined as a result of judicial decision. Center B, Policlinico Bancario Hospital, is a medical center belonging to the Banking Employees Union. Clinical infectological and immunological analyses were made. A neuropsychological series of studies was also carried out together with a psychiatric examination.

Conclusions: Fifty out of 66 patients (75.75%) were intravenous drug addicts; 34 patients were judicially confined in hospitals, and 14 revealed imprisonment antecedents. The most frequent crimes (drug possession and marketing) were observed as antecedents in those patients confined in Center A. These patients had a lower less economic and cultural status. Center B patients were middle class patients and revealed less imprisonment antecedents, but higher costs regarding drugs consumed. Both groups demonstrated very similar behavioral patters. Five patients showed psychotic disturbances due to drug consumption. Four were mentally ill and had AIDS. The remainder showed different levels of cognitive deterioration. It was demonstrated that patients in the 20–29 yr use range were the most frequent drug-dependent group. Sexually-transmitted diseases were observed in Center B while infectious blood disease, prevailing STD (Sexual Diseases).

NR102 Monday, May 6, 3:00 p.m.-5:00 p.m.

Therapy Completion Rates in Patients Prescribed Isoniazid and SSRIs

Michael E. Doyle, M.D., Psychiatry, Walter Reed VAMC, Borden Pavilion, Washington DC 20307; Daniel W. Hicks, M.D., Naomi Aronson, M.D.,

Summary:

Objective: Recognizing a potential interaction between isoniazid (INH) and selective serotonin reuptake inhibitors (SSRI), we assessed therapy completion rates in HIV infected individuals taking an SSRI, INH, or both.

Method: Treatment records were retrospectively case-control reviewed to determine if drug therapy was completed in accordance with a treatment plan (e.g., 12 months of INH therapy). Patients on both medications constituted the sample population; patients taking either an SSRI or INH alone comprised comparison populations.

Results: There were no significant differences between the populations based on age, gender, or CD4%. Three of the 10 patients in the sample population completed therapy, which was significantly less (Fisher Exact test, two tailed) than the 11 of 13 in the SSRI group ($p = 0.0131$) and the 14 of 18 subjects who completed therapy with INH ($p = 0.0204$).

Conclusion: Therapy completion rates for patients prescribed an SSRI coincident with INH were significantly lower than for those prescribed these separately. These differences cannot be accounted for on the basis of age, gender, or CD4%, but may be due to increased side effects caused by interactions between these medications.

NR103 Monday, May 6, 3:00 p.m.-5:00 p.m.

Recognition of Severe Depression and Suicidal Ideation in HIV-Infected Patients

Mark H. Halman, M.D., Psychiatry, The Wellesley Hospital, 160 Wellesley St. East, JB#334, Toronto ON M4V 1J3, Canada; Ronald J. Heslegrave, Ph.D.,

Summary:

Objective: To examine predictors of severe depression and suicidality and their recognition in HIV-infected patients attending a newly established HIV psychiatry service.

Methods: Seventy-seven consecutive HIV-infected patients referred by their primary care physician for psychiatric assessment, completed a demographics questionnaire, CAGE survey, and Beck Depression Inventory (BDI) prior to undergoing a semistructured psychiatric interview. Multiaxial diagnoses (DSM-IV, CDC HIV staging, ADC staging and GAF) were determined. Severe depression was defined as BDI > 27, and suicidality was assessed by endorsements on BDI item nine. Family physicians completed a referral triage form inquiring about suicidality in a subset of 38 patients.

Results: The sample was 98% male, 89% white, mean age of 37 ($\pm$ 8) years, mean education of 14 ($\pm$ 4) years, and 95% identified as men who have sex with men. Forty-eight percent perceived themselves as having poor or no social support. Sixty-seven percent had a psychiatric history and 61% had a positive family history. Forty-six percent had asymptomatic HIV disease, 22% had symptomatic non-AIDS-defining conditions and 32% had AIDS. Mean BDI was 23 $\pm$ 9, mean GAF was 53 $\pm$ 16. Significant predictors (chi square analyses) of severe depression (36% of sample) included perception of poor social support ($p \leq .001$), not working ($p \leq .01$), living alone ($p \leq .01$), knowing < 10 HIV-positive people ($p \leq .04$), psychiatric history ($p \leq .03$), and concern over drug use ($p \leq .04$). Significant predictors of suicide were BDI > 27 ($p \leq .001$) and psychiatric history ($p \leq .03$). Referring physicians recognized suicidality in only 52% of patients who endorsed some level of suicidal ideation on the BDI.

Conclusion: Poor psychosocial supports and isolation were predictive of depression in this sample of HIV-infected patients. Severe depression and psychiatric history were predictive of suicidal ideation, though referring physicians recognized suicidal ideation at only chance levels.

NR104 Monday, May 6, 3:00 p.m.-5:00 p.m.

Congenital HIV: Effect of Knowledge of Diagnosis on Mood and Social Function

Cathy A. Mercaldi, M.D., Psychiatry, New York Hospital, 445 E 68th St #6J, New York NY 10021; John C. Markowitz, M.D., Ladd Spiegel, M.D.,

Summary:

Objective: This poster presents preliminary data from a study of children with congenital HIV infection, an essentially unstudied population. We assessed what children know about their illness and how this knowledge affects their mood and function. Based on research with pediatric cancer patients, we hypothesized that children knowing more about their illness would show less depression and better function.

Method: Guardians (G) and social work therapists (SW) of ten congenitally infected patients (ages 7 to 11) completed questionnaires to assess knowledge of illness. Each guardian completed Achenbach's Child Behavior Checklist (CBCL) to measure social functioning. Child patients completed Kovac's Children's Depression Inventory (CDI) as a depression screen.

Results: Children knew an average of 2.2 ± 2.7 (according to G) or 2.6 ± 2.1 (SW) concepts about their illness. Four (40%, G) and seven (70%, SW) saw themselves as seriously or always ill. None of the children screened positive for depression on the CDI (mean 8 ± 2.4) and only one, who has attention deficit hyperactivity disorder, screened positive for social dysfunction on the CBCL (mean 3.6 ± 3.0).

Conclusion: Preliminary data suggest that these children are doing well psychiatrically regardless of knowledge level. However, given the wide range noted in knowledge, we expect additional data to allow correlation between knowledge level and depression/function. This study is ongoing.

NR105 Monday, May 6, 3:00 p.m.-5:00 p.m.

Possible Alzheimer's Disease Resembles Probable Alzheimer's Disease with Respect to Clinical Features and Rate of Progression

Carmen M. Rodriguez, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue, Ste. 702, Miami FL 33136; Steven Sevush, M.D., A.N. Choudhury, M.D., Ian Treasaden, M.B., Dhrubo J. Bagchi, D.P.M., K.K. Ghosh, M.B., K.D. Sen, D.P.M.,

Summary:

Objectives: NINCDS criteria exclude a diagnosis of probable Alzheimer's disease (PAD) if cerebrovascular disease (CVD) is present. It is unclear, however, whether excluded patients differ clinically from those with PAD. We addressed this issue by comparing PAD with CVD patients with respect to clinical features of their illness.

Methods: 130 patients with NINCDS PAD and 40 patients with CVD were studied. The Hachinski Ischemic Scale, modified by inclusion of MRI data, was used to identify CVD. Groups were compared with respect to delusions of theft (Variable 1), repeating of questions over and over (Variable 2), denial of deficit (Variable 3), and rate of disease progression (Variable 4), calculated as the decline in Mini-Mental Status Examination (MMSE) score over one year (available for 118 PAD and 18 CVD patients). Analysis of covariance, controlled for initial MMSE score, was used to compare groups with respect to the clinical measures.

Results: PAD patients failed to differ from CVD patients with respect to any of Variable 1 ($F = 1.05$, $p = .3$), Variable 2 ($F = 0.45$, $p = .5$), Variable 3 ($F = 0.65$, $p = .4$), or Variable 4 ($F = 0.65$, $p = .4$).

Conclusions: These data suggest that exclusion of patients from PAD because of evidence of CVD may be arbitrary. Specifically, CVD patients may suffer primarily from AD despite the additional presence of CVD pathology.

NR106 Monday, May 6, 3:00 p.m.-5:00 p.m.

A Cognitive-Behavioral Approach to Panic Attacks in Chronic Schizophrenia

Phyllis B. Arlow, C.S.W., Queens Day Center, Hillside Hospital, 87-80 Merrick Blvd., Jamaica NY 11432; Mary E. Moran, Ph.D., Paul C. Bermanzohn, M.D., Samuel G. Siris, M.D.,

Summary:

Objective: Panic attacks contribute to overall severity and dysfunction in schizophrenia. The Epidemiological Catchment Area surveys found prevalence rates of 28% to 63%, depending upon the site. In nonschizophrenic populations with panic disorder, cognitive behavioral therapy is considered the treatment of choice, based upon reports of beneficial short-term and long-term effects. However, in schizophrenic patients with panic disorder, the efficacy of cognitive behavioral therapy has not been established. This poster reports on an open clinical trial using cognitive behavioral therapy with patients diagnosed with schizophrenia and panic disorder. A case study is also presented.

Method: In a 16-week clinical trial, eight patients were given CBT. All met DSM-III-R criteria for schizophrenia and panic disorder. Patients received the Westergaard (CBM-WASPA) at baseline (pretreatment) and 16 weeks posttreatment to systematically assess panic.

Results: Pilot analyses were computed and demonstrated that CBT reduced the frequency and intensity of overall panic symptomatology 16 weeks posttreatment. Patients demonstrated a statistically significant reduction in panic symptoms and an overall diminution in panic attacks from baseline to four months posttreatment.

Conclusions: These results suggest that CBT is a most promising component in the integrated of patients with a diagnosis of schizophrenia and panic disorder.

NR107 Monday, May 6, 3:00 p.m.-5:00 p.m.

The Differential Effectiveness of Social Skills Training for Schizophrenia: Deficit Versus Nondeficit Negative Symptoms

Alex J. Kopelowicz, M.D., San Fernando MHC, 15535 San Fernando Mission, Mission Hills CA 91345; Robert P. Liberman, M.D., Roberto Zarate, M.A., Jim Mintz, Ph.D.,

Summary:

The efficacy of social skills training (SST) for the negative symptoms of schizophrenia is not universally accepted. The present study is an attempt to determine whether patients with equal severity but different quality of negative symptoms (i.e., deficit vs. nondeficit) have divergent responsiveness to SST.

Six male outpatients with chronic schizophrenia (three with the deficit syndrome and three with nondeficit negative symptoms) underwent SST twice weekly for 12 weeks using a multiple baseline across target behaviors design. Social skills were evaluated with a modified version of the Behavioral Assessment Test-Revised. Negative symptoms were rated with the Schedule for the Assessment of Negative Symptoms (SANS).

Subjects with nondeficit negative symptoms significantly improved on each of the behaviors trained and remained improved six months later, while deficit syndrome subjects did not change from baseline. Similarly, subjects with nondeficit symptoms had improved SANS scores immediately after completing training and at follow-up, while deficit syndrome subjects showed no change.

These data suggest that patients with nondeficit negative symptoms may be more amenable to SST than patients with the deficit syndrome. The deficit/nondeficit distinction may allow for the identification of those individuals whose negative symptoms would most benefit from social skills training.

NR108 Monday, May 6, 3:00 p.m.-5:00 p.m.

Effect of Patients Observing Their Videotaped Behavior

Stephanie A. Davidoff, M.D., Psychiatry, McLean Hospital, 19 Strawberry Hill Road, Natick MA 01760; Brent Forrester, M.D., S. Nassir Ghaemi, M.D., J. Alexander Bodkin, M.D.,

Summary:

Objective: Many patients with psychotic disorders lack an awareness of being ill. We explored whether exposing patients to videotapes of themselves, made while they were in an acutely psychotic state, might increase their insight into the nature of their illness.

Methods: 16 psychotic inpatients were assigned randomly to a control or experimental group. All were interviewed on videotape shortly after admission, while in an acutely psychotic state, using instruments measuring insight (Insight and Treatment Attitudes Questionnaire) and psychopathology (Brief Psychiatric Rating Scale). One to four weeks later, when judged to be significantly improved, each subject in the experimental group was shown his/her videotape made after admission; the control group was shown a comedy videotape. All subjects then participated in a discussion of their illness. Between 24–48 hours after viewing the videotapes subjects were reinterviewed on videotape and again evaluated with the BPRS and ITAQ to evaluate insight and psychopathology.

Results: The mean changes in BPRS scores for the control and experimental groups were 7.33 (5.8%), and 10.57 (8.4%), respectively ($p = 0.072$, Student's t-test). The mean changes in ITAQ scores for the control and experimental groups were 2.88 (8.7%) and 7.37 (22.3%), respectively ($p = 0.059$).

Conclusion: Exposure of hospitalized patients to videotapes of their own psychotic behavior may be a cost-effective educational tool for the development of insight into psychiatric illness.

NR109 Monday, May 6, 3:00 p.m.-5:00 p.m.

Abnormal Parietal Lobe Asymmetry in Schizophrenia

Robert M. Donnino, B.A., Psychiatry, Brockton VAMC, 940 Belmont Street, Brockton MA 02401; Martha E. Shenton, Ph.D., Dan V. Iosifescu, M.D., Ota Hirokazu, M.D., Ronald Kikinis, M.D., Robert W. McCarley, M.D.,

Summary:

This MRI study examined the parietal lobe in 15 schizophrenic and 15 control subjects, all right-handed males, matched for age and social class of origin. Gray matter volumes of parietal regions were assessed, including the postcentral gyrus, superior parietal gyrus, and inferior parietal lobule (IPL) (comprised of the supramarginal and angular gyri), with a focus on the IPL.

MR scans were obtained on a 1.5 Tesla magnet using 3DFT SPGR and stored as coronal slices (1.5mm thick). Postprocessing of MR images included using an algorithm for semiautomated segmentation, an algorithm allowing slice-editing in multiple planes, and a surface rendering algorithm that created 3D representations of relevant brain structures. All volumes were corrected for total intracranial space to account for variation in head size. No significant volume differences were observed for overall parietal gray matter or for the IPL. Schizophrenics did, however, exhibit a reversal of normal controls' (left > right) asymmetry of the IPL, yielding a significant group X laterality interaction ($F(2, 28) = 6.23$, $p = .019$). A similar group X laterality interaction (trend) was observed for the whole parietal lobe ($F(2,28) = 3.70$, $p = .065$). These results are consistent with recent reports implicating parietal lobe abnormalities—specifically parietal asymmetry—in the pathogenesis of schizophrenia.

NR110 Monday, May 6, 3:00 p.m.-5:00 p.m.

Medical Comorbidity and Psychotic Illness in an Outpatient Clinic Sample

Calvin J. Flowers, M.D., Psychiatry, LA County USC Medical Center, 1937 Hospital Place, Los Angeles CA 90033; Lawrence S. Gross, M.D., Mina Tasic, M.D., George M. Simpson, M.D.,

Summary:

Introduction: There is evidence from recent research that psychiatric patients may have an increased risk for certain chronic and serious comorbid medical conditions. There has been, however, relatively little work done investigating the relationship between chronic psychotic illness (i.e. schizophrenia) and coexisting physical illness.

Methods: We collected data on 294 patients at a major urban outpatient psychiatric clinic who were identified as being on maintenance therapy with antipsychotic medications. Demographic, diagnostic, and treatment data were collected cross-sectionally from chart reviews.

Results: The sample included 138 males and 156 females with a mean age of 44 years (range 18–84). The ethnic distribution was as follows: 17% white, 21% black, 54% Hispanic, and 7% Asian-Pacific. Of 294 patients identified as being on maintenance neuroleptic therapy, 211 (72%) had one or more comorbid medical conditions. The most frequent medical diagnosis was hypertension (17%), followed by diabetes mellitus (8.5%), and hypothyroidism (3.4%). These prevalence figures are significantly higher than published estimates for the general population.

Conclusions: This study suggests that a subset of psychiatric patients, (i.e., those maintained on neuroleptics for psychotic illness) may be at greater risk for certain comorbid medical illnesses compared with the general population.

NR111 Monday, May 6, 3:00 p.m.-5:00 p.m.

Positive and Negative Syndrome Scale Symptom Factors in Schizophrenia

Diane Fredrikson, Psychiatry, University of BC, 2660 Oak Street, Vancouver BC V6H 3Z6, Canada; William G. Honer, M.D., Peter F. Liddle, M.D., James M. Steiger, Ph.D., Lili C. Kopala, M.D., Siemion Altman, M.D.,

Summary:

Objective: To replicate the five-factor model of schizophrenia (Kay & Sevy, 1990).

Method: Subjects included chronically ill in patients with DSM-III-R schizophrenia (n = 164) and nonschizophrenic psychoses (n = 55: schizoaffective n = 37, bipolar n = 11, and psychotic depression n = 7). Positive and Negative Syndrome Scale (PANSS) ratings were completed during an acute exacerbation of illness and used for principal components analysis (schizophrenic subjects) and subsequent between-group comparisons (all subjects).

Results: Factor analysis yielded five independent symptom factors: Negative (N1-N4, N6, G7), Positive (P1, P3, P5, P6, G9), Cognitive (N5, P2, G10, G11), Excitement (P4, P7, G8, G14), and Depression (G2, G3, G6), largely replicating previous results. Cognitive and negative factor scores discriminated between paranoid (n = 43) and disorganized (n = 34) schizophrenia, with the paranoid subgroup scoring lower on each factor. However, no difference was found between groups on the depression factor. High depression factor scores differentiated patients with a depressive syndrome (n = 28) from those with either a manic (n = 18) or no (n = 150) affective syndrome. Similarly, low negative factor scores, or high excitement factor scores, discriminated patients with a manic syndrome from those with either a depressive or no affective syndrome.

Conclusions: The five-factor model appears to be a valid construct of schizophrenic symptoms. In addition, the independence of a negative and depression factor is supported by the data.

NR112 Monday, May 6, 3:00 p.m.-5:00 p.m.

Medical Illness in Relatives of Schizophrenics, Affective Disorders and Normal Controls

Janet E. Johnson, M.D., Med Geriatrics, NY State Psychiatric Institute, 722 West 168th Street, Unit 58, New York NY 10032; Elizabeth Squires-Wheeler, Ph.D., Simone A. Roberts, B.A., L. Erlenmeyer-Kimling, Ph.D.,

Summary:

Many studies have been conducted examining the prevalence of various medical disorders in psychiatric patients (Tsuang, 1983). A decreased prevalence of rheumatoid arthritis in schizophrenia has been consistently demonstrated. Associations of migraine, diabetes, and cancer with affective illness and schizophrenia have also been reported but with less consistent results. However, few studies have examined the rate of medical illness in relatives of psychiatric patients.

Methods: We conducted family history interviews with schizophrenic and affectively ill probands, their spouses, and normal controls from the New York High Risk Project to obtain information about medical illnesses in their parents and siblings.

Results: Migraine was found to occur at an increased rate in relatives of schizophrenic patients, as compared to affective disorder, well spouses, and normal controls ($p < .05$). Asthma and thyroid disease also occurred at a significantly increased rate in siblings of schizophrenic patients.

Discussion: Demonstration of familial patterns of medical illness in schizophrenia and affective disorders may help elucidate etiology. Of particular interest are the autoimmune disorders, given the recent report of putative linkage of schizophrenia to chromosome 6 and the HLA region. Both asthma and thyroid disease involve autoimmune mechanisms.

NR113 Monday, May 6, 3:00 p.m.-5:00 p.m.

The Effects of Risperidone Versus Haloperidol on Measures of Prefrontal Functioning in Treatment-Resistant Schizophrenia

Susan R. McGurk, Ph.D., B151H Bldg 210, BR15, Brentwood VA Med Ctr, 11301 Wilshire Blvd., Los Angeles CA 90073; 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:

Spatial working memory tasks require subjects to briefly view a target stimulus and then indicate after a delay the location of the target. Accurate performance on this task requires the formation of an internal representation of spatial location to guide the delayed response. This function is supported by the dorsolateral prefrontal cortex and is impaired in schizophrenia. Animal studies indicate a role for both dopamine and acetylcholine in performance of this task. The current study involved inpatients who were participating in a double-blind comparison of risperidone vs. haloperidol ($N = 44$; 20 subjects were receiving risperidone). Measures of working memory were administered during a seven-day wash-out prior to random assignment and following four weeks of double-blind fixed-dose medication. The design of this study allowed for assessment of the separate effects of risperidone and benztropine mesylate on performance of the neurocognitive measures. An analysis of covariance indicated a trend for a beneficial effect for risperidone and a highly detrimental effect of benztropine mesylate on spatial working memory performance. Additionally, the spatial working test was significantly correlated, at baseline, with three other putative prefrontal measures including Verbal Fluency ($r = 0.24$), Wisconsin Card Sort ($r = 0.48$, number of correct responses), and Trailmaking "B" ($r = -0.45$). These results suggest a role for acetylcholine in spatial working memory. Additionally, the pattern of intercorrelations suggests that performance on the spatial working memory task is reflecting prefrontal functioning in this sample.

NR114 Monday, May 6, 3:00 p.m.-5:00 p.m.

Trends and Patterns of Substance Use Amongst Schizophrenic Patients: A Ten-Year Study of Emergency Room Visits

Ashwin A. Patkar, M.D., Psychiatry, Jefferson Med College, 111 South 11th Street, Philadelphia PA 19107; Robert C. Alexander, M.D., Kenneth M. Certa, M.D., C. Boardman, Ph.D.,

Summary:

Objective: Most studies of substance use in schizophrenia have focused on prevalence issues, clinical and demographic correlates, and the negative effects of substance use. The goal of this study was to investigate whether there was a change in patterns of substance abuse among schizophrenic patients over a ten-year period.

Method: The subjects were selected by a retrospective review of records of visits to the crisis center of a university hospital during 1984–1994. The sample was all individuals with a diagnosis of schizophrenia (DSM-III and DSM-III-R) who visited the crisis center during the first half of alternate years of the study period. Substance use was diagnosed and categorized on the basis of urine toxicology screens.

Results: There was a significant increase in schizophrenic patients testing positive for illicit drugs. Moreover, cocaine and cannabis use showed a significant increase. Amphetamine and barbiturate use decreased significantly while opiate and benzodiazepine use was unchanged. There were no significant racial differences in substance use.

Conclusions: First, there has been a significant increase in schizophrenic patients testing positive for illicit drugs during emergency room visits from 1984–1994. Second, this increase seems to be due to an increase in cocaine and cannabis use.

NR115 Monday, May 6, 3:00 p.m.-5:00 p.m.

Referential Activity of Language in Schizophrenic Outpatients

Lisseth Rojas-Flores, M.A., Derner Institute, Adelphi University, Hy Weinberg Bldg, Garden City NY 11530; Wilma Bucci, Ph.D., Lewis A. Opler, M.D., Jill R. Linder, M.D., Frank Cory, Psy.D.,

Summary:

Objective: This study aimed to examine schizophrenic language and psychiatric symptoms using computer generated Referential Activity (CRA), a measure of linguistic and emotional features of texts based on the multiple-code theory. All three subscales of the Positive and Negative Syndrome Scale (PANSS) were rated to determine whether degree of general psychopathology or phenomenological positivity and negativity would covary with levels of Referential Activity (CRA).

Method: Nineteen stable outpatient schizophrenics and schizoaffectives were rated on the PANSS and asked to provide four monologues about their childhood memories. Narratives were analyzed using computer assisted procedures for referential activity (CRA).

Results: Results revealed inverse correlations between levels of PANSS General Psychopathology Scale and CRA for each narrative provided. CRA totaled across texts yielded statistically

significant findings (r = -.47; p = .05). Contrary to expectations, no correlations between CRA scores and degree of positive and negative symptoms were found.

Conclusions: Preliminary data analyses confirmed the applications of multiple-code theory and CRA as a useful paradigm in schizophrenia research. Moreover, these results are congruent with contentions that cognitive functions fail with high levels pathology, particularly with regards to affective expression.

NR116 Monday, May 6, 3:00 p.m.-5:00 p.m.

No Association Between Null Allele at the Dopamine D4 Receptor and Schizophrenia

Walter G. Rooney, B.A., ETB, NIH, 9000 Rockville Pike, Bethesda MD 20892–1380; Anil K. Malhotra, M.D., David S. Goldman, M.D., Robert W. Buchanan, M.D., Alan F. Breier, M.D., David Pickar, M.D.,

Summary:

Objective: The goal of this study was to determine if there is a significant association between a mutation in exon 1 of the dopamine D4 receptor and schizophrenia. This mutation is a 13 base-pair deletion causing a frameshift, which results in a premature stop codon. It is predicted that this mutation renders the receptor non-functional (known as a null allele).

Methods: Genomic DNA was collected and extracted from 131 patients who were diagnosed with schizophrenia or schizoaffective disorder according to DSM-III-R criteria. The candidate region was then amplified using the polymerase chain reaction. The PCR product was denatured and resolved by polyacralymide gel electrophoresis using single-stranded comformational analysis (SSCP). A positive SSCP result was confirmed using 5% polyacrylamide gel electro-phoresis.

Results: One patient out of 131 was found to be heterozygous for this mutation and no homozygotes were identified. The allelic frequency of the null allele was .0038. We are examining the heterozygote for clinical variables including neuropsychological testing and response to antipsychotic medications.

Conclusions: This study suggests that a null allele in the first exon of the dopamine D4 receptor gene is not significantly associated with schizophrenia. This conclusion is consistent with Nothen et al.[1]

NR117 Monday, May 6, 3:00 p.m.-5:00 p.m.

Clinical Predictors of Acute Risperidone Response in Elderly Patients with Schizophrenia and Schizoaffective Illnesses

Sean P. Stanton, B.S., Psychiatry, University of Cincinnati, 231 Bethesda Avenue ML559, Cincinnati OH 45267; Daniel R. Wilson, M.D., Paul E. Keck, Jr., M.D., Susan L. McElroy, M.D., Danielle L. Kizer, B.S., Tony M. Balistreri, B.S.,

Summary:

Risperidone has been shown to be as effective as conventional antipsychotic agents in the treatment of patients with schizophrenia and to cause fewer and less severe extrapyramidal side effects. (Marder SR, et al., 1994, Chouimard G, et al., 1993). To our knowledge no studies have examined the efficacy of riperidone in geriatric patients with schizophrenia or schizoaffective disorder. With its favorable side effect profile risperidone was hypothesized to be a useful treatment for elderly patients with schizophrenia and schizoaffective disorder.

Methods: We evaluated the efficacy of risperidone in geriatric patients with schizophrenia (N = 15) and with schizoaffective disorder (N = 15). These patients were treated at a state psychiatric hospital in Cincinnati, Ohio, in 1994. Response to risperidone was assessed by independent raters who also consulted with each patient's treating psychiatrist.

Results: Forty percent of patients were refractory to previous trials of standard antipsychotics. Fifteen patients (50%, six with schizophrenia, nine with schizoaffective disorder) displayed a moderate to marked response to risperidone. A moderate to marked response was significantly associated with shorter length of hospitalization prior to risperidone treatment ($p < 0.003$), combination therapy ($p < 0.03$), and fewer number of failures to previous antipsychotics ($p < 0.01$). The average length of stay for these patients was 3.8 years: treatment response was sufficient to allow discharge from the hospital in 30% of patients who had been in the hospital for at least ten weeks, and 21% of patients who had been in the hospital for more than one year before being treated with risperidone.

Conclusions: Risperidone is a useful therapeutic agent in the treatment of geriatic patients with schizophrenia and schizoaffective disorder refractory to previous standard antipsychotic agents.

NR118 Monday, May 6, 3:00 p.m.-5:00 p.m.

MRI Study of Auditory Memory in Schizophrenia

Alexander A. Stevens, Ph.D., CSC, Yale University, 230 South Frontage Road, New Haven CT 06520; Patricia Goldman-Rakic, Ph.D., John C. Gore, Ph.D., Bruce E. Wexler, M.D.,

Summary:

Substantial evidence suggests that individuals with schizophrenia are particularly impaired on auditory and verbal functions. Functional imaging techniques can elucidate the neural systems involved in these capacities. The present study investigated the neural basis of auditory verbal and nonverbal memory in patients with schizophrenia. Using functional magnetic resonance imaging with an echo-planar sequence, cerebral blood flow in patients with schizophrenia (n = 6) and age- and education-matched controls (n = 7) was assessed during performance of procedurally identical auditory verbal and nonverbal memory tasks. For the nonverbal memory task three tones were presented followed by a variable retention interval, after which one of the three tones was repeated. Subjects indicated the position of the repeated tone in the list (first, second, or third) by extending the appropriate number of fingers. The verbal memory task required subjects to perform the same task with four words presented. Two sequences for each task were run and during each imaging sequence tasks were preceded and followed by a baseline matched for auditory stimulation and motor response.

Ten axial slices were acquired parallel to the anterior-posterior commissure in a Signa 1.5 tesla scanner with the following parameters: TR = 1500 msec; flip angle = 60; 80 images per/slice; FOV = 128 x 64. The signal of each pixel during baseline was subtracted from task activation and was retained if the difference reached a t-value greater than one on both imaging sequences for it and five adjacent pixels. Twenty-four regions of interest (ROI) were identified and analyzed for each task. Results revealed a Group-by-Hemisphere trend in the tone task ($F(1, 11) = 3.942$, $p = .073$) reflecting relatively more left hemisphere activation in controls and greater right hemisphere activation in patients. For the word task, a trend in the Group-by-ROI-by-Hemisphere interaction ($F(9, 99) = 1.811$, $p = .075$) reflected greater signal in the right frontal lobe (Broca's Areas 45, 46) of the patients. Results suggest the patients showed abnormal right frontal lobe activity primarily in areas previously implicated in a working memory function.

NR119 Monday, May 6, 3:00 p.m.-5:00 p.m.

Neurological Soft Signs and Formal Thought Disorder in Schizophrenia

Raffaella Valigi Bjorck, M.D., Psychiatry, Karolinska Institute, Huddinge Hospital, S-14186 Huddinge, Sweden; Conny Nordin, M.D.,

Summary:

Compared with controls, patients with schizophrenia have a higher prevalence of non-focal neurological abnormalities called "soft signs". The significance of those signs is unclear, but it is commonly accepted that they are expressions of an impairment of several brain systems.

Objectives: We wanted to investigate the prognostic role of soft signs in patients with schizophrenia.

Methods: 40 schizophrenic (DSM-III-R) patients were included. All underwent a standardized neurological examination. Schizophrenic symptoms were evaluated using the SAPS and SANS scales. We obtained a formal thought disorder total score by adding the positive thought disorder subscale score (SAPS) and the alogia subscale score (SANS).

Results: We found a positive correlation between formal thought disorder total score and soft signs total score ($r_s = 0.40$; $p < .05$). This correlation was mainly accounted for by the positive thought disorder score, which was significantly ($p < .05$) higher in females.

Conclusion: Our results are preliminary but in line with earlier reports on an association between thought disorder and neurological soft signs. The correlation between soft signs and positive formal thought disorder might indicate a prognostic role of soft signs that has to be further explored in prospective studies.

NR120 Monday, May 6, 3:00 p.m.-5:00 p.m.

Medication Compliance and Self-Structure in Schizophrenia

Mary E. Witt, M.D., Psychiatry, UMDNJ-RW Johnson Med, 671 Hoes Lane, Piscataway NJ 08855; Stuart R. Schwartz, M.D., Michael Gara, Ph.D., Shula Minsky, Ph.D.,

Summary:

Objective: To learn about factors influencing medication compliance in patients with schizophrenia

Methods: A sample of subjects, diagnosed with schizophrenia, were assessed for self structure using a questionnaire with hierarchical classes analysis (HICLAS) and were rated for compliance by the treatment team

Results: Eight subjects, who had schizophrenia for at least ten years, were rated as compliant with recommendations for medication.

Of the eight subjects, all but one described being a patient in as elaborate a manner as the self. In fact, in half, the identity as patient could not be distinguished from the self. The self was described by most as having both positive and negative attributes. The ideal self and the psychiatrist were another pair perceived as very similar by all eight. One-fourth also perceived the psychiatrist like the parents. However, unlike the patient-self structure, the ideal self-psychiatrist pair was described in a positive manner.

The discussion will contrast these findings with results for non-compliant subjects and include other factors which may discriminate the groups (global assessment of function, family support, utilization of services).

Conclusions: Examination of the structure of self merits further investigation in understanding patients' compliance with medication recommendations for schizophrenia.

NR121 Monday, May 6, 3:00 p.m.-5:00 p.m.

Hippocampal Synaptic Proteins in Schizophrenia

Clint E. Young, B.Sc., Psychiatry, University of British Columbia, 2660 Oak Street, Vancouver BC V6H 3Z6, Canada; Kunimasa Arima, M.D., William S. Trimble, Ph.D., Peter Falkai, M.D., William G. Honer, M.D.

Summary:

Objective: Presynaptic proteins are altered in amount and distribution in the hippocampus in Alzheimer's disease and temporal lobe epilepsy. Since considerable evidence indicates hippocampal abnormalities in schizophrenia as well, we studied the levels and distribution of three presynaptic proteins in this region.

Method: Homogenates made from postmortem samples of hippocampus were available from 13 cases of schizophrenia and 13 controls. In addition, paraffin embedded hippocampal sections were studied from 12 cases of schizophrenia and 12 controls. Monoclonal antibodies were used to quantify the presynaptic proteins synaptophysin, SNAP-25, and syntaxin in homogenates with an ELISA, and in the dentate gyrus with image analysis.

Results: The ELISA findings indicated mean reductions in the synaptophysin (30%) and SNAP-25 (20%) immunoreactivities in the hippocampus in schizophrenia. The overall effect of diagnosis (MANOVA, $p < .05$) was significant, covarying for age and postmortem interval. Immunocytochemical studies of the dentate gyrus indicated significantly reduced synaptophysin ($p < .05$) and SNAP-25 ($p < .05$) immunoreactivities in the inner molecular layer in schizophrenia.

Conclusions: The immunoreactivity of proteins found in presynaptic terminals was reduced in the hippocampus in schizophrenia. Further investigations are required to determine if these changes represent a process intrinsic to the hippocampus, or if they are secondary to loss of connections from elsewhere.

NR122 Monday, May 6, 3:00 p.m.-5:00 p.m.

A Central Hypothesis for the Charles Bonnet Syndrome

Gil Lichtshein, M.D., Psychiatry, Univ. of Maryland, 2811 Baneberry Court, Baltimore MD 21209; Antony Fernandez, M.D., Lisa B. Dixon, M.D.

Summary:

Introduction: The Charles Bonnet Syndrome (CBS) is an underrecognized psychiatric syndrome characterized by vivid visual hallucinations without significant psychopathology or disturbed consciousness. The prevalence of CBS in geriatric populations ranges from 1% to 12%. This report reviews the literature on CBS and describes a case of an individual with CBS who was evaluated with advanced neuroradiologic techniques and with SPECT, a novel functional neuroimaging test. Our overall goal is to advance a new model for understanding the pathophysiology and diagnosis of CBS.

Methods: A literature review and case report are presented. The literature review was conducted using an extensive Medline search from the years 1966–1995 with key words: CBS, visual hallucinations, elderly, and eye disease. Experts in the field were consulted.

Results: The literature review revealed no consensus on the etiology and pathophysiology of CBS and, in particular, whether opthalmologic and/or brain insults are necessary. SPECT study revealed localizing cortical functional abnormalities in our CBS patient presenting without localizing CNS pathology evident on neurological exam or via CT or MRII.

Conclusion: These findings suggest a possible cortical etiology of CBS. Duplication of these findings by evaluation with functional neuroimaging techniques of other CBS patients could lead to reconceptualization of the etiology and pathophsyiology of CBS.

NR123 Monday, May 6, 3:00 p.m.-5:00 p.m.

Sickness Behaviors As Manifestations of Immunoendocrine Dysregulation in Somatic and Psychologic illness

Andrew N. Dentino, M.D., Center for Aging, Duke University Medical Ctr, Box 31051, DUMC, Durham NC 27710

Summary:

"Sickness behaviors" are formulated as the generalizable compendium of physical and psychologic symptoms that accompany any state of 'dis-ease,' be it major depression, chronic medical illness (diabetes/arthritis), acute infection (influenza), or even the 'normal' physiologic process of aging itself.

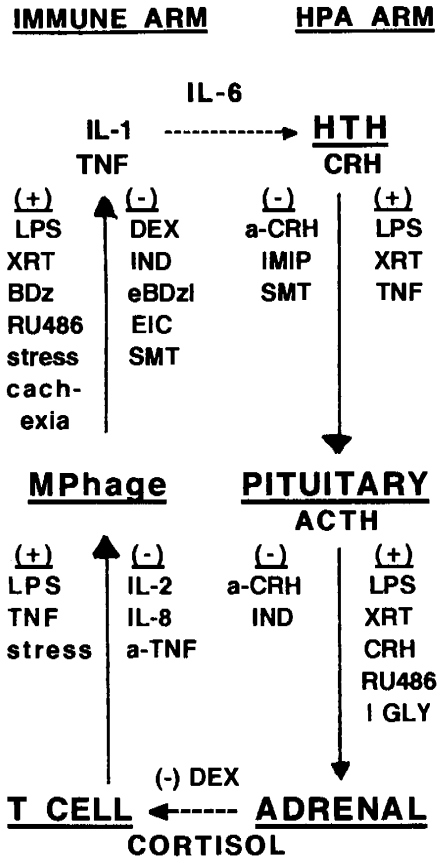
Sickness behaviors (evolutionarily potentially conferring some protective organismal adaptational advantage under stress) include anergia, malaise, dysphoria, sleep dysfunction, appetite changes, weight loss, and somatic pain sensations such as headache.

This study addresses the increasing body of literature etiologically implicating reciprocal dysregulated changes in several immunoendocrine axes, which act as multilevel, nonspecific mediators of various somatic and psychologic symptoms and behavior, in both animal and human models.

Methods involve Medline (all articles in English literature meshing under " 'cytokines' - 'depression' - 'aging' ") and supporting secondary literature review (over 500 articles).

A potential unitary psychopathophysiologic model of immunoendocrine dysregulation in major depression, referent to generalizable sickness behaviors in other illnesses and subsyndromal states, and to aging in general, results (Figure 1, text).

Prospective studies of rational therapeutic-antidepressant strategies to symptomatically and physiologically ameliorate these dysregulated processes in various conditions manifesting such sickness behaviors are discussed.



(+) LPS, TNF, ACTH, STRESS

1. IMMUNOENDOCRINE DYSREGULATORY ('POSITIVE FEEDBACK') MODEL OF MAJOR DEPRESSION (abbreviations in text)

NR124 Monday, May 6, 3:00 p.m.-5:00 p.m.

Alcohol Abuse in An Inpatient Geriatric Psychiatry Unit

Edward W. Cowen, B.S., Penn State College of Med, 189 University Manor East, Hershey PA 17033; Paul A. Kettl, M.D.

Summary:

Alcohol abuse in geriatric psychiatry is an under-recognized clinical syndrome. Since the bulk of geriatric psychiatry practice involves affective and cognitive disorders, a better understanding of the prevalence of alcohol abuse in these patients is essential.

191 patients consecutively admitted to a university-based geriatric psychiatry service were prospectively evaluated for the presence of alcohol abuse. The CAGE questionnaire and DSM-III-R criteria were used to assess alcohol abuse. Demographic data, diagnosis, length of stay, family history, and past psychiatric and medical history were reviewed, as well as MCV, ALKP, SGOT, and total bilirubin levels. Data were assessed using Chi-square analysis as well as two-tailed T-tests.

Twenty percent (39/191) of those admitted to the geriatric inpatient psychiatry service suffered from alcohol abuse. Alcohol abusers in general were younger than other patients ($p = .002$), were more likely to be male ($p = .009$), and had higher bilirubin levels on admission ($p = .05$). Alcohol abuse was not associated with a longer hospital stay, psychiatric diagnosis, or medical, psychiatric, and family history.

As in other medical services, a large number of those admitted to geriatric psychiatry service suffer from alcohol abuse. Although similar in many ways to other individuals, alcohol use in this group must be addressed for optimal care.

NR125 Monday, May 6, 3:00 p.m.-5:00 p.m.

Outcome of Psychiatric Hospitalization for Very Low-Functioning Demented Patients

Ayman Abdel Bakey, M.D., Psychiatry, Baylor College Med, One Baylor Plaza, Houston TX 77030; Mark E. Kunik, M.D., Victor Molinari, Ph.D., Claudia Orengo, M.D., Richard H. Workman, Jr., M.D., Joseph D. Hamilton, M.D.

Summary:

The characteristics and outcome of the lowest-functioning patients with dementia admitted to a geropsychiatric inpatient unit were examined. Sixty-nine consecutive admissions with a diagnosis of dementia and a Global Assessment of Functioning (GAF) score of 20 or less on admission received a standardized battery consisting of the Mini-Mental State Examination (MMSE), the Hamilton Rating Scale for Depression (HAM-D), the Brief Psychiatric Rating Scale (BPRS), the Cohen-Mansfield Agitation Inventory (CMAI), and the Rating Scale For Side Effects (RSSE). Mean BPRS, HAM-D, and CMAI scores decreased significantly from admission to discharge, indicating reductions in general psychiat-

ric symptoms, depression, and agitation, respectively. Mean GAF scores increased significantly between admission and discharge, reflecting improvement in patients' global functioning. Mean scores on the MMSE and RSSE remained unchanged, suggesting no untoward side effects with treatment. About three-quarters of the patients required discharge to a nursing home setting—not unexpected for this very low-functioning population. More noteworthy, however, is that nearly one-quarter could be discharged to home or a personal care home after the behavioral disturbances troublesome to caregivers improved with hospital treatment. It appears that even in this very low-functioning population, inpatient geropsychiatric treatment produces clinically significant behavioral improvement that can enhance the quality of life for patients and their often overburdened caregivers.

NR126 Monday, May 6, 3:00 p.m.-5:00 p.m.

Anxiety Sensitivity in Elderly Presenting to a Primary Care Clinic

William J. Apfeldorf, M.D., Psychiatry, Cornell University Med, 21 Bloomingdale Road, White Plains NY 10605; George F. Brady, M.A., M. Philip Luber, M.D., Barnett S. Meyers, M.D., Mary E. Charlson, M.D., George S. Alexopoulos, M.D.

Summary:

Objective: To determine whether high anxiety sensitivity, a pathologic form of anxiety associated with panic disorder, occurs in elderly patients presenting to a primary care setting.

Methods: Patients presenting for an initial evaluation at a university-based general medicine clinic were asked to complete a brief one-page questionnaire. The questionnaire gathers demographic information and includes the following items: 1) the 16-item Anxiety Sensitivity Index, with a range of 0 – 64; 2) "do you have any problems with your emotions or nerves"; 3) "have you ever had an anxiety attack"; 4) "have you ever had Panic Disorder"; and 5) "in the past month, have you seen a health professional for your emotions or nerves." Kruskal-Wallis "analysis of variance" by ranks was chosen to test significance.

Results: Seven hundred eighteen patients completed the questionnaire. For the entire sample, the mean ASI score was 20.8 with a standard deviation of 14.7. The elderly subsample reported a mean ASI score of 22.4 ± SD 15.9, and the younger subsample reported a mean ASI score of 20.5 ± SD 14.5 (*t*-test, p = ns). Anxiety sensitivity showed a significant weak positive correlation with age ($r = 0.14$, $p < 0.001$). The percent of elderly patients reporting emotional problems was 29% with ASI 32.0 ± 16.1 SD. The ASI score for elderly reporting emotional problems was significantly higher than the ASI score for those elderly answering no, ASI 17.7 ± 14.5 ($H = 11.43$, $p < 0.01$). The percentage of elderly self-reporting anxiety attacks was 24%, with the highest ASI score for those answering yes to anxiety attacks, ASI 31.8 ± 17.1, compared with those who answered no, ASI 17.7 ± 14.2, or those who answered unsure, ASI 26.8 ± 14.9 ($H = 11.13$, $p < 0.01$). A lower percentage of elderly reported having panic disorder, 10%, with higher ASI score reported for those answering yes, 31.8 ± 15.9, or unsure, 36.3 ± 12.4, compared with those who answered no, 18.7 ± 15.1 ($H = 13.34$, $p < 0.01$). Nine of 85 (11%) elderly respondents reported seeing a health professional for emotions or nerves in the previous month; those answering yes reported higher anxiety sensitivity, ASI 34.8 ± 13.1, compared with those who answered no, ASI 20.8 ± 15.8 ($H = 5.99$, $p < 0.02$).

Discussion: The study finds that emotional problems are common, may be self-identified in elderly primary care patients, and are associated with higher anxiety senstivity. For many elderly patients, anxiety attacks and panic disorder may also be self-reported and their presence appears associated with higher anxiety sensitivity scores.

NR127 Monday, May 6, 3:00 p.m.-5:00 p.m.

Asystole Incidence in the Elderly Receiving ECT

Jeremy A. Burd, Hershey Med Ctr, Penn State University, PO Box 850, Hershey PA 17033; Paul A. Kettl, M.D.

Summary:

Electroconvulsive therapy is a very effective form of treatment for depression in the elderly. However, cardiac complications in the elderly receiving ECT have been much debated in the lay and professional literature. We prospectively investigated the incidence of asystole of five seconds or greater in elderly receiving ECT. Patients were examined for age, sex, medical history, medications, and findings on EKG documenting rhythm and cardiac disturbance. Those who had asystole were compared using Chi square analysis with those who did not.

Results: 65.8% (25 of 38 total patients over 51 series of treatments) experienced asystole during the course of ECT. The asystole group was significantly younger (average age 72.2 vs. 77.0) and less likely to have cardiac rhythm disturbances on EKG ($p = 0.05$). Medical history, history of cardiac disease, thyroid disease, diabetes, hypertension, or the use of a wide variety of cardiac medications did not predict asystole. Unilateral/bilateral electrode placement, number of ECT treatments, and sex did not predict asystole either.

Conclusion: Asystole is a common side effect of ECT in the elderly. Those with cardiac disease are not more likely to experience asystole and may in fact be less likely to experience the phenomenon. Clinically, asystole in this series was not medically relevant to any significant outcome. Asystole following ECT in the elderly is a common but clinically nonsignificant experience during ECT.

NR128 Monday, May 6, 3:00 p.m.-5:00 p.m.

Thyroid Screening in a Geriatric Psychiatry Unit

Craig S. Feaster, B.S., Psychiatry, Penn State University, 211 University Manor East, Hershey PA 17033; Paul A. Kettl, M.D.

Summary:

Introduction: Thyroid screening is often ordered on admission to a geriatric psychiatry unit. An attempt was made to determine the prevalence of thyroid abnormalities in those admitted.

Method: The records of 227 consecutive admissions to a university geriatric psychiatry unit were retrospectively analyzed to determine the frequency of thyroid abnormalities in this population. Length of stay data were analyzed to determine if those with thyroid abnormalities had a different length of hospital stay. TSH levels were available for 200 of these admissions and T_4 levels were available for 197 of these admissions.

Results: 57 patients (25.1%) were found to have thyroid abnormalities. Of these 57 patients, 27 patients (11.9%) had a known history of thyroid disease and 30 patients (13.2%) had previously undiagnosed thyroid abnormalities. Lengths of stay for all patient groups, i.e., those without thyroid abnormalities, previously diagnosed thyroid disease, and undiagnosed thyroid disease were the same: 16 days.

Conclusion: Because 13.2% of patients admitted to a geriatric psychiatry unit had previously undiagnosed thyroid abnormalities tests to screen for them are useful. However, the detection of thyroid abnormalities does not affect length of stay.

NR129 Monday, May 6, 3:00 p.m.-5:00 p.m.

Direct Assessment of Function in Older Schizophrenia Patients

Joshua C. Klapow, Ph.D., Psychiatry, UCSD/ San Diego VAMC, 3350 La Jolla Village Drive, San Diego CA 92161;

Jovier D. Evans, Ph.D., Thomas L. Patterson, Ph.D., Robert K. Heaton, Ph.D., Robert M. Kaplan, M.D., Dilip V. Jeste, M.D.

Summary:

Aim: A growing trend in medicine is to evaluate the impact of illness on functional abilities. Because measures of function frequently rely on self-report, few studies have *directly* assessed behavioral outcomes in psychiatric patients, especially older ones who may be at increased risk for functional disability.

Methods: Subjects were 47 outpatients with DSM-III-R schizophrenia (n = 30) or mood disorder (n = 17), and 24 normal comparison subjects, all over the age of 45. Subjects completed the Direct Assessment of Functional Status (DAFS) Scale, a standardized, direct assessment of behavior during simulated daily activity tasks (time orientation, communication, finances, shopping, eating, grooming, and transportation skills).

Results: Schizophrenia patients had significantly greater disability than mood disorder patients and normal subjects ($p < .01$). An evaluation of specific behaviors indicated that schizophrenia patients were significantly more limited in financial, shopping, and transportation skills ($p < .05$). The overall disability was significantly associated with scores on the Quality of Well-Being Scale ($r = .59$, $p < .05$), but not with age or education ($p > .05$).

Discussion: The DAFS is a promising instrument for functional assessment in psychiatric patients. Our findings of significant functional disability in older schizophrenia patients have implications for treatment as well as allocation of health care resources.

NR130 Monday, May 6, 3:00 p.m.-5:00 p.m.

An Open-Label Study of Risperidone for the Treatment of Agitation in Dementia

Helen Lavretsky, M.D., Psychiatry, UCLA-VA, 1401 S Bentley Ave #101, Los Angeles CA 90025–3406; David L. Sultzer, M.D.

Summary:

Objectives of the study were to determine the efficacy and side effects of risperidone for the treatment of agitation in patients with dementia.

Research methodology. We conducted a 10-week, open-label clinical trial of risperidone in 15 elderly patients, all of whom met DSM-IV criteria for a specific dementia subtype, and a minimum score criteria on the Cohen-Mansfield agitation scale. Neuropsychiatric assessment included behavioral rating scales (Cohen-Mansfield Agitation Inventory, Overt Aggression Scale, Clinical Global Impression), cognitive scales (Mini-Mental State Examination), side effect checklist, and the Unified Parkinson's Disease rating scale. The study included a three-week dose-finding phase, followed by a six-week extended treatment phase. Risperidone dose was adjusted during the first three weeks, according to efficacy and side effects.

Results: Thirteen patients completed the ten-week trial. All 13 patients were improved or very much improved according to CGI ratings at week 10. One patient dropped out due to marked extrapyramidal side effects (EPS) on the lowest dose of 0.5 mg/day. Four patients developed significant EPS on the lowest dose. No patient required more than 1.5 mg twice a day. Overall, patients were 50% improved on the OAS after two weeks of treatment, while 50% improvement on CMAI and CGI occurred during the eighth week. Mean UPDRS scores increased and mean MMSE scores decreased over the ten weeks.

Conclusion: Our data suggest that risperidone is effective for treatment of agitated behaviors in dementia. Aggressive behaviors responded to treatment before overall agitation. Elderly patients with dementia are very susceptible to EPS and may show decline in cognition with risperidone treatment.

NR131 Monday, May 6, 3:00 p.m.-5:00 p.m.

Premorbid Personality of Dementia Patients and Caregiver Burden

Ziad H. Nahas, M.D., Psychiatry, Baylor College Med, One Baylor Plaza, Houston TX 77030; Victor Molinari, Ph.D., Mark E. Kunik, M.D.

Summary:

Objective: Investigate the relationship between premorbid personality of patients with dementia and caregiver burden.

Method: Analyses were conducted in the HVAMC geropsychiatric unit database on identified patients with a primary DSM-III-R (and later DSM-IV) diagnosis of dementia (n = 80). Caregivers were mailed a measure of the patient's premorbid personality, the Personality Disorder Questionnaire-Revised (PDQ-R), and a measure of caregiver burden, the Burden Interview (BI). As a measure of behavioral disturbance, we used the patient's admission rating on the Cohen-Mansfield Agitation Inventory (CMAI).

Results: We found no significant differences between the 22 patients whose caregivers responded to the survey (28%) and the 58 who did not. The log BI correlated with the log PDQ-R total trait score ($r = 0.470$; $p = 0.027$), and histrionic personality disorder traits ($r = 0.479$; $p = 0.023$). Log cluster B traits correlated with log BI ($r = 0.523$; $p = 0.012$), and accounted for 38% of the log BI variance in the regression equation ($t = 3.29$; $p = 0.004$). Only CMAI non-aggressive physical agitation correlated with paranoid personality traits ($r = 0.724$; $p = 0.034$).

Discussion: The positive correlation between premorbid personality and caregiver burden suggests that the caregiver's perception of the patient's traits may be an important contributor to the burden, particularly for caregivers of patients with cluster B traits.

NR132 Monday, May 6, 3:00 p.m.-5:00 p.m.

Depression in Demented and Non-Demented Inpatients

Ziad H. Nahas, M.D., Psychiatry, Baylor College Med, One Baylor Plaza, Houston TX 77030; Claudia Orengo, M.D., Mark E. Kunik, M.D., Victor Molinari, Ph.D., Richard H. Workman, Jr., M.D.

Summary:

Objective: Compare the presentation and course of treatment of depression in two subgroups of geriatric patients.

Methods: Analyses were conducted comparing depressed non-demented patients (n = 23) and depressed demented patients (n = 35) in the HVAMC geropsychiatric unit database on MMSE, CMAI, HDRS, and RSSE. Tests scores in each group were compared at admission and discharge, as well as amount of change from admission to discharge by using T-tests.

Results: The two groups were the same in regards to age, sex, marital status, living arrangements, and number of medical problems. Both groups present the same in regard to HDRS; however, the depressed group with dementia presents with significant more agitation as measured by CMAI. After multimodal treatment, both groups improved significantly in HDRS and RSSE; however, the depressed group with dementia improved significantly on CMAI Fac 1 - physical agression ($p = 0.014$), Fac 2 - non-aggressive physical agitation ($p = 0.0091$), and total CMAI ($p = 0.0074$). When amount of change from admission to discharge was compared, no significant difference between groups was noted.

Conclusions: The presentation of depression in demented patients may include an increased agitation with considerable improvement after antidepressant treatment.

rating perspectives (IE ratings shown). The improvement in hyperarousal in notable.

Given a low placebo response rate (10%–20%) in previous studies, the high response rate suggests true efficacy of paroxetine for PTSD, and a controlled trial is warranted.

	Independent Evaluator Ratings					
	CGI Sev	DAV-A Freq/Sev	DAV-H Freq/Sev	DAV-I Freq/Sev	HAM-A	HAM-D
PRE	5.0	16.0/15.5	12.5/11.7	7.0/8.5	18.7	15.8
POST	2.7***	6.7**/4.3**	5.2***/2.8**	1.5*/1.8**	9.7**	8.2**

CGI=global improvement scale, **DAV**=Davidson PTSD Scale with, **A**=avoidance, **H**=hyperarousal, **I**=intrusion, **Freq**=frequency of symptoms, **Sev**=severity of symptoms, **HAM-A**=Hamilton Anxiety Scale, **HAM-D**=Hamilton Depression Scale *p<.10,**p<.05;***p<.01.

NR148 Monday, May 6, 3:00 p.m.-5:00 p.m.

Comorbid Major Depression and OCD in Pregnancy and the Puerperium

Susan F. Diaz, M.D., Psychiatry, Brown University, 345 Blackstone Blvd, Providence RI 02906; Lee S. Cohen, M.D., Deborah A. Sichel, M.D., Laura M. Robertson, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: Pregnancy has typically been thought of as a period of emotional well-being. However, data describing mood and anxiety disorders during pregnancy are sparse and conflicting. Postpartum worsening of mood and anxiety disorders has been described by several investigators. The purpose of this investigation was to described the relationship between major depression and obsessive-compulsive disorder in a cohort of 20 patients with a primary diagnosis of OCD followed naturalistically during pregnancy and the puerperium.

Methods: Twenty patients with obsessive-compulsive disorder were prospectively assessed across pregnancy and during the first nine postpartum months. Structured clinical instruments, including the SCID-P, Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and Hamilton Depression Rating Scale (HDRS), were administered at multiple points during the study. Pharmacological treatment across pregnancy and the puerperium was also recorded.

Results: Of the 20 patients with a primary diagnosis of OCD, 18 (90%) had a lifetime history of comorbid major depression. During pregnancy, major depression appeared most commonly during the first trimester (n = 7). Antidepressant discontinuation prior to conception (n = 9) often lead to relapse of depression in the first trimester (n = 5). During the postpartum period, rates of depression were low (n = 2). However, 76% of the sample continued to meet criteria for OCD postpartum despite frequent use of antiobsessional drugs (n = 13).

Conclusions: Despite high rates of lifetime comorbid major depression, patients with primary diagnoses of OCD did not appear to demonstrate puerperal worsening of mood, though they did demonstrate postpartum exacerbation of obsessive-compulsive symptoms. The extent to which postpartum anxiety disorders should be considered as discrete nosologic entities warrants further investigation.

NR149 Monday, May 6, 3:00 p.m.-5:00 p.m.

Pharmacotherapy During Pregnancy in Women with OCD

Lynn R. Grush, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street WACC 815, Boston MA 02114; Deborah A. Sichel, M.D., Lee S. Cohen, M.D., Laura M. Robertson, B.A., Carol S. Birnbaum, M.D., Lisa S. Weinstock, M.D.

Summary:

Few guidelines exist for clinicians about the use of pharmacotherapy during pregnancy in women with obsessive-compulsive disorder. We report on the use of pharmacotherapy in 19 pregnant women with histories of pregravid OCD as determined by DSM-III-R SCID criteria.

Women were assessed prospectively at each trimester using the YBOC Scale, Clinical Global Impression, and SCID. Pharmacotherapy was recorded at each visit. Results suggest that women with pregravid OCD are not likely to improve during pregnancy. Worsening or maintenance of symptoms occurred in 58% of women by the third trimester. Pharmacotherapy appeared to have little impact on symptoms. Further study is required to assess the impact of worsening OCD on pregnancy outcome and to formulate safe and effective treatment strategies during pregnancy.

NR150 Monday, May 6, 3:00 p.m.-5:00 p.m.

Premenstrual Dysphoric Disorder and Its Relationship to Schizophrenia Symptom Severity

Andiea Hedayat-Harris, Ph.D., Psychiatry, NYH-Cornell Med Ctr, 21 Bloomingdale Road, White Plains NY 10605

Summary:

Objective: In this study, menstrually related affective, behavioral, and physiological changes were analyzed to determine whether cyclical biological and psychological changes covary with changes in the severity and frequency of symptoms in schizophrenic women, with the expectation of significant psychotic symptom exacerbation premenstrually.

Method: Thirty-nine inpatient schizophrenic women were examined longitudinally at two consecutive menses to assess differences between pre- and post-menstrual phases on the Brief Psychiatric Rating Scale (BPRS) and the retrospective and prospective versions of the Premenstrual Assessment Form (PAF and DRF), using ANOVA, with repeated measures.

Results: The results indicated that similar to normal and depressed women, the symptoms that were most exacerbated were affective and somatic in nature, rather than psychotic symptoms that are characteristic of schizophrenic symptomatology. Furthermore, most of the symptoms were increased perimenstrually and menstrually.

Conclusion: Overall the findings suggest that consistent with the DSM-IV research category of premenstrual dysphoric disorder, menstrually related changes seem to be a discrete phenomenon with its own symptomatology, which may be superimposed on psychiatric disorders, both those with and without a predominant affective component. However, clearer guidelines are necessary for determining the degree of associated impairment in functioning before this diagnosis can be made validly and reliability.

NR151 Monday, May 6, 3:00 p.m.-5:00 p.m.

Disorders of Extreme Stress in Anxiety Disorder Patients

Kevin B. Handley, M.A., Psychiatry, North Shore Univ Hospital, 400 Community Drive, Manhasset NY 11030; Juliana R. Lachenmeyer, Ph.D., Regina Ucello, Andrew Shack, M.A., David Pelcovitz, Ph.D., Fran Mandel

Summary:

Disorders of extreme stress (DES) is a proposed diagnostic category designed to describe the impact of prolonged types of trauma on functioning, as opposed to current diagnostic criteria for PTSD, which are limited to the effects of acute time-limited traumas. DES symptoms are referenced in DSM-IV as possible complications associated with PTSD, particularly in individuals

whose trauma experiences are interpersonal in nature (POW, prolonged physical or sexual abuse, torture). The clinical presentation of DES includes symptom clusters representing problems with affect regulation, attention, self-perception, relations with others, somatization, and systems of meaning. The similarity between this symptom picture and symptoms associated with anxiety disorders raises questions about the specificity of the DES. The current study examines the diagnosis of DES in non-PTSD anxiety disorder patients. All 16 subjects had experienced a high-magnitude-stressor trauma event. Preliminary results offer support for the DES diagnosis. Subjects whose trauma was interpersonal in nature on average scored higher on a structured clinical interview for DES than those subjects whose experienced high-magnitude trauma was not interpersonal in nature. The implications for DES construct validity and the ability of DES to discriminate between different types of trauma experiences will be discussed.

NR152 Monday, May 6, 3:00 p.m.-5:00 p.m.

Deficiencies of Categorical Boundaries in Phoneme Perception in Schizophrenia

Angel Cienfuegos, M.D., Psychiatry, Bronx Psych Ctr, 1500 Waters Place, Bronx NY 10461; Daniel C. Javitt, M.D., Anne-Marie Shelley, Ph.D., L. March, Ph.D.

Summary:

Normal volunteers asked to discriminate between phonemes with nine graded changes, from /ba/ to /da/, abruptly switch from perceiving "ba" to perceiving "da" towards the center of the continuum (Picton, 1995). This change represents the categorical boundary between /ba/ and /da/. When normal subjects are prestimulated with pure /ba/s or pure /da/s the categorical boundary shifts in the opposite direction—a process known as adaptation. Experiment 1 of the present study compared categorical perception in 15 schizophrenics and 14 controls. While patients and controls were equally consistent in identifying pure forms of both phonemes, patients showed a greater number of ambiguous responses and significantly less sharp shifting around the categorical boundary. This suggests an abnormality of phonemic boundary definition. Experiment 2 found that schizophrenics and controls did not differ in their ability to adapt their phonemic boundary when previously exposed to the pure forms of /ba/ and /da/. The ability of schizophrenics to utilize and discriminate different categories of speech sounds appears to be impaired already at a phonemic level. The mechanism underlying this deficit may contribute to impaired sematic processing in schizophrenia.

NR153 Monday, May 6, 3:00 p.m.-5:00 p.m.

Psychiatric Disorders in PMS: Five-Year Follow-Up

Catherine A. Roca, M.D., BPB/SBE, NIMH, 10 Center Drive MSC 1276, Bethesda MD 20892; Peter J. Schmidt, M.D., David R. Rubinow, M.D.

Summary:

Objective: To determine whether: 1) women with prospectively confirmed PMS developed more psychiatric disorders than controls, and 2) whether PMS is a stable diagnosis over time.

Methods: Patients with prospectively-confirmed PMS (n = 26) and normal volunteers (n = 19) were evaluated using the Structured Clinical Interview for DSM-III-R (SCID) and longitudinal ratings (data not yet available) 5–12 years after their initial participation in PMS studies.

Summary: New onset psychiatric disorders occurred in 54% of PMS patients compared with 32% of controls. During the follow-up period, 38% of PMS patients had an episode of major depression (MDE) compared with 21% of controls; 11% of the patients had a new onset depression compared with 16% of controls. These differences were not statistically significant (Fisher's exact test). 8/45 subjects reported Axis I disorders that preceded the follow-up period and yet were not reported in the initial diagnostic interview.

Conclusions: While a type II error cannot be excluded, preliminary data suggest that women with PMS are not significantly more likely to develop psychiatric disorders than controls. Discrepancies between symptom reports in first and second interviews are consistent with observations of state dependent access to autobiographical memory and suggest potential limitations of single cross-sectional diagnostic interviews.

NR154 Monday, May 6, 3:00 p.m.-5:00 p.m.

OCD in Pregnancy, the Puerperium and the Premenstruum: A Pilot Study

Katherine E. Williams, M.D., Psychiatry, Stanford University, 401 Quarry Road, Stanford CA 94305; Lorin M. Koran, M.D.

Summary:

Objectives: Recent reports suggest that pregnancy and the puerperium may precipitate or exacerbate obsessive-compulsive disorder (OCD). We examined the course of OCD during reproductive events including the premenstruum, pregnancy, and postpartum and assessed the prevalence of postpartum depression.

Methods: Female outpatients (N = 57) at a university specialty clinic who met DSM-III-R criteria for OCD completed an 18-question telephone interview retrospectively investigating the effect of reproductive events on OCD and depression.

Results: 38 women had been pregnant at least once: 31 had delivered at least one child. OCD began during pregnancy in five women (13.2%). A total of 69% of women with pre-existing OCD described no change in symptoms during pregnancy; 17% described worsening. No women reported postpartum onset of OCD; exacerbation of symptoms in women with preexisting OCD occurred in 29%, 33% reported postpartum depression, and 41% of all women described premenstrual exacerbation of OCD.

Conclusion: Women with OCD appear to be at risk for the onset of postpartum depression and exacerbation of OCD symptoms during the premenstrual and postpartum periods. Future prospective, longitudinal research is needed to confirm these findings and investigate the biological and psychological factors associated with the course of OCD in women.

NR155 Monday, May 6, 3:00 p.m.-5:00 p.m.

Reduced EEG Coherence in Narcolepsy Measured with Computerized EEG Mapping Technique

Do-Un Jeong, M.D., Psychiatry, Seoul National Univ Hospital, 28 Yongon-Dong, Chongro-Gu, Seoul 110–744, South Korea; Doo-Heum Park, M.D., Jun Soo Kwon, M.D., Tak Youn, M.D.

Summary:

Objective: To find characteristic features of quantitative electroencephalography (QEEG) in narcoleptic patients in wakeful state, diagnosed with ICSD(1990) criteria, nocturnal polysomnography, and multiple sleep latency test (MSLT).

Method: Twelve drug-free narcoleptic patients were compared to sex- and age-matched controls, using computerized electroencephalographic mapping technique with spectral analysis based on the International 10–20 system. Absolute power, relative power, interhemispheric asymmetry, and coherence and intrahemispheric coherence in each frequency band (delta, theta, alpha, and beta) were measured and analyzed.

Results: In narcoleptic patients, monopolar interhemispheric coherences of all frequency bands were decreased in occipital area. Intrahemispheric coherences of alpha band were decreased in left hemispheric areas. Absolute power of beta band was increased in right temporal area.

Conclusions: Decreased interhemispheric coherence in occipital area and decreased left intrahemispheric coherence may indicate the effects of fewer interhemispheric occipital neuronal connections ("visual" coherence) and fewer intrahemispheric neuronal connections ("fascicle" coherence), respectively.

NR156

WITHDRAWN

NR157 Monday, May 6, 3:00 p.m.-5:00 p.m.

Double-Blind Crossover Study of Mirtazapine, Amitriptyline and Placebo in Patient with Major Depression

Mark L. Catterson, M.D., Psychiatric Research, 1100 N. St. Francis, Ste 200, Wichita KS 67214; Sheldon H. Preskorn, M.D.

Summary:

There is no single antidepressant that treats all patients with major depression. There are limited data from prospective, double-blind, controlled studies to guide physicians about what to do should a patient not respond to one specific antidepressant. This study was carried out to address this issue with regard to nonresponse to amitriptyline and the new antidepressant, mirtazapine. This study was a follow-up protocol for patients with major depression (DSM-III criteria) who did not experience a response during a six-week, double blind study of mirtazapine versus amitriptyline versus placebo. Without breaking the blind, amitriptyline and placebo nonresponders (n = 49 and 74, respectively) were crossed over to mirtazapine treatment; mirtazapine nonresponders (n =) were crossed over to amitriptyline treatment. At the end of eight weeks of treatment, the response rate (defined as a 50% reduction in the 17-item Hamilton Depression Rating Scale done at the time of the crossover) was 71% and 59%, respectively, for the placebo and amitriptyline nonresponders treated with mirtazapine and 55% for the mirtazapine nonresponders crossed over to amitriptyline. Discontinuation rates due to adverse effects was 7% and 10%, respectively, for placebo and amitriptyline nonresponders switched to mirtazapine and 17% for mirtazapine nonresponders switched to amitriptyline. Patients lost to follow up were 6–7% for all three groups. Based on these results, there is not a complete overlap in the antidepressant spectrum of activity for amitriptyline and mirtazapine consistent with their different neuropsychopharmacology.

NR158 Monday, May 6, 3:00 p.m.-5:00 p.m.

Acute Cardiovascular and Noradrenergic Effects Following the Alpha-2 Antagonist Ethoxyidazoxan in Humans

Libby A. Jolkovsky, B.A., Bldg 10, Room 2D-46, NIMH, 9000 Rockville Pike, Bethesda MD 20892; Mark E. Schmidt, M.D., Michael Henry, M.D., Hyung G. Kim, M.D., Bradley S. Folley, B.S., William Z. Potter, M.D.

Summary:

Drugs that block alpha-2 adrenoceptors (A2ARs) have recently shown promise for the treatment of depression. Moreover, A2AR antagonists have been used as probes in studies of mood and anxiety disorders. Recently ethoxyidazoxan (ETX), a highly selective A2AR antagonist, has been made available for use in humans. This is a study of the dose dependence of sympathetic responses to acute ETX in humans.

Methods: 12 male volunteers (26 ± 7 yrs) received infusions of ETX (4, 6, 9, or 12 μg/kg) or placebo (normal saline) over 30 minutes. Blood pressure, plasma norepinephrine (NE), plasma glucose (GLU), and subjective effects were measured over three hours at multiple time points.

Results: Diastolic pressure increased after all doses, and after 9 μg/kg for systolic. NE increased in a dose dependent fashion. GLU decreased only following 6 and 9 μg/kg of ETX (all reported changes: $p < 0.05$). There were no significant changes in subject state ratings.

Discussion: The pressor and noradrenergic responses are consistent with central and/or peripheral A2AR blockade. These data suggest that ETX is a highly potent A2AR antagonist in humans. ETX may be useful for the study of A2AR function in psychiatric disorders.

NR159 Monday, May 6, 3:00 p.m.-5:00 p.m.

Sleep Electroencephalography in Depressed Versus Adolescents: Reanalyses of Sleep Data Collected During Adolescence After Longitudinal Follow-Up

Susan I. Wolk, M.D., NYS Psychiatric Institute, 722 West 168th Street, New York NY 10032–2603; Jeremy D. Coplan, M.D., Raymond R. Goetz, Ph.D., Neal D. Ryan, M.D., Ronald E. Dahl, M.D., Myrna M. Weissman, Ph.D.

Summary:

In the adolescents studied between 1978 and 1984 by Dr. Puig-Antich and colleagues, Goetz et al. found greater REM density (REMDEN) during the first REM period in depressed than in normal adolescents (unpublished data). REM latency (REMLAT) did not differ between the groups. Through clinical follow-up of this cohort in adulthood, we can redefine the original diagnostic groups using longitudinal diagnoses. Eighty-two subjects have follow-up data available. Twelve (40%) of the normal control (NC) subjects (N = 30) went on to develop MDD during the follow-up period. These subjects (NCs MDDs) do not differ from the "pure" NCs with respect to REMDEN during the first REM period. When the NCs MDDs were reassigned to a lifetime MDD group, there was a near-trend ($p = 0.11$) for the adolescents with lifetime depression to have a shorter REMLAT (mean 79.7 mins) than the pure NC adolescents (mean 95.8 mins). Further, REMLAT is significantly associated with the outcome of suicide attempts, such that depressed suicide attempters had a longer REMLAT than depressed subjects who were not suicidal.

These data suggest that REMDEN during the first REM period may be a state marker for major depression/suicidality in adolescents. In contrast, the non-significant difference in REMLAT between the diagnostic groups became apparent only after the NCs MDDs were reassigned to the depression group and compared a "pure" NC group. This suggests that REMLAT may be a trait marker for major depression and may be expressed premorbidly in adolescents.

NR160 Monday, May 6, 3:00 p.m.-5:00 p.m.

Sleep-Related Growth Hormone Secretion in Depressed Versus Normal Adolescents: Reanalysis of Biological Data Collected During Adolescence

Susan I. Wolk, M.D., NYS Psychiatric Institute, 722 West 168th Street, New York NY 10032–2603; Jeremy D. Coplan, M.D., Raymond R. Goetz, Ph.D., Neal D. Ryan, M.D., Ronald E. Dahl, M.D., Myrna M. Weissman, Ph.D.

Summary:

In the adolescents studied between 1978 and 1984 by Puig-Antich et al., Dahl et al. (1992) reported sleep-related growth hormone (GH) hyposecretion in suicidal adolescents. Through

clinical follow-up of this cohort in adulthood, we can redefine the original diagnostic groups using longitudinal diagnoses. Final analyses of 62 of an original 94 adolescent subjects who participated in sleep-related GH secretion studies are presented here. An unexpected 38.7% of the normal adolescents developed MDD during the follow-up period and as a group exhibited a significantly earlier peak of sleep-related GH secretion than normal adolescents who remained healthy (N = 19) (83.3 minutes vs. 120 minutes from sleep onset, $p < 0.05$). Adolescents who were currently depressed (N = 31) also exhibited a significantly earlier sleep-related GH peak than normal controls (N = 19), once normal controls with latent depression were removed (mean 82.9 minutes vs. 120 minutes from sleep onset, $p < 0.01$). Latent (N = 12) and currently depressed adolescents (N = 31) were indistinguishable. Lifetime normal controls (N = 19) were then compared to lifetime MDD subjects (N = 43) split on the basis of suicidality. Only current attempters (N = 12) displayed a pattern of GH response indistinguishable from lifetime normal controls (N = 19).

The cross-sectional comparison between depressed and healthy adolescents reported sleep-related GH hyposecretion in suicidal adolescents. Reclassification using longitudinal clinical diagnoses indicate that 1) Both latent and current MDD in comparison to lifetime normals is associated during adolescence with an early peak in sleep-related GH secretion; 2) Curiously, current attempters are indistinguishable from lifetime normals and have a relatively-delayed sleep-related GH peak when compared with other depressive groups. Suicidality during adolescence may be associated with a "pseudonormal" intermediate pattern of sleep-related GH secretions on a continuum between prepubertal hyper- and adult hypo-secretion of nocturnal GH.

NR161 Monday, May 6, 3:00 p.m.-5:00 p.m.

Delirium Detection in Elderly Emergency Room Patients

Francois Rousseau, M.D., Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal Quebec H3T 1M5, Canada; Michel Elie, M.D., Martin G. Cole, M.D., Francois J. Primeau, M.D., Jane McCusker, M.D., Francois Bellavance, Ph.D.

Summary:

Objective: To determine the sensitivity (Se) and specificity (Sp) of a conventional clinical assessment (CCA) by an emergency room (ER) physician for detection of delirium (D) in ER patients aged 65 years and over.

Method: All elderly patients presenting to the ER of a primary acute care university-affiliated hospital between 24h:00 and 15h:00 Monday to Friday and triaged to the observation room on a stretcher because of severity of their illness were screened for D by a psychiatrist using the Confusion Assessment Method (CAM). The charts of interviewed patients with D and of a randomly chosen subgroup of patients without D were then reviewed systematically by an investigator blind to the screening results. Diagnosis of D or an equivalent by the ER physician was noted if present. Prevalence of D and the Se and Sp of the CCA were calculated with a 95% confidence interval (CI). We are presenting preliminary analysis of the first 250 patients out of an expected total of 500.

Results: The overall prevalence of D in the ER is 10% (95% CI: 6, 3%; 13, 7%). The Se and Sp of the CCA for D is 20% (95% CI: 11, 3: 28, 7%) and 94, 7% (95% CI: 94, 6; 94, 8%), respectively.

Conclusion: Despite a relatively high prevalence of D in the elderly ER patients, the Se of a CCA for this condition is low. There is a need for means to improve the detection of D in the ER.

NR162 Monday, May 6, 3:00 p.m.-5:00 p.m.

Psychiatric Emergency Services and Medical Comorbidity

Thomas A. Armistead, M.D., Psychiatry, Jefferson Med College, 111 South 11th Street, Philadelphia PA 19107; Kenneth M. Certa, M.D.

Summary:

Objectives: Currently, many managed care plans are attempting to devise plans and capitation rates for carving out mental health and substance abuse services. Our experience in an urban psychiatric emergency service led us to question the amount of primary care medicine needs we identify (and sometimes treat) in our service.

Method: Charts of all patients presenting to a university psychiatric emergency service for six months were retrospectively reviewed, representing over 1000 visits. Note was taken of several indicators of a need for active current medical treatment. Charts were also screened for evidence of the patient receiving that treatment.

Results: Depending upon the criteria used to assign need for active medical treatment, 20% to 60% of patients presenting were suffering from comorbid medical conditions. Fewer than half of those gave any evidence of receiving care outside of the psychiatric system.

Conclusions: Many patients in a psychiatric emergency service have basic medical care needs that are either unmet or are met by the psychiatric care system. Designs for systems of care and reimbursement should consider this situation.

NR163 Monday, May 6, 3:00 p.m.-5:00 p.m.

Substance Use by Seriously Mentally Ill Patients and Their Families

Laura T. Rachuba, B.A., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Lisa B. Dixon, M.D., Anthony F. Lehman, M.D., Leticia Postrado, Ph.D.

Summary:

Objective: The prevalence and adverse sequelae of co-morbid substance use disorders (SUD) in persons with serious mental illnesses (SMI) are well-established. To elucidate the context of this co-morbidity, we aimed to determine patients' perceptions of familial substance use in a cohort of SMI persons receiving treatment for mental illness.

Methods: Eighty patients living in inner-city Baltimore (mean age = 39, 56% male, 61% schizophrenic) randomly recruited from inpatient (47%) and outpatient (53%) settings were interviewed about their substance use and their knowledge about substance use in their families. Twenty-eight families provided information on familial substance use.

Results: 58% of patients had a DSM-III-R SUD. A total of 92% of all patients reported substance use by a family member (49% mother, 64% father, 77% sibling); 42% reported alcohol use only. Patients' report of family substance use was not associated with the presence/absence of a patient SUD. A total of 57% of families reported substance use by a family member (excluding the patient). Although patients were more likely than families to report maternal substance use ($p < .000$), patients and families agreed on the presence of any family substance use in the majority of cases.

Discussion: Patients with serious mental illness in the inner city report an extremely high rate of substance use in their families. This has important implications for treatment and prevention of substance use in SMI patients. Further research in this area is essential.

NR164 Monday, May 6, 3:00 p.m.-5:00 p.m.

Depression in General Medical Settings: Diagnostic Limitations of Non-Psychiatric Physicians

David B. Arciniegas, M.D., Psychiatry, University of Colorado, 4200 E. Ninth Avenue, Denver CO 80262; Thomas P. Beresford, M.D.

Summary:

Objective: Evaluation of depression is a common reason for patient referral to general hospital psychiatric consultation services. Depressed mood is often recognized by nonpsychiatric physicians, but is a nonspecific symptom, not necessarily indicating a true depressive disorder nor need for antidepressant therapy. Despite this, many general physicians, without benefit of a psychiatric consultation, will prescribe antidepressant medication for a depressed mood alone, subjecting their patients to unwarranted medical risks. Based on this, we hypothesized, nonpsychiatric physicians recognizing depressed mood in their medially ill patients would overdiagnose depressive disorders and overprescribe antidepressants.

Method: We reviewed 49 university hospital cases referred for "depression," measured frequencies of psychiatric consultants' diagnoses, referring physicians' discharge diagnoses, and examined subsequent antidepressant prescription patterns of referring physicians.

Results: Psychiatric consultants diagnosed depressive disorders (major depression, depression N.O.S.) in 18.4% of cases. Seventy-five percent with a consultant-diagnosed depressive disorder, and 25% without diagnosable depression, were prescribed antidepressants by referring physicians. Depressive disorder was excluded by consultant but included by referring physician in 28.6%; 43% of these patients were prescribed antidepressants by the referring physician. Diagnosis and prescription patterns between psychiatric consultants and nonpsychiatric referring physicians varied significantly ($X2 = 7.56$, $p < .01$; and $X2 = 10.21$, $p < .01$, respectively).

Conclusions: Nonpsychiatric physicians are not skilled at generating a mood-related differential; hence, they overdiagnose depressive disorders and overprescribe antidepressants. These results support using psychiatric consultation to evaluate depression and argue against a trend in managed care to increase the proportion of depressed patients treated by nonpsychiatric physicians.

NR165 Monday, May 6, 3:00 p.m.-5:00 p.m.

Quality of Life in Fibromyalgia Patients

Megan M. Dwight, M.D., Psychiatry, University of Cincinnati, P.O. Box 670559, Cincinnati OH 45267; Lesley M. Arnold, M.D., Megan G. Murray, M.A., Emily Park-Morris, B.A., Hadley O'Brien, M.S.H.P/A,

Summary:

Objective: We tested the hypothesis that fibromyalgia patients with Axis I psychiatric disorders would have a significantly more impaired quality of life than those without psychiatric comorbidity.

Method: Fifteen outpatients with fibromyalgia were recruited through a newspaper advertisement. They were interviewed at the University of Cincinnati Biological Psychiatry Program using the Structured Clinical Interview for DSM-IV and the Psychosocial Adjustment to Illness Scale (PAIS). Results were analyzed with a paired two tailed t-test.

Results: Ten of 15 patients had lifetime Axis I diagnoses, including major depression ($n = 6$), dysthymia ($n = 4$), generalized anxiety disorder ($n = 3$), panic disorder ($n = 1$), and specific phobia ($n = 3$). Patients with a lifetime history of Axis I disorders had a significantly decreased quality of life as rated by the PAIS compared with patients with no psychiatric history ($t = 2.16$, $p = .02$).

Conclusion: Our results indicate that screening for psychiatric comorbidity is important in assessing the quality of life of fibromyalgia patients and that treatment of comorbid psychiatric diagnoses may improve overall treatment outcome.

NR166 Monday, May 6, 3:00 p.m.-5:00 p.m.

Risk Factors for Postpartum Depressive Symptoms in an Urban Minority Population

Janine S. Mele, B.A., Psychiatry, UMDNJ-NJMS, 5141 Broadway, Allen Pavilion, New York NY 10034; Rhilina Ghosh, B.A., Veronika Solt, M.D.

Summary:

The prevalence of postpartum depression during the first six months after childbirth has been reported in the range of 7% to 15%. As postpartum depressive symptoms (PPDS) are prevalent, identifying vulnerability factors of PPDS is of particular interest. The present study was designed to test the hypothesis that certain vulnerability factors are more likely to be present in women with postpartum depressive symptoms compared to a non-depressed postpartum population.

Mothers (54 African American and 17 Hispanic women) returning for their four to six weeks postpartum visit were asked to complete the Edinburgh Postnatal Depression Scale (EPDS). Twenty women (28%) had a positive EPDS score (> 12). Patients' charts were reviewed without prior knowledge of EPDS scores and data about social status, medical, obstetric and pregnancy history, delivery, and infants' characteristics were obtained. EPDS scores were subsequently assigned to respective patients and the above factors were compared between women with PPDS and those without depressive symptoms.

Women with PPDS when compared to non-depressed mothers, were more likely to be single ($p < 0.05$; $DF = 1$), to have lack of social support ($p < 0.05$; $DF = 1$), and to have an unwanted pregnancy ($p < 0.05$; $DF = 1$). Patients with PPDS attended significantly fewer prenatal visits ($p = 0.04$; $DF = 67$), were more likely to attend their first prenatal visit after 20 weeks gestation ($p < 0.03$; $DF = 1$), have delivery stressors ($p < 0.03$; $DF = 1$), and infants with lower Apgar scores ($p < 0.02$; $DF = 65$) as well as lower average birth weight ($p < 0.04$; $DF = 67$).

The high prevalence of PPDS in our postpartum population warranted the exploration of the above described factors. The identified vulnerability factors may enable us to detect those at risk for PPDS and offer timely preventive measures.

NR167 Monday, May 6, 3:00 p.m.-5:00 p.m.

Attitudes and Beliefs About Mental Illness Among Caribbean Immigrants

Sonia L. Cole, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Lisa B. Dixon, M.D.

Summary:

Objective: To determine the attitudes, beliefs, nosology, and behavioral responses pertaining to mental illness (MI) among the English-speaking Caribbean community in an East Coast urban community.

Methods: We created an anonymous 15-item, self-report survey, including choices from both the traditional and dominant American cultures. We sampled three community sites: a West Indian grocery store; a nearby West Indian bakery, and the Baltimore-West Indian Carnival of 1995.

Results: A total of 30 respondents described themselves as English-speaking Caribbean (56% > 35 years, 52% in U.S. > 10 years; 67% had some college; 58% had income < $30,000; 68% raised in rural setting). Stress (85%), childhood trauma (70%),

drugs (70%), "loss" (61%), and hereditary factors (45%) were most frequently endorsed as causal factors for MI, while only 30% endorsed magical beliefs. Individuals with only high school educations tended to endorse magic more frequently ($p < .10$), and those in the U.S. < 10 years tended to endorse inheritance more frequently ($p < .10$) as causal for MI. Those in the U.S. < 10 years ($p < .05$), younger ($p < .05$) and raised in a rural setting ($p < .02$) were more likely to believe that spiritual healing is an important treatment.

Discussion: This study, though small, suggests that immigrants from Caribbean countries frequently assume beliefs and attitudes of the dominant American culture. However, variations in retention of traditional beliefs persist, which may relate to demographic and economic characteristics.

NR168 Monday, May 6, 3:00 p.m.-5:00 p.m.

Psychiatric Disorders in an Arctic Community

John M. Haggarty, M.D., Geriatrics, London Psych Hospital, 850 Highbury Street, London Ontario N5V 5D8, Canada; Harold Merskey, M.D., Zach Cernovsky, Ph.D., Patricia Kermeen, M.Sc.

Summary:

Objective: The prevalence of psychiatric disorders among the Arctic Inuit has rarely been explored in epidemiological studies; studies based on modern DSM nosology and related screening tools are much needed.

Method: A random sample of 161 residents between the ages of 14 to 71 was interviewed in a Canadian Inuit Arctic community (population of approximately 1,100) to assess the prevalence of depression, anxiety, suicidal ideation, and alcohol abuse. The survey tools were the Hospital Anxiety and Depression Scale (HAD), the CAGE questionnaire, and an item focusing on suicidal ideation. Ninety-four percent were Inuit and 64% chose English as the language for the survey interview. All questionnaires were available both in English and in Inuktitut translation. A subsample of 22 participants were also examined using the Structured Clinical Interview for the DSM-III-R (SCID) to estimate the concurrent validity of the HAD survey and to determine the best cut-off scores on the HAD in this sample.

Results: Kappa coefficients indicated satisfactory agreements ($p < .025$) between HAD and SCID classifications. The community survey indicated a prevalence of 45.6% for suicidal ideation, 26.5% for depression (HAD depression > 8), 14.8% for anxiety (HAD anxiety > 11), and a lifetime prevalence of 30.6% for alcohol abuse.

Conclusions: Significant psychiatric morbidity exists in the Arctic.

NR169 Monday, May 6, 3:00 p.m.-5:00 p.m.

Ethnicity and Self-Injurious Behaviors

Antonio A. Menchaca, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Harold W. Koenigsberg, M.D., Tatsuyuki Kakuma, Ph.D.

Summary:

Objective: Understand the impact of culture and ethnicity upon self-injurious behaviors (SIB) in borderline personality disorder (BPD).

Method: We reviewed retrospectively 82 charts (40 Caucasians, 42 Hispanics), with the diagnosis of BPD upon discharge from an inpatient service. The subjects were matched by sex, age, and discharge year. We compared rate and type of SIB (overdose, cutting, burning, and others).

Results: We found a high rate of SIB in both samples (Caucasians 87.5%, Hispanics 95.24%). We found a significant difference in the form of SIB between the groups: 70% of the Caucasians cut themselves versus 48% of the Hispanics ($x^2 = 4.2$, 1df, $p < 0.04$). If we eliminate the seven patients who did not hurt themselves, this difference is greater: 80% of the Caucasians cut themselves versus 50% of the Hispanics ($x^2 = 7.29$, 1df, $p < 0.007$). There is no difference in the frequency of burning, overdosing, or other types of SIB.

Conclusions: SIB, particularly overdosing and self-cutting, are common in patients with BPD. This significant difference in self-cutting behavior between Hispanics and Caucasians should be investigated in future research; this may help predict such events and may have treatment implications.

NR170 Monday, May 6, 3:00 p.m.-5:00 p.m.

Elevated Plasma Chloride in Psychiatric Patients

Medhat Aziz-Esaak, M.D., Psychiatry, Maimonides Medical Center, 914 48th Street, Brooklyn NY 11219

Summary:

Objective: To demonstrate the difference in plasma chloride level between psychiatric and medical patients; to compare any difference in the chloride among psychiatric diagnostic categories.

Method: A comparison between the plasma chloride levels of 60 psychiatric patients (aged 18–70) comprising inpatient psychiatric admissions during a consecutive 10-week period and matched 60 control patients admitted to a nonpsychiatric floor within 48 hours of admission of the subject. None of the control patients had a psychiatric disorder. Patients with medical illnesses, who used medication that affects the chloride homeostasis, or who abused substances were excluded from both groups. All analyses were performed using the same analyser within 48 hours after admission.

Results: Plasma chloride levels of psychiatric patients are significantly higher than those of nonpsychiatric controls, with means of 103.40 mEq/L and 101.13 mEq/L, respectively ($t = 3.98$, $p < 0.001$). The bipolar patients showed the highest mean serum chloride levels (104.75 mEq/L) of all diagnostic groups, with statistically significant difference from the mean of the unipolar depressed patients (101.00 mEq/L) ($t = 2.5$, $p < 0.05$).

Conclusion: To our knowledge, this is the first study demonstrating these findings. Previous studies have concentrated on cations (sodium, potassium, and calcium) in patients with affective disorders. Our findings may reflect the respective anion movement, but would imply that it is consistent across diagnostic categories. The significant difference between patients with bipolar and unipolar disorders confirms that these are both clinically and biochemically separate disorders.

NR171 Monday, May 6, 3:00 p.m.-5:00 p.m.

Predictive Validity of Axis III Physical Disorders

Javier E. Saavedra, M.D., Cayetano Heredia, Peruvian University, Lima, Peru; Juan E. Mezzich, M.D., Ihsan M. Salloum, M.D., Levent Kirisci, Ph.D.

Summary:

Objective: Little empirical research has been carried on the clinical validity of Axis III physical disorders and the most effective way to formulate this axis. This paper reports on the validity of various approaches to the formulation of Axis III to predict functioning outcomes at a 33-month follow-up.

Method: A sample of 515 general psychiatric patients presenting at a psychiatric institute was assessed with a semistructured procedure to cover all DSM-III diagnoses and axes, and was subsequently followed up for 33 months. Outcome was assessed with several measures of adaptive functioning. Axis III was analyzed according to 1) presence of any physical disorder, 2) number of

these, 3) presence of major chronic physical disorder, and 4) number of these.

Results: Prediction of impairment in functioning (as measured at follow-up with the Strauss-Carpenter Scale) for the total sample of general psychiatric patients ranged from a correlation coefficient of 0.17 when Axis III was expressed as the presence of any physical disorder to 0.35 when the number of major chronic physical disorders was considered. Furthermore, when conducting these analyses within groups of patients with specific psychiatric disorders at baseline, it was found that number of major chronic physical disorders reached a predictive validity of 0.55 for patients with dysthymic disorder, 0.44 for those with anxiety disorders, and 0.41 for those with major depression. Comparative regression analyses also considering other variables at baseline such as age, social class, number of symptoms, clinical setting, and average functioning within each specific category of psychiatric disorder showed that number of major chronic physical disorders was the most important predictor of functioning outcome among patients with dysthymic disorder and for those with major depression, but not for those with anxiety disorders for whom average functioning at baseline was the best predictor.

Conclusion: The number of major chronic physical disorders seems to be an important predictor of future functioning, particularly for patients with certain psychiatric disorders. This points out the importance of considering the relationship between psychiatric and physical disorders when conducting systematic clinical assessment with the goal of predicting course and outcome.

NR172 Monday, May 6, 3:00 p.m.-5:00 p.m.

Clinical Factors Associated with Positive Neuroimaging Studies in Psychiatric Inpatients

Michael Golding, M.D., Psychiatry, University of NC, Box 7160 Med School Wing B, Chapel Hill NC 27599; John H. Gilmore, M.D., Ann M. Kopanski, M.A., Susan G. Silva, Ph.D.

Summary:

Computerized tomography (CT) and magnetic resonance imaging (MRI) of the brain are frequently used in psychiatry. Previous studies have questioned the utility of neuroimaging in psychiatric patients, as the results are often negative or of little clinical value. To understand clinical factors that predict positive neuroimaging studies, clinical information and neuroimaging findings were reviewed in all adult psychiatric inpatients from 1991 through 1995. Analysis of the first 132 records revealed that 63% had an abnormality, with most of the abnormal scans showing atrophy. Abnormal neuroimaging findings were associated with an abnormal neurologic exam ($P = 0.004$) and a history of neurological events ($P = 0.08$). Patients with positive findings were older than those with negative studies. These and other clinical factors predictive of positive neuroimaging studies will be presented in the complete study.

NR173 Monday, May 6, 3:00 p.m.-5:00 p.m.

Screening for Psychiatric Disorders in Medical Outpatients: A Patient Acceptance Study

Joseph V. Penn, M.D., Psychiatry, Brown University, 345 Blackstone Blvd, Providence RI 02906; Mark Zimmerman, M.D., Jill I. Mattia, M.A.

Summary:

Although psychiatric disorders are among the most common disorders in patients seeing primary care physicians, they are often underdiagnosed and undertreated. One method of increasing the rate of detection of psychiatric disorders is by using self-report screening questionnaires. There have been few studies examining the acceptability of mental health screening in primary care outpatients. A consecutive series of outpatients attending the medicine clinic at Rhode Island Hospital were approached to participate in a control group design trial to examine: 1) the acceptability of a brief self-report questionnaire that screens for several psychiatric disorders (the SCREENER), 2) the effect of this intervention on patient-physician interaction, 3) patient level of comfort in discussing mental health issues with their primary care physician, and 4) level of involvement expected from physicians should mental health treatment be indicated. There were no significant demographic differences in acceptability of mental health screening. 87% were "not at all," 11% were "a little," and only 2% were "somewhat," annoyed, embarrassed, upset, or uncomfortable being asked about mental health problems. 55.5% indicated it would be "neither easy nor difficult," to bring up depression, anxiety/nerves, drugs/alcohol with their primary care physician (17.7% "difficult/very difficult," 26.6% "easy/very easy"). 95.6% expected their primary care physician to be at least "somewhat involved" if the patient experienced a mental health problem (4.4% "not involved," 31.1% "somewhat involved," 28.9% "involved, 35.6% "very involved"). Further analyses with inter-group comparisons will be presented. These results suggest that medical outpatients are amenable to screening for mental health problems. Implications of these findings for mental health screening in primary care medicine will be discussed.

NR174 Monday, May 6, 3:00 p.m.-5:00 p.m.

Domains of Psychopathology: Is Schizophrenia Different From Other Psychoses?

Santhi S. Ratakonda, M.D., Psychiatry, Columbia University, 722 West 168th Street, Unit 2, New York NY 10032; Xavier F. Amador, Ph.D., Jack M. Gorman, M.D.

Summary:

Previous factor analytic studies of schizophrenia symptoms have consistently demonstrated the existance of three independent factors or psychopathological domains (positive, negative, and disorganization). Treatment response, course, and neuropsychological test findings provide some evidence that these domains may be pathophysiologically independent. However, the specificity of these domains for schizophrenia has not been adequately examined. In this study, we used factor analysis to examine data from the DSM-IV field trial, involving SAPS and SANS ratings of 221 patients with DSM-III-R diagnosis of schizophrenia and 191 patients with other diagnoses. An identical three factor structure was seen in both "schizophrenia" and "other diagnoses" groups. Sub-group analysis showed a similar structure for "primary mood disorders" (N = 65) and "schizoaffective disorders" (N = 49). Individual domains were differentially associated with age at onset, premorbid function, and course of illness. Such associations were independent of diagnostic groupings. We suggest that future research examine the validity of these psychopathological domains and the degree to which they are independent of current diagnostic categorizations. Establishing the validity of these domains and their independence from current diagnostic groupings would have implications for psychiatric nosology, by indicating that these domains could form the basis for a more valid classification of psychotic disorders.

NR175 Monday, May 6, 3:00 p.m.-5:00 p.m.

Archives of General Psychiatry: A Prevalence Study of Trials 1956–1995

Irshad Ahmed, M.D., Psychiatry, U-Conn Health Ctr, 263 Farmington Avenue, Farmington CT 06030; Clive E. Adams, M.B, Rochelle Seifas, Karla V. Soares, M.D.

Summary:

Background: Randomized controlled trials (RCTs) are the most powerful design by which mental health care is evaluated and often guide clinical practice. This study used 'Archives' as a sampling frame to survey trends in the use of RCTs over four decades.

Objective: To describe all controlled trials in Archives from 1956–1995 with particular attention to the a) participants b) quality of reporting of randomization; c) inteventions; d) sample size; and e) trial length.

Method: Archives was thoroughly handsearched. Specific variables for every study were reliably recorded. Prespecified questions were asked of the data and analysis conducted in Epi-info6.

Results: Archives published 621 clinical trials, 483 were stated to be randomized; 27% RCTs were about schizophrenia (decreased over time p = .0007) and 25% affective disorders (stable over time (p = .11). Drug trials (84%) are increasing over time (p = .01). Trials are small (median = 43) with no change over time (p > 0.37). Most trials (81%) were less than six months and length was decreasing latterly (p = .01). The quality of reporting of randomization was poor and declining (p = .03).

Conclusions: This study provides no evidence that the reporting and conduct of trials within psychiatry is improving and some evidence of a shift in emphasis away from schizophrenia.

NR176 Monday, May 6, 3:00 p.m.-5:00 p.m.

Thyroid Function Tests in First-Episode Mania

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Mauricio Tohen, M.D., Silvina B. Zarate, M.D.

Summary:

Because of abnormalities of thyroid function tests (TFTs) reported to occur in affective disorders and the confounding effects of chronicity of illness and exposure to psychotropic medications, the authors studied TFTs in patients experiencing a first manic or mixed episode.

Methods: Admission TFTs were reviewed in patients participating in a first-episode mania study. TFTs were compared in patients with manic (N = 57) vs. mixed (N = 15) bipolar states.

Results: Patients with bipolar disorder, mixed type, were more likely to have an elevated abnormal thyroid-stimulating hormone (TSH) level than bipolar manic patients (33% vs. 7%; p = 0.016). In addition, bipolar mixed patients were more likely to have higher mean TSH levels than bipolar manic patients (p = 0.04). There were no significant differences in the other mean TFTs levels between the two groups.

Conclusions: These preliminary data suggest that abnormalities in TSH are present in early mixed manic-depressive states.

NR177 Monday, May 6, 3:00 p.m.-5:00 p.m.

A Family Study of First-Episode Psychoses/Mania

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Bruce M. Cohen, M.D., Mauricio Tohen, M.D., Jennifer Sahatjian, Silvina B. Zarate, B.S.

Summary:

Objective: The goal of this study was to determine 1) whether there is a difference in the relative risk of psychosis in first-degree relatives of probands with first-episode psychosis/mania, and 2) whether the number of psychiatrically ill first-degree relatives predicts outcome in probands.

Methods: The first-degree relatives (N = 439) of probands with first-episode psychosis/mania (N = 95) were interviewed with the Diagnostic Interview for Genetic Studies and/or Family Interview for Genetic Studies by a rater who was blind to the probands' diagnosis and outcome.

Results: BP probands with one or more psychiatrically ill first-degree relatives were more likely not to have recovered by discharge than BP probands without psychiatric illness in first-degree relatives (p = 0.0001). There was no difference in the relative risk of psychosis among the first-degree relatives of probands with first-episode psychosis/mania.

Conclusions: 1) The density of psychiatrically ill first-degree relatives for probands with BP was highly predictive of probands' recovery at discharge. 2) Psychosis does not appear to be familial as there was no difference in the relative risk of psychosis in the relatives of the probands with a first episode of psychosis.

NR178 Monday, May 6, 3:00 p.m.-5:00 p.m.

Competency to Consent to Hospitalization and SPECT Scans Findings in Schizophrenia

Carlos A. Rueda, M.D., Psychiatry, St. Vincent's Med. Ctr., 101 West 15th Street, #6ES, New York NY 10011; Stephen B. Billick, M.D., Carlos Blanco, M.D., James J. Daly, M.D., Woodward Burgert, B.A.

Summary:

Objective: To compare regional cerebral blood flow (rCBF) differences in the frontal lobes of competent and incompetent schizophrenic inpatients.

Method: Eighteen inpatients clinically diagnosed with schizophrenia and confirmed by administration of the Structured Clinical Interview for Axis I DSM-III-R disorders, (SCID), were studied with the use of SPECT scans. The patients were also given the Competency Questionnaire to determine objectively the patient's capacity to consent to hospitalization, need for treatment, roles of medication, and the patient's legal rights. Regional CBF was measured as a ratio of regional tracer uptake to the cerebellar tracer uptake. Cerebral SPECT scans were performed with Tc99m HMPAO as the tracer. The rCBF was measured bilaterally in the superior, mid-, and inferior prefrontal regions, the orbitofrontal regions, and the frontal lobes as a whole.

Results: No statistically significant differences emerged in the rCBF when comparing competent versus incompetent patients. There was no significant correlation between rCBF abnormalities and incompetent patients. No significant differences were found between left or right areas of interest when comparing competency. However, all patients studied showed significant hypoperfusion in the frontal lobes.

Conclusions: These results suggest that SPECT scans cannot differentiate significant frontal hypoperfusion patterns in competent and incompetent patients with schizophrenia.

NR179 Monday, May 6, 3:00 p.m.-5:00 p.m.

Limbic System-Associated Membrane Protein in Human Brain: An Immunocytochemical Study

E.M. Kemether, M.D., Psychiatry, Mt. Sinai Medical, One Gustave Levy Place, New York NY 10029; William M. Byne, M.D.

Summary:

The limbic system-associated membrane protein (LAMP) is a cell adhesion molecule expressed by limbic-associated cortical and subcortical neurons in rat and monkey. Cell adhesion molecules underlie the molecular mechanisms that mediate cell migration, and cell-cell and cell-matrix adhesion. LAMP is unique among cell adhesion molecules in its ability to selectively influence limbic neurons.

Objective: To determine whether LAMP-immunoreactivity in autopsied human brain is selective for limbic and limbic-associated regions.

Method: Monoclonal antibody directed against LAMP was employed in immunocytochemistry to map the distribution of LAMP-immunoreactivity in formalin-fixed autopsied human brain.

Results: Regional immunostaining showed a strong correlation between the presence of immunoreactivity and conventionally defined limbic regions as well as areas receiving limbic connections.

Conclusions: LAMP-immunoreactivity in the human appears to be expressed by a subset of functionally related neurons. This distribution suggests that aberrant developmental expression of LAMP could give rise to anomalies in diverse brain regions. For example, LAMP is expressed in hippocampus, mediodorsal thalamic nucleus, and prefrontal cortex, regions strongly implicated in schizophrenia.

NR180 Monday, May 6, 3:00 p.m.-5:00 p.m.

Tardive Suppression of Dopamine Neurons in Substantia Nigra but not Ventral Tegmental Area Following Neuroleptic Administration

Anthony J. Levinson, M.A., Medicine, McMaster Med Ctr, 1200 Main Street East, Hamilton Ontario L8N 3Z5, Canada; Sarah Garside, M.D., Patricia I. Rosebush, M.D., Michael Mazurek, M.D.

Summary:

Objective: To determine whether haloperidol (HAL) treatment produces changes in midbrain dopaminergic neurons that persist after withdrawal of the drug.

Methods: Male Sprague-Dawley rats received daily intraperitoneal injections of saline (n = 18) or HAL 2mg/kg/day (n = 30) for eight weeks. Cohorts of saline- and HAL-treated rats were sacrificed at 2, 4, or 12 weeks *after* the final injection. Sections from SN and VTA were immunohistochemically stained for tyrosine hydroxylase (TH), a marker for dopamine neurons. Blinded counts of TH-positive cells were carried out on six sections per animal with a kontron video analysis system. Data were analysed by ANOVA and post-hoc t-test.

Results: The number of TH immunoreactive neurons in SN was 31% lower in HAL-treated rats than controls at two weeks withdrawal ($p < 0.001$); 49% lower at four weeks withdrawal ($p < 0.0001$); but only 12% lower at 12 weeks withdrawal ($p = 0.19$). There was no difference in VTA cell counts.

Conclusion: HAL produces selective down regulation of dopamine neurons in SN that persists after discontinuation of the drug. This TH-suppressing effect may play a role in the neurobiology of the persistent tardive syndromes associated with the use of neuroleptics.

NR181 Monday, May 6, 3:00 p.m.-5:00 p.m.

Diurnal Variation in Vagolytic Response to Lorazepam 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., Eva Petkova, Ph.D., Richard P. Sloan, Ph.D.

Summary:

To determine whether the cardiac autonomic response to lorazepam (LZ) demonstrates a diurnal variation, a double-blind, randomized, placebo-controlled study was conducted. Seven healthy volunteers received LZ (3 mg qd) or placebo for one week, a week taper, then crossed over. Following each drug, heart rate and heart period variability (HPV) were measured over 24 hours using ambulatory ECG monitoring. Two-tailed paired t-tests revealed: an increase in heart rate on LZ vs PL for the period between 9 a.m. and 3 p.m. ($p < 0.0001$); and a corresponding decrease in Root Mean Square Successive Difference (an index of cardiac vagal modulation) on LZ vs PL between the hours of 9 a.m. and 4 p.m. ($p < 0.01$). These results demonstrate a diurnal variation in the cardiac autonomic response to lorazepam, with a pronounced vagolytic effect occuring during the hours between 9 a.m. and 4 p.m. These findings suggest that during the daytime hours, a period which coincides with hypothalamic-pituitary-adrenal axis activation and a relative increase in activity compared to nightime hours, the vagal limb of the autonomic nervous system displays a greater sensitivity to the pharmacologic effects of benzodiazepine.

NR182 Monday, May 6, 3:00 p.m.-5:00 p.m.

Effects of Prefrontal Repetitive Transcranial Magnetic Stimulation (rTMS) on Mood and Anxiety in Healthy Volunteers: A Replication Study

Juliet E. Dearing, B.S., Clinical Neuropsych, NIMH, Bldg 10/3D41, Bethesda MD, 20892; Mark S. George, M.D., Benjamin D. Greenberg, M.D., Eric M. Wassermann, M.D., Thomas E. Schlaepfer, M.D., Robert M. Post, M.D.

Summary:

Background: The prefrontal cortex has been implicated in normal and pathological mood regulation. rTMS permits noninvasive stimulation of cortical neurons, either enhancing or inhibiting function depending on the stimulation parameters. Previous studies of healthy controls have found that left prefrontal cortex rTMS was associated with sadness, and right with happiness. We attempted to replicate these earlier findings.

Methods: Nine right-handed healthy volunteers free of psychopathology had rTMS using a figure-eight shaped electromagnetic coil over the right and left prefrontal cortex and sham stimulation, 20 minutes apart, in random order. rTMS was given at 80% motor threshold, 20 Hz, 2 seconds/minute x 20 over 20 minutes. Subjects serially self-rated their mood and anxiety. Randomly, and on a different day, these same subjects had the same stimulation using a larger, tear-drop-shaped coil.

Results: Twenty-minutes after stimulation with the figure-eight-shaped coil, happiness ratings decreased after left prefrontal rTMS compared with right prefrontal rTMS ($p < 0.05$). Anxiety increased after right rTMS compared with left ($p < 0.05$). No significant mood changes were seen following rTMS with the tear-drop-shaped coil.

Conclusions: These findings are consistent with previous rTMS studies examining differential prefrontal effects on mood and imply that the site of stimulation, as well as perhaps the focal nature, is a critical component in these mood changes.

NR183 Monday, May 6, 3:00 p.m.-5:00 p.m.

Auditory Event-Related Potentials in An Oddball Paradigm in Children with Tourette's Syndrome

M. Yanki Yazgan, M.D., Child Psychiatry, Marmara University Hospital, Tophanelioglu CD Altunizade, Istanbul 81190, Turkey; Sennur Zaimoglu, M.D., Sacit Karamursel, M.D.

Summary:

We investigated in Tourette Syndrome (TS) selective and divided attention using AEP in an oddball paradigm and specific neuropsychological measures.

Methods: Fifteen TS children (9 boys, 6 girls; age 110 + / – 32 months) diagnosed according to DSM-IV criteria, and their individually age-, sex-, and education-matched normal controls participated. AEPs were evoked in an oddball paradigm (Donchin, 1981) in which subjects hear standard and deviant tones, and respond to deviant tones as "target" stimuli. A neuropsychological battery of specific laterality measures (Yazgan 1995) and tests of

executive function and attention (CPT, Stroop, WCS, word fluency) were also administered.

Results: TS children showed significantly reduced N1 in standard central derivations. (p = .03) The index computed by subtracting standard N1 latency from deviant N1 latency was also significantly (p = .03) greater in the TS group. TS + OCD group (N = 5) showed reduced cN1 latency relative to TS-only children, but this difference did not reach significance (p = .08). Patients also differed from the normals significantly on word fluency and CPT (p = .04). They also did not show the normal symmetry for this age group on laterality measures (p = .04). (All p's are two-tailed)

Conclusions: The electrophysiological findings were suggestive of increased distractibility and increased attention to background stimuli in the TS group relative to the normal controls. The neuropsychological findings were parallel to previous reports of altered laterality and impaired executive function in TS. These findings were more pronounced in TS children with OCD comorbidity.

NR184 Monday, May 6, 3:00 p.m.-5:00 p.m.

Dermatologic QA Screening in 50 Psychiatric Inpatients

Sandra O. De Jesus, M.S., Psychiatry, NY Medical College, 123 Bank Street, Apt. 220, New York NY 10014; Stephen B. Billick, M.D., Sandra M. Bruni, M.S.

Summary:

Background: Psychiatric illness has been shown to coexist with or manifest as dermatoses in the field of psychodermatology. Any association between specific psychiatric diagnoses and discrete dermatological disease has not, however, been extensively investigated.

Objective: We determined the frequency of dermatological disease in psychiatric inpatients and, in addition, assessed the psychiatry residents' abilities to detect and diagnose cutaneous lesions.

Methods: 50 psychiatric inpatients were examined for dermatological disease. Findings were compared with those of the psychiatry resident MD.

Results: A significant association was observed between schizophrenia and pruritus. Mood disorder and dementia were also found to be associated with dermatologic disease. Psychiatry residents failed to detect dermatologic disease in 86% of patients examined.

Conclusion: There is a real relationship between psychiatric and dermatologic illnesses, but more extensive research is needed. Additionally, our study confirmed earlier studies that nondermatologists perform poorly in detection of skin disease. Psychiatry residents should receive better training in physical diagnosis of the skin to provide proper and adequate care to patients exhibiting psychodermatology.

NR185 Monday, May 6, 3:00 p.m.-5:00 p.m.

Patients Subjective Illness Concepts About Chronic Schizophrenia: A Comparison of Views Seen by Patients and Psychiatrists in Office Practice

Bettina Ripke, M.A., Psychiatry, Dresden University, Markt 2, 01109 Cresden 01109, Germany; Julia Schellong, M.D., Antje Triemer, M.A., Franco Glasner, M.A., Otto Bach, Ph.D.

Summary:

Background: The subjective point of view in patients and therapists about illness and therapy is of a considerable significance with respect to a psychotherapeutic co-treatment for chronic schizophrenic persons.

Samples and method: 25 schizophrenics (clinical obvious schizophrenia according to DSM-IV criteria with at least one relapse) and 38 psychiatrists in office practice in the area of the cities Dresden and Leipzig were interviewed in the framework of a pilot study. All patients were interviewed by means of the Dresden Semistructured Interview (Ripke, Gläsner 1993) while psychiatrists received a questionnaire with items about information transfer to their patients, about content and meaning of illness concepts and their significance in the outpatient treatment.

Results: The knowledge of the patients about their disease varied considerably but the majority of subjects (75%) desired more information and communication. Most of the therapists consider this as important, too (50% as important, 34% individually selected information, 13% totally oppose to that) and express to be interested in doing so in practice. An accordance was also found for the schizophrenia illness concept which, is following the vulnerability-stress-hypothesis. As to the treatment process the most obvious effects were ascribed to the pharmacologic treatment. Nevertheless, the patients more likely believe that an improvement could arise from augmenting the verbal communication (also in groups) while clinicians don't consider such possibilities of therapy as notable in like manner.

Conclusion: In spite of different interviewing methods we found a distinct accordance of the samples in regard to clinical information management and illness concept. This fact should be conceived of as an encouragement to a psychotherapeutical oriented relation which is perceived by patients and therapists to be helpful and desirable in the structural context of forming a therapeutical alliance.

NR186 Monday, May 6, 3:00 p.m.-5:00 p.m.

Changes of Interleukin Levels in Serum of Schizophrenic Patients Before and After Haloperidol Treatment

Yong-Ku Kim, M.D., Psychiatry, Korea University, 17-202, Woosung Atp, Suhcho-Do, Sucho-Ku, Seoul 137 072, Korea; Min Soo Lee, M.D.

Summary:

We have previously reported that Korean schizophrenic patients have low production of Il-2 in vitro suggestive of autoimmunity to the pathogenesis of the disorder. In an attempt to further explore this issue, we measured in vivo serum level of interleukin (IL-1beta, IL-2, and IL-6) using a quantitative "sandwich" enzyme immunoassay (ELISA) in 26 male schizophrenic patients before and after four weeks of haloperidol treatment. Patients met DSM-IV criteria for schizophrenia and were drug free for at least six months. The severity of symptoms was assessed by SANS SAPS. We found a significant increase of IL-2 level (p 0.05) and a slight increase of IL-6 (p 0.1) in schizophrenic patients as compared with age-matched normal controls. In schizophrenic patients, no significant differences were found in IL-1beta, IL-2, and IL-6 levels before and after haloperidol treatment. There were significantly positive correlations between IL-2, IL-6, and negative symptom scores. There were no correlations between age, age at onset, duration of illness, and interleukin levels.

Our results may support the hypothesis of an autoimmune dysfunction in schizophrenia. It is suggested that haloperidol treatment may not change interleukin levels. The correlations of IL-2 and IL-6 level and negative symptoms suggest that increased IL-2 and IL-6 may be associated with specific clinical features in the schizophrenic syndrome.

NR187 Monday, May 6, 3:00 p.m.-5:00 p.m.

Epinephrine Increases Plasma Interleukin-6 in Major Depression

Gregory H. Pelton, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06519; Lawrence H. Price, M.D., George R. Heninger, M.D.

Summary:

We examined mechanisms of stress induced alterations in immune function by assessing epinephrine (E) induced release of Interleukin-6 (IL-6) in healthy controls (HC) and patients with major depression (PMD).

Methods: HC's and drug free PMD underwent randomized double-blind testing with a 60-min continuous i.v. infusion of 0.1 to 0.2 ug/kg/min of E or saline. Plasma levels of E and norepinephrine (NE), cortisol, IL-6, blood pressure (BP), heart rate (HR), and emotional state were measured before and after E.

Results: E produced a dose related increase in IL-6, systolic BP, and HR in HC's. In five PMD, increases in IL-6 levels and HR did not correlate like they did in HC's. E did not produce consistent cortisol and emotional responses in HC or PMD.

Discussion: This is the first demonstration that E causes an increase in plasma IL-6 levels in both HC and PMD. The E-induced increase in IL-6 occured without changes in plasma cortisol, indicating that stress effects on the immune system can be mediated directly through E release, without involvement of the HPA axis.

NR188 Monday, May 6, 3:00 p.m.-5:00 p.m.

Schizophrenia Research Subjects: Gender Differences

Patrick T. Dooley, M.A., Psychiatry, Harvard Med School, 74 Fenwood Drive, Boston MA 02115; Jayendra K. Patel, M.D., Anthony G. Kalinowski, Ph.D., Rahim Shafa, M.D., Carla M. Canuso, M.D., Alan I. Green, M.D.

Summary:

Objective: Obtaining adequate numbers of subjects of both sexes is especially important in studies of schizophrenia because of the clear gender-based differences in the expression of the disorder and in its response to treatment. Nonetheless, many clinical research studies of psychotic patients include more men than women. We report here our experience in recruiting psychotic patients for our clinical research studies.

Method: Over a 16-month period, we have employed various strategies to recruit men and women subjects from private hospitals, state hospitals, and outpatient clinics to participate in: a) clinical/neuropharmacological studies of new antipsychotic drugs; and b) a neuropharmacological study of clozapine. Eligible subjects for these studies require a diagnosis of schizophrenia or schizoaffective disorder that is either treatment responsive or treatment refractory. For this analysis, data from our recruitment logs were reviewed, and the distribution of our referred subjects by gender was assessed.

Results: 482 subjects were referred for our studies. Of these subjects, 305 (63%) were men and 177 (37%) were women ($p < .01$). Among subjects over age 50, however, there were slightly more women (n = 41) referred for study than men (n = 29); among subjects under 50, 274 (67%) were men and 136 (33%) were women.

Conclusion: These data suggest that despite our attempt to recruit equal numbers of men and women for our studies, the subjects referred have been predominantly men, except in the over-50-year-old category. Our recruitment data will be presented in detail, and their implications for clinical research programs focusing on psychotic subjects will be discussed. In addition, the possible implications of our data for the "estrogen hypothesis" of schizophrenia will be reviewed.

NR189 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Bupropion Plus Bromocriptine for Treatment of Cocaine Dependence

Ivan D. Montoya, M.D., NIH, PO Box 5180, Baltimore MD 21224; David A. Gorelick, M.D., Kenzie L. Preston, Ph.D., Edward Cone, Ph.D., Richard B. Rothman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat cocaine dependence using the dopaminergic medications bupropion and bromocriptine.

Summary:

Objective: To evaluate the safety and efficacy of the medication combination bupropion plus bromocriptine for treatment of cocaine dependence.

Method: Twenty-six cocaine-dependent (DSM-III-R) outpatients (69% male, 58% African American, mean age 33.4 years, lifetime cocaine use 6.3 years) received eight weeks of weekly drug abuse counseling plus the open-label combination of bupropion (up to 300 mg daily) and bromocriptine (up to 7.5 mg daily) according to a dose escalation schedule that took either three weeks (slow dose escalation [SDE], n = 13) or one week (rapid dose escalation [RDE], n = 13) to reach maximum dose. The primary outcome measures were cocaine use (by self-report and urine toxicology), cocaine craving, and treatment retention.

Results: Both groups tolerated the medications well with no serious adverse events, and had significant decreases in self-reported cocaine craving and cocaine use. The RDE group had significantly longer treatment retention, but there were no other significant group differences.

Conclusions: The combination of two dopaminergic medications, bromocriptine plus bupropion, is safe for use in cocaine addicts, and warrants further study for the treatment of cocaine dependence.

References:

1. Giannini AJ, Baumgartel P, DiMarzio LR: Bromocriptine therapy in cocaine withdrawal. J Clin Pharmacol 27:267–270, 1987.

2. Margolin A, Kosten T, Petrakis I, et al.: Bupropion reduces cocaine abuse in methodone-maintained patients. Arch Gen Psychiatry 48:87, 1991.

NR190 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Use of Alcohol Detox Protocol on a Medical Unit

Lisa R. Fenton, P.S.D., YPI/CRU, Yale University, 914.5 Howard Avenue, New Haven CT 06519; Judy Ebbets, M.S., Wayne S. Fenton, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how the use of a structured protocol for treating alcohol withdrawal may reduce morbidity associated with withdrawal related adverse events.

Summary:

Background: Adverse events related to alcohol withdrawal cause significant morbidity in general medical settings. In this study we evaluate the effects of introducing a structured protocol for the treatment of emergent withdrawal in a med-surg inpatient unit.

Methods: The Withdrawal Assessment Scale and Titration Protocol was implemented on a general medical unit at Hartford Hospital. The charts of consecutive patients before (N = 20) and after (N = 36) introduction of the protocol who received at least one benzodiazapine dose for alcohol withdrawal were reviewed for

withdrawal-related adverse events. Using a quasi-experimental design, patients on an adjacent unit (N = 42) served as controls.

Results: Patients' mean age was 46, most were male (75%) and single (76%) Pancreatitis and/or GI disorders were most common diagnoses. AMA discharges decreased significantly ($p < .005$) on the experimental unit after protocol implementation (32% to 6%) with no significant changes on the control unit; the overall frequency of adverse events increased significantly ($p < .04$) on the control unit (23% to 65%) but did not change on the experimental unit.

Conclusions: A structured alcohol withdrawal protocol in the medical setting may result in improved patient outcome by reducing the frequency of withdrawal-related adverse events and AMA discharges.

References:

1. Kinney J, Severinghaus J (1991): Clinical medical management. In, J. Kinney (ed.) *Clinical Manual of Substance Abuse* (pp. 91–118). Boston: Mosby York.

2. Cushman P. (1987). Delirium tremens: Update of an old disorder. Post-Graduate Medicine, 2, 117–122.

NR191 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Prior Abstinence and Post-Transplant Drinking: Six Months of Abstinence Does Not Predict Alcoholic Relapse

Thomas P. Beresford, M.D., Psychiatry, VAMC/U of Colorado, 1055 Clermont Street, Denver CO 80220; Michael R. Lucey, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should acquire sufficient empirical understanding to discard the Six Month Prior Abstinence rule as a useful guide for selecting alcohol dependent patients for liver transplant.

Summary:

Objective: Most liver transplant teams in the U.S. require a six-month period of abstinence before listing alcohol dependent (AD) persons for transplant. This practice derives from a single report with brief follow-up, inadequate numbers of subjects, and no use of standard diagnostic and prognostic protocols. We hypothesized that abstinence of more than six months prior to transplant evaluation is of no prognostic value in predicting return to drinking after transplant.

Method: We conducted a study of 47 AD (DSM-III-R, DSM-IV) liver transplant recipients and followed them prospectively for three years on average. Alcohol use data were collected at multiple follow-up visits from index patients and from a significant other person. Patients were grouped as 1) abstinent, 2) any alcohol use and 3) alcohol use with either resumption of addictive drinking or physical sequellae due to use.

Results: At three years, 31 were completely abstinent, 11 had brief, limited exposure to alcohol without resumption of addictive drinking, and five had returned to pathological use. With seven cases in the smallest cell, Chi-square analysis revealed that six months abstinence prior to transplant was no better than chance alone in predicting return to alcohol use.

Conclusions: These data suggest that there is no empirical justification for excluding AD patients lacking six months of prior abstinence from this lifesaving procedure. A wiser, more humane approach is to assess the likelihood of long-term AD remission through social and psychological factors that predict abstinence empirically.

References:

1. Lucey MR, Merion RM, Beresford TP. *Liver Transplantation For the Alcoholic Patient*, Cambridge University Press, Cambridge, 1994.

2. Beresford TP and Lucey MR: Alcoholics and liver transplant. *Addiction*, 89:1043–48, 1994.

NR192 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Double-Blind Fluoxetine in Depressed Alcoholics

Jack R. Cornelius, M.D., Dept. of Psychiatry, WPIC Room 1092, 3811 O'Hara Street, Pittsburgh PA 15213-2593; Ihsan M. Salloum, M.D., Joan G. Ehler, M.D., Patricia J. Jarrett, M.D., James Perel, Ph.D., Michael E. Thase, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: 1. Learn the therapeutic response of depressed alcoholics to fluoxetine, as compared to placebo. 2. Learn the clinical profile of patients with comorbid major depressive disorder and alcohol dependence.

Summary:

The selective serotonergic agonist (SSRI) fluoxetine has demonstrated efficacy in the treatment of depression and obsessive-compulsive disorder, and has suggested efficacy in the treatment of alcoholism. However, no large-scale double-blind, placebo-controlled trials with any SSRI have been reported in depressed alcoholics. In the current ongoing study, 41 patients with MDD and alcohol dependence were randomized to fluoxetine (N = 20) or placebo (N = 21) in a double-blind, parallel group trial (AA09127). Weekly ratings of symptoms were performed for 12 weeks. All patients were initially started on one capsule (20 mg fluoxetine or placebo), which could be increased to two capsules after two weeks if depressive symptoms persisted. The fluoxetine group demonstrated a significantly greater improvement on the HAM-D-24 ($\Delta = -6.75$ vs -1.48; $F = 4.06$; $df = 1, 25$; $p = 0.05$), the SCL-90 depression subscale ($\Delta = -.60$ vs $-.14$; $F = 4.97$; $df = 1, 25$; $p = 0.04$), and the SCL-90 obsessive-compulsive subscale ($\Delta = -.57$ vs $-.12$; $F = 9.38$; $df = 1, 25$; $p = 0.005$). Level of drinking was significantly associated with level of depressive symptoms and with level of obsessive-compulsive symptoms at baseline and during the medication trial. Total alcohol consumption during the 12-week study was significantly lower in the fluoxetine group than the placebo group ($X = 61$ vs 220 drinks; $F = 5.47$; $df = 1, 13$; $p = 0.036$). These findings suggest efficacy for fluoxetine for treating the depressive symptoms, the obsessive symptoms, and the excessive alcohol use of depressed alcoholics.

References:

1. Cornelius JR, Salloum IM, Cornelius MD, et al.: Fluoxetine Trial in Suicidal Depressed Alcoholics. *Psychopharmacol Bull* 29:195–199, 1993.

2. Cornelius JR, Salloum IM, Mezzich JE, et al.: Disproportionate Suicidality in Patients with Comorbid Major Depression and Alcoholism. *Am J Psychiatry*, 152:358–364, 1995.

NR193 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Development of a Therapeutic Cocaine Vaccine

Barbara S. Fox, Ph.D., Discovery, Immunologic Pharm, 610 Lincoln Street, Waltham MA 02154; Kathleen M. Kantak, Ph.D., Thomas J. Briner, Ph.D., Mark A. Exley, Ph.D., Philip A. Swain, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand and appreciate a promising new approach to the treatment of cocaine addiction. This treatment stimulates the patient's own immune system to produce anti-cocaine antibodies that will antagonize the reinforcing properties of cocaine.

Summary:

There are currently no effective therapies for the treatment of cocaine addiction. A novel strategy is to inhibit the reinforcing activity of the drug by inducing anti-cocaine antibodies with a therapeutic vaccine. A model system demonstrates that antibodies can rapidly and effectively extinguish cocaine self-administration in rats (passive transfer of a monoclonal antibody specific for cocaine). To induce anti-cocaine antibodies in vivo, a cocaine vaccine was synthesized by conjugating cocaine to a protein carrier. Immunized mice achieved high titers of anti-cocaine antibodies that were maintained for several months after the last boost. The anti-cocaine antibodies caused a significant change in cocaine pharmacokinetics, with decreased levels of cocaine measured in the brain of immunized vs. control mice 30 seconds after i.v. injection of [^{3}H] cocaine. The anti-cocaine antibodies did not detectably affect either the pattern of cocaine metabolism or the rate of loss of cocaine from the plasma, and cocaine administration did not reduce the level of circulating anti-cocaine antibody. These data demonstrate the feasibility of a cocaine vaccine and suggest that it will be a powerful new tool for the treatment of cocaine addiction.

References:

1. Slusher, B.S. and P.F. Jackson. A shot in the arm for cocaine addiction. Nature Medicine 2:26-27 (1996)

2. Johanson, C.E. and M.W. Fischman. The pharmacology of cocaine related to its abuse. Pharmacological Reviews. 41:3-52 (1989)

NR194 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Electrocardiographic Findings in Chronic Heavy Cocaine Abusers

Faiq A. Hameedi, M.D., Psychiatry, Yale School of Medicine, 34 Park Street, New Haven CT 06519; Lynn C. Winther, M.D., Conor K. Farren, M.D., Rukhshinda R. Hameedi, M.D., Elinore F. McCance-Katz, M.D., Thomas R. Kosten, M.D.

Educational Objectives:

At the end of this presentation the participant should be able to describe how a certain percentage of cocaine abusers have electrocardiographic abnormalities.

Summary:

Background: About 30% of cocaine abusers have evidence for significant electrocardiographic (EKG) abnormalities. We report prevalence of EKG abnormalities in young asymptomatic chronic heavy cocaine abusers rejected from our studies due to these EKGs.

Methods: EKGs from 45 asymptomatic subjects with a mean ± SD age (33 ± 6) years and 8.9 ± 5.7 gm of cocaine/wk were reviewed.

Results: Preliminary analysis reveals that four (9%) of the subjects had sinus bradycardia, two (4.5%) had sinus arrhythmia, one (2%) had atrial fibrillation, and two (4.5%) had premature ventricular contractions. Fourteen (31%) of the subjects had right bundle branch block (RBBB). Thirteen (29%) met minimal criteria for left ventricular hypertrophy (LVH). Twenty-four (53%) of the subjects had ST-T wave abnormalities while nine/24 (37%) of these changes were consistent with myocardial ischemia. A total of 4/45 (9%) had evidence for old myocardial infarction. In our sample RBBB was linked to higher gm/wk of cocaine use while LVH was related to product of gm/wk x duration of cocaine use.

Conclusion: Prevalence of medically significant EKG abnormalities is high in young asymptomatic chronic cocaine abusers. The prevalence of ST-T wave changes was similar to other studies but RBBB and old infarctions appear to be higher in our sample. Detailed analysis will be presented.

References:

1. Isner JM, Chokshi SK. Cardiovascular Complications of Cocaine. Curr Prob Cardiol 16:91–123, 1991.

2. Chakko S, Fernandez A, Mellman TA, Milanes FJ, Kessler KM, Myerberg RJ. Cardiac Manifestations of Cocaine Abuse: A Cross Sectional Study of Asymptomatic Men with a History of Long-Term Abuse of "Crack" Cocaine. J Am Coll Cardiol 20:1168–74, 1992.

NR195 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Pharmacokinetic and Pharmocodynamic Effects of Co-Administration of Nefazodone and Desipramine to Normal Volunteers

Sheldon H. Preskorn, M.D., Psychiatric Res Ctr, 1100 North St. Francis Ste 200, Wichita KS 67214-3199; Ryan D. Magnus, M.D., Dale Horst, Ph.D., Jane Rosenblum, Darlene Jody, M.D., John R. Ieni, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the results of the study which will help guide clinicians about combination antidepressant treatment for non- or partially-responsive depressed patients.

Summary:

Tricyclic antidepressants (TCAs) are still widely used to treat depressed patients, and there is a tendency to prescribe additional agents for those depressed patients who are either nonresponsive or partially responsive to a single antidepressant agent. Thus, nefazodone could be co-prescribed with TCAs, such as desipramine. While nefazodone or its metabolites are extremely weak in vitro inhibitors of CYP2D6, the isoenzyme principally responsible for the metabolism of TCAs, it is important to evaluate in vivo the potential for pharmacokinetic (PK) and/or pharmacodynamic interaction between nefazodone and TCAs.

Methods: Eligible male and female volunteers were randomized to one of two treatment sequences. Group A subjects received desipramine (50 mg qd) for two days followed by desipramine (75 mg qd) for 17 days. On Day 10, nefazodone (100 mg bid) was added to the desipramine treatment. The nefazodone dose was increased to 150 mg qd on Day 15. PK parameters were determined on Days 9, 14, and 19. Group B subjects received nefazodone (100 mg bid) for five days followed by nefazodone (150 mg bid) for 14 days. On Day 11, desipramine (50 mg qd) was added to the nefazodone dose. On Day 13, the desipramine dose was increased to 75 mg qd. PK parameters were determined on Days 10 and 19.

Results: Nefazodone (150 mg bid) increased Area Under the Curve (AUC) and Cmax of desipramine by 8.5% and 10.1%, respectively (n.s.). AUC and Cmax of 2-OH-desipramine were not affected. Desipramine (75 mg qd) decreased the AUC and Cmax of nefazodone by 22% (n.s.) and 16% (n.s.), respectively, and decreased the AUC and Cmax of OH-nefazodone by 19.3% ($p < .05$) and 16% (n.s.), respectively. In addition, desipramine increased the minor nefazodone metabolite, m-CPP, by 39.6% ($p < .002$) and 42.9% ($p < .003$), respectively. No statistical changes in vital signs were observed when nefazodone was added to desipramine treatment. However, a small but significant elevation of supine diastolic BP (+ 7 mm Hg) and supine pulse rate (+ 7

bpm) were observed when desipramine was added to nefazodone. Adverse events, insomia and tachycardia, were increased by the addition of desipramine to nefazodone. One patient withdrew from the study for an adverse event (tachycardia) while being treated with desipramine alone. Based on these data, nefazodone, in a therapeutic dose of 150 mg bid, did not increase plasma levels of desipramine, a drug principally metabolized by CYP2D6, in contrast to previous research indicating drug interactions of desipramine with fluoxetine and paroxetine. Nefazodone may be relatively safe to use in combination with desipramine. However, desipramine may affect the metabolism of nefazodone which could result in increased rates of some adverse events.

References:

1. Brosen K. Recent developments in hepatic drug oxidation: implications for clinical pharmacokinetics. *Clin Pharmacokinet* 18(3):220–239, 1990.

2. Preskorn SH. What is the message in the alphabet soup of cytochrome P450 enzymes? *Jrnnl Pract Psych Behav Hlth.* 238, 1995. In press.

NR196 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Optimal Target Dose of Imipramine in Panic Disorder with Agoraphobia

Matig R. Mavissakalian, M.D., Psychiatry, Ohio State University, 473 West 10th Avenue, Columbus OH 43210-1252; James Perel, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to present new data of practical relevance to the selection of an optimal target dose of imipramine in the treatment of panic disorder.

Summary:

Objective: Our dose-ranging study with imipramine in panic disorder found that the fixed, weight-adjusted dose 1.5mg/kg/d had similar therapeutic effects, but significantly lower dropout rates than 3.0mg/kg/d and suggested that an intermediate dose of the drug may increase the likelihood of achieving optimum plasma concentrations [110–140ng/ml]. The aim of the present study was to follow up on this suggestion with a target dose of 2.25 mg/kg/d.

Method: 110 consecutive patients with panic disorder with agoraphobia entered the open, fixed-dose protocol with 2.25mg/kg/d of imipramine. Assessments included patient and clinician rated scales of symptom severity, and the determination of plasma concentrations of imipramine and desmetylimipramine at Week 8 of the protocol.

Results: 77 patients completed the trial of whom 46 [60%] were marked responders. Twenty-seven [24.5%] patients dropped out due to drug side effects. The average actual dose of imipramine was 165.3 ± 42.5 mg/d for the entire sample. The mean total plasma concentration at Week 8 [n = 74] was 175.1 ± 132.7 ng/ml. The regression equation relating dose to plasma concentration was plasma = 23.2 + 0.94 dose, R^2 = 8.4%. Regression models relating plasma to Week 8 scores revealed neither linear nor quadratic effects approaching significance.

Conclusion: The results demonstrate that the 2.25mg/kg/d protocol was successful in controlling the bio-availability of the drug. Although better tolerated, the therapeutic effects were similar to 3mg/kg/d. It is suggested that dosages between 1.75 to 2.0mg/kg/d would yield optimal plasma and therapeutic results.

References:

1. Mavissakalian MR, Perel JM: Dose-response characterization of antipanic effects of imipramine. Psychopharmacology Bulletine 30:171–174, 1994.

2. Mavissakalian MR, Perel JM: Imipramine treatment of panic disorder with agoraphobia: dose-ranging and plasma level response relationships. American Journal of Psychiatry 152:673–682, 1995.

NR197 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Fluvoxamine in the Treatment of OCD in Children and Adolescents: A Multicenter, Double-Blind, Placebo-Controlled Trial

Mark A. Riddle, M.D., Psychiatry, Johns Hopkins Med Inst, 600 N Wolfe Street CMSC 346, Baltimore MD 21287; Pediatric OCD Research Group,

Educational Objectives:

At the end of the presentation, the participant should be knowledgeable about the use of fluvoxamine in the treatment of children and adolescents with obsessive compulsive disorder.

Summary:

Objective: To assess the safety and efficacy of fluvoxamine (50–200 mg/day) in children and adolescents 8–17 years old with obsessive-compulsive disorder (OCD).

Methods: Subjects entered the study, if they had a minimum six-month history of OCD and had not failed a previous medication trial for OCD. After a one- to two-week placebo washout/screening period, 120 subjects were randomized into the 10-week (four weeks titration, six weeks maintenance) double-blind, placebo-controlled trial. The intent-to-treat, last-observation-carried-forward method of data analysis was used to assess outcome.

Results: The primary efficacy variable, Children's Yale-Brown Obsessive Compulsive Scale, showed significant differences from placebo ($p < 0.05$) at weeks 1 to 4, 6, and 10. Efficacy was also supported by a number of secondary outcome variables. Four subjects (three fluvoxamine, one placebo) discontinued participation due to side effects, none of which was considered serious. Side effects more common fluvoxamine included insomnia, agitation, hyperkinesia, somnolence, and dyspepsia.

Conclusions: Fluvoxamine was found to be efficacious in the treatment of OCD in children and adolescents as young as age 8. Side effects were, in general, mild. The design, subjects, and results of this study will be compared with those of other published, controlled, medication trials for OCD in children and adolescents.

References:

1. DeVeaugh-Geiss J, Moroz G, Biederman J et al.: Clomipramine hydrochloride in childhood and adolescent obsessive-compulsive disorder - a multicenter trial. J Am Acad Child Adolesc Psychiatry, 31(1):45–49, 1992.

2. Riddle MA, Scahill L, King R et al.: Double-blind crossover trial of fluoxetine and placebo in children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry, 31(6):1062–1069, 1992.

NR198 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Serotonergic Antidepressants in Obsessive Personality

Marc M. Ansseau, M.D., Psychiatric Unit, University of Liege, Chu Du Sart Tilman, Liege B-4000, Belgium

Educational Objectives:

At the conclusions of this presentation, the participants should be aware of the usefulness of serotonergic antidepressants, such as fluvoxamine, in the treatment of obsessive-compulsive personality disorder.

Summary:

Objective: A large body of evidence suggests that "serotonergic" antidepressants represent the most effective pharmacological agents in the treatment of obsessive-compulsive disorders. In the traditional psychoanalytic explanation of obsessive-compulsive disorders, obsessive-compulsive personality has been seen as a predisposing feature. In a recent study, we reported that in depressive patients, the presence of an underlying compulsive personality predicted a particular benefit with selective serotonin re-uptake inhibitors (SSRIs). A possible interpretation for these findings was that SSRIs improved the personality disorder. Therefore, the objective of the present study was to test the therapeutic usefulness of SSRIs, such as fluvoxamine, in obsessive-compulsive personality disorder (OCPD) without associated depression.

Method: 24 outpatients who fulfilled DSM-IV criteria for OCPD were included in the study: 15 males and 9 females, aged from 24 to 62 years (mean = 44.3 ± 11.7). All patients were devoid of significant depressive symptomatology, as evidenced by scores less than 7 on the 17-item Hamilton Depression Scale. The patients were randomly assigned to either fluvoxamine (50 mg during the first week then 100 mg) (n = 12) or placebo (n = 12) in double-blind conditions. The duration of the study was three months. Initial and final assessments were performed by rating each of the eight features of DSM-IV OCPD on a five-point scale (0 = absent, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe).

Results: Three patients did not complete the study (two in the fluvoxamine group and one in the placebo group). Changes over time in OCPD scores showed a significant superiority of fluvoxamine over placebo : from 18.6 to 13.7 in the fluvoxamine group vs from 18.5 to 17.7 in the placebo group ($t = 4.39$, $p = 0.0003$). Side effects were more frequent with fluvoxamine (13 vs 3), mainly of the gastrointestinal type (7 vs 2).

Conclusion: These results support a beneficial activity of SSRIs in OCPD. These findings favor the possibility that at least some elements of personality disturbances have a biological component. In the case of OCPD, serotonergic dysfunction could play a role.

References:

1. Ansseau M, Troisfontaines B, Papart P, von Frenckell R: Compulsive personality as predictor of response to serotonergic antidepressant. *Br Med J* 303:760–761, 1991.

2. Pollit J, Tyrer P: Compulsive personality as predictor of response to serotonergic antidepressants. *Br J Psychiatry* 161:836–838, 1992.

NR199 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Double-Blind, Controlled Comparison of Haloperidol and Pimozide in Children with Gilles de la Tourette's Syndrome

Floyd R. Sallee, M.D., Psychiatry, MUSC, 171 Ashley Avenue, Charleston SC 29425-0002; Lori Nesbit, Pharm D., Cherry Jackson, Pharm D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the limitations of pharmacotherapy and to assess the risk/benefit of neuroleptic treatment of Tourette in this population

Summary:

This study compares the efficacy and safety of pimozide and haloperidol in the treatment of Gilles de la Tourette's syndrome (GTS) in children. Although haloperidol is cited as being the drug of first choice, the relative efficacy and side effect profiles for haloperidol and pimozide have not been determined in this population.

Methods: A double-blind, 24-week, crossover study with biweekly assessment and flexible dose titration was completed in 22 GTS subjects (10.2 ± 2.5 years). Final outcome was determined after six weeks on each treatment (placebo, pimozide, haloperidol).

Results: Pimozide demonstrated superior relative efficacy, based on a threefold higher incidence of treatment-limiting side effects associated with haloperidol treatment. Pimozide was equivalent to haloperidol in tic and behavioral efficacy. Dose range and potency of pimozide and haloperidol were found to be equivalent (3.4 ± 1.6 mg/day versus 3.5 ± 2.2 mg/day), with effective dose ranges lower than previously reported. Cognitive function and school performance deficits were not detected at the low dose ranges used.

Conclusions: At equivalent dosages lower than previously reported, both pimozide and haloperidol are effective in controlling symptoms of GTS in children and adolescents.

References:

1. Sallee FR, Dougherty D, Sethuraman G, Vrindavanam N. Prolactin monitoring of haloperidol and pimozide treatment in children with Tourette Syndrome. *Biological Psychiatry.* In Press.

2. Shapiro E, Shapiro AK, Fulop G, Hubbard M, Mandeli J, Nordlie J, and Phillips RA. Controlled Study of Haloperidol, Pimozide, and Placebo for the Treatment of Gilles de la Tourette's Syndrome. *Archives of General Psychiatry.* 46:722–730, 1989.

NR200 Tuesday, May 7, 9:00 a.m.-10:30 a.m.

Predictors of Response to Paroxetine Therapy in the Treatment of Panic Disorder

Martin Steiner, Ph.D., Clinical Develop., Smith Kline Beecham, P.O. Box 5089, Collegeville PA 19426; Rosemary Oakes, M.S., David E. Wheadon, M.D., Ivan P. Gergel, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the potential usefulness of paroxetine, a selective serotonin reuptake inhibitor, in the treatment of panic disorder, and to recognize baseline demographic and disease characteristics that may predict response to pharmacologic therapy in the treatment of panic disorder.

Summary:

Baseline demographic and clinical variables have been shown to be predictive of treatment outcome in psychiatric disorders such as depression and OCD. Psychotherapy, TCAs, MAOIs, benzodiazepines, and more recently SSRIs, all have shown to be effective in the treatment in panic disorder (PD); however, a significant proportion of patients fail to achieve a therapeutic response or do so transiently.

Objective: To determine the importance of baseline demographic and clinical variables in predicting the response to paroxetine therapy in the treatment of PD.

Method: A retrospective analysis of two U.S. multicentered trials was performed via logistic regression. Variables included: gender, race, age, history of PD, prior response to treatment, baseline number of panic attacks, and other baseline efficacy measures. Response was defined as zero full panic attacks, and other baseline efficacy measures. Response was defined as zero full panic attacks at endpoint (LOCF dataset).

Results: Two-hundred eighteen (218) paroxetine-treated patients were considered in the analysis. Sixty-one percent (61%, 132/218) met the response criteria. The stepwise logistic regression model revealed effects for baseline number of panic attacks and gender. Increased symptom severity was predictive of a poorer outcome. More males met the response criteria than did

females (72% vs. 55%) and odds ratios indicated that males are almost twice as likely to respond as are females.

Conclusions: As with other psychiatric disorders, increased symptom severity in PD is associated with a poorer outcome. The data also suggest that male and female patients with PD respond differentially to paroxetine, although the basis of the difference and its significance remain unclear. An understanding of baseline variables and how they may influence outcome is an important feature in evaluating a patient's treatment regimen.

References:

1. Yonkers KA, Kando JC, Cole JO, Blumenthal S: Gender differences in pharmacokinetics and pharmacodynamics of psychotropic medication. *Am J Psychiatry* 149:587–595, 1992.

2. Steiner M, Oakes R, Gergel IP, Burnham DB, Wheadon DE. A fixed-dose study of paroxetine (10 mg, 20 mg, 40 mg) and placebo in the treatment of panic disorder. Presented at the 1995 Annual Meeting of the American Psychiatric Association; Miami, FL; May 24, 1995.

NR201 Tuesday, May 7, 12 noon-2:00 p.m.

Treating Depression in HIV-Positive Patients

John C. Markowitz, M.D., Psychiatry, Cornell Med College, 445 East 68th Street Ste 3K, New York NY 10021; Baruch Fishman, Ph.D., James H. Kocsis, M.D., Lawrence B. Jacobsberg, M.D., Lisa A. Spielman, Ph.D., Samuel W. Perry III, M.D.

Summary:

Objective: Almost no psychotherapy research examines depressed HIV-positive patients. Preliminary findings of our current study showed differential improvement between interpersonal psychotherapy (IPT) and supportive therapy (SP). We now present results from all four cells of this study modeled on the NIMH Treatment of Depression Collaborative Research Program.

Methods: HIV-positive patients (n = 77) with 24-item Ham-D scores ℓ 15 and clinical diagnosis of major depression or dysthymia were randomized to 16 weeks of IPT, cognitive behavioral therapy (CBT), SP, or SP plus imipramine (IMI). Independent raters were used and therapist adherence monitored.

Results: All cells improved over time: Ham-D fell from 20.7 $\pm$ 5.0 to 11.8 $\pm$ 8.1. In completer analyses (n = 55), ANOVA showed a significant effect for treatment ($p = .039$); IPT was superior to both SP and CBT, without other pairwise differences between therapies ($p < .02$).

Significance: Depression in HIV-positive patients responds both to psychotherapy and medication. Psychotherapy patients completing treatment did best in IPT.

NR202 Tuesday, May 7, 12 noon-2:00 p.m.

Mediators of Bereavement Distress in a Gay Man Sample

Vicki L. Gluhoski, Ph.D., Psychiatry, Cornell Med College, 445 East 68th Street Ste 3K, New York NY 10021; Baruch Fishman, Ph.D., Samuel W. Perry III, M.D.

Summary:

Objective: Limited research has examined bereavement in gay male samples. However, bereavement is a significant stressor for these men, particularly dur to AIDS. This project examined two factors, hardiness and social support, believed to influence bereavement distress.

Method: 278 gay men participating in a longitudinal study of AIDS and distress completed measures of social support (the Interpersonal Support Evaluation List), hardiness (Hardiness Questionnaire), number of losses (Psychiatric Epidemiological Research Interview), and psychological distress (depression: Beck Depression Inventory, Hamilton Rating Scale for Depression; anxiety: Spielberger Anxiety Inventory—State and Trait; global distress: Brief Symptom Inventory).

Results: Significant main effects were found for hardiness, social support, and number of losses. HIV status did not have a significant effect on these variables. There were no interaction effects for loss x social support nor loss x hardiness on any of the dependent variables.

Conclusion: The results indicate that individuals with high levels of social support or hardiness will be less distressed than individuals with low levels. In addition, individuals with high levels of loss will have more symptoms than individuals with low levels of loss. Although all subjects report some distress associated with loss, individuals low in hardiness and social support experience significantly more symptoms when loss occurs.

NR203 Tuesday, May 7, 12 noon-2:00 p.m.

Depression, Viral Load and Other AIDS Illness Markers

Judith G. Rabkin, Ph.Ds, Psychiatry, Cornell Med College, 445 East 68th Street, Ste 3K, New York NY 10021; Stephen J. Ferrando, M.D., Baruch Fishman, Ph.D.

Summary:

Objective: To assess the association of immune measures (CD4, HIV RNA viral load), DHEA sulfate, and nutritional status with depression and distress in a cohort of men with AIDS.

Method: 110 men received comprehensive psychiatric evaluations including the Structured Clinical Interview for DSM-IV, Hamilton Depression Rating Scale, Beck Depression Inventory, and Endicott's quality of life scale. Nutritional status was assessed with bioelectric impedance analysis. Laboratory tests included T cell subsets, HIV RNA assay by PCR and DHEA sulfate.

Results: Of these gay/bisexual men, 44% were minority, 87% had attended at least some college, mean age was 40. Mean CD4 cell count was 150 (SD=133), and median viral load count was 144,583 copies/ml. Rate of major depression was 7% current and 36% lifetime. Mean 17-item HAM-D was 5.8 (SD=5.2), and mean BDI was 10.8 (SD=7.5). Although CD4 cell count, DHEA sulfate, and viral load were intercorrelated, none was significantly associated with any measure of depressive symptomatology or disorder. No association was found between degree of malnutrition and any measure of depression.

Conclusion: The observed rate of current major depression of 7% is consistent with other studies of HIV+ men, both asymptomatic and ill. Overall, the "invisible" markers of illness progression we examined do not appear to influence or be influenced by psychiatric status.

NR204 Tuesday, May 7, 12 noon-2:00 p.m.

A Comparative Analysis of Standard and Alternative Antidepressants in the Treatment of HIV Patients

Glenn J. Wagner, Ph.D., Psychiatry, NYS Psychiatry Institute, 722 West 168th Street Unit 35, New York NY 10032; Judith G. Rabkin, Ph.D., Richard Rabkin, M.D.

Summary:

Objective: This paper reports secondary analyses of data pooled from our trials of standard (imipramine, fluoxetine, sertraline) and alternative (dextroamphetamine, testosterone replacement therapy) antidepressants in the treatment of clinical depression among HIV patients, with the purpose of comparing the antidepressant efficacy of these various agents.

Methods: In all trials, a DSM-III-R depressive disorder was the primary criterion for study entry. The flouxetine and imipramine trials were double-blind and placebo controlled, while the others were open trials. Sample sizes ranged from 18 (dextroamphetamine) to 50 (fluoxetine).

Results: Each treatment resulted in significant improvement after both two and six weeks of treatment according to the Hamilton Depression Rating Scale. Response rates for the standard antidepressants ranged from 70% to 74%, with similar, high response rates found in the trials of dextroamphetamine (93%) and testosterone (81%)—all of which were superior to those of placebo (33%). Each treatment was well tolerated in terms of side effects.

Conclusions: Differences in trial design and entrance criteria require that caution be used in interpreting these results; nonetheless, each of the five treatments studied demonstrated strong efficacy and possesses relatively unique benefits, giving health care providers valuable treatment options in addressing the individual needs of patients.

NR205 Tuesday, May 7, 12 noon-2:00 p.m.

Somatic Symptoms, Depression and HIV Illness Markers

Stephen J. Ferrando, M.D., Psychiatry, Cornell Med College, 445 East 68th Street Ste 3K, New York NY 10021; Judith G. Rabkin, Ph.D., Baruch Fishman, Ph.D.

Summary:

Purpose: To examine the relationships between the somatic symptoms of fatigue and restrictions on physical activity, and measures of HIV illness progression and depression.

Method: Subjects were 137 HIV+ men, 110 of whom had AIDS. Stepwise multiple regressions were performed, with dependent variables being fatigue, as measured by the Chalder Fatigue Scale, and restrictions on physical activity, as measured by the RAND Physical Limitations Index. Independent variables were nonsomatic depressive symptoms, as measured by teh cognitive/affective subscales of the Beck (BDI-cognitive) and Hamilton Depression (HAM-D-affective) scales, and markers of HIV illness progression, CD4 count and HIV RNA viral load.

Results: In this 40% minority sample of gay/bisexual men, mean CD4 count was 199 cells/ cu mm and median viral load was 119,079 copies. Fatigue was not associated with cognitive/affective depression, CD4 count, or viral load. Physical restriction was associated with cognitive/affective depression (BDI-cognitive: F = 2.72, p = 0.0472 HAM-D-affective: F = 2.94, p = 0.0359), but not with markers of HIV illness progression.

Conclusion: In this sample of men with advanced HIV illness, fatigue and physical restriction were independent somatic symptoms, and were not associated with "invisible" markers of HIV progression. Reported physical restriction, in the absence of an obvious medical cause, may indicate a need for assessment for clinical depression.

NR206 Tuesday, May 7, 12 noon-2:00 p.m.

Fatigue in Ambulatory AIDS Patients

William Breitbart, M.D., Psychiatry, Memorial Hospital, 1275 York Avenue Box 421, New York NY 10021-6007; Margaret McDonald, M.S.W., Barry Rosenfeld, Ph.D., Steve Passik, Ph.D., Monique Kaim, Ph.D., Paulette Murphy, Psy.D.

Summary:

Objective: To examine the prevalence and correlates of fatigue in AIDS patients. *Method:* 436 ambulatory AIDS patients were interviewed using: 1) AIDS Physical Symptom Checklist; 2) Karnofsky Performance Rating Scale (KPRS); 3) Beck Depression Inventory (BDI); 4) Brief Symptom Inventory (BSI); 5) Beck Hopelessness Scale (BHS). Patients were classified into fatigue/no fatigue groups based on their respose to a criterion fatigue question. *Sample Characteristics:* Mean age: 38.8; Gender: 64% male, 36% female; Race: 38.3% white, 36.9% black, 22.5% Hispanic; HIV risk factor: 52.7% injection drug use (IDU), 29.2% homosexual contact, 16.8% heterosexual contact; CD4+ cell counts: 40% < 100, 25% = 100–199, and 35% > 200. All patients met 1993 CDC case definition for AIDS.

Results: 55% of patients (N = 244) reported fatigue. Fatigue was more often reported by women (Chi-Square = 6.23, df = 1, $p < .05$) and IDUs (Chi-Square = 5.18, df = 1, $p < .05$). Fatigue was associated with number of AIDS-related physical symptoms $\pm(434) = 7.9$, $p < .0001$), treatment for HIV-related medical disorders (Chi-Square = 11.77, df = 1, $p < .0001$), functional disability (KPRS: $\pm(430) = -6.14$, $p < .0001$), psychological distress (BSI: $\pm(433) = 9.04$, $p < .0001$), depressive symptoms (BDI: $\pm(434) = 7.63$, $p < .0001$), and hopelessness (BHS: $\pm(434) = 5.4$, $p < .0001$). No significant associations were found between fatigue and CD4+ cell count, duration of HIV+, CDC category, or antiretroviral use.

Conclusions: Fatigue is a highly prevalent symptom in ambulatory AIDS patients and is associated with significant physical and psychological morbidity.

NR207 Tuesday, May 7, 12 noon-2:00 p.m.

Undertreatment of Pain in AIDS

William Breitbart, M.D., Psychiatry Serv Box 421, Memorial Hospital, 1275 York Avenue, New York NY 10021-6007; Steve Passik, Ph.D., Barry Rosenfeld, Ph.D., Margaret McDonald, M.S.W., Howard Thaler, Ph.D., Russell Portenoy, M.D.

Summary:

Objective: To examine the adequacy of analgesic therapy for pain in AIDS. *Method:* 235 ambulatory AIDS patients reporting frequent or persistent pain during the previous two weeks were surveyed with the following measures: 1) AIDS-related medical data; 2) HIV risk factor; 3) Karnofsky performance score; 4) Brief Pain Inventory (BPI); 5) Analgesic Medication Record; 6) Pain Management Index (PMI). *Sample Characteristics:* Gender: 73% male, 27% female; Race: 39% white, 36% black, 23% Hispanic, 2% other; Age: *M* = 39(18–63); Education: *M* = 12.9(7–20); Risk factor: 59% intravenous drug use (IVDU), 30% homosexual contact, 9% heterosexual contact, 2% other; Karnofsky: 72% > 70; BPI mean pain intensity: "on average" = 5.2, "at its worst" = 7.3.

Results: Frequency of analgesics prescribed: none = 28%, NSAID = 42%, antidepressant = 6%, weak opioid (e.g. codeine) = 19%, strong opioid (e.g. morphine) = 5%. For those reporting BPI "worst pain" in the severe range (8–10; n = 114, 49%): none = 26%, NSAID = 41%, antidepressant = 6%, weak opioid = 24%, strong opioid = 6%; 85% were undermedicated (PMI score = –1, –2, –3), 49% "severe undermedication" (PMI score = –2, –3). Factors associated with "severe undermedication" included: female gender ($p < .05$), less education ($p < .01$), IVDU as HIV risk factor ($p < .05$), and higher pain intensity ($p < .05$). Race, age, and Karnofsky score were not associated with undermedication.

Conclusion: Pain in AIDS is vastly undermedicated with only 15% of patients receiving adequate analgesic therapy (PMI), and only 6% of those reporting severe pain receiving a strong opioid.

NR208 Tuesday, May 7, 12 noon-2:00 p.m.

Pain in Women with AIDS

William Breitbart, M.D., Psychiatry Serv Box 421, Memorial Hospital, 1275 York Avenue, New York NY 10021-6007; Margaret McDonald, M.S.W., Barry Rosenfeld, Ph.D., Steve Passik, Ph.D., Jaqueline Calle, B.A., Howard Thaler, Ph.D., Russell Portenoy, M.D.

Summary:

Objective: To survey the prevalence and describe the characteristics of pain in women with AIDS. *Method:* 171 female ambulatory AIDS patients were assessed for "persistent or frequent pain" during the preceding two weeks including location, frequency, and intensity of pain(s). They were also administered the Brief Pain Inventory (BPI), the Beck Depression Inventory (BDI), the Brief Symptom Inventory (BSI), the Beck Hopelessness Scale (BHS), and demographic and AIDS-related medical data were gathered. *Patient Characteristics:* Age: M = 37 (range: 25–69); HIV risk factor: 39% heterosexual contact, 33% injecting drug use, 26% multiple risk (heterosexual contact and injecting drug use), 2% other; Race: 46% black, 30% Hispanic, 23% white.

Results: 67.8% (N = 116) reported persistent or frequent pain in the two weeks preceding interview, with an average of 2.6 pains and mean pain intensities of 6.1 "on average" and 7.8 "at its worst" (BPI). More than 70% experienced their primary pain frequently or constantly, and 24.1% reported experiencing their worst pain constantly. Severe pain was most commonly reported in the following sites: leg(s) (25%), head (23%), abdomen (11.5%), and lower back (8.6%). Pain was associated with a history of IDU (p < .05), history of at least one major opportunistic infection (p, .05), significantly higher levels of psychological distress (p < .0001), hopelessness (p < .05), and depression (p < .0001). Pain intensity was significantly correlated with increased levels of functional interference (r = .45, p < .0001).

Conclusion: Pain is a highly prevalent, often severe, and highly distressing symptom in women with AIDS.

NR209 Tuesday, May 7, 12 noon-2:00 p.m.

Brief Cognitive Therapy After HIV Antibody Testing

Baruch Fishman, Ph.D., Psychiatry, Cornell Univ Med Ctr, 445 E. 68th Street Ste 3K, New York NY 10021; Samuel W. Perry III, M.D.

Summary:

Objective: To test the efficacy of brief Cognitive Behavioral Therapy (CBT) for reducing emotional distress in patients infected with Human Immunodeficiency Virus (HIV) shortly after HIV testing and notification.

Method: Subjects were 54 emotionally distressed HIV seropositives randomly assigned to receive either a six-session individual CBT program (N = 24) or other forms of HIV-related psychoeducation (N = 30). The patients were assessed before the treatment and about two, six, and 12 months later on several measures of emotional distress, including the Brief Symptom Inventory (BSI). Only patients who scored above 1.0 on the BSI at intake were included in this analysis.

Results: Patients who received CBT scored significantly lower on the BSI (controlling for initial BSI score) at two (p < .01) and six (p < .02) months, but not at 12 months after intake.

	BSI Mean (SD)		
	2 mos.	6 mos.	12 mos.
CBT	.76(.54)	.68(.43)	.86(.57)
Other	1.08(.63)	1.08(.69)	1.02(.64)

Conclusion: A brief CBT intervention is effective for reducing emotional distress in HIV seropositives in the immediate and intermediate post-notification period. The beneficial effect seems to diminish by 12 months post notification. Repeating a brief CBT for distressed patients every six months during the course of HIV infection may prevent excessive distress in vulnerable patients.

NR210 Tuesday, May 7, 12 noon-2:00 p.m.

Stress-Associated Changes in Neuropsychological Functioning in HIV-1 Infection

Susan G. Silva, Ph.D., Psychiatry, University of NC, Medical School CB# 7160, Chapel Hill NC 27599; Eric D. Jackson, B.S., Jane Leserman, Ph.D., Robert A. Stern, Ph.D., Robert N. Golden, M.D., Dwight L. Evans, M.D.

Summary:

Objective: We recently reported that stress may alter cell-mediated immunity in HIV-1 infection (Evans et., 1995). To determine whether stress is associated with HIV-related neurocognitive decline, we studied 48 HIV-1 seropositive gay men participating in the Coping in Health and Illness Project (CHIP).

Method: Initially asymptomatic HIV-infected subjects were evaluated every six months over three years. Individuals with a history of substance abuse, mild head injury, CNS disorder, or learning disability were excluded. A semistructured interview was used to rate the objective context of stressful life events and difficulties. Seven neurocognitive functions (attention, psychomotor speed, verbal learning/memory, motor speed, manual dexterity, self-report mood, and general intellectual ability) were examined with a comprehensive battery of neuropsychological tests. For analysis purposes, subjects were divided into two groups: low and high stress. Stress level was defined by average level of stress over the three-year period.

Results: High-stress subjects showed a diminution of intellectual ability over the three-year period compared with low-stress subjects (ANCOVA, P = .04). Between-group differences were not detected on the remaining neuropsychological measures.

Conclusions: The results suggest that stress may be related to cognitive disturbances in HIV-1 infection. The clinical significance of stress-associated changes in neuropsychological functioning warrants further study.

NR211 Tuesday, May 7, 12 noon-2:00 p.m.

Psychological Functioning and HIV Risk Behavior Among Substance Abusers with HIV Infection

Julie A. London, Ph.D., Psychiatry, UC San Francisco, 3180 18th Street, Ste. 205, San Francisco CA 94110; James L. Sorensen, Ph.D., Meridith Miller, B.A., Kevin Delucchi, Ph.D., James W. Dilley, M.D., Bonnie Schwartz, M.S.W.

Summary:

Objective: The objective of this analysis was to examine the relationship of psychological functioning to HIV risk behavior among substance abusers with HIV infection.

Method: The analysis comes from a randomized, two-group, controlled trial of a case management (Sorensen, et al., 1993) service intended to improve the treatment of substance abusers with HIV infection (Sorensen, London, Okin & Batki, 1994). Study participants were recruited from the emergency department as well as outpatient and inpatient programs at San Francisco General Hospital. This work reports on preliminary data from the first 137 participants. Psychological functioning was measured by (1) the psychiatric severity scale of the Addiction Severity Index (ASI), (2) Beck Depression Inventory (BDI), (3) Social Support Network (SSN), (4) the cognitive functioning, mental health, and energy/fatigue scales from the Health Status Questionnaire (HSQ). HIV risk behavior was defined as the number of times in a 30-day period that illicit drugs were injected and syringe needles shared.

Results: One hundred (73%) participants were male, the majority were either homeless (28%) or lived in a hotel or motel (36%), and African-Americans and Caucasians made up 84% of the sample (42% each). Just over half (54%) were heterosexual and all subjects averaged 38.5 years of age. Measures of psychological functioning were both significantly correlated among each other

and demonstrated acceptable levels of internal consistency. The relationships between psychological functioning and HIV risk behavior were not strong, with the exception that greater scores on the ASI psychiatric severity scale were associated with decreased likelihood of injection drug use. Measures of HIV risk behavior indicated that while 103 subjects (75%) reported injecting illicit drugs in the previous 30 days, only nine (9%) participants admitted to sharing needles.

Conclusion: The frequency of HIV-related risk behavior involving illicit drug use among this sample of HIV-infected substance abusers is noteworthy. While the relationship between psychological functioning and HIV risk behavior (when operationalized by injection drug use) is not striking, the association between measures may be fortified by extending this measure of HIV risk behavior by including risky sexual practices. Lastly, the psychiatric severity scale of the ASI may be a more sensitive measure of psychological functioning when examined within the context of injection drug use.

NR212 Tuesday, May 7, 12 noon-2:00 p.m.

Safety of Risperidone in Patients with HIV and AIDS

Ashok N. Singh, M.D., Psychol. Med., Chelsea and Westminister, Fulham Road, London SW10, United Kingdom; Jose Catalan, M.B.

Summary:

Objective: To study the safety of risperidone in patients with HIV-related psychosis. *Methods:* Consecutive case histories of all patients referred to the department of psychological medicine who were receiving risperidone were evaluated. *Results:* We have treated 12 acutely manic male patients, mean age 41.2 years (range 30–52). All but three had full-blown AIDS (CD4 counts 0–96), the others had CD4 counts of 319–592. Conventional neuroleptics had been used in two cases but caused severe or moderate extrapyramidal side effects (EPS). Patients responded rapidly to low doses of risperidone (1–6 mg/day, mean daily dose 3.25 mg). No serious adverse effects were reported, but two patients complained of excess salivation, one of stiffness, and one of drowsiness. These all resolved spontaneously or when the risperidone dose was lowered (from 3 mg twice daily to 1 mg once daily). No hematologic effects were seen despite the patient's already compromised status.

Conclusion: Risperidone appears safe in patients with HIV-related mania who may be sensitive to EPS from conventional neuroleptics.

NR213 Tuesday, May 7, 12 noon-2:00 p.m.

Emotional Distress in Seropositive Patients Who Both Monitor or Blunt Information

Lara A. Warburton, M.S., Psychiatry, Cornell Medical, 445 East 68th Street, Ste 3K, New York NY 10021; Baruch Fishman, Ph.D., Judith G. Rabkin, Ph.D.

Summary:

Objective: This study examines the relationship between the coping styles of monitoring and blunting, and emotional distress. Monitoring consists of seeking information about a threat, and blunting is characterized by avoidance of attention to a threat. Individuals who are both highly vigilant and attempt to avoid thinking about HIV-related information may cope ineffectively and experience more distress.

Method: This hypothesis was examined in a sample of 53 HIV-positive gay men, who were recruited as part of a longitudinal HIV research program in New York City. Monitoring and blunting were measured by a modified version of the Miller Behavioral Style Scale. Distress was assessed by the Beck Depression Inventory, Hamilton Rating Scale for Depression, Impact of Events Scale, Spielberger State Trait Anxiety Inventory, and the Brief Symptom Inventory (BSI).

Results: T-tests revealed that seropositives who scored high on both monitoring and blunting reported significantly more distress on all measures than those who scored low on both monitoring and blunting. For example, those who scored high on both monitoring and blunting had a higher mean on the BSI ($M = .67$, $SD = .52$) than those who scored low on both monitoring and blunting ($M = .39$, $SD = .34$), $t(51) = 2.31$, $p < .05$).

Conclusion: Seropositive gay men who use high levels of monitoring and blunting are more anxious and depressed. High scores on both monitoring and blunting may be a manifestation of ineffective coping.

NR214 Tuesday, May 7, 12 noon-2:00 p.m.

Risperidone for AIDS-Associated Dementia: A Case Series

Louis Belzie, M.D., Linroc Nursing Home, 650 Amboy Street, Brooklyn NY 11212

Summary:

Objective: To determine the effects of low doses of risperidone on behavioral disturbances in patients with AIDS-associated dementia. Because the AIDS virus attacks the basal ganglia, these patients are highly susceptible to neuroleptic-induced movement disorders. Risperidone at low doses reportedly carries little risk of movement disorders.

Method: Nine nursing-home patients with AIDS-associated dementia received risperidone for behavioral disturbances (psychomotor agitation, aggressiveness, social withdrawal, uncooperativeness), or psychotic symptoms. The patients were aged 28 to 57 years. Seven were switched to risperidone because their symptoms did not respond to conventional neuroleptics and adjunct medications; one patient was switched because of a neuroleptic-induced movement disorder, and one was receiving no antipsychotic medication.

Results: The risperidone dose ranged from 0.5 to 1 mg daily. Most patients also received an adjunct benzodiazepine, antidepressant, or mood stabilizer. Within one or two weeks of receiving risperidone, six of the nine patients exhibited brighter mood, were less agitated or aggressive, were more cooperative, and participated more frequently in social activities. Two patients became increasingly agitated or psychotic; these symptoms were controlled when risperidone was replaced with haloperidol. One patient was transferred to a psychiatric unit because of increased paranoid delusions and auditory hallucinations.

Conclusions: Risperidone effectively controlled behavioral disturbances in six of nine patients with AIDS-associated dementia. Risperidone may be an alternative to conventional neuroleptics in patients who are susceptible to neuroleptic-induced movement disorders or unresponsive to treatment.

NR215 Tuesday, May 7, 12 noon-2:00 p.m.

Gender Differences in Hyperactivity in Children

Carol A. Glod, Ph.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Martin H. Teicher, M.D., Cynthia E. McGreenery, Matthew Ducsik, B.A., Carl M. Anderson, Ph.D., Ann Polcari, M.S.

Summary:

Attention-deficit hyperactivity disorder (ADHD) is estimated to affect 6% of children, predominantly males. Our hypothesis was that ADHD was equally prevelant in boys and girls, but that teachers were more likely to detect symptoms in boys. To date, 277 first and second graders participated (145 M; 132 F). Children

completed a 15 minute continuous performance test (CPT) at school, while head movements were tracked using an infrared motion analysis system, which discriminated ADHD from normal with 95% accuracy (Teicher et al., 1996). Teachers completed Connor's and IOWA ratings. Connor's scores were 90% higher in boys than girls ($p = 0.00006$), and ratings of inattention and aggression were equally skewed. Boys did not differ from girls on CPT errors of omission, accuracy, or response variability. Boys made 24% more commission errors, but were 8% faster ($p = 0.00003$). Boys made 14% more movements and covered a 20.2% larger area ($p = 0.007$). However, using the same absolute criteria, as many girls as boys had abnormally high activity. For example, five girls and five boys moved more than 2470 times, and covered an area greater than 52.5 cm^2. Teachers rated many more boys as symptomatic. This may lead to overdiagnosis in boys and underdiagnosis in girls.

NR216 Tuesday, May 7, 12 noon-2:00 p.m.

Characteristics of Juvenile Delinquents Admitted to an Adolescent Psychiatric Inpatient Unit

Wun Jung Kim, M.D., Div Of Child Psych, Medical College Of Ohio, P.O. 10008, Toledo OH 43699; Youngsik Lee, M.D., Michael P. Carey, Ph.D.

Summary:

Objectives: This study was performed to identify and understand the characteristics of adolescents who had a history of police arrest and/or were adjudicated unruly/delinquent.

Method: The study employed a retrospective review of computer-recorded data set on 210 consecutive admissions to an adolescent psychiatric inpatients unit. Three groups (No Police Contact, N = 115; Police Contact Only, N = 60 ; Adjudicated, N = 35) were compared on demographic variables, WISC-III, Kaufman Test of Educational Achievement, Millon Adolescent Personality Inventory, Reynolds Adolescent Depression Scale, Revised Children's Manifest Anxiety Scale, Suicide Ideation Questionnaire, Suicide Behavior Interview, Life Events Checklist, and Family Environmental Scale. A subgroup of the subjects, 60 cases, also received a standardized interview by Child Assessment Schedule.

Results: The statistically significant findings of the delinquent group (the police contact and adjudicated subjects) included (1) a high rate of adoption, sexual promiscuity, out of home placement, and repeated psychiatric hospitalization, (2) low verbal IQ scores and educational achievements, (3) high impulsivity, low social conformity, and high forcefulness in a personality inventory, (4) low activity-recreation orientation and low moral religious emphasis in family environment, (5) a high frequency of adverse life experiences, (6) among the three groups, the Police Contact Only group showed the lowest depression, anxiety, and suicidal ideation scores, (7) a high diagnostic frequency of conduct disorder, ODD, and ADHD.

Conclusions: The adolescent psychiatric inpatients with delinquent histories presented with certain clinical characteristics that warrant specific intervention strategies for their cognitive deficits, an impulsive personality style, family dysfunction with adverse life experiences, and disruptive behavioral disorders, different from the rest of adolescent psychiatric inpatients.

NR217 Tuesday, May 7, 12 noon-2:00 p.m.

Olfaction in Tourette's Syndrome: ADHD and Controls

F. Xavier Castellanos, M.D., Child Psychiatry, NIMH, 10 Center Drive 6N240, Bethesda MD 20892; Nancy E. Harnett, Ph.D., William E. Klein, R.N., Margaret DeMayo, Judith L. Rapoport, M.D.

Summary:

We previously found that 10 boys with Tourette's syndrome (TS) comorbid with attention deficit hyperactivity disorder (ADHD) had a significantly decreased descending olfactory threshold compared with eight ADHD boys without tics (APA, 1995). To replicate this finding, 16 children with TS (ages 6–16) were compared with 17 age- and gender-matched healthy controls (three females/group) using the same method (Olfacto Labs, El Cerrito, CA).

Initial analysis did not reveal differences between groups. However, nine TS subjects without ADHD (TS-ADHD) had significantly lower detection thresholds than seven subjects with ADHD + TS and 17 controls for carbinol. TS-ADHD subjects also had a significantly lower threshold for (*E*)-3-methyl-2-hexenoic acid compared with ADHD + TS (2-tailed, $p < .05$).

Though these results remain preliminary, they objectively confirm TS patients' reports of olfactory hyperacuity and support attempts to incorporate sensory systems into pathophysiologic models of tic and movement disorders.

NR218 Tuesday, May 7, 12 noon-2:00 p.m.

Predicting Unmet Service Needs for ADHD Among Children in Special Education: Who Is at Risk?

Regina Bussing, M.D., Psychiatry, University of Florida, 1329 SW 16th Street, Gainesville FL 32610-0234; Amy Perwien, B.A., Thomas Belin, Ph.D.

Summary:

Objective: Exceptional Student Education (ESE) settings in public schools service children with varying disabilities and can serve as a community census of students with severe attention deficit hyperactivity disorder (ADHD). This study examines service needs as well as services use for ADHD in an entire county population of elementary school ESE students and identifies relevant predictors of unmet need for services among this high-risk group.

Methods: Employing a two-stage design we screened all ESE students using parent and teacher questionnaires to identify children already under ADHD treatment as well as untreated children at high risk for the condition. Those identified were subsequently invited to a comprehensive, second-stage follow-up, containing a formal diagnostic interview and assessment of services use, as well as relevant child self-reports measures.

Results: 25% of the ESE population was reportedly under treatment for ADHD, mostly with stimulants. An additional 15% were at risk for ADHD based on extreme screener results, and not under treatment, indicating unmet need for services. Female gender, low socioeconomic status, and HMO coverage significantly increased the risk for unmet service needs, even after controlling for other factors through logistic regression analyses.

Conclusion: Improving access to care for this treatable condition will require policy interventions in the health care and education sectors.

NR219 Tuesday, May 7, 12 noon-2:00 p.m.

Clinical Characteristics and Treatment Courses of the Children with Selective Mutism

Kang-E M. Hong, M.D., Psychiatry, Seoul Univ Hospital, 28 Yunkun-Dong, Chongro-Ku, Seoul 110-744, South Korea; Sun-Ju Chung, M.D.

Summary:

The present study investigates clinical characteristics, treatment methods, and outcome of 23 children who were diagnosed as having selective mutism by DSM-IV criteria. As shown in past work, the sex ration was female dominant, and 26% of subjects had a history of delayed language development. Some of subjects

(26%) had experienced physical or psychological trauma before age 3. A few of subjects had enuresis (30%). Many (65%) subjects had symbiotic relationships with their mother. The outstanding characteristics of families are dominant mother and passive father, parental shyness, and lack of communication. The personality traits of subjects were frequently described as follows: shy (100%), anxious (83%), stubborn (83%), immature (65%), overdependent (65%), irritable (52%), manipulative (39%), and depressive (39%). When subgrouped by IQ, we could find some difference in language development, personality trait, family dynamics, and treatment outcome between the mental retardation and normal intelligence groups. Play therapy was the treatment method most frequently used (65%). At the time of treatment termination, most of the children were improved (91%). But at follow-up interview, only half of the children (55.7%) remain improved. The clinical variable that correlated most highly with treatment outcome was intelligence.

NR220 Tuesday, May 7, 12 noon-2:00 p.m.

Positive Cognition in Depressed Adolescents

John B. Jolly, Psy.D., Psychology, Missippi College, 105 Lowrey Hall, Clinton MS 39058; Thomas A.M. Kramer, M.D., David C. Weisner, Ph.D., Jane H. Feldman, M.D.

Summary:

Objective: Despite a new interest in examining positive cognitive variables in adult psychopathology, studies examining the role of positive cognition in children and adolescents are almost nonexistent.

Method: The psychometric properties of the Automatic Thoughts Questionnaire-Positive (ATQ-P; Ingram & Wisnicki, 1988) were examined in 206 adolescent inpatients. Subjects were read randomized packets of depression, anxiety, and affective self-report measures, in addition to the ATQ-P, and were administered the K-SADS (Last, 1986) blind to the self-report data.

Results: ATQ-P scores converged significantly with positive emotionality and inversely with a variety of negative affect measures. Discriminant validity was demonstrated by significantly stronger relationships among ATQ-P scores and depressive constructs than ATQ-P scores and anxious constructs. When depression was partialled from the ATQ-P and anxiety relationships, ATQ-P scores were independent of anxious constructs. ATQ-P scores were significantly lower in adolescents with major depressive disorder (MDD) than non-MDD adolescents, though this relationship was moderated by gender. Factor structure of ATQ-P items was consistent with adult samples and reflected the inverse of Beck's (1976) cognitive triad of depression.

Discussion: Results support the psychometric properties of the ATQ-P and the use of positive cognitions to discriminate depression from anxiety in adolescents.

NR221 Tuesday, May 7, 12 noon-2:00 p.m.

Perinatal and Obstetric Events As Predictors of Onset of Tourette's Symptoms

Raul R. Silva, M.D., Child Psychiatry, St. Luke's - Roosevelt, 1111 Amsterdam Avenue, New York NY 10025; Lorraine Wolf, Ph.D., Dinohra M. Munoz, M.D., E. Steven Dummit III, M.D., Jim Kim

Summary:

Introduction: Tourette's disorder (TD) is characterized by motor and vocal tics, with typical age of onset (AO) at approximately 7 years old. Earlier age of onset may be associated with increased severity. Individual disease expression may be tempered by prenatal or perinatal events. The present study explores the relationship among perinatal events and the AO in TD.

Method: Records of 50 patients (35 males, 15 females) meeting DSM-III-R criteria for TD were reviewed. Mean motor tic AO was 7.8 ± 4.72, mean vocal tic AO was 9.6 ± 6.45. A composite AO was calculated by averaging AO of motor and vocal tics. Due to a skewed distribution, this was normalized by log-transformation. Items from the perinatal events section of the TS Questionnaire were examined with multiple regression analyses (MRA).

Results: Significant effects were found for two obstetric events: premature delivery (Beta = 16.5; $p < .005$) and low birth weight (Beta = .87; $p < .001$). Post—term delivery (Beta = -.08; $p < .16$) was negatively related to AO. The overall effect of the MRA using these three items was highly significant ($F = 97.98$; Multiple $r = .94$; $r^2 = .88$ $p < .001$).

Conclusions: These data suggest that adverse perinatal events, particularly low birth weight, influence disease severity as reflected by AO. Obstetric complications may exert this effect either through direct or indirect mechanisms, which may be mediated by heterogeneity in the TD population.

NR222 Tuesday, May 7, 12 noon-2:00 p.m.

Sertraline Treatment in Children and Adolescents: Tolerability, Efficacy and Pharmacokinetics

Jeffrey A. Alderman, Ph.D., Central Res, Pfizer Inc., 235 East 42nd Street, New York NY 10017; Robert Wolkow, M.D., Hugh F. Johnston, M.D., Murray H. Rosenthal, D.O., James M. Ferguson, M.D., Floyd R. Sallee, M.D., Jeffrey Blumer, M.D.

Summary:

Sixty-one children and adolescents 6–17 years of age with a DSM-III-R diagnosis of major depression or obsessive-compulsive disorder (OCD) were administered open-label sertraline. All patients received an initial single dose of 50 mg sertraline and, seven days later, began five weeks of treatment using titration regimens that started at either 25 mg/day or at 50 mg/day. The initial 50 mg dose was tolerated by all patients, and forced titration to 200 mg was tolerated by 95% of the patients. The adverse experience profile consisted primarily of gastrointestinal and psychiatric complaints, with no differences on the basis of age or titration regimen. In OCD patients, mean Children's Yale-Brown Obsessive Compulsive Scale ratings decreased from 25 to 13, while in depressed patients, Clinical Global Impressions of Improvement mean ratings at endpoint were 2.2 (2 = much improved). Mean sertraline pharmacokinetic parameters after chronic 200 mg/day dosing were similar to those of previously studied healthy young adults:

	Cmax (ng/ml)	AUC(24) (ng-hr/ml)	T½(hr)
Pediatric	143	2682	27.1
Adult	141	2570	27.2

However, some low bodyweight patients exhibited sertraline plasma levels substantially higher than the group mean. In conclusion, sertraline was well tolerated by 6–17 year olds over the 50–200 mg/day therapeutic dose range, and mean pharmacokinetic parameters were similar to adult values.

NR223 Tuesday, May 7, 12 noon-2:00 p.m.

Drug and Alcohol Trends in Adolescents

Norman S. Miller, M.D., Psychiatry, M/C 913 U of IL Chicago, 912 South Wood St, Chicago IL 60612; Mark S. Gold, M.D.

Summary:

The 1993–94 National Parents' Resource Institute for Drug Education (PRIDE) survey was drawn from a database of 197,735 surveys from 34 states. The Chi-Square test of Independence was used to test the null hypothesis that the observed differences

in the number of students who used a certain drug in 1992–93 and the number who used the same drug in 1993–94 were due to sampling variation. The null hypothesis was refuted at an alpha level of 0.05

Prevalence of use of every illicit drug included on the questionnaire (marijuana, inhalants, cocaine, hallucinogens, uppers, and downers) increased significantly for both junior high (6th-8th grade) and senior high (9th-12th grade) school students. Three illicit drugs showing the most substantial relative increases among 6th-12th grade students were marijuana, inhalants, and cocaine. These findings reflect the most dramatic increase in use PRIDE has found in three consecutive years of steadily rising drug usage.

Of 79, 661 6th-8th students surveyed about suicide, 5,177 students reported thinking often or a lot about committing suicide (6.6% of total responding). Of the 5,177 students who reported thinking often or a lot about suicide, 2,626 reported using liquor (51.6%), 1,521 reported using marijuana (29.9%), 686 reported using hallucinogens (13.5%), and 645 reported using cocaine (12.7%).

NR224 Tuesday, May 7, 12 noon-2:00 p.m.

The Lack of Effect of Methylphenidate on the Growth Hormone Axis

Paz Toren, M.D., Mental Health Ctr, Tel-Aviv Community, 9 Hatzvl Street, Tel-Aviv 67197, Israel; Aviva Silbergeld, M.Sc., Sofia Eldar, M.D., Nathaniel Laor, M.D., Ronit Weizman, M.D.

Summary:

Objective: To assess the growth hormone (GH) axis in methylphenidate (MPH)-treated and untreated boys with attention deficit hyperactivity disorder (ADHD), by evaluating serum GH, GH binding protein activity (GHBP), and insulin-like growth factor-I (IGF-I) levels, and compare them with age-matched normal controls.

Method: Blood samples were taken from 38 boys (aged 6–15 years) diagnosed as ADHD according to DSM-III-R criteria, and confirmed using the K-SADS. Eighteen subjects were treated with MPH (5–20 mg/day; 0.15–0.77 mg/kg/day) for three days to 30 months (on drug-holiday protocol), and 20 were drug-naive. Forty-six age-matched normal boys at height and weight within normal range served as controls.

Results: No significant differences were detected among the MPH-treated ADHD children, the untreated ADHD children, and the control subjects on fasting serum GH levels, GHBP activity, or IGF-I levels.

Conclusions: Active treatment with MPH in ADHD children on drug holiday protocol does not cause growth retardation or changes in GH axis as manifested by normal values of GH, GHBP, and IGF-I.

NR225 Tuesday, May 7, 12 noon-2:00 p.m.

Cognitive Impulsivity in Adolescent Inpatients

David L. Pogge, Ph.D., Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; Susan R. Borgaro, M.A., William Horan, B.A., Joel Lord, M.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D.

Summary:

Impulsive behavior is a central feature of many disorders of childhood and adolescence. Certain errors of commission on the Continuous Performance Test (CPT) have been used to measure impulsive tendencies, with adolescents having diagnoses of conduct disorder and substance abuse making considerably more CPT errors of commission. The mechanism that produces these errors is unclear, since impulsive responses can be initiated by either premature responses based on inadequate information or failures to inhibit a response that the subject knows is incorrect. In this study, 200 adolescent psychiatric inpatients with diagnoses of major depression, conduct disorder, or substance abuse (age range = 13–17; all IQ > 80) were examined with a visual continuous performance test with a 3–7 target sequence, and the latency of their errors was examined. Three types of errors of commission were identified and their latency of response was compared to correct detections of the target stimuli. Error responses to the first half of the sequence (3 no 7) had a reaction time that was significantly shorter than correct detections ($t = 5.28$, $p < .001$), and error responses to the second half of the target sequence (7 no 3) had significantly longer reaction times than correct detections ($t = -6.24$, $p < .001$). The third type of errors of commission were correct responses to the 3–7 target sequence that were so slow that the next target stimulus had already been presented. Thus, different types of errors have distinct latencies, suggesting that excessively rapid responding and failures to inhibit incorrect responses contribute to different types of impulsive errors on the CPT.

NR226 Tuesday, May 7, 12 noon-2:00 p.m.

Pilot Trial of Risperidone in Children and Adolescents with Pervasive Developmental Disorder

Richard I. Perry, M.D., Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Caroly S. Pataki, M.D., Dinohra M. Munoz, M.D., Jorge L. Armenteros, M.D., Raul R. Silva, M.D.

Summary:

Introduction: Antipsychotic medications have received much attention in the treatment of the pervasive developmental disorders (PDD). To date, haloperidol has emerged as the most useful agent in treating many target symptoms of autism. Risperidone is a new, high-potency antipsychotic with less potential risk for tardive dyskinesia than haloperidol. This preliminary trail is designed to investigate the safety and efficacy of risperidone in PDD.

Method: The design was open-label pilot trial. Subjects were started on risperidone at a dosage of 0.5 mg once or twice daily and dosage was raised by increments of 0.5 mg/day every few days. Subjects were rated on the Clinical Global Impressions (CGI) and on selected items from the Children's Psychiatric Rating Scale (CPRS) on baseline and while on optimal dosage.

Subjects: Five males and one female aged 7.3 to 14.8 years (mean, 10.7) who met DSM-III-R criteria for a PDD diagnosis. Five subjects were refractory to other prior medications. Five subjects were neuroleptic free for 11 days preceding the trial.

Results: Optimal doses ranged from 1 to 6 mg/day. Mean total duration of risperidone administration was 5.2 months. On the CPRS, there were significant decreases in the mean scores of two items: angry affect ($p = .04$) and lability of affect ($p = 0.03$). A statistical trend in the reduction of the mean hyperactivity scores was noted. Mean CGI Clinical Global Improvement scale scores were significant ($p < .001$). Side effects included weight gain, transient sedation, increased salivation, and stereotypies.

Discussion: Pharmacologic alternatives to treating behavioral symptoms in PDD are needed, and atypical neuroleptics may be a promising possibility.

NR227 Tuesday, May 7, 12 noon-2:00 p.m.

Placebo Response and Hyperactivity in Aggressive Conduct Disorder

Richard P. Malone, M.D., Psychiatry, MCP and Hahnemann University, Mail Stop 403, Broad and Vine, Philadelphia PA 19102; Louisa Seraydarian, Ph.D., Mary A. Delaney, M.D., Krista A. Biesecker, B.A., James F. Luebbert, M.D., Amy B. Rowan, M.D.

Summary:

Objective: Prior treatment studies of lithium in aggressive conduct disorder suggest a high placebo response and hyperactivity during the placebo baseline phase of an ongoing trial of lithium for aggressive conduct disorder (DSM-III-R).

Method: Forty-eight inpatients (41 males, seven females), aged 9.83 to 17.14 years (mean = 12.67 ± 1.94) participated in a six-week, double-blind, placebo-controlled trial of lithium. During the two-week, single-blind, placebo baseline period, subjects were rated weekly for hyperactivity using the Conners Teacher Questionnaire (CTQ) and the IOWA Conners (IOWA). Aggression was rated continually using the Overt Aggression Scale.

Results: Twenty-two subjects (baseline responders) did not demonstrate sufficient aggression for randomization to the treatment phase, and 26 were baseline nonresponders. A one-way MANOVA indicated an overall multivariate group effect (baseline responders and nonresponders) for total CTQ and IOWA scores (Wilks's lambda = .813, $F(2, 45) = 5.16$, $p < .01$). Follow-up univariate tests yielded significant differences between the groups.

Conclusions: Results suggest that for aggressive conduct disorder, poor response to placebo is associated with hyperactivity. The significance of these results is discussed.

NR228 Tuesday, May 7, 12 noon-2:00 p.m.

Buspirone in Adolescents with Anxiety Disorders

Manuel P. Bouvard, Psychiatry, R Debre Hospital, 48 BD Serurier, Paris 19 75019, France; Alain-Jean Braconnier, M.D., Catherine Dissoubray

Summary:

Generalized anxiety disorder (GAD) is not rare in adolescents. Prevalence rates are estimated from 2 to 19% in general population (Anderson et al., 1987). There are few reports concerning potential effects of anxiolytic agents in adolescents. Buspirone is a novel anxiolytic agent effective in GAD in adults, without major side effects. Buspirone does not interact with benzodiazepine GABA receptors and has minimal abuse potential. In open studies and single case reports, Buspirone has been shown to be effective in a various anxiety disorders in children and adolescents, such as social phobia or generalized anxiety disorder.

Methods: We have conducted a double-blind study comparing buspirone (30 mg/day) to placebo during six weeks. The first objective was to evaluate efficacy and tolerance of buspirone versus placebo during the first six weeks. The second objective of this study was to rate eventual withdrawal effects with a 15-day placebo period post-treatment. Fourty-two adolescents (age from 15 to 18 years) meeting DSM-III-R criteria for GAD have been randomized and enrolled in this study. All patients were rated with Hamilton Anxiety Scale, Clinical Global Impression, Global Assessment Functionning, and a withdrawal-specific questionaire. Eight patients have dropped out between D0 and D42 (in the treatment group and four in the placebo group) for adverse effects or noncompliance with the study.

Results: After the treatment period, no significant differences have been found between buspirone and placebo. More precisely, improvement in the buspirone group (52%) was superior to the placebo group (45, 7%) but without statistical difference. No differences has been found between buspirone and placebo concerning adverse effects, with a good tolerance. Withdrawal symptoms were slightly superior in buspirone group than in placebo group but not statistically differents.

Conclusion: This study is, to our knowledge, the first double-blind, placebo-controlled study with buspirone in an adolescent population. If buspirone seems to be effective and well tolerated in adolescents with GAD, we observed an important placebo effect in this population. This study confirms in adolescents, the minimal withdrawal effects of buspirone. Considerations about methodology required in further pharmacological studies in anxiety disorders (e.g. elimination of placebo responders) will be discussed.

NR229 Tuesday, May 7, 12 noon-2:00 p.m.

Psychopathology in Incarcerated Youth

Andres J. Pumariega, M.D., William S Hall Psych Inst, 1800 Colonial Dr, PO Box 202, Columbia SC 29202; D. Lanette Atkins, M.D., Larry Montgomery, M.D., Kenneth T. Rogers, D.O., W. Franklin Sease Jr, B.S., Gary Jeffers

Summary:

Objective: The incarceration of mentally ill youth is a serious problem not receiving the same attention as in adults. In this study, we examine the prevalence of psychopathology and level of behavioral symptomatology in incarcerated youth versus youth receiving community mental health services.

Method: We randomly recruited youth from middle South Carolina served by a local CMHC and youth in the S.C. Dept. of Juvenile Justice facilities from the same region. The DISC-PC 2.3 and the CBCL were administered to evaluate symptomatology and DSM-III-R diagnoses.

Results: Incarcerated youth have higher number of diagnoses (jailed = 2.3, CMHC = 1.5, N.S.) and significantly higher symptoms (jailed = 30.3, CMHC = 18.5, $p < .01$) than CMHC youth. Level of "caseness" (at least one diagnosis) was slightly higher in the incarcerated (68%) youth than in CMHC (60%) youth. The groups did not differ in CBCL mean total T (jailed = 64.3, CMHC = 66.9), mean internalizing T (jailed = 59.3, CMHC = 61.1), and mean externalizing T scores (jailed = 66.4, CMHC = 67.1).

Conclusions: Our results indicate the comparability in level of psychopathology in incarcerated and community-treated populations of youth, and the need to develop diversionary programs to prevent the entry of such youth into the juvenile justice system.

NR230 Tuesday, May 7, 12 noon-2:00 p.m.

Services Utilization in Incarcerated Youth

Andres J. Pumariega, M.D., William S Hall Psych Inst, 1800 Colonial Dr, PO Box 202, Columbia SC 29202; D. Lanette Atkins, M.D., Larry Montgomery, M.D., Susan Appenzeller, M.S.W., Robert Caesar, Ph.D., Donald Millus, B.S.

Summary:

Objective: Lack of community mental health services for poor and minority youth is thought to contribute to their risk for incarceration, but little is known about the level of prior service utilization in this population. In this study, we examine mental health and other service utilization in jailed versus community-treated youth.

Method: Incarcerated youth and youth served by a CMHC from middle South Carolina were randomly recruited. The DISC-PC 2.3 and the CBCL were used as measures of psychopathology. Parents completed lifetime history of human services for their child. Mean number of episodes of service across different categories was calculated.

Results: CMHC-treated youth utilized fewer overall services (jailed = 5.7, CMHC = 4.3, $p < .05$) and fewer residential services (jailed = 1.2, CMHC = 0.33, $p < .001$) and equal levels of educational, social, and volunteer services. Jailed youth used significantly fewer previous outpatient and acute mental health services (jailed = 1.0, CMHC = 1.6; $p < .05$). When juvenile justice records were reviewed for the incarcerated youth, we found that one-third of them had received psychiatric referral, with 17 (21%) having received pharmacotherapy for psychiatric disturbance.

Conclusions: Youth at risk for incarceration may utilize more services than anticipated, but may benefit from intensive mental health services to prevent out-of-home placement and later incar-

ceration. There is also a clear need for mental health service in juvenile correction facilities.

NR231 Tuesday, May 7, 12 noon-2:00 p.m.

Self-Reported Pathology and Psychiatric Assessment Among Special Education Students in a School-Based Clinic

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 relationship between self-reported pathology and psychiatric assessment among special education students in school mental health clinics.

Method: Subjects (N = 33) were 12–15 year old boys ($\bar{x}$ = 13.3 years). They were assessed through a psychiatric interview and standardized instruments = Youth Self-Report (YSR), Brief Psychiatric Rating Scale-Child (BPRS-C). Data analysis consisted of correlation procedures and descriptive statistics.

Results: Our results showed that: 1) DSM-IV diagnoses did not correlate significantly with any of the YSR scales; 2) BPRS-C items correlated with various YSR scales (uncooperativeness, hostility, feelings of inferiority, hyperactivity, and distractibility correlated with aggressive behavior; feelings of inferiority correlated with delinquent problems; hyperactivity correlated with attention problems); 3) several DSM-IV diagnoses correlated with various BPRS-C items (ADHD) correlated with hyperactivity and distractibility; conduct disorder correlated with manipulativeness; dysthymia correlated with suicidal ideation; major depression correlated with depressive mood and suicidal ideation

Conclusions: In this sample of special education students, self-reported pathology tended to correlate significantly with psychiatric assessment of specific symptoms, but not with DSM-IV diagnoses. Clinically meaningful correlations occurred also among standardized symptom assessment and formal psychiatric diagnoses. Further systematic studies are needed to explore the implications of these findings.

NR232 Tuesday, May 7, 12 noon-2:00 p.m.

Attachment and Drug Use in Detained Youth

Adrienne E.R. Sheldon-Keller, Ph.D., Psychiatry, University of Virginia, Box 16 Blue Ridge Hospital, Charlottesville VA 22901; Randolph J. Canterbury, M.D., Elizabeth L. McGarvey, Ed.D., Dennis Waite, Ph.D.

Summary:

Objective: To investigate differential risk of substance use due to differences in attachment patterns in a sample of incarcerated youth.

Method: Approximately 1,000 incarcerated adolescents participated in individual interviews to assess attachment patterns and substance use. The sample included 291 white males, 453 black males, 75 white females, and 57 black females. Data are from The Personal Experiences Screen Questionnaire (PESQ) and The Adolescent Attachment Questionnaire (AAQ).

Results: For black and white females, attachment variables associated with anxious attachment account for 28% (R^2 = .28; F(3, 51) = 6.36; p = .001) and 23% (R^2 = .23; F(5, 65) = 3.77; p = .005) of the variance in drug use, respectively. For black males, 7% of the variance (R^2 = .071; F(2,429 = 16.37; p < .0001) is accounted for by avoidant attachment. For white males, 6% of the variance (F(1,275) = 17.79; p < .0001) is accounted for by ambivalent attachment.

Conclusion: Attachment patterns account for a significant amount of the variance in reported drug use in this sample of high-risk adolescents. This suggests that understanding adolescents' attachment patterns is an important focus for successful intervention.

NR233 Tuesday, May 7, 12 noon-2:00 p.m.

Sport, Coping Strategies and Depression in Adolescence

Fabien Durif, M.D., Psychiatry, Hospital Purpan, Place Du Docteur-Baylac, toulouse 31059, France; Pierre Tap, Ph.D., Jean-Philippe Raynaud, M.D., Laurent Schmitt, M.D., Pierre Moron, M.D.

Summary:

Objective: Adolescence is a period of development and change. Risks of depression are higher because of negative coping strategies. The aim of this study is to prove that high competition sports protect adolescents against depression.

Method: This study includes 176 subjects aged 15 to 18 years divided into two groups: 90 high-competition athletes and 86 non-athletes. Athletes attend a college for high-level athletes and play more than 10 hours of sports per week. Nonathletes have less than four hours of sports per week in their college. We use the Beck Depression Inventory, the Catell Anxiety Scale, and the Toulouse Coping Scale for Adolescents to investigate six coping strategies: focalisation, social support, control, conversion, denial, withdrawal.

Results: Our study shows that 23.6% of the athletes and 51.2% of the nonathletes express depressive feelings. Athletes are significantly less anxious than nonathletes (p < 0, 01). Athletes use significantly more positive coping strategies: social support, active focalisation, emotional control. Nonathletes use more negative coping strategies: withdrawal, denial.

Conclusions: High-competition sports seem to protect adolescents from emergence of anxiety and depression due to better coping strategies. It is proposed that not only competitive but also leisure sports are good for adolescents' mental health. Further longitudinal studies evaluating protective value of sport in adolescence are needed.

NR234 Tuesday, May 7, 12 noon-2:00 p.m.

Pilot Project Examining the Effectiveness of an Intensive Day Program for Truant, Severely Disturbed Adolescents

Frederick J. Matzner, M.D., Child Psychiatry, St. Luke's-Roosevelt, 1111 Amsterdam Avenue, New York NY 10025; Matthew Silvan, Ph.D., Raul R. Silva, M.D., Joanne Weiner, Jacqueline Bendo, Murray Alpert, Ph.D.

Summary:

Introduction: Studies have demonstrated the effectiveness of adult day treatment. However, there is less literature on child day treatment, despite that fact that there may be over 300 programs now functioning. This is a pilot study examing the response to treatment in a population of truant adolescents with severe disturbance treated for six months in an adolescent day program.

Method: A chart review of consecutive admissions to the program was performed to abstract demographic data, diagnosis, and percentage of days truant, and contrasted with same subjects' truancy during six months of nonday treatment serving as a control. Clinical Global Improvement (CGI) severity and improvement ratings and Global Assessment of Functioning (GAF) scores were obtained on admission and at six months, using a pretest-posttest design.

Subjects: There were 21 females and 10 males, diagnostically heterogeneous, aged 14 to 19 years (mean, 16.2). Ethnic composition included Hispanic (42%) and African-American (51%).

Results: All 31 patients completed the six months of treatment. Significant improvement was seen in truancy ($p = .0001$), GAF ($p = .002$), as well as CGI Severity of Illness ($p = .001$), and Global Improvement ($p = .02$).

Conclusions: Combined academic and psychiatric treatment resulted in clinically significant improvement in truancy and psychiatric symptoms. Details of the program and results will be elaborated.

NR235 Tuesday, May 7, 12 noon-2:00 p.m.

Treatment of Childhood and Adolescent Depression with Sertraline: Possible Therapeutic Range of Plasma Concentration

Vincenzo F. DiNicola, M.D., Adolescent Psychiatry, Queen's University, 166 Brock St Brock 5, Kingston ON K7L 5G2, Canada; Irvin Epstein, M.D., James Owen, Ph.D., Kevin Parker, Ph.D., Kelly Driver, B.Sc.

Summary:

While tricyclic antidepressants have been utilized in the treatment of childhood and adolescent depression, recent studies have determined that they have clinical efficacy equal to placebo. The advent of newer serotonin reuptake inhibitors (SSRIs) has provided an opportunity to treat depression in this population with an agent that has a better side effect profile, better tolerability, and improved compliance rates. There are few studies in the literature utilizing SSRIs in the treatment of depression, and no reported investigations of the relationship between plasma concentration and clinical efficacy.

We recently completed a study of 10 depressed children and adolescents who were treated with sertraline, to determine whether a relationship exists between plasma levels of the medication and clinical efficacy. A repeated case study design was used in conjunction with evaluation of objective measures, including sertraline plasma concentration taken every two weeks and assessment of severity of the depression using the Children's Depression Inventory (CDI). A Clinical Global Improvement score was assigned for each psychiatric assessment session and was used to evaluate clinical efficacy.

Results of our study showed a positive clinical response in seven of 10 patients, with mean CDI scores of 18.25 and GDI scores of 85.5. The mean sertraline plasma levels were 118.9 nmol/l and five of the seven responders had plasma levels below 150 nmol/l. There is a weak relationship (Pearson's $r = .35$) between sertraline dose and plasma concentration.

Sertraline is a safe and effective medication that was well tolerated and showed a 70% clinical response.

NR236 Tuesday, May 7, 12 noon-2:00 p.m.

Characteristics of Korean Learning Disordered Children

Ji-Hae Kim, Ph.D., Psychiatry, Samsung Med Ctr, 50 Ilwon-Dong, Kangnam-Ku, Seoul, Korea; Young-Ran Lim, M.D., S. Peter Kim, M.D.

Summary:

Objective: Children with learning disorder (LD) exhibit a heterogeneous group of various cognitive deficits and sometimes have concurrent attention problems. It is not yet well known whether LD and attention deficit hyperactivity disorder (ADHD) have a common neurological origin or if etiologic factors of both disorders are mutually exclusive. Our study defined LD as a specific information-processing deficit. We classified LDs according to phonological processing, spatial cognition, attention problem, and memory. Through neuropsychological tests, we evaluated LD subtype's cognitive characteristics and attention deficits that co-occur with LD.

Method: The results of intelligence tests, academic achievements, behavior evaluation, and neuropsychological tests of 60 school-aged children diagnosed as LD and ADHD were analyzed. According to multifactorial criteria, they were divided into three groups: verbal type, nonverbal type, and mixed type. We then studied the comorbidity of LD and ADHD groups. By discriminant and cluster analysis, we attempted to find the discriminating factors among the groups.

Results: Verbal types in the LD group have difficulties in reading, word recognition, and verbal tasks that need phonological processing. Nonverbal types in the LD group showed poor visual-motor skills, sensory perception, and spatial cognition. Mixed types in the LD group showed more global deficits. When attention deficits co-occur with LD, this group showed both executive function deficits and linguistic problems.

Conclusions: LD subgroups of Korean children show similar deficits or patterns to those of children in the U.S., indicating little cultural influence on LD symptoms. It suggests the importance of theoretical framework to identify the LD's neuropsychological phenotypes.

NR237 Tuesday, May 7, 12 noon-2:00 p.m.

Predictors of Neuroleptic Response in Psychiatrically Hospitalized Children

Dinohra M. Munoz, M.D., Psychiatry, NYU Medical School, 20 Knickerbocker Road, Tenafly NJ 07670; Raul R. Silva, M.D., Murray Alpert, Ph.D., Daniel M. Medeiros, M.D., Lissa Lacher, Richard I. Perry, M.D.

Summary:

Introduction: Neuroleptics are effective for a wide range of disorders in children and adolescents. In adults, it has been shown that chronicity and severity of illness as measured by length of stay predict responsiveness to neuroleptics. Little is known about which variables might predict the outcome of neuroleptic treatment in children. The purpose of this study was to investigate this relationship in a mixed sample of child psychiatric inpatients.

Method: 72 diagnostically heterogeneous child psychiatric inpatients (mean age, 7.8 ± 2.4 years) were evaluated on a number of clinical and demographic variables, including SES, gender, race, residence, length of stay (LOS), level of suicidality and assaultiveness, IQ, as well as diagnosis, to determine which variables were associated with good response to neuroleptics. Responsivity was expressed as the number of different neuroleptics the child received, as a greater number of medications reflects a more treatment-refractory patient. Multiple regression analysis was used to determine statistical results.

Results: The total number of neuroleptics ranged from 1–3 (mean 1.1). Age was associated with increased responsiveness (Beta .38, $p = .009$). Longer LOS was associated with poor response (Beta .33, $p < .001$), as were higher IQ (Beta .36, $p < .02$), presence of disruptive behavior (Beta .07, $p < .05$), and pervasive developmental disorder (Beta .19, $p < .02$). Interestingly, children with psychotic features did not have a uniformly predictive response pattern to neuroleptics (Beta .08, $p < .14$).

Discussion: The reason why different clinical and independent variables may mediate neuroleptic responsivity in child psychiatric inpatients will be discussed.

NR238 Tuesday, May 7, 12 noon-2:00 p.m.

Predictors of Length of Stay in Child Psychiatry Inpatient Hospitalization

Ilisse R. Perlmutter, M.D., Psychiatry, Mt. Sinai, 178 E 80th Street #26-F, New York NY 10021-0450; Dean McKay, Ph.D., John D. O'Brien, M.D.

Summary:

Objective: Providing good clinical care while attempting to reduce length of psychiatric hospital stay is a major challenge confronting child and adolescent psychiatrists. Identifying predictors of length of stay can potentially facilitate cost-effective treatment planning. This study seeks to identify variables predicting a longer hospitalization for children.

Method: Records of 89 subjects, ages 5–12, consecutively admitted to the child psychiatry inpatient unit of a large city hospital, were evaluated for age, gender, length of stay, DSM-III-R diagnosis, and disposition. Data analysis was completed by Kruskal-Willis nonparametric analysis of variance, and data were converted to correlations for estimates of prediction.

Results: Our results show that: 1) diagnosis predicted length of stay with $r = .34$, $p = .002$. Children diagnosed with attention deficit/hyperactivity disorder remained longest; those with post-traumatic stress disorder stayed the shortest; 2) disposition predicted length of stay with $r = .39$, $p < .001$; 3) age and length of stay were not related ($r = .05$, p = ns); 4) age was correlated with diagnosis ($r = .46$, $p < .001$), with younger children more likely to be diagnosed with affective disorders or conduct/impulse control disorders.

Conclusions: Diagnosis and disposition significantly predict length of hospitalization. Awareness of these factors may enable clinicians to make more appropriate treatment interventions and long-term plans when children are hospitalized.

NR239 Tuesday, May 7, 12 noon-2:00 p.m.

The Factorial Composition of Thought Disorder in Adolescence

David S. Medoff, Ph.D., Psychiatry, Mass General Hospital, 40 Parkman Street, Ste 120, Boston MA 02114; David L. Pogge, Ph.D.

Summary:

This study examined the factorial structure of thought disorder in 101 adolescent psychiatric inpatients. Assessment instruments included several well-known and commonly used clinical measures of thought disorder including: a) The Scale for the Assessment of Thought, Language, and Communication (TLC), b) The Goldstein-Sheerer Object Sorting Test, c) The Gorham Proverbs Test, and d) The Comprehensive System for The Rorschach Inkblot Test.

Findings revealed that the TLC, a commonly used measure of thinking disturbance in adults, detected little to no thought disorder in adolescents. The measure most sensitive to thought disorder in this sample was the Rorschach Comprehensive System. Analysis of the thought disorder variables of this instrument generated a four-factor model that was difficult to interpret and did not fit any known or hypothesized model of thought disorder.

Results suggest that the thinking disturbance in adolescence may be qualitatively different than that of adulthood. The exact nature of these differences may be due to either maturational influences or normative distinctions in these two populations. It is suggested that there may be a developmental discontinuity of some kind in which the manifestation of thought disorder in adolescence may not reflect the same pathological processes or symptoms as in adulthood.

NR240 Tuesday, May 7, 12 noon-2:00 p.m.

Cognitive Impulsivity in Adolescent Conduct Disorder

Susan R. Borgaro, M.A., Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; David L. Pogge, Ph.D., William Horan, B.A., John Stokes, Ph.D., Joel Lord, M.A., Philip D. Harvey, Ph. D.,

Summary:

Adolescent substance abuse is associated with several concurrent psychiatric conditions, including major depression and conduct disorder. Several recent studies have also suggested that specific profiles of attentional impairment and cognitive impulsivity are present in adolescent psychiatric patients with conduct disorder and substance abuse. These studies suggested that CPT errors of commission predicted polysubstance abuse, although CPT errors were not subdivided on the basis of whether they reflected impulsivity or simple careless responding. Adolescent psychiatric patients were subdivided on the basis of whether they abused alcohol alone ($N = 22$), multiple substances ($n = 56$), or no substances ($n = 78$). Of the total of 156 cases, 70 met criteria for conduct disorder and 86 did not. Cognitive functioning was measured with Continuous Performance Test (CPT), with CPT performance divided into errors of omission and several subtypes of errors of commission that had been previously validated for their differential correlation with impulsivity. Errors of omission and errors of commission reflecting careless or random responding did not correlate with either conduct disorder or substance abuse. For cases that did not meet criteria for conduct disorder, impulsive tendencies failed to predict substance abuse. However, there were significant 2-way interactions of conduct disorder × substance abuse for both alcohol abuse and multiple substance abuse (both $F's > 5.0$, both $p < .01$) when impulsive errors of commission were examined. These interactions reflected specific elevations in impulsive errors of commission were examined. These interactions reflected specific elevations in impulsive errors of commission in substance abusers who also met criteria for conduct disorder, relative to individuals with conduct disorders without substance abuse and substance abuse without conduct disorder. These data may suggest that impulsivity is a risk factor for substance abuse, which is expressed only which is expressed only in those persons who also have tendencies toward antisocial behavior.

NR241 Tuesday, May 7, 12:00 noon-2:00 p.m.

Zinc Deficiency in ADHD

Sofia Eldar, M.D., Tel-Aviv Community Mtl Hlth, 9 Hatzvi Street, Tel-Aviv 67197, Israel; Paz Toren, M.D., Ben-Ami Sela, Ph.D., Leo Wolmer, M.A., Ronit Weizman, M.D., Nathaniel Laor, M.D.

Summary:

Objective: To evaluate serum zinc levels in children and adolescents with ADHD and compare them with age-matched normal controls.

Method: Blood samples were taken from 43 children (aged 6 through 16 years) diagnosed as ADHD according to DSM-III-R criteria, and confirmed using the K-SADS. Twenty-eight age-matched normal children served as controls. Serum zinc levels were measured by atomic absorption spectrophotometry.

Results: Serum zinc levels of the ADHD group (mean ± SD: 77 ± 27 μg/dl, range: 31–141 μg/dl) were significantly lower ($p < 0.05$) than levels of the control group (mean ± SD: 86 ± 13 μg/dl, range: 60–125 μg/dl). Moreover, 30% of ADHD children had serum zinc levels of less than 55 μg/dl.

Conclusions: A subtype of ADHD with zinc deficiency may exist. Further studies are required to confirm this finding. The ADHD

children with zinc deficiency might benefit from a therapeutic trial with zinc supplementation.

NR242 Tuesday, May 7, 12:00 noon-2:00 p.m.

Brain EEG Abnormalities in 300 Hospitalized Preadolescents

Noelle K. Gehm, B.S., Psychiatry, Ohio State University, 1670 Upham Drive, Columbus OH 43210; Henry A. Nasrallah, M.D.

Summary:

In an era of managed health care, the cost-effectiveness of every laboratory procedure must be established. An electroencephalograph (EEG) is an expensive but potentially useful diagnostic tool in psychiatric brain disorders. We conducted a study to examine the yield of brain abnormalities detected by EEG in preadolescent patients.

Methods: The records of all consecutive admissions to our preadolescent psychiatric unit over a period of five years (n = 300) were studied. Demographic and clinical variables as well as abnormal findings on EEG's were recorded. A total of 79% of the patients were male, 21% female, 88% white, 11% black, and 66% had an onset of illness by age 6 and 34% between ages 7–12. EEG's were obtained on 274 patients (91% of the sample).

Results: Only 16 of the 274 EEG's were found to be abnormal (6% yield). A statistical analysis using classification and regression trees showed that highest yield was found if 1) the current age is greater than 7.5 years and 2) there is a diagnosis of organic mood disorder. For equal costs, the effect on the tree is that out of any 274 set of subjects there is a statistical probability of eight normal being misclassified as abnormal and 29 abnormal being misclassified as normal. The clinical and economic implications of the findings for the use of EEG in preadolescents will be discussed.

NR243 Tuesday, May 7, 12:00 noon-2:00 p.m.

Depressive Symptoms in Adolescent Conduct Disorder

William Horan, B.A., Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; David L. Pogge, Ph.D., Susan R. Borgaro, M.A., Joel Lord, M.A., John Stokes, Ph.D., Philip D. Harvey, Ph.D.

Summary:

Although depressive symptoms are known to be present in adolescents with conduct disorders and other antisocial behaviors such as substance abuse, there have been few studies of the relationship between these symptom domains. This is particularly true for features of cognitive impairments in these two disorders. This study compared adolescents with major depression (n = 56), conduct disorder (n = 43), and both diagnoses (n = 20) in their attentional performance on tests of vigilance (i.e., single and dual task Continuous Performance Tests [CPT]). Specific patterns of impulsive CPT errors have previously been found to be elevated in adolescent psychiatric patients who have symptoms of conduct disorder, including multiple substance abuse. Data were examined in terms of errors reflecting failures to respond, impulsive responses, and long-latency responses.

Across all three groups these three types of errors were uncorrelated, suggesting independent dimensions of attentional dysfunction. Adolescent dual-diagnosis patients had a pattern of responding that included both more impulsive errors and more long-latency errors than either the pure depressed or pure conduct disordered groups, with no differences in failures to respond to target stimuli. Examination of their reaction times implicated a deficit in response inhibition that was not present in either of the other two groups, in that they had longer reaction times while making impulsive errors than either the depressed or conduct disordered groups. These results suggest that the concurrent presence of conduct disorder and depression leads to a pattern of impulsive errors that is greater than seen in each group alone. Furthermore, there is evidence of an additional pattern of cognitive impairment that may be unique to these dual-diagnosis subjects, suggesting that group may be different from either of the two single-diagnosis groups and worthy of further research attention.

NR244 Tuesday, May 7, 12:00 noon-2:00 p.m.

Financial Efficacy of Treatment Foster Care for Emotionally Disturbed Children and Adolescents

Edwin J. Mikkelsen, M.D., Mentor Clinical Care, 313 Congress Street, 5th Floor, Boston MA 02210; Wayne J. Stelk, Ph.D., Lynn Morton-Epps, M.E.D.

Summary:

This study evaluates the financial efficacy of specialized treatment foster care for emotionally disturbed children. We accomplished this by comparing the average per diem cost for the residential services they received prior to admission with the average per diem cost of their discharge placement. The total N was 412, with an average length of stay of 12.6 months. The demographic information is as follows: age:--13% under 6, 31% age 6–12, 56% age 13–18; race:——52% Caucasian, 45% African-American, 1% Hispanic, 2% other; and gender:——52% male, 48% female.

The preadmission [%] and post-discharge (%) distribution of residential settings is as follows: psychiatric hospital—[16%] and (12%); residential treatment center—[14%] and (12%); crisis shelter—[17%] and (5%); group home—[10%] and (5%); foster care—[30%] and (10%); bio family—[9%] and (31%); relatives [4%] and (13%); and adoptive [1%] and (8%).

The estimated per diem cost savings per 100 clients discharged from the mentor treatment foster care program was $6,279 (average preadmission per diem cost per 100 clients $15,211 vs. discharge per diem cost of $8,932.) The savings was largely accomplished by the 52% of children who were discharged to biological family, relatives, or adoptive home, whereas only 14% were admitted from these locations.

NR245 Tuesday, May 7, 12 noon-2:00 p.m.

Family and Peer Influences in Adolescent Drug Use

Ramon U. Florenzano, M.D., 584 Ricardo Matte, Providencia, Santiago 00068, Chile; Paulina Z. Pino, Ph.D., Milka D. Kaplan, M.Sc., Perla C. Ben Dov

Summary:

Objectives: To describe the frequency of risk behaviors among Santiago de Chile adolescents and their association with family characteristics and attribution of peer use.

Methods: This case-control clinical epidemiology survey was applied to a representative sample of Santiago de Chile school-attending adolescents. They answered the Chilean adaptations of the Minnesota Adolescent Survey, and the FACES III, a family function instrument that measures perception of family cohesion and adaptability. The 2030 adolescents surveyed were a representative sample of school attenders in metropolitan Santiago. They were compared in their level of emotional symptoms, report of peer and self alcohol, tobacco and drug use, as well as in their perception of family functioning, religiosity, and sociodemographic characteristics. The two dimensions of family functioning were summarized in three groups: balanced, intermediate, and extreme families.

Results: Marihuana consumption decreased as cohesion increased: children from detached families consumed more (12.1%) than those from separated (6.6%), connected (4.2%), and amalgamated (2, 7%) families ($p < 0.00001$). With regards to adaptabil-

ity, children from rigid families consumed more (10.7%) than those from structured (9.8%), flexible (4.2%), and chaotic (4.3%) families ($p < 0.0004$). With regard to drug use, children who thought their classmates or friends used drugs consumed much more themselves (31.5%) than those who thought their peers did not use them (4.8%). A logistic regression analysis found a major odds ratio for peer consumption (5.86) family rigidity (3.02), and lack of religiosity (2.77).

Conclusions: This research demonstrates the comparative influence of family and peers in adolescent drug consumption. This design does not predicate causality, but reafirms the importance of both variables in the design of preventive interventions.

NR246 Tuesday, May 7, 12 noon-2:00 p.m.

Olanzapine: Molecule to Drug Candidate

Charles M. Beasley, Jr., M.D., DC: 0538, Eli Lilly & Co., Lilly Corp Center, Indianapolis IN 46285; Gary D. Tollefson, M.D., Pierre V. Tran, M.D., Winston G. Satterlee, M.D., Todd Sanger, Ph.D.

Summary:

Olanzapine, a thienobenzodiazepine, has been extensively investigated as a potential atypical antipsychotic. Phase II & III clinical trials, completed in February 1995, consisted of five acute studies of which three also included double-blind, long-term maintenance phases. These studies included 2,500 olanzapine-treated patients (1,122 patient years of treatment), 810 haloperidol-treated patients (193 patient years of treatment), and 236 placebo-treated patients (27 patient years of treatment). The integrated results of the four of these studies evaluating olanzapine in the treatment of schizophrenia will be presented with respect to both efficacy and safety.

Olanzapine was superior to placebo with respect to all symptom domains and superior to haloperidol with respect to total and negative symptoms, while being comparable with respect to positive symptom effects. At an effective dose of 10 mg/day, no adverse event was reported in association with olanzapine at a rate statistically significantly greater than with placebo. At higher doses (15–20 mg/day) somnolence (39.1%), dizziness (17.4%), and constipation (14.5%) were reported with olanzapine at rates statistically significantly greater than with placebo. At all doses investigated (5–20 mg/day), olanzapine was associated with actual mean decreases from baseline in parkinsonism and akathisia and in long-term use was associated with a statistically significantly lower rates of treatment-emergent dyskinesia than was haloperidol.

NR247 Tuesday, May 7, 12 noon-2:00 p.m.

Multiple DWI Arrests in Minority Offenders

Hyung K. Lee, M.D., Psychiatry, Bronx-Lebanon Hospital, 1276 Franklin Avenue 5th Flr, Bronx NY 10486; Ali Khadivi, Ph.D.

Summary:

Objective: Very little is known about the clinical and demographic characteristics of driving while intoxicated (DWI) offenders in an inner city. The purpose of the study was to compare multiple DWI offenders with a group of one-time offenders on a number of clinical and psychosocial variables.

Method: The data were collected from a retrospective review of the records of all nonoverlapping adult patients (N = 612) who were court mandated to the Bronx-Lebanon Hospital DWI outpatient program from 1990 to 1993.

Results: The sample was 99% male, 60% married, 98% employed, and predominately Hispanic (64%) and Afro-American (23%). The multiple arrest group (DWI arrest > 1, N = 231) was significantly older ($p = .001$), had a longer duration of drinking ($p < .0001$), was more likely to describe themselves as daily drinkers ($p = .001$), reported more severe alcohol problems as measured by the modified version of Michigan Alcohol Screening Test ($p < .0001$), and were more likely to have had a history of alcohol treatment than the single arrest group (DWI arrest = 1, N = 381). The two groups were not significantly different on the age of onset of drinking, family history of alcoholism, non-DWI-related arrests, drug abuse, or alcohol-related medical problems. Strikingly, 78% of the multi-arrest group did not consider themselves to be alcoholics and 77% reported no past alcohol treatment.

NR248 Tuesday, May 7, 12 noon-2:00 p.m.

Factor Analysis of the Addiction Severity Index

Juris P. Mezinskis, Ph.D., Psychology, VA Medical Center, 3200 Vine Street 116B, Cincinnati OH 45220; Jennifer Lewis, B.S., Eugene C. Somoza, M.D., Sue R. Dyrenforth, Ph.D., Mark Cohen, Ph.D.

Summary:

The Addiction Severity Index (ASI) is a widely used assessment instrument in the field of substance abuse treatment (e.g., it has been translated into nine languages, McLellan et al., 1992). The ASI is a structured interview that evaluates patient functioning in seven problem areas: medical, employment, drug, alcohol, legal, family/social, and psychiatric. When using the ASI for research, a summary composite score is calculated for each of the problem areas using mathematical formulas. The intent of the present study was to determine whether these composite scores are unitary factors, or whether the composite scores are combinations of multiple underlying factors. Therefore, a factor analysis was performed using the 55 ASI items used in calculating the seven composite scores. The data set consisted of intake ASIs given to 1,013 patients entering chemical dependence treatment at an urban VA medical center. Using the principle components method, 17 factors, with eigenvalues > 1.0, were found. Factor loadings for individual items were determined using verimax rotation. The proportion of variance explained by each factor ranged from 13.0% (factor 1) to 1.9% (factor 17). The 17 factors accounted for a total of 62.4% of the variance. Finding 17 factors suggests a more complicated structure for the ASI than the seven factors originally proposed. Items from two of the ASI composite score areas loaded on a single factor: alcohol (factor 3) and medical (factor 4). However, the other five composite score areas broke up into two or more factors: psychiatric (factors 1 & 5), drug (factors 2, 7, 11, & 14), legal (factors 5 & 10), social (factors 6 & 13), employment (factors 8 & 9). The results suggest that when using the ASI for outcomes research, investigators may choose to look at this 17-factor structure of the ASI as a way of obtaining more finely graded information about changes in patient functioning.

NR249 Tuesday, May 7, 12 noon-2:00 p.m.

Harm Reduction As an Outcome of Methadone Maintenance Treatment of Geriatric Heroin Addicts

Chandresh Shah, M.D., Psychiatry, VA Outpatient Clinic, 351 E. Temple Street, Los Angeles CA 90012; David Highfill, M.A., Lena Simitian, Ph.D.

Summary:

To study the outcome of long-term methadone maintenance treatment (MMT) among geriatric heroin addicts, 20 male patients were followed for 12 months. Urine samples were collected randomly and screened for toxicology. The patients were 67.35 ± 2.87 years old and had been on MMT for 95.36 ± 69.79 months. The first use of heroin was at the age of 25.05 ± 9.61 years and then continued for the next 36.80 ± 15.06 years. They tried detoxification at least 1.55 times but had failed and subsequently started the MMT. During the study period, five patients were totally

abstinent. Even though the other 15 patients had continued to use heroin, the frequency of use was only 11.10 ± 11.19% of the time. They used to use heroin 23.25 ± 8.63 days per month before starting the MMT. Since their participation in the treatment, the use was significantly ($p < .0001$) reduced to 0.25 ± 0.72 days per month.

These results show that MMT may not produce total abstinence in all patients but reduces heroin use significantly in most geriatric addicts, thus may greatly reduce mortality and morbidity. This is of paramount significance when heroin users are at risk of diseases like AIDS. Therefore, partial abstinence among heroin addicts should not be viewed as failure but as a harm-reduction outcome.

NR250 Tuesday, May 7, 12 noon-2:00 p.m.

Bromocriptine for Treatment of Cocaine Abuse

David A. Gorelick, M.D., NIDA Addiction Reser Ctr, PO Box 5180, Baltimore MD 21224–0180; James L. Hill, Ph.D., Jeffery N. Wilkins, M.D.

Summary:

Objective: To evaluate the efficacy and safety of the dopamine agonist bromocriptine as treatment for cocaine abuse, for which existing clinical data are inconclusive.

Method: We conducted a double-blind, randomized clinical trial in 70 cocaine-abusing (DSM-III) men (86% African-American, mean age 34 years, 39 months of regular cocaine use, 16 days of cocaine use in prior month) with no other current substance dependence except tobacco (n = 23). Subjects received four weeks of inpatient treatment, taking bromocriptine (titrated up to 2.5 mg po tid) (n = 35) or placebo (n–35) during the last two weeks, followed by 24 weeks of outpatient treatment on medication plus weekly group therapy. The primary outcome measure was cocaine use (urine toxicology, self-report).

Results: Both medication groups decreased their cocaine use, but there were no significant group differences in treatment retention, proportion of urine samples positive for cocaine (either in all subjects or in the 19 completers), adverse reactions, or reasons for leaving the study.

Conclusions: These findings do not support the efficacy of bromocriptine in treating cocaine abuse, although it appears safe and well tolerated when used with a gradual dose escalation regimen. (Supported by a grant from Sandoz.)

NR251 Tuesday, May 7, 12 noon-2:00 p.m.

Phenomenology of Inpatient Cocaine Withdrawal

David A. Gorelick, M.D., NIDA Addiction Reser Ctr, PO Box 5180, Baltimore MD 21224–0180; Robin Stauffer, R.N., Jon-Kar Zubieta, M.D., James J. Frost, M.D.

Summary:

Objective: To evaluate prospectively the clinical phenomenology and time course of inpatient cocaine withdrawal.

Method: Fourteen physically healthy, cocaine-dependent (DSM-III-R), medication-free subjects (12 men; mean age 30 years) with no other current substance dependence (except nicotine) were housed on a closed research ward for 28 days and evaluated twice daily for pulse, blood pressure (BP), mood (Beck Depression Inventory, Profile of Mood States), cocaine craving (Minnesota Craving Scale), and psychomotor performance (computerized digit symbol substitution test [DSST]), and daily for sleep characteristics (St. Mary's Sleep Questionnaire). Subjects had used cocaine on 3.7 ± 1.6 days of the seven preceding admission (a total of 3.5 ± 2.9 grams), with last use 16.6 ± 18 hours before admission.

Results: Pulse and BP stabilized in the normal range over the first two to three days. DSST performance and sleep duration and quality improved over the first three to five days. Mood scores (within normal range at admission) and cocaine craving progressively declined over the first seven to 10 days. All variables remained stable over the last two to three weeks.

Conclusions: Signs and symptoms of moderate cocaine withdrawal progressively normalize over seven to 10 days without medication in an inpatient setting.

NR252 Tuesday, May 7, 12 noon-2:00 p.m.

Plasma Butyrylcholinesterase Activity in Drug Abusers

David A. Gorelick, M.D., NIDA Addiction Reser Ctr, PO Box 5180, Baltimore MD 21224–0180; Gilberto Carmona, M.S., Raymond Woosley, M.D., Kenneth Dretchen, Ph.D., George Belendiuk, M.D., Nicholas Carriero, Ph.D.

Summary:

Objective: To evaluate factors influencing the activity and stability over time of plasma butyrylcholinesterase (BChE), the major cocaine-metabolizing enzyme in humans.

Method: BChE activity was assayed using a colorimetric method with butyrylthiocholine as substrate in 20 nonaddicted controls and 132 subjects (127 men, 118 African-American, 31 white, mean [SD] age 33.8 [6.2] years) who met DSM-III-R criteria for substance dependence: 80 cocaine (including 23 with secondary alcohol abuse), 19 alcohol only, 12 heroin and/or marijuana, 21 nicotine only. Venous blood was drawn at study entry, when subjects were medication- and drug-free with normal liver function, and at one, six, and 12 months.

Results: Plasma BChE activity was 2.11–7.13 U/L, within the range of published norms in nonsubstance abusers and significantly correlated with body weight ($r = 0.18$, $p = 0.03$). There were no significant differences in enzyme activity by primary drug of abuse, age, race, sex, or height. Enzyme activity did not change significantly over time.

Conclusions: Cocaine addicts have normal plasma BChE activity, which remains stable over a one-year period.

NR253 Tuesday, May 7, 12 noon-2:00 p.m.

Brazilian Medical Students: Alcohol and Drug Use

Florence Kerr-Correa, M.D., Neuro-Psiquia, Botucatu Medical School, FAC Medicina Botucatu Unesp, Botucatu SP 18618–000, Brazil; Artur G. Andrade, M.D., Ana Z. Bassit, Psy.

Summary:

Objective: To analyze the prevalence of drug use by medical students at Botucatu Medical School compared with students at eight medical schools of São Paulo State (at lifetime, last 12 months, and last 30 days).

Background: Serious accidents, including deaths, involving drugs use among medical students in Botucatu caused increased attention to this problem.

Methods: Research was carried out in 1994 and 1995, with 5,227 student using anonymous self-completed questionnaires, including one from the World Health Organization. The completion rate was of 71% (3.725).

Results: There were no significant statistical differences among schools, and the last 30 days drug use rate showed the following results, for Botucatu and other schools (drug use range) respectively: alcohol in 50% (42%–50%); tobacco in 7% (7%–13%); inhalants in 8% (7%–12%); cannabis in 6% (6%–16%); benzodiazepines (BZD) in 3% (2%–8%); cocaine in 0.5% (0.2%–4%); amphetamines in 1% (0%–1%). Though there was increased drug

use from first to sixth year, especially BZD, most of the students did not approve of using drugs.

Conclusions: Although the research found drug use (not abuse or dependence), the results suggest the necessity of developing prevention programs for the this population.

NR254 Tuesday, May 7, 12 noon-2:00 p.m.

Alcohol Severity in Comorbidity Depressed Patients

Helen M. Pettinati, Ph.D., Psychiatry, University of Penn, 3900 Chestnut Street, Philadephia PA 19104; Richard Saini, M.D., Alexia L. Wolf, B.A., Ann E. Semwanga, B.A., Alan Sharf, B.S.

Summary:

Objective: This study examined whether the higher degree of problem severity typically seen in comorbidly depressed alcohol dependent patients is due primarily to the additional depressive symptoms, or does the depressive disorder also exacerbate the alcohol problems, increasing the level of alcohol problem severity in depressed alcoholics?

Methods: Pre-treatment profiles of alcohol severity were evaluated in 47 male and female outpatients with a DSM-III-R diagnosis of alcohol dependence, 25 of whom also met DSM-III-R criteria for major depression. Depressed vs. nondepressed patients were compared on the amount of consumption (Timeline Followback) and severity of consequences from their alcohol drinking (Short Michigan Alcoholism Screen Test and the Addiction Severity Index).

Results: Findings showed no significant differences between depressed and nondepressed patients in their amount of drinking in the month prior to treatment, or on the two measures of alcohol severity. However, there were gender differences. Alcohol severity scores on the Short Michigan Alcoholism Screen Test were higher in males compared to females (M = 9.1 vs. M = 6.7, respectively, $t = 2.3$, $df = 24$, $p < .01$), although the number of standard drinks in the month prior to treatment was comparable between males and females. Within the depressed group, there was a higher proportion of depressed females than males (70% vs. 25%, respectively; *chi square* = 8.1, $df = 2$, $p < .01$), and depressed females endorsed significantly more depressive symptoms than depressed males on the Beck Depression Inventory (M = 23.6 vs. M = 14.8, respectively, $t = 2.5$, $df = 24$, $p < .02$).

Conclusions: The higher problem severity of the depressed alcohol dependent patients is due to the addition of depressive symptoms but was not associated with a greater drinking problem compared to nondepressed alcoholics. There were gender differences in both depressed and nondepressed alcohol dependent patients in their alcohol severity and depressive symptoms.

NR255 Tuesday, May 7, 12 noon-2:00 p.m.

Perceived Need for Substance Abuse and Mental Illness Treatment Among Dually-Diagnosed Psychiatric Inpatients

Jill Rachbeisel, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Lisa B. Dixon, M.D., Jean Gearon, Ph.D.

Summary:

Objective: This study examined the awareness of psychiatric inpatients dually diagnosed with mental illness (MI) and substance abuse (SA) disorders regarding: 1) their perceptions of the *presence* of MI and SA problems; and 2) their perceived need for treatment for MI and SA disorders.

Methods: A cohort of psychiatric inpatients (N = 264) admitted to a university hospital and diagnosed with a MI and SA disorder were referred to an inpatient dual diagnosis program. Patients were assessed for awareness of MI and SA disorders, need for treatment, and severity of illness. Patients were a mean age of 34.7 (SD 8.7) years, 70% male, 68% black, and 72% single.

Results: The majority of patients acknowledged a SA problem and need for SA treatment, and a MI problem and need for MI treatment. Acknowledgment of a SA problem was associated with perceived need for SA treatment ($p < .001$), diagnosis of substance dependence rather than abuse ($p < .001$), higher MAST scores ($p < .0001$), greater current use ($p < .01$) and perception of having a MI ($P < .005$) but not need for MI treatment. Perception of a MI was associated with the need for MI treatment ($p < .001$), but not psychiatric severity indicators.

Conclusions: The high level of illness awareness and consent for treatment observed suggests that treatment readiness may be optimal in the inpatient setting and underlines the importance of initiating inpatient dual diagnosis treatment. Insight into SA difficulties appears to be related to SA severity measures, a relationship not found with MI. More research on treatment response will be presented.

NR256 Tuesday, May 7, 12 noon-2:00 p.m.

Reduced Blue Cone Electroretinogram in Cocaine Patients

Alec Roy, M.D., Psychiatry, East Orange VAMC, 385 Tremont Avenue, East Orange NJ 07018; Monique Roy, M.D., John A. Williams, M.D., Larry Wineberger, Ph.D., David Smelson, Psy.D.

Summary:

Background: The main reinforcing effect of cocaine is by altering dopaminergic neurotransmission in the brain reward systems. Since dopamine is found in high concentrations in the retina, we investigated whether cocaine dependence may be associated with abnormalities of the electroretinogram (ERG).

Methods: We compared recently withdrawn cocaine dependent patients (N = 20) with age; sex; and racially-matched normal controls (N = 20) for responses of cone photoreceptors to light flashes on full field ERG.

Results: Cocaine dependent patients had significantly reduced blue cone ERG responses compared with matched controls.

Conclusion: This result suggests that in cocaine dependent patients there is dysregulation of blue cone function. The ERG may be useful in future studies of cocaine dependent patients.

NR257 Tuesday, May 7, 12 noon-2:00 p.m.

Why Do Alcoholics Get Depressed?

Alec Roy, M.D., Psychiatry, East Orange VAMC, 385 Tremont Avenue, East Orange NJ 07018

Summary:

Objective: Secondary depression is common among primary alcoholics. However, it's etiology is poorly understood.

Methods: Forty primary alcoholics, abstinent for two weeks or more, with a secondary major depressive episode were compared with 40 matched nondepressed and never-depressed primary alcoholic controls for risk factors for depression and recent life events.

Results: In the six months before the onset of depression depressed alcoholics had experienced significantly more life events, more life events with negative impact, more dependent events caused by alcohol, and more independent events. Significantly more depressed alcoholics than controls had a family history of depression, a family history of suicidal behavior, and had themselves attempt suicide.

Conclusion: Having recent life events, particularly events with negative impact, and a family history of depression are risk factors for secondary depression in alcoholics.

NR258 Tuesday, May 7, 12 noon-2:00 p.m.

Oral Morphine Maintenance Program

Gabriela Forster, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18–20, Vienna 1090, Austria; Gabriele Fischer, M.D., Karin Diamant, M.D., Corinna Schneider, M.D., Lukas Pezawas, M.D., Siegfried Kasper, M.D.

Summary:

In 1963, Dole and Nyswander suggested substitution treatment with methadone for opiate addicts. Since then, approximately 80,000 patients have been treated with this substance in the United States. In Austria, substitution treatment has been permitted by law since 1987. To date 3,000 patients have been treated in different substitution programs. Methadone has many advantages, including a long half-life of 24 to 36 hours, it is an inexpensive substitute and it is easily differentiated from other opioids in urine samples. Methadone also shows some disadvantages: many patients have developed side effects such as weight gain up to 20 kilos, depressive mood disorders, apathy, and sleep disorders. It therefore became necessary to look for alternatives.

Since 1990, oral morphine in slow release tablets has been used in a maintenance program. Patients, who showed side effects on methadone have been switched to oral morphine. In our study, 100 patients have been treated with morphine, 130 with methadone. The mean daily dosage of morphine is 470 mg and the mean daily dosage of methadone is 90 mg. Side effects disappeared within a short period after patients were switched to morphine. In addition, the abuse of illicit substances was reduced in morphine maintained subjects in comparison to methadone maintained patients (MMP): 63% of the patients treated with morphine did not take any other drugs, whereas only 38% in the MMP proved negative for other substances in supervised urine samples. Morphine maintenance showed efficacy, was well accepted in the study population, and seems to be an alternative for maintenance therapy in opiate dependent subjects.

NR259 Tuesday, May 7, 12 noon-2:00 p.m.

MRI Evidence of "Silent" Neurotoxicity in Cocaine Dependence

George Bartzokis, M.D., Research, West LA VAMC, 11301 Wilshire Blvd (B-151H), Los Angeles CA 90073; Mace Beckson, M.D., Darwood Hance, M.D., Walter Ling, M.D., Stephen R. Marder, M.D.

Summary:

In preliminary studies supported by the West Los Angeles VA Medication Development Unit cocaine dependent (CD) subjects were evaluated with a single high-field (1.5 Tesla) MRI instrument in order to investigate whether gross anatomic evidence of neurotoxicity could be observed. Preliminary data analysis was carried out on 23 male CD subjects, and 11 normal male control subjects. The groups had the same age range (30–66) and did not significantly differ in age, race, or height.

The subjects had no history of major medical or neurologic illness or head trauma and no evidence of neurologic impairment on clinical exam. Despite these exclusion criteria, seven of the 23 CD subjects were noted to have severe structural brain pathology. The gross structural abnormalities are suggestive of "silent" vascular events possibly related to the vasoconstrictive effects of cocaine. The affected subjects had lesions in occipital white matter, temporal pole cortex, occipital and parietal cortices, left insula, and left putamen. Two subjects had a very large number of multiple, diffuse, confluent cerebral white matter lesions in a classic watershed distribution. The CD group also had an apparent increase in the prevalence of small T_2 hyperintense lesions in the ventral putamen/globus pallidus regions on qualitative evaluation of the scans. These lesions correspond to an area supplied by the anterolateral branches of the mid and anterior cerebral arteries, often a site of intracerebral hemorrhage in this population (Brown et al., 1992). Although "subclinical," these lesions may affect treatment response to medication and behavioral interventions. Data from a larger sample will be scored and available for presentation.

NR260 Tuesday, May 7, 12 noon-2:00 p.m.

Clinical Effects of Repeated Cocaine and Alcohol Use

Elinore F. McCance-Katz, M.D., Psychiatry, Yale University, 184 Liberty Street, New Haven CT 06519; Thomas R. Kosten, M.D., Peter I. Jatlow, M.D.

Summary:

Objective: This study of repeated cocaine administration in the presence of steady-state ethanol concentration approximates street use and explores effects of combined cocaine and ethanol use and the role of cocaethylene.

Method: Six cocaine dependent, alcohol abusing subjects participated in this randomized, double-blind, within-subjects study with three sessions (each 480 minutes): four doses of intranasal cocaine (1 mg/kg) every 30 minutes with oral ethanol (1 g/kg) administered following the initial cocaine dose and a second ethanol drink (120 mg/kg) at + 60 minutes to maintain plasma ethanol concentration during cocaine administration, cocaine with placebo ethanol, and cocaine placebo with ethanol. Area under the curve values representing responses to successive doses of cocaine and residual effects were calculated.

Results: Plasma cocaine concentration during cocaine/ethanol administration exceeded that for cocaine administration. Cocaethylene concentrations ranged from 22% to 40% that of cocaine. Heart rate increased following each dose of study drug for cocaine/ethanol administration relative to cocaine or ethanol alone ($p < .05$). Cocaine/ethanol administration increased ratings of "Any High" and "Feel Good" ($p < .05$) relative to cocaine or ethanol administration.

Conclusion: Findings are consistent with clinical reports indicating increased toxicity during binge use of cocaine and ethanol.

NR261 Tuesday, May 7, 12 noon-2:00 p.m.

Comorbidity in Adult Inpatient Drug Abusers

Carlos M. Grilo, Ph.D., Psychiatry, Yale Psychiatric, P.O. Box 208038, New Haven CT 06520; Steve Martino, Ph.D., Daniel F. Becker, M.D., Martha L. Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To assess DSM-III-R axis I and axis II co-occurrence and comorbidity in young adult psychiatric inpatients with substance use disorders (SUD).

Method: A consecutive series of 118 inpatients (Mean age = 23.6 yrs, SD 5.6) were assessed with structured diagnostic interviews for axis I (SCID-P) and axis II personality disorders (PDE). Diagnoses were reliable; kappas for inter-rater reliability ranged from .65 to 1.0 (average kappas were .77 and .84 for axis I and II, respectively). Final research diagnoses were based on the best-estimate method, following the LEAD standard.

Results: 71 subjects met criteria for a SUD (SUD group) and 47 did not (nonSUD group). The two groups did not differ in age, gender, enthnicity, SES, age of first psychiatric treatment, or GAF at admission. A high rate of co-occurrence of axis I disorders was observed——ranging from eating disorders (23%) to major depression (44%)——but *no* axis I disorder co-occurred in the SUD group at a significantly higher rate than in the nonSUD comparison group. In contrast, Cluster B personality disorders and

borderline personality disorder were diagnosed significantly more frequently in the SUD group (66% and 61%) than in the nonSUD group (19% and 15%)(x^2 = 25.10 and 24.16, respectively, p < .001).

Conclusions: Axis I co-occurrence is frequent in inpatients with SUD but no more so than is axis I disorder occurrence among adult psychiatric inpatients. Only Cluster B and borderline personality disorders among axis II appear to have a significantly different co-occurrence (i.e., comorbidity) with SUD.

NR262 Tuesday, May 7, 12 noon-2:00 p.m.

Personality Disorders in Adults: Gender Effects

Carlos M. Grilo, Ph.D., Psychiatry, Yale Psychiatric, P.O. Box 208038, New Haven CT 06520; Daniel F. Becker, M.D., Martha L. Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To examine gender differences in DSM-III-R personality disorders in young adult inpatients.

Method: A consecutive series of 118 inpatients (Mean age = 23.6 yrs, SD = 5.6) were assessed with structured diagnostic interviews for axis I (SCID-P) and axis II personality disorders (PDE). Diagnoses were reliable; kappas for inter-rater reliability ranged from .65 to 1.0. Final research diagnoses were based on the best-estimate method, following the LEAD standard. In order to reduce potential variability in the assessment of personality disorders due to heterogeneity of axis I diagnoses, we re-tested for gender differences in a subgroup of 51 consecutive patients with major depression.

Results: Overall, men were significantly more likely to meet criteria for cluster A, schizotypal, and antisocial personality disorders. Among depressed patients, men were more likely to meet criteria for Cluster A, schizotypal, and Cluster C, personality disorders.

Conclusions: Women were not observed to have a higher frequency of any personality disorder than men in either study group. A greater frequency of Cluster A and schizotypal personality disorders, and, depending on whether depressed or not, Cluster C and antisocial personality disorders, was observed in men.

NR263 Tuesday, May 7, 12 noon-2:00 p.m.

Pregnancy and Opiate Dependence

Corinna Schneider, M.D., Psychiatry, University of Vienna, Wahringer Guertel 18–20, Vienna 1090, Austria; Gabriele Fischer, M.D., Karin Diamant, M.D., Gabriela Forster, M.D., Lukas Pezawas, M.D., Siegfried Kasper, M.D.

Summary:

Methadone treatment has been used as treatment for heroin addiction for over a decade. The combination of illicit drug abuse, drug dependence, and pregnancy presents a major problem, since abusing drugs during pregnancy yields a high risk for the unborn child. Data presented in different studies demonstrate that infants born to addicted mothers are more severely affected by the intrauterine exposure to methadone than to heroin. However, methadone is associated with better prenatal care, improved fetal growth, and reduced fetal mortality. Thirty-four pregnant, opiate-dependent (DSM IV, 304.0; 304.8) women, enrolled through the drug addiction outpatient clinic, were studied over a period of two years. At the first contact females were abusing illicit drugs and the pregnancy averaged 13 weeks. The mean age of the subjects was 27 years, the mean duration of opiate dependence 68 months (range: 18–228 months). Eighteen women were enrolled in a methadone maintenance program, with an average daily methadone dosage of 33 mg at delivery time. Thirteen women have been treated with morphine daily, with an average dosage of 300 mg. The mean birth weight of the 18 infants born to date was 2.807 g; no congenital anomalies appeared.

All newborn children showed an opiate neonatal withdrawal syndrome but more complications were associated with the intrauterine exposure to methadone. The application of morphine should be an alternative in order to reduce the appearance of the withdrawal syndrome in methadone exposed newborns. In addition, pregnant patients in a morphine maintenance program showed less additional consumption of illicit drugs during pregnancy.

NR264 Tuesday, May 7, 12 noon-2:00 p.m.

Type-B Alcoholics Have Poorer Drinking-Related Outcomes with Fluoxetine Treatment

Henry R. Kranzler, M.D., Psychiatry, Univ of CT Health Center, 263 Farmington Avenue, Farmington CT 06030–2103; Joseph A. Burleson, Ph.D., Joseph Brown, Ph.D., Thomas F. Babor, Ph.D.

Summary:

Objective: To test the hypothesis that fluoxetine treatment differentially affects drinking among Type B (i.e., high risk/severity) alcoholics.

Methods: Using a k-means clustering procedure, alcohol-dependent subjects who had participated in a 12-week, placebo-controlled trial of fluoxetine were grouped into low risk/severity (Type A: n = 60) and high risk/severity (Type B: n = 35) groups. MANCOVA was used to examine the effects of alcoholic subtype, medication group, treatment completion, and their interactions on measures of drinking and psychiatric symptoms.

Results: Subjects who completed the treatment trial showed significantly better drinking outcomes and greater reductions in anxiety and depressive symptoms [$F(4, 81) = 6.18$, $p < .001$ and $F(3, 83) = 3.76$, $p = .014$, respectively]. After controlling for the effects of treatment completion, there was also an interaction of alcoholic subtype by medication group [$F(4, 81) = 2.77$, $p = 0.33$], such that among Type B subjects, fluoxetine treatment resulted in poorer drinking-related outcomes. This was particularly evident for GGTP levels, which in Type B subjects were decreased by an average of 28.1 U with placebo treatment and 12.9 U with fluoxetine treatment.

Conclusions: Fluoxetine may interact with serotonergic abnormalities in Type B alcoholics, thereby limiting the beneficial effects of relapse prevention psychotherapy.

NR265 Tuesday, May 7, 12 noon-2:00 p.m.

Targeted Naltrexone in Combination with Coping Skills Training in Early Problem Drinkers

Henry R. Kranzler, M.D., Psychiatry, Univ of CT Health Center, 263 Farmington Avenue, Farmington CT 06030–2103; Howard Tennen, Ph.D., Christopher Penta, M.A., Michael J. Bohn, M.D.

Summary:

Objective: To evaluate the potential utility of targeted (i.e., intermittently administered) naltrexone in the context of coping skills training to treat early problem drinkers.

Methods: Twenty-one subjects (52% male; 52% with mild alcohol dependence, 33% with alcohol abuse, and 15% heavy drinkers) received brief coping skills training weekly during the four-week treatment period. Subjects also received naltrexone 50 mg, to use two to five times per week in anticipation of high-risk drinking situations.

Results: Two subjects discontinued medication treatment due to adverse effects. During the month prior to treatment, subjects drank an average (± SD) of 5.0 (± 2.5) standard drinks on 22.6

(± 8.3) days. During treatment this declined to 2.5 (± 1.9) drinks on 10.0 (± 8.7) days. In addition, ASI alcohol severity scores declined from 0.58 (0.72) to 0.22 (0.20). Paired t-tests were significant ($p < .001$) for all three alcohol-related measures.

Conclusions: Low-intensity treatment with targeted naltrexone and brief counseling may be useful for treatment of early problem drinkers, many of whom are seen in the primary care medical setting.

NR266 Tuesday, May 7, 12 noon-2:00 p.m.

Cardiovascular Interactions of Cocaine with Antidepressants

Richard A. Nelson, M.D., NIH, PO Box 5180, Baltimore MD 21224; David A. Gorelick, M.D., Gilberto Carmona, M.S., Robert Keenan, M.D., Lino Covi, M.D.

Summary:

Objective: To retrospectively evaluate subacute cardiovascular interactions of cocaine with fluoxetine and desipramine.

Method: Heart rate (HR), blood pressure (BP), and urine toxicology data were collected from charts of 91 physically healthy, cocaine-dependent (DSM-III-R) outpatients in double-blind, placebo-controlled clinical trials of fluoxetine (20, 40, or 60 mg daily) or desipramine (up to 300 mg daily) for treatment of cocaine dependence. Urine samples had been tested for benzoylecgonine with a radio-immunoassay that detected cocaine use within the prior two to three days.

Results: The 55 subjects with cocaine-positive urine tests at trial entry had significantly higher diastolic BP (6.5 mm Hg) and mean arterial pressure (6.3 mm Hg) than the 36 subjects with cocaine-negative urine tests. Among the 47 subjects who took medication for at least two weeks and had medication blood levels indicating good compliance, there were no significant differences in HR or BP between pairs of clinic visits (no more than two weeks apart) with cocaine-positive and cocaine-negative urine tests.

Conclusions: Fluoxetine and desipramine, at usual doses, do not accentuate the subacute HR and BP of cocaine use in physically healthy outpatients.

NR267 Tuesday, May 7, 12 noon-2:00 p.m.

Safety of Depakote in Bipolar Patients with Comorbid Alcohol Abuse/Dependence

Susan C. Sonne, Ph.D., Psychiatry, Med University of SC, 171 Ashley Avenue, Charleston SC 29425–0742; Kathleen T. Brady, M.D.

Summary:

Depakote, or divalproex sodium (DVPX), was recently approved by the FDA for the treatment of acute manic episodes associated with bipolar disorder. Because a large number of bipolar patients abuse alcohol and other drugs, the safety of Depakote in bipolar patients with comorbid alcohol dependence has been an issue.

Objective/Method: In order to evaluate the effect of DVPX on liver function and other lab tests in bipolar patients with comorbid alcohol abuse or dependence, the charts of 20 patients were reviewed. All patients had baseline labs and at least one set of follow-up labs for comparison.

Results: Patients were followed for an average of five months, with an average DVPX dose of 1562.5 mg/day. There was no statistical difference in AST, GGT, LD, ALT, or total bilirubin. There was a statistically significant decrease ($p < 0.001$) in platelet count from an average of 286.6 K/CUMM at baseline to 229.5 K/CUMM at follow-up. This finding is of questionable clinical significance as none of the platelet counts decreased below the normal range of 140–440 K/CUMM.

Conclusion: While limited by the small sample size, this study provides preliminary evidence for the safety of DVPX in the acute treatment of bipolar episodes complicated by alcohol abuse/dependence.

NR268 Tuesday, May 7, 12 noon-2:00 p.m.

Eriksonian Stages of Psychosocial Development, Defense Styles and Mood States in Alcoholics: Repeated Measures

Paul W. Ragan, M.D., NIAAA/LCS, Bldg 10 Rm 3B19, 10 Center Drive MSC 1250, Bethesda MD 20892; Linda Doty, R.N., Nancy E. Harnett, Ph.D., Dell Wright, B.S.N., Sandy Birdsong, B.S.N., Chris Geyer, R.N.

Summary:

We found in a group of 34 alcoholics at the time of admission for treatment that they demonstrated greater immaturity on measures of psychosocial development and ego defenses. Concurrent mood states associated with alcohol withdrawal could influence response to these measures; therefore, depression and anxiety symptoms were measured in the alcoholics at admission and at weekly intervals for three weeks. The MEPSI, MPD, DMI, and the DSQ also obtained within 72 hours of admission were readministered three weeks later. Over the three weeks of the study, there was a significant drop in the Beck Depression Inventory (from 15 ± 8 to 5 ± 7), Hamilton Rating Scale for Depression (from 17 ± 10 to 8 ± 7), State Anxiety Inventory (from 47 ± 14 to 38 ± 13), and the Trait Anxiety Inventory (from 47 ± 11 to 39 ± 11), all with $p < .001$. Over the same time period, there were *no* significant differences in the repeated measures of any of the subscales of the MEPSI, MPD, DMI, or DSQ. There were small improvements at the trend level in the trust subscale of the MEPSI ($p = .1$) and in the projection subscale of the DMI ($p = .09$). These findings strongly suggest that the measures of psychosocial maturation and ego defensive functioning in alcoholics are more likely to reflect traits stable over the course of this study and are not due to acute state changes. How these measure in alcoholics relate to later relapse await further study.

NR269 Tuesday, May 7, 12 noon-2:00 p.m.

A Study on Ego Defense Mechanisms of Alcohol Abuse Patients by Ewha Defense Mechanism Test in Korea

Kun Hoo Rhee, M.D., Neuropsychiatry, EWHA Womans Hospital, 70 Chongro 6-KA, Seoul 110, Korea

Summary:

Objective: This study was designed to evaluate the ego defense mechanisms of alcohol abuse patients by Ewha Defense Mechanism Test (EDMT) in Korea.

Method: Subjects consisted of 172 patients meeting DSM-IV criteria for alcohol abuse and 206 comparison subjects without a history of alcohol abuse matched on sex, age, and education level. The ego defense mechanisms were evaluated by EDMT, which consisted of 20 scales.

Results: The scores of the supression, rationalization, dissociation, acting out, and avoidance scales were significantly higher for the alcohol abuse group than the comparison group, whereas the sublimation scale was significantly higher for the comparison group than the alcohol abuse group. Twenty scales of EDMT were divided into four factors by factor analysis. Acting out and dissociation scales were loaded as a first factor (an unstable factor). Supression, rationalization, and avoidance scales were loaded as a fourth factor (a behavior-inhibited factor). Sublimation scale was a second, ego-expansive factor. The score of the behavior-inhibited factor was significantly higher for the alcohol abuse

group than the comparison group. The behavior-inhibited factor was significantly correlated with the frequency of drinking, age of drinking onset, and habitual drinking age, as well as the unstable factor.

Conclusion: The results suggest that the drinking behaviors are correlated with the behavior-inhibited and the unstable type of defenses.

NR270 Tuesday, May 7, 12 noon-2:00 p.m.

Psychosocial and Pharmacological Treatments for Cocaine Abuse: A Review of Empirical Research

Joy M. Schmitz, Psychiatry, University of Texas, 1300 Moursund, Houston TX 77030; Patrick Bordnick, Ph.D., Bruce Thyer, Ph.D., Donald M. Dougherty, Ph.D.

Summary:

Objective: The primary purpose of this paper was to provide a comprehensive empirical review of the treatments for cocaine dependence. Recommendations regarding treatment efficacy will be presented to provide clinicians with information to make more informed treatment decisions.

Method: This review encompassed current theories and approaches used to treat cocaine dependence, and critically examined current treatment outcomes research on both pharmacological and psychosocial interventions. Studies were selected based on scientific merit and demonstrated efficacy.

Results: Currently, an effective intervention has not been developed. However, some pharmacological and behavioral interventions have demonstrated limited efficacy for cocaine dependence. Behavioral treatment approaches which utilize contingent reinforcement and skills training appear to produce the most efficacious outcomes. Strong empirical evidence supporting the use of pharmacological agents to treat cocaine dependence is lacking, and no medication has been proven to be efficacious at this time.

Conclusions: Of the alternatives currently available, behavioral interventions appear to be the best choice for the treatment of cocaine dependence. Recommendations for future outcome research include the need for controlled trials, so that more definitive conclusions regarding treatment efficacy can be reached.

NR271 Tuesday, May 7, 12 noon-2:00 p.m.

A Comparison of Three Months Versus Six Months of Outpatient Alcohol and Drug Treatment

Sheku G. Kamara, Ph.D., The Washington Institute, University of Washington, 9601 Steilacoom Blvd. SW, Tacoma WA 98498

Summary:

Objective: Alcohol and drug patients were randomized into two groups, one receiving three months and the other six months of outpatient treatment, to determine if there were differences in outcomes. Most clients in both had received prior 30 days of inpatient treatment.

Method: Patients were contacted after the first 70 days of outpatient treatment; 12 patients refused participation. Consenters were randomized and assigned into control (63 patients) and experimental (90 patients) groups, and interviewed at discharge, and three and six months later. A gratuity of $10.00 was offered after a completed phone interview. Data were analyzed using chi-square, t-test, and logistic regression techniques.

Results: Drop-out rates were lower for controls than for experimentals. Follow-up attrition rates were lower for experimentals than for controls. There were no major differences between the two groups in the numbers employed, subsequently using drugs, or having legal or medical problems. However, experimentals had better outcomes with respect to problems at work, arrests, visits to doctors' office, months worked, being a homemaker, treatment re-entry, and living arrangement.

Conclusion: Regardless of group distinction, longer treatment was associated with desirable outcome.

NR272 Tuesday, May 7, 12 noon-2:00 p.m.

Gamma Hydroxybutyric Acid for Detoxification Treatment of Opiate-Dependent Patients

Gabriele Fischer, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna 1090, Austria; Corinna Schneider, M.D., Karin Diamant, M.D., Richard Frey, M.D., Angela Heiden, M.D., Siegfried Kasper, M.D.

Summary:

The quality of opiate detoxification treatment is still unsatisfactory. Detoxification treatment with neuroleptics or α-adrenergic drugs could not be well established due to major side effects and inefficacy. The treatment based on a daily reduction with methadone yields to good compliance during the withdrawal treatment because there are no major side effects, but the mean duration of staying on an inpatient basis is more than three weeks. Gamma nydroxybutyric acid (GHB) has been demonstrated to suppress ethanol withdrawal symptoms in rats and humans. Interesting data have been reported about GHB-mechanism of action. The variety of studies suggests for GHB GABA-like activity, dopamine release, increased dopamine concentration in the brain or serotonin stimulating action. We investigated ten opiate dependent patients (DSM IV: 304.0) applying GHB orally on an inpatient basis. Drug history was evaluated by Europe Addiction Severity Index (ASI), withdrawal rating scale WANG has been applied frequently. Blood pressure and heart rates were monitored during detoxification treatment. First, GHB was applied every four hours (Somsanit®). Initially, we administered a dose of 150 mg per kg per day, which showed efficacy, but the successful suppression of withdrawal syndromes lasted only up to two hours after application of GHB. We increased the dosage to a maximum of 100 mg per kg per single dosage, changed the scheme, and applied it orally every two hours. Using this dosage of GHB, no major withdrawal syndromes were noticed during the detoxification treatment period. Urine samples were negative for opiates on day 5. No additional medication has been necessary, with exception of oxacepam for the treatment of sleep disturbances. GHB was discontinued on day 8 without reoccurance of any symptoms; patients were discharged on day 10. GHB appears to be a useful approach for opiate detoxification.

NR273 Tuesday, May 7, 12 noon-2:00 p.m.

Methylphenidate Treatment of Cocaine-Abusing Adults with ADHD

Frances R. Levin, M.D., Psychiatry, Columbia University, 722 West 168th Street, Unit 66, New York NY 10032; Suzette M. Evans, Ph.D., Helga Yuan, B.A., Madeline Rhum, M.A., Nicole D. Regent, B.A., Herbert D. Kleber, M.D.

Summary:

Clinicians have hypothesized that some individuals with adult ADHD symptoms might be self-medicating their distressing symptoms with psycho-active substances, including cocaine. The purpose of this single-blind pilot study was to evaluate the efficacy of methylphenidate (MPH) in reducing cocaine abuse among adults with persistent ADHD symptoms. To date, five subjects have been evaluated. Using the SCID for DSM-IV, a SCID-like module for adult ADHD symptoms, and an ADHD symptom checklist, individuals with cocaine abuse/dependence and adult ADHD were admitted into the study. Using a titrated dosing schedule, subjects were maintained on divided daily doses of sustained-

release MPH, ranging from 60 to 80 mg/day. MPH blood levels for the group averaged 8.77 ng/ml. Subjects were also offered weekly relapse prevention psychotherapy. Comparing the first three weeks of evaluation to the last three weeks of treatment, ADHD symptom scores dropped 57%, overall global severity of symptoms decreased 11%, and cocaine craving declined 66%. On average, subjects attained 50 continuous days of cocaine abstinence based on urine toxicology results. These results suggest that MPH improves ADHD symptoms and decreases cocaine use. However, further research with a double-blind study of a larger sample is warranted.

NR274 Tuesday, May 7, 12 noon-2:00 p.m.

Characteristic Features of Responders to Acupuncture Detoxification for Acute Heroin Withdrawal Symptoms

Joselito B. Domingo, M.D., Psychiatry, East Orange VA, Tremont Avenue, East Orange NJ 07019; Cheng-Jen Chen, M.D.,

Summary:

Objective: This presentation will demonstrate that acute withdrawal symptoms in certain heroin addicts can be relieved immediately and persistently by one or two acupuncture treatments.

Method: 31 heroin addicts in a VA psychiatric inpatient unit were treated with one or two sessions of both body and ear acupuncture during the entire course of detoxification. Withdrawal symptoms were recorded with a symptom checklist both before and after treatment, and also on the second and third day after treatment.

Results: The total success rate was 52%. These successfully treated patients were characterized by a shorter history of heroin abuse, a smaller average daily dose, and a smaller last dosage. Among the patients who used no more than five bags/day, 90% had an immediate response, and 71% had persistent symptom relief. In contrast, when patients used more than five bags/day of heroin, only 50% had immediate responses and 12.5% had persistent symptom relief.

Conclusion: This special type of acupuncture detoxification can achieve immediate and persistent relief of acute heroin withdrawal symptoms with only one or two treatments, especially in patients who use no more than five bags/day of heroin.

NR275 Tuesday, May 7, 12 noon-2:00 p.m.

EEG Signs of Cocaine Dependence

Ronald I. Herning, Ph.D., Clinical Neuropsychiatry, NIH, PO Box 5180, Baltimore MD, 21224; David A. Gorelick, M.D., Xiaoyan Guo, M.D., Linda L. Weinhold, Ph.D., Jean L. Cadet, M.D.,

Summary:

Objective: To evaluate EEG patterns associated with chronic cocaine use and withdrawal.

Method: Resting, eyes closed EEG at eight scalp sites was recorded from 33 medication-free, cocaine-dependent (DSM-IIIR) men (22 also nicotine-dependent) after 7.1 ± 4.6 days of monitored abstinence on a closed research ward, from 17 drug-free, non-cocaine-dependent drug abusers (12 marijuana, 5 opiates) also housed on the research ward, and from 10 medication-free, non-substance-abusing controls tested as outpatients. Mean percent EEG activity was calculated using a modified zero cross technique for four frequency bands: delta (1.3–3.5 Hz), theta (3.6–7.5 Hz), alpha (7.6–13.5 Hz), and beta (13.6–50.0 Hz). The association between EEG activity and cocaine use characteristics was evaluated with principal components analysis.

Results: The cocaine-dependent group had significantly greater beta activity, especially in frontal areas, than the other two groups. Increased beta activity was positively correlated with longer duration of substance use and greater recent cocaine use.

Conclusions: Cocaine-dependent men have increased EEG beta activity, which may be a neurophysiological marker of cocaine dependence.

NR276 Tuesday, May 7, 12 noon-2:00 p.m.

EEG and Evoked Potentials in Chronic Cocaine Abuse

John J. Straumanis, Jr., M.D., Psychiatry, Tulane Med Ctr Psych, 1430 Tulane Ave-SL23, New Orleans LA 70112–2699

Summary:

Quantitative EEG (QEEG) and cerebral evoked potentials (EP's) were recorded in 24 chronic (mdn. 8 years) cocaine preferring substance abusers. The EP's were: 1) auditory and visual P300, 2) auditory P50 recovery.

The main QEEG findings in the chronic cocaine users were: 1) increased posterior absolute alpha and beta power, 2) decreased relative theta power, 3) increased frontal delta power, 4) increased central interhemispheric coherence.

Both auditory and visual P300 amplitudes were lower in cocaine users; there were no significant latency differences. The cocaine users had a more posterior distribution of both auditory and visual P300.

With the auditory P50 recovery paradigm, the cocaine users showed an average of 33% suppression of S2 versus S1, compared to about 80% suppression in normals.

The increased alpha power replicates findings of Alper and Lukas with chronic and acute cocaine intoxication. The significantly increased frontal delta power could be due to functional hypoactivity or structural damage of the frontal cortex with chronic cocaine use. The lower auditory and visual P300 amplitudes might reflect impaired cognitive function. The P50 recovery findings, similar to schizophrenia, suggest impaired signal gating/processing with chronic cocaine use.

NR277 Tuesday, May 7, 12 noon-2:00 p.m.

Medication Adherence in Bipolar Substance Abusers

Roger D. Weiss, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178–1048; Shelly F. Greenfield, M.D., Cathryn Hufford, B.A., Lisa M. Najavits, Ph.D., Mauricio Tohen, M.D., Jose Martinez-Raga, M.D., Jose Soto, B.A.

Summary:

Although many patients with bipolar disorder have a coexisting substance use disorder, little is known about this subgroup of dually diagnosed patients. Therefore, as part of a project to develop a relapse prevention group therapy for patients with current bipolar disorder and substance use disorder, we followed a control group of 18 such patients receiving "treatment as usual." As one aspect of this study, we asked patients and their prescribing psychiatrists monthly for six months about their adherence to their medication regimens. Fifty-four of the 82 patient self-reports (66%) indicated medication adherence "at least two-thirds of the time," while the psychiatrists reported a similar level of adherence only 41% of the time; there was little monthly variation in either group of reports. Since there were some months in which either patient or psychiatrist reports were missing, we examined all 48 instances in which we had both patient and psychiatrist reports; patients were significantly more likely to report high (more than two-thirds of the time) adherence than were their psychiatrists (79% vs. 42%, $p = .02$). Our main findings were that (a) medication adherence among bipolar substance abusers was relatively consistent, and (b) patients were significantly more likely than their psychiatrists to report high adherence.

NR278 Tuesday, May 7, 12 noon-2:00 p.m.

Distribution of Substance-Abusing Inpatients Along a Stages-of-Behavioral Change Continuum

Eve J. Wiseman, M.D., Psychiatry, John L. McClellan VA, 4300 West Seventh Slot 116E, Little Rock AR 72205; Margaret J. Briggs, L.P.N.

Summary:

Objective: The objective of this study was to determine how substance-abusing inpatients were distributed along a stages-of-change (SOC) continuum for condom use.

Methodology: As part of a facility-based HIV/AIDS education demonstration project funded by the VA, 100 consecutively admitted inpatients from a substance abuse rehabilitation program consented to an SOC risk assessment.

Results: Patients were less likely to report always using condoms with a partner they considered their primary sex partner (9%) than to report always using condoms with other partners (26%); similarly, they were more likely to report never using condoms with their primary partner (54%) than to report never using condoms with other partners (38%). More than two-thirds (68%) of patients with primary partners were in the precontemplative SOC about always using condoms; i.e., they never or almost never used condoms and reported no intention to always use condoms. Of those patients with partners not considered to be their primary partner, 38% were in the precontemplative SOC about always using condoms.

Conclusions: Because many substance-abusing patients are in the precontemplative SOC, interventions targeted to this stage may produce changes in condom-use intentions and behavior.

NR279 Tuesday, May 7, 12 noon-2:00 p.m.

Behaviorally Contingent Pharmacotherapy for Opioid Abusers: An Outpatient Randomized Clinical Trial

Van L. King, Jr., M.D., Psychiatry, Johns Hopkins - Bay VW, 5510 Nathan Schock Dr #1500-G1, Baltimore MD 21224; Robert K. Brooner, Ph.D., Michael Kidorf, Ph.D.

Summary:

Objective: This clinical trial evaluated the effectiveness of a treatment model, Behaviorally Contingent Pharmacotherapy, that makes continued pharmacological treatment (i.e., methadone) contingent on compliance with psychosocial treatment (i.e., counseling and medical care).

Method: Data are available for 73 patients in methadone substitution therapy stratified on baseline cocaine use and antisocial personality disorder and randomly assigned to the control (N = 38) or experimental (N = 35) group. Demographics and mean methadone dose were comparable between groups. Patients in both groups who continued to use drugs or missed counseling sessions were referred for increased intensity of weekly counseling. Experimental group patients were informed that continuation of methadone substitution was contingent on attending all weekly counseling (routine clinic treatment). Patients in the control group were informed that continuation of methadone substitution was independent of their compliance with the weekly counseling.

Results: Outcome data were available for the first 90 days of study participation. Weekly counseling compliance was significantly higher in the experimental vs. control group (85% vs. 35%, $p < .001$). Patients in the experimental group also had significantly fewer urines positive for drugs of abuse (43% vs. 67%, $p = .002$).

Conclusion: These results support using Behaviorally Contingent Pharmacotherapy in opioid substitution programs.

NR280 Tuesday, May 7, 12 noon-2:00 p.m.

Serum Cholesterol and Impulsive Aggressive Behavior in Personality Disorder Patients

Carol F. Zale, M.D., Psychiatry, Mt. Sinai Med Ctr, One Gustave Levy Place, New York NY 10029; Antonia S. New, M.D., Robert L. Trestman, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Summary:

Background: Low or reduced serum cholesterol has been associated with impulsive and aggressive behaviors. Diminished central serotonergic activity, as reflected by prolactin response to fenfluramine, has been associated with impulsive aggression in patients with personality disorders (Coccaro et al., 1989). The present study explores the relationship between serum cholesterol and measures of impulsive and aggressive behaviors in patients with personality disorders.

Method: Seventy-two personality-disorder patients with or without borderline personality disorder (BPD-DSM III), (39 males, age 44.1 ± 12.3:9BPD, 30OPD and 33 females, age 38.6 ± 12.7; 13BPD, 20OPD) were examined for evidence of irritability and aggression by self-report as measured by the Buss-Durkee Hostility Inventory (BDHI), for evidence of impulsivity by self-report as measured by the Barratt Impulsivity Scale. Central serotonergic activity was measured by the prolactin response to fenfluramine challenge. Serum cholesterol was measured as part of initial medical screening and was measured by standard enzymatic assay.

Results: There was a positive correlation between serum cholesterol levels and age ($r = .33$, $p < .01$). Therefore, all analyses were performed controlling for age. An ANCOVA was performed with factors gender and borderline diagnosis with age as a covariate was performed. There was a significant effect for diagnosis with borderline patients having lower cholesterol levels (174.9 ± 34.1) than non-borderline patients (209.7 ± 40.9; $F[1, 67] = 6.03$, $p < .02$). Female patients also demonstrated reduced cholesterol levels (183.4 ± 38.3) compared to male patients (212.3 ± 40.7; $F[1, 67] = 3.98$, $p < .05$). There was no significant interaction effect between gender and diagnosis. Controlling for age there was no statistically significant correlation between cholesterol levels and prolactin response to fenfluramine ($r = -.23$, $n = 36$, $p = ns$) and measures of impulsivity as measured by the BDHI; however, for women there was an inverse correlation between cholesterol and the Barratt impulsivity scale ($r = -.43$, $n = 33$, $p < .05$), for men the correlation was positive not for the total score but for the motor subscale of the Barratt ($r = .41$, $n = 39$, $p < .04$).

Conclusions: This study provides preliminary evidence that in a subpopulation of personality disordered patients with borderline personality disorder, serum cholesterol may be lower than in normals. There is no evidence to support a relationship between low serum cholesterol and aggression or impulsivity in this personality disordered population, nor is there evidence to support an association between low serum cholesterol and reduced central serotonin activity as measured by prolactin.

NR281 Tuesday, May 7, 12 noon-2:00 p.m.

Validity of DSM-III-R Personality Disorders in Adolescents: Results From Follow-Up Two Years After Hospitalization

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:

Objective: To examine the validity of the DSM-III-R personality disorder constructs in late adolescents via follow-up of inpatients treated at the Yale Psychiatric Institute. Baseline admission evalu-

cultural roles. Together these factors may account for a special vulnerability to traumatic stress conferred by young adulthood.

NR296 Tuesday, May 7, 12 noon-2:00 p.m.

Trauma, PTSD and Axis II Disorders in Addicts: Patterns of Comorbidity

Elisa G. Triffleman, M.D., CTU, Yale Univ. Sch. of Med., 914 1/2 Howard Avenue, New Haven CT 06519

Summary:

Trauma exposure, PTSD, and personality disorders are common among substance dependent patients. Few studies, however, have examined the frequencies of personality disorders among those with PTSD, nor have civilian, mixed gender, treatment-seeking addicts been the primary focus of study. This paper presents the findings of a multi-site study of these issues.

Methods: 371 addicts were interviewed with the SCID I, II and PTSD module, and measures of civilian trauma. The SCID II was double-coded for symptoms and diagnoses presenting when sober versus only during drug use, and for DSM-III-R and DSM-IV criteria.

Results: 95% of subjects were trauma exposed. Median first age of exposure was at 9 yo. Mean total types of traumatic exposures were 4.3 ± 2.6 (range: 0–11). A total of 20% (n = 74) had lifetime PTSD (L-PTSD); 8% had current PTSD. 46% had at least one personality disorder. Total types of traumatic exposures were associated with first age of traumatic exposure (rho = -0.55, $p < .0001$), several Cluster B and C disorders, and with total number of personality disorders. L-PTSD was associated with borderline personality disorder regardless of diagnostic system, and with drug-related DSM-III-R and DSM-IV conduct disorder, but not with antisocial personality disorder. No association was observed between specific Axis II disorders and primary drug of choice.

Conclusions: Trauma exposure and Axis II disorders occur with high frequency in this population. PTSD is associated with more specific patterns of comorbidity, in contrast to trauma exposure in general. Associations of PTSD and substance dependence will also be presented.

NR297 Tuesday, May 7, 12 noon-2:00 p.m.

Childhood Abuse and Subsequent Axes I-II Disorders

Lynn A. Lyons, M.S., Psychiatry, Yale University, CMHC 34 Park Street, New Haven CT 06519; Heather Z. Lyons, Carolyn M. Mazure, Ph.D., Bruce E. Wexler, M.D.,

Summary:

Physical and/or sexual abuse during childhood is a traumatic event. If development of some but not other Axis I and Axis II disorders is influenced by such events, then the incidence of these disorders should be different among patients who have been abused than among patients who have not. We tested this hypothesis in a large sample (n = 967) of outpatients in an urban mental health center. Clinicians very familiar with the patients, and often in long established treatment relationships, provided developmental histories as well as clinical diagnoses. Men and women with histories of abuse were more likely to have diagnoses of major depressive disorder and less likely to have diagnoses of schizophrenia ($p < .0001$), and more likely to have Cluster B personality disorders and less likely to have Cluster A or C disorders ($p = .005$) than were individuals without childhood abuse. Gender-specific effects were evident in the greater impact of childhood abuse on women than men in the incidence of alcohol or substance abuse ($p < .001$), suicidal behavior ($p < .001$), and poor heterosexual relations ($p < .001$). The assumption that the study sample is representative of psychiatric patients in general is supported by the greater incidence in the sample of abuse in women than men (33% vs. 21%), the greater incidence of depression than of schizophrenia in women (1.8:1), and the greater incidence of schizophrenia than of depression in men (2.2:1). These results indicate that childhood abuse is associated with the development of major depressive disorder, Cluster B personality disorders, and substance abuse in women, but not in the development of schizophrenia, other personality disorders, or substance abuse in men.

NR298 Tuesday, May 7, 12 noon-2:00 p.m.

Adult Serotonergic Correlates of Childhood Abuse in Male Alcoholics and Cocaine Addicts

Leonard Handelsman, M.D., Psychiatry, Mt. Sinai School of Med, One Gustave Levy Place, New York NY 10029; David P. Bernstein, Ph.D., Paul Rinaldi, Ph.D., Stevan Gabriel, Ph.D., Karen Holloway, M.D., Christopher Sturiano, A.B.,

Summary:

A history of childhood abuse is a common feature in substance abusers; however, little is known about the biological correlates of maltreatment. Using a valid and reliable self-report instrument to assess the magnitude of several types of childhood trauma, we examined the correlations of child abuse and neglect with markers of CNS serotonin activity: prolactin, cortisol, and temperature responses to meta-chlorophenylpiperazine (MCPP) challenge in adult alcoholics (n = 11) and adult cocaine addicts (n = 12) after two weeks abstinence. In adult alcoholics, childhood physical abuse was correlated inversely with cortisol response to MCPP (partial $r = -.52$, $p < .04$); but in cocaine addicts, positively correlated with cortisol (partial $r = .47$, $p < .07$) and prolactin (partial $r = .49$, $p < .05$) responses. In contrast to physical abuse, sexual abuse and cortisol response were correlated positively in alcoholics (partial $r = .90$, $p < .01$), but inversely in cocaine addicts (partial $r = -.75$, $p < .01$). Previously, we reported similar patterns of correlation between adult trait hostility and prolactin responses in the respective groups. Although these findings are clearly preliminary, they raise the possibility that childhood maltreatment may modify serotonin activity in adulthood in alcoholics and cocaine addicts.

NR299 Tuesday, May 7, 12 noon-2:00 p.m.

An Examination of Clinical and Personality Characteristics Among Couples with a History of Less Violent Abusive Interaction in a Military Population

Charles D. Magruder, M.D., Clinical Serv, DoD HA, 2009 Alabaster Drive, Silver Spring MD 20904; Roslyn Tartaglione, M.A., Gary Southwell, Ph.D., Robert Mays, Ph.D.,

Summary:

Objective: A number of Axis I and Axis II disorders have been associated with perpetrators and victims of violent physical abuse. This study determines the extent to which psychopathology and certain personality traits are present in couples involved in other types of abusive situations.

Methods: Couples in substantiated, abusive relationships, as defined by military protocols, were asked to participate. All cases were categorized as emotional or mild, physical abuse. Each partner completed the Millon Clinical Multiaxial Inventory III (MCMI-III), which renders personality patterns and clinical syndromes.

Results: 25 couples, approximately 20% of those eligible, agreed to participate. Of these, all completed the MCMI-III. All situations involved male abuse of the female. Only one severe syndrome, a delusional disorder, was found among men. Among women, three had a delusional disorder and 20% were diagnosed with major depression. Anxiety disorder was the most common clinical syndrome found in both partners (24%). Depressive and

self-defeating personality patterns were found more frequently among women (28% vs. 8% and 20% vs. 0%).

Conclusions: Depressive characteristics and disorders were not uncommon in this population, particularly among women. It is likely more psychopathology would be found in couples who chose not to participate. More extensive mental health evaluations should be considered for couples found in abusive relationships.

NR300 Tuesday, May 7, 12 noon-2:00 p.m.

Characteristics of Childhood Sexual Abuse and Adult Psychopathology

Jill Pettigrew, F.R.A., 84 Queen Street, Berry 2535, Australia; Joyce Burcham, Ph.D.,

Summary:

Objective: This study investigated the relationship of characteristics of childhood sexual abuse and subsequent psychopathology.

Method: Referrals to a female psychiatrist in private practice in an urban working class area provided 73 adult female subjects who reported having been sexually abused in childhood. Data were collected on age at onset, duration, physical invasiveness of the abuse, violence, and the number and relationship of abusers.

Results: Having had multiple abusers in childhood was significantly ($p < 0.01$) associated with every outcome measure of severe psychopathology: an initial Global Assessment Functioning score of 50 or below; both single and repeated incidents of deliberate self-harm; overdose; self-mutilation; and psychiatric hospital admission. Notably, multiple abusers was the only characteristic showing a reliable independent association with any of these measures.

Conclusions: The characteristic of childhood sexual abuse with the most effect on subsequent psychopathology in adulthood is multiple abusers.

NR301 Tuesday, May 7, 12 noon-2:00 p.m.

A Longitudinal Study of Clinical Outcome Indicators and Rating Scales in Chronic State Hospital Inpatients

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 purpose of this paper is to report the results of a longitudinal study of a chronic state hospital unit, with average census 42 (60% female), age 46, and length of stay 15 years. Diagnoses include uncomplicated psychosis (54%) and other or mixed diagnoses (46%).

Method: Over a 41-month period, clinical indicators, including episodes of agitation, violence, prn medications and seclusions, and serial ratings with the MMSE, BPRS, and GAF were collected and analyzed longitudinally using correlation coefficients and the paired t-test.

Results: Episodes of seclusion decreased significantly for all patients (0.50/pt/mo. vs. 0.06/pt/mo., $p = 0.038$) while violence rates showed a significant decline only for patients with uncomplicated psychosis (1.01/pt/mo. vs. 0.19/pt/mo., $p = 0.009$). Agitation and prn medication rates showed no change, although the minimum monthly values for uncomplicated psychotic patients declined significantly ($p < 0.001$ and $p = 0.022$, respectively). Insignificant improvement was found in GAF (mean 21.3 vs. 21.7) and MMSE (mean 20.8 vs. 21.9) scores. No significant correlation was found between test scores and clinical outcome measures.

Conclusion: Clinical outcome measures showed improvement, more pronounced for patients with uncomplicated psychosis. We found no correlation over time between test scores and clinical indicators. However, longer longitudinal studies in this area are warranted.

NR302 Tuesday, May 7, 12 noon-2:00 p.m.

PTSD in Spanish Policeman

Inmaculada Gilaberte-Asin, M.D., Medical, Eli Lilly & Co, Avda. Industria N30, Alcobendas 28100, Spain; Enrique Baca, M.D., Asuncion Abril, M.D., Carlos Blanco, M.D., Alfonso Calve, M.D.,

Summary:

We studied the incidence and risk factors for DSM III-R defined PTSD in Spanish policemen. All policemen who experienced a traumatic event during 1990 were studied ($n = 94$). Cattell personality inventory, Paykel life events, severity of traumatic event, and social support questionnaires were used. Sociodemographic data, personal and family history were obtained. Two groups were defined depending on whether they met DSM III-R diagnosis for PTSD. Chi square, t-tests analysis were used to compare the characteristics of the two groups, and logistic regression was used to assess the risk factors. Thirty-one (32.98%) of the 94 policemen met criteria for PTSD. This represents 6% of the Spanish police force. Feelings of death during the event (OR = 22.3), increase in family conflicts (OR = 6.6), and change in work conditions (OR = 5.4) appeared as risk factors after controlling for personality traits and characteristics of the events. Social support (OR = 75.8) appeared to be a protective factor for this population. Exposure to traumatic events is associated with a high incidence of PTSD in Spanish policemen. Feelings of death during the event constitute the main risk factor for development of PTSD, whereas presence of good social support can act as a protective factor.

NR303 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Psychiatric Comorbidity of Atypical Depression

Isabel Lagomosino, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street ACC 815, Boston MA 02114

Summary:

Objective: To assess whether major depressive disorder with atypical features presents with a psychiatric comorbidity profile that is distinct from that of major depression without such features.

Method: We studied 245 drug-free adult outpatients with major depressive disorder (MDD) participating in a treatment study at the Depression Clinical and Research Program of the Massachusetts General Hospital by administering both the Structured Clinical Interview for DSM-III-R-Patient Edition (SCID-P) and the Structured Clinical Interview for DSM-III-R-Personality Disorders (SCID-II). Patients were classified as either having definite, probable, or no atypical features (including mood reactivity) according to the Atypical Depression Diagnostic Scale. We compared the prevalence of comorbid Axis I and II disorders in patients with and without atypical features, thereby excluding from the analyses those subjects with only probable atypical features.

Results: We found that depressed outpatients with atypical features were significantly ($p = .05$) more likely to meet criteria for bulimia nervosa than nonatypical patients and also showed a trend ($p = .08$) toward a significantly higher rate of social phobia. As far as personality disorder comorbidity was concerned, patients with atypical features were significantly more likely to meet criteria for avoidant and dependent personality disorders than those without such features ($p = .002$ and .008, respectively).

Conclusion: It appears that the presence of atypical features is associated with a distinctive psychiatric comorbidity. In particular, compared with nonatypical depressives, atypical depressives have higher rates of bulimia nervosa and social phobia as well as of avoidant and dependent personality disorders.

NR304 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Contributions of Family Burden and Denial of Illness to Outpatient Service Use in Bipolar Affective Disorder

JoAnne Sirey, Ph.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605

Summary:

Introduction: Research has demonstrated that families of chronic mental patients influence their use of outpatient psychiatric services (Horowitz, 1988), but little is known about how this occurs. We investigated associations between outpatient service use and two potentially influential factors: family insight into the illness and subjective burden regarding the illness.

Methods: Subjects were 286 patients with RDC-diagnosed bipolar affective disorder recruited for study upon admission to a university-based psychiatric hospital and its outpatient clinics. Patients and identified family caregivers were assessed on measures of psychiatric status, family burden, denial of illness, and one month of outpatient service use.

Results: Two-way (denial X burden) ANOVA revealed a significant main effect for denial ($F = 6.79$, $p < .01$), with greater service use for patients with low than with high denial caregivers. Multiple regression analyses within denial groups revealed different predictors of service use: higher BPRS scores ($F = 6.99$, $p < .01$) and female patient gender ($F = 4.66$, $p < .05$) were associated with greater service use for low denial (MultR = .42, Rsq = .17), while frequency of patient-caregiver contact was (positively) associated with frequency of service use for high denial ($F = 6.42$, $p < .05$; MultR = .40. Rsq = .16).

Conclusion: These data suggest that family influences on outpatient service use are greatest for caregivers who are educated about their relatives' illness and who have frequent contact with them.

NR305 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Sociodemographic Predictors of Response to Antidepressant Treatment

Maya Spillmann, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street ACC 815, Boston MA 02114

Summary:

Objective: To assess whether sociodemographic variables such as age, gender, marital status, level of education, and employment status are related to the changes in functioning that have been reported after drug treatment in outpatients with major depressive disorder.

Method: We studied 164 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 Structured Clinical Interview for DSM-III-R-Patient Edition (SCID-P), and patients were required to have a 17-item Hamilton Rating Scale for Depression (HAM-D-17) score ℓ 16 at study entry. All subjects were administered the HAM-D-17 and the Social Adjustment Scale-Self-Report (SAS-SR) before and after treatment with fluoxetine.

Results: We found that SAS-SR scores decreased significantly following treatment with fluoxwtine from a mean score at baseline of 2.6 ± 0.7 to a mean score at endpoint of 2.3 ± 0.6. After adjusting for the degree of change in HAM-D-17 scores, we found a significant relationship between degree of change in SAS-SR and level of education. No statistically significant relationships were observed between SAS-SR change and age, gender, marital status, and employment status.

Conclusion: The degree of improvement in psychosocial functioning observed in depressed outpatients following antidepressant treatment appears to be related to the level of education at study entry, but not to other sociodemographic variables. Further studies need to investigate the nature of this relationship.

NR306 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Differences in Expressed Emotion of Spousal Versus Parental Caregivers in Bipolar Affective Disorder

John F. Clarkin, Ph.D., Psychiatry, New York Hospital-CMC, 21 Bloomingdale Road, White Plains NY 10605

Summary:

Introduction: Research on expressed emotion (EE) has focused on parental caregivers of schizophrenic patients. Because spouses also function as caregivers in bipolar illness, we examined the influence of caregiver relationship to the patient as well as gender on indices of EE in this illness.

Methods: Subjects were family caregivers (63 spouses, 39 parents) for 100 patients with RDC-diagnosed bipolar affective disorder, recruited on admission to a teaching hospital and its outpatient clinics. The Camberwell Family Interview was administered and scored by certified raters.

Results: Parental caregivers scored significantly higher than spousal caregivers on indices of emotional overinvolvement (EOI—$t = 3.64$, $p < .001$) and warmth ($t = 2.33$, $p < .03$), with no significant differences for critical comments (CC). Female caregivers ($N = 64$) also scored higher than males ($N = 36$) on EOI ($t = 3.96$, $p < .001$) and CC ($t = 2.51$, $p < .02$). Additional caregiver attributes were differentially related to EE indices: Caregiver burden was positively associated with CC ($p < .01$), but not significantly associated with EOI or warmth, while caregiver age was positively associated with warmth ($p < .003$) and EOI ($p = .05$), but not CC.

Conclusion: The differences in EE indices obtained may relate to differences in affectional bonds and/or needs of caregivers vis-a-vis clients that are intrinsic to specific gender and/or relationship roles. They also argue for more differentiated family interventions.

NR307 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Determinants of Family Burden in Male Versus Female Caregivers of Persons with Bipolar Affective Disorder

Deborah A. Perlick, Ph.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605

Summary:

Introduction: Prior work (Noh & Avison, 1988) found marked gender effects in factors contributing to subjective burden for caregivers of patients with major mental disorders. We examined predictors of subjective burden for male vs. female caregivers of bipolar disorder patients.

Methods: Subjects were the primary caregivers of 286 patients with RDC-diagnosed bipolar affective disorder, recruited for study upon admission to a psychiatric teaching hospital and its outpatient clinics. Patients and caregivers were assessed on measures of psychiatric status, family burden, and one month of outpatient service use.

Results: Hierarchical multiple regression analyses demonstrated gender-specific contributants to caregiver burden: for males sociodemographic variables including male client gender, black or Hispanic client ethnicity, and being married were associated with increased burden. For women, living in the same household increased the sense of burden, while being the client's parent ameliorated it. For both genders, burden was positively associated with outpatient service use and caregiver insight into the patient's illness. Both equations were significant, accounting for 37% of the variance for men (adjusted Rsq = .25) and 34% of the variance for women (adjusted Rsq = .27).

Conclusions: Male and female caregivers are vulnerable to different aspects of the strains of caregiving and may, therefore, require gender-specific interventions.

NR308 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Outpatient Service Use As a Predictor of Psychiatric Hospitalization in Bipolar Illness

Deborah A. Perlick, Ph.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605

Summary:

Introduction: Few studies of risk factors for rehospitalization in bipolar disorder have considered use of outpatient psychiatric services. We investigated the association between outpatient service use and six-month psychiatric hospitalization in a naturalistic outcome study.

Methods: Subjects were 96 patients with RDC-diagnosed bipolar affective illness recruited for study upon admission to a university-based psychiatric hospital and its outpatient clinics. Patients and identified family caregivers were assessed on measures of psychiatric status, family burden, and outpatient service use over one month and were followed for six months to determine readmission status.

Results: Fifteen patients were hospitalized during the six-month period. Logistic regression analysis employed to evaluate the utility of service use and other variables in predicting hospitalization correctly classified 90% of hospitalized cases (sensitivity = .53; specificity = .96). A greater frequency of outpatient service use and having a married caregiver were negatively associated with hospitalization ($p = .01$), with trends ($p = .08$) for patient gender (females were less likely) and BPRS (higher scorers were more likely). Number of admissions in the past two years, household composition, and caregiver social support and stigma were not significant predictors.

Conclusions: These data suggest that use of outpatient psychiatric services helps prevent rehospitalization in bipolar disorder.

NR309 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Thyroid and Cognitive Therapy for Depression

Russell T. Joffe, M.D., Psychiatry, McMaster University, 1200 Main Street West, Rm3G56, Hamilton ON L8N 3Z5, Canada

Summary:

The treatment of major depression with various somatic antidepressant treatments is associated with significant but limited decreases in thyroid hormone levels, particularly in measures of thyroxine (T4). Cognitive behavior therapy (CBT) has been shown to be effective in the treatment of mild to moderate depression. We therefore investigated whether changes in thyroid hormone levels would occur during a course of cognitive behavior therapy for the treatment of major depression.

Thyroid hormone levels were measured before and after 20 weekly sessions of CBT in 30 outpatients who filled criteria for unipolar nonpsychotic, major depressive disorder. There were significant decreases in measures of thyroxine, with significantly greater decreases in responders than nonresponders to CBT.

It is concluded that cognitive behavior therapy has a similar effect as somatic antidepressant treatment on the thyroid axis when used for the treatment of depression.

NR310 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Degree of Assertiveness in Major Depression

Asha I. Parekh, M.D., Psychiatry, Mass General Hospital, 15 Parkman Street ACC 815, Boston MA 02114

Summary:

Objective: To evaluate whether the degree of assertiveness in depressed outpatients is related to the severity of depressive or anxious symptoms and whether treatment with antidepressants is followed by a significant improvement in assertiveness.

Method: We studied 144 drug-free depressed outpatients participating in a study involving treatment with fluoxetine 20 mg/day for eight weeks. Diagnosis of major depressive disorder was made with the use of the Structured Clinical Interview for DSM-III-R-Patient Edition (SCID-P), and patients were required to have a 17-item Hamilton Rating Scale for Depression (HAM-D-17) score ℓ 16 at entry. All subjects were administered the Rathus Assertiveness Scale (RAS), the Symptom Questionnaire (measuring depression, anxiety, hostility, and somatic symptoms), and the HAM-D-17 before and after fluoxetine treatment.

Results: We found that treatment with fluoxetine was followed by a significant increase ($t = 6.0$; $p < .0001$) in RAS scores among our depressed outpatients. After treatment, RAS scores were significantly related to severity of depression, anxiety, and hostility. However, the degree of change in RAS scores did not correlate significantly with the degree of change in HAM-D-17 scores.

Conclusion: Assertiveness in depressed patients appears to improve significantly following antidepressant treatment and to be related to the severity of anxiety, depression, and hostility. Interestingly, the change in assertiveness with treatment does not seem to be significantly related to the symptomatic improvement of depression.

NR311 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Gabapentin Does Not Alter Lithium Pharmacokinetics

Mark A. Frye, M.D., NIMH, Building 10 Room 3N212, Bethesda MD 20892

Summary:

Adjunctive treatments to lithium carbonate for mood stabilization often include anticonvulsants. Lithium and gabapentin are both exclusively eliminated by renal excretion. Thus, when used in combination, a competitive drug-drug interaction could alter renal excretion. Given the low therapeutic index of lithium carbonate, any such pharmacokinetic interaction may have important clinical implications. We studied single-dose pharmacokinetic profiles of lithium in six patients on placebo and again on steady-state gabapentin. We determined C_{max}, (maximal concentration of lithium), T_{max} (time to reach peak lithium concentration), and AUC (area under the curve, quantitative exposure to lithium).

Both on placebo and steady-state gabapentin (3600 mg per day), each patient received a single oral 600 mg dose of lithium carbonate with subsequent blind plasma lithium level determinations @ 0.5, 1, 2, 3, 4, 8, 12, 24, 48, and 72 hours post ingestion.

On gabapentin, mean C_{max} was 0.67 (+/- 0.12) and did not differ from the placebo mean C_{max} of 0.67 (+/- 0.10). On gabapentin, mean T_{max} was 1.42 hours (+/- 0.66) and did not differ significantly from the placebo mean T_{max} of 1.17 hours (+/- 0.41). On gabapentin, the mean AUC at 8 hours was 3.28 (+/- 0.60) and did not differ significantly from the mean placebo AUC at 8 hours of 3.23 (+/- 0.29).

These data suggest that gabapentin therapy at 3600 mg qd does not cause clinically significant alterations in lithium pharmacokinetics. We are continuing this study to increase statistical power and confirm these preliminary data.

NR312 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Increasing Use of Polypharmacy for Refractory Mood Disorders: Twenty-Five Years of Study

Mark A. Frye, M.D., NIMH, Building 10 Room 3N212, Bethesda MD 20892

Summary:

Patients with mood disorder commonly need multiple medications for adequate symptom control as in done in the management of cancer, epilepsy, congestive heart failure, tuberculosis, and AIDS. A review of 180 patients hospitalized for refractory mood disorders at the NIMH between 1970–1994 was conducted to assess the need for and efficacy of "add on" polypharmacy.

Following monotherapy investigational protocols, sequential combination therapy was used in an "add on" basis to achieve maximal mood stabilization. Each patient's retrospective life chart and prospective double-blind NIMH data were reviewed and degree of improvement at discharge was assessed by a CGI rating. Seventy-eight percent of 180 patients had moderate or marked improvement when compared to their placebo phase of illness. Adjunctive discharge medications to four major treatment groups (lithium, carbamazepine, divalproex, and lithium/divalproex) included: antidepressants (17%), anticonvulsants (19%), calcium channel blockers (5%), and thyroid supplementation (29%). A pattern of increasing number of medications at discharge was observed in successive five-year epochs. That is, monotherapy was sufficient for 82% of patients in 1970–1975, 69% of patients in 1975–1979, 38% of patients in 1980–1984, 29% of patients in 1985–1989, and only 24% of patients in 1990–1994. This increasing polypharmacy over time might be explained by changing referral patterns, birth cohort effect, changes in comorbidity, or pharmacotherapy-induced cycle acceleration.

Further studies, including new clinical trial methodologies, are required to assess the efficacy of combination treatments and thus allow the development of rational polypharmacy for the management of refractory mood disorders.

NR313 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Postpartum Prophylaxis in Women with Histories of Major Depressive Disorders

Lee S. Cohen, M.D., Psychiatry, Mass General Hospital, 15 Parkman St. WACC 815, Boston MA 02114; Laura M. Robertson, B.A., Deborah A. Sichel, M.D., Carol S. Birnbaum, M.D., Lynn R. Grush, M.D., Lisa S. Weinstock, M.D.,

Summary:

Introduction: The postpartum period has typically been described as a period of risk for development of affective disorder. While the benefit of postpartum prophylaxis with mood stabilizers has been described for women suffering from bipolar disorder, the efficacy of prophylactic intervention with antidepressants during the postpartum period in women with unipolar depression has not been adequately investigated.

Methods: This report describes the course of 28 women with histories of major depressive disorder (MDD) who were prospectively followed in a longitudinal study of mood and anxiety disorders during pregnancy and the postpartum period. Patients were assessed using the SCID-P at three-month intervals across pregnancy and the first nine postpartum months. Changes (if any) in pharmacotherapy were also noted. Relapse rates of MDD were compared using Kaplan-Meier survival analysis for women who received prophylactic intervention with antidepressants within the first 24 hours postpartum and women who did not receive prophylaxis in this time period.

Results: Of 28 women in the sample, 64% (N = 18) were euthymic at delivery. Nine of these women were prophylaxed with antidepressant medications during the acute 24 hours postpartum. The remaining nine women did not receive immediate puerperal prophylaxis with antidepressants. Of those women who did receive prophylactic intervention, 78% (n = 7) relapsed in the first three postpartum months. Of the nine women who did not receive prophylaxis, 33% (n = 3) relapsed in the first three postpartum months. Kaplan-Meier survival analysis failed to demonstrate a significant difference between time to relapse in women who did or did not receive prophylactic intervention. Differences in benefit from prophylactic intervention with antidepressants could not be accounted for by differences in lifetime chronicity of major depression, presence of depression during pregnancy, or subsyndromal illness at the third trimester assessment. Findings of greater severity of worst episode of major depression and greater incidence of past double depression in women who received prophylaxis approached significance.

Conclusions: Multiple factors may enhance risk for postpartum worsening of mood. Severity of history of major depression, presence of double depression, and other factors may exceed the prophylactic efficacy of antidepressant use for some patients. The implications of these findings with respect to treatment guidelines for postpartum women are discussed.

NR314 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Impact of Pregnancy on Risk for Relapse of Major Depressive Disorder

Lee S. Cohen, M.D., Psychiatry, Mass General Hospital, 15 Parkman St. WACC 815, Boston MA 02114; Laura M. Robertson, B.A., Deborah A. Sichel, M.D., Carol S. Birnbaum, M.D., Lynn R. Grush, M.D., Lisa S. Weinstock, M.D.,

Summary:

Introduction: While pregnancy has frequently been referred to as a time of emotional well-being, recent studies suggest that depression during pregnancy is not uncommon and that it may be an important risk factor for postpartum depression. The implications of these findings for women with histories of major depressive disorder who plan to conceive and who choose to either stay on maintenance antidepressant treatment or to attempt antidepressant discontinuation are significant.

Methods: This report describes the course of 28 women with histories of major depressive disorder (MDD) who were prospectively followed in a longitudinal study of mood and anxiety disorders during pregnancy and the postpartum period. Using a diagnostic timeline keyed to the SCID-P, presence of MDD was recorded retrospectively for the nine months prior to conception, and then prospectively at three-month intervals across pregnancy and the first nine postpartum months. Changes (if any) in pharmacotherapy for this 18-month period were also noted. Relapse rates of MDD were compared using Kaplan-Meier survival analysis during pregnancy and the nine months prior to conception in those women who discontinued or maintained antidepressant treatment.

Results: Of 28 women, 60.7% (N = 17) were on maintenance treatment and euthymic nine months prior to conception. Eleven of these women continued antidepressant treatment through conception, while six discontinued antidepressant treatment. During the nine pregravid months, 83.3% of those who attempted to discontinue antidepressant experienced a relapse of MDD compared with 45.5% of those who continued maintenance treatment. Of women on maintenance treatment and euthymic at the time of conception (N = 18), six continued taking antidepressants throughout pregnancy, while 12 discontinued treatment. In both groups, 83.3% experienced relapse. No significant difference in time to relapse was found between pregnancy and the nine months prior to pregnancy in the women who discontinue antidepressant treatment. However, pregnant women on maintenance treatment experienced a significantly shorter time to relapse than women on maintenance treatment prior to pregnancy.

Conclusions: Rates of relapse appear high in the setting of antidepressant discontinuation during pregnancy. Maintenance treatment does not necessarily confer protection against relapse of MDD in gravid women.

NR315 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Deliberate SSRIs Added to Tricyclic Antidepressant: A Combination to Achieve Therapeutic Tricyclic Antidepressant Levels in Rapid Metabolizers

Robert P. Kraus, M.D., Psychiatry, Victoria Hospital, 375 South Street, London ON N6A 4G5, Canada; Paula Diaz, MRPharmS,

Summary:

Background: Interindividual variability in TCA metabolism can result in nontherapeutic plasma levels on standard doses. We noted some "treatment-resistant" depressed patients were rapid antidepressant metabolizers, with subtherapeutic TCA levels despite high doses. We deliberately added fluoxetine or paroxetine, SSRI's known to inhibit TCA metabolism, to a TCA in order to raise TCA levels into the therapeutic range.

Patients and Results: Eight case studies will illustrate this combination strategy. Fluoxetine or paroxetine 20 mg/d was added to pre-existing desipramine. Mean desipramine dose prior to combination therapy was 312 mg/d; mean plasma level 257 nmol/L (therapeutic range 550–1100 nmol/L; 150–300 ng/ml). The mean desipramine dose on combination therapy was 252 mg (mean plasma level of 947 nmol/L). Six patients had a very good or excellent response. In one nonresponder a therapeutic range plasma level was never achieved. The combination therapy was well tolerated, even if TCA levels "overshot" the therapeutic range.

Discussion: This combination strategy was successful in six out of seven patients who achieved therapeutic range TCA plasma levels. Whether the therapeutic response primarily reflects the therapeutic TCA level and/or a synergistic action between the noradrenergic antidepressant and the SSRI is uncertain.

NR316 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Family Functioning and Chronic Depression

Gabor I. Keitner, M.D., Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Christine E. Ryan, Ph.D., Ivan W. Miller, Ph.D., Martin B. Keller, M.D.,

Summary:

As part of a multisite clinical trials study we examined family functioning in outpatients diagnosed with chronic depression (N = 96) or double depression (N = 91) at baseline interview and after 12 weeks of randomized treatment with imipramine or sertraline. At the acute stage, patients with chronic depression rated all family dimensions on the Family Assessment Device (FAD) as unhealthy; those with double depression rated all but one dimension (Behavior Control) as unhealthy. This was the only dimension that showed significant differences between the two groups. After 12 weeks of treatment, those with chronic depression viewed their family's functioning as significantly better in all seven family dimensions. In contrast, patients with double depression improved significantly in only two dimensions. Also, those with double depression reported significantly poorer functioning than patients with chronic depression in Communication. Since depressive symptoms improved equally in both groups from baseline to week 12, the change in family functioning is not due to symptom change. In addition, outpatients with chronic or double depression perceived the same degree of family dysfunction as a comparison group of inpatients with major depression. Patients with chronic forms of depression experience considerable family dysfunction, and pharmacotherapy for these depressions is associated with significant improvement in perception of family functioning.

NR317 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Pharmacotherapy and Psychotherapy Response in Atypical Depression: Findings From the NIMH Treatment of Depression Collaborative Research Program

Stuart M. Sotsky, M.D., Psychiatry, George Washington Univ, 2150 Pennsylvania Avenue NW, Washington DC 20037–2396; Sam Simmens, Ph.D.,

Summary:

The validity of diagnostic criteria for atypical depression and the efficacy of pharmacotherapy and psychotherapy for this disorder were studied in the NIMH Treatment of Depression Collaborative Research Program. Outpatients with major depressive disorder (*N* = 239) entered a 16-week clinical trial and were randomly assigned to interpersonal psychotherapy, cognitive-behavior therapy, and imipramine or placebo with clinical management. Features of atypical depression were rated on the SADS and ISI, and clinical outcome was measured on the HRSD, GAS, and BDI. Atypical features of mood reactivity and at least one reversed vegetative symptom of hypersomnia, hyperphagia, or weight gain (25.2% patients) were predictive of pharmacotherapy nonresponsiveness with imipramine compared to placebo. The additional features of diurnal mood variation, "leaden paralysis," and "rejection sensitivity" did not further distinguish an imipramine nonresponsive subgroup. Whereas both imipramine and interpersonal psychotherapy showed significant effectiveness compared to placebo among nonatypical depressives, there was no significantly better outcome among atypical depressives with either of the psycho-therapies or imipramine pharmacotherapy than with placebo. There appeared to be a substantial placebo treatment response among patients with atypical depression.

NR318 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Safety and Tolerability of the Sustained-Release Formulation of Bupropion in Depression: Results of Three Clinical Trials

Edmund C. Settle, Jr., M.D., General Division, Medical Staff Off Pavilion, 415 Morris Street Ste 306, Charleston WV 25301; Stephen M. Stahl, M.D., Sharyn R. Batey, Pharm D., J. Andrew Johnston, Pharm D., John A. Ascher, M.D.,

Summary:

Objective: The immediate-release formulation of the antidepressant bupropion hydrochloride has been demonstrated to be effective and well-tolerated in clinical trials and medical practice. In three randomized, double-blind, placebo-controlled clinical trials (n = 1420), the safety and tolerability of the recently developed sustained-release (SR) formulation of bupropion were evaluated in depressed patients.

Methods: Following a one-week, single-blind, placebo treatment period, patients received placebo or bupropion SR (Study 1: 150 or 300 mg/day; Study 2: 100, 200, 300, or 400 mg/day; Study 3: 50–150 or 100–300 mg/day) for eight weeks. Safety and tolerability assessments included adverse events, patient discontinuation rates, changes in weight, vital signs, and results of clinical laboratory tests.

Results: The most frequently reported adverse events were headache, constipation, and dry mouth. No seizures were reported. Ninety-seven percent of adverse events in the bupropion SR groups were considered to be mild or moderate in intensity. Seven percent of bupropion-treated patients and 6% of placebo-treated patients discontinued treatment due to adverse events. Bupropion SR was not associated with weight gain. No consistent patterns of change in vital signs or in the results of clinical laboratory tests were observed.

Conclusion: These data from three large-scale clinical trials demonstrate that bupropion SR is safe and well-tolerated.

NR319 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Serotonergic Autoreceptor Blockade in the Reduction of Antidepressant Latency: A Controlled Trial

Michael T. Isaac, M.D., Psychiatry, VMDS Guys Hospital, Suite 6, Lewisham Hospital, London SE13 6LH, United Kingdom; Maria B. Tome, M.D., Rosarii Harte, M.D.,

Summary:

Objective: To study augmentation of the antidepressant paroxetine with pindolol, a $5HT_{1A}$ autoreceptor blocker. Open studies suggest that for SSRI antidepressants the two- to three-week latency of antidepressant effect may be reduced if pindolol is taken simultaneously.

Method: Double-blind, randomized, placebo-controlled trial. All patients (n = 80; mean age 36 [range 19–65]; asthma, diabetes, cardiopulmonary disease *excluded*) met criteria for major depression and received paroxetine (20 mg *o.d.*) plus, randomly, either pindolol (2.5 mg *t.d.s.*) or placebo. Assessment: days 4, 7, 10, 14, 21, 28, 42, using clinical measures, the Montgomery-Åsberg Depression Rating Scale [MADRS] and the Beck Depression Inventory.

Results: Compared with day 0, 20% of subjects showed a fall in MADRS score > 50% by day 4. By day 7, 30%, and on day 10, 40% of the patients scored > 50%, rising to 48% at day 14. On days 21, 28 and 42, 52%, 56% and 70% of patients registered a fall in MADRS score > 50%. Other measures showed comparable changes. Patients were followed up for six months, allowing assessment of long-term safety, tolerability and optimal dosage regimes, and subsequent service usage.

Conclusions: The implications for the management of depression are considerable. Larger multicenter trials are warranted.

NR320 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Cost-Benefit Analysis of a Novel Antidepressant Regime

Michael T. Isaac, M.D., Psychiatry, VMDS Guys Hospital, Suite 6, Lewisham Hospital, London SE13 6LH, United Kingdom; Maria B. Tome, M.D.,

Summary:

Objective: To analyze the costs and benefits of augmentation of the antidepressant paroxetine with the $5HT_{1A}$ receptor blocker pindolol.

Method: Randomized, placebo-controlled trial. Eighty outpatients meeting ICD-10 criteria for depressive disorder and scoring > 18 in the Montgomery-Åsberg Depression Rating Scale (MADRS) were recruited from primary care populations. All patients received paroxetine 20 mg. *o.d.* and either pindolol 2.5 mg *t.d.s.* or placebo. The trial period was six weeks, during which the patients were monitored for changes in depressive symptoms using the MADRS and the Beck Depression Inventory. All patients, whether they completed the study or not, are followed up for six months. The economic analysis incorporates all the costs involved, including clinical and laboratory costs, costs of infrastructure, and drugs. We applied the techniques of shadow pricing and intertemporal discounts of social taxes.

Results: The chief benefits are the speed and magnitude of improvement of quality of life and leisure, together with savings in clinical resource utilization.

Conclusion: Novel treatments are amenable to economic analysis, and clinical trials should include them wherever possible.

NR321 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Comparison of Serotonin Levels in Depression Treated by New and Standard Antidepressant Regimes

Michael T. Isaac, M.D., Psychiatry, VMDS Guys Hospital, Suite 6, Lewisham Hospital, London SE13 6LH, United Kingdom; Maria B. Tome, M.D., Roy Sherwood, M.D., Paul Eldridge, Ph.D.

Summary:

Objective: We test the hypothesis that augmentation of paroxetine, a selective serotonergic reuptake inhibitor, with pindolol, a specific $5\text{-}HTI_A$ blocker, increases levels of serotonin in the brain, as measured in the periphery, during the early phase of treatment. Open studies indicate that this combination may reduce the traditional latency of onset of substantive antidepressant action.

Method: Using high-performance liquid chromatography, we measured blood serotonin levels on days 0, 4, 7, and 14 of the 42-day trial period in 20 subjects from a randomized, placebo-controlled, double-blind evaluation of the pindolol/paroxetine combination. All subjects (n = 80; mean age 36 [range 19–65]) met criteria for major depression and received paroxetine (20 mg o.d.) plus, randomly, either pindolol (2.5 mg t.d.s.) or placebo.

Results: We observed accelerated antidepressant response in significant numbers of our patients, where 20% showed a fall in Montgomery- Åsberg Depression Rating Scale [MADRS] score > 50% by day 4 of the study; 30% by day 7; 40% by day 10; and 48% by day 14. We have attempted to correlate these clinical measures and whether the subject was taking pindolol or placebo, with blood serotonin levels.

Conclusions: Central changes in serotonin reflected in the periphery may aid monitoring of antidepressant therapy.

NR322 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Depression: A Disorder of Coincidence Detection?

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: Molecular coincidence detectors are proteins that integrate two (or more) convergent inputs by generating an output signal that differs from the output signal generated by any individual input (Bourne & Nicoll, 1993). To explore this, we compared signal integration by adenylate cyclase (AC) in depressed patients and control subjects.

Method: Using AC activities in both platelets and mononuclear leukocytes, we developed a new measure that may reflect the activity of the inhibitory G-protein Gi.

Results: Our findings, based on this measure, suggest that platelet AC acts as a coincidence detector to integrate signals from both Gi and the stimulatory G-protein Gs in control subjects (N = 19), but not in depressed patients (N = 23). For example, we observed that the relative increase in prostaglandin (PG)-stimulated platelet AC activity (i.e., PG-stimulated AC:basal AC), which is regulated by Gs and may correspond to the signal-to-noise ratio of the receptor——G protein——AC enzyme complex, was positively correlated with our measure of Gi activity (r = .41 to .71, p = .05 to .001) in control subjects, reflecting the integration of signals from both Gs and Gi by AC. Thus, in control subjects, AC appears to act as a coincidence detector. However, in depressed patients, the relative increase in PG-stimulated platelet AC activity was not correlated with our measure of Gi activity, suggesting an impairment of coincidence detection.

Conclusions: The impairment of coincidence detection by AC may be an important component of the pathophysiology of depressive disorders.

NR323 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Bupropion SR Response in Depression: Diagnosis and Biochemistry

Paul J. Goodnick, M.D., Psychiatry, University of Miami, 1400 NW 10th Avenue #304, Miami FL 33136; Roberto A. Dominguez, M.D., Yolanda M. Don, M.D., C. Lindsay DeVane, Ph.D., Charles L. Bowden, M.D., Joseph Henry, M.D.

Summary:

Bupropion is a unique antidepressant with predominant effect on norepinephrine and dopamine reuptake and with few 5HT effects. Previous work has shown bupropion to be useful in bipolar and atypical depression (Goodnick & Extein 1989; Haykal & Akiskal 1990; Sachs et al., 1994). Blood levels may be associated with response (Preskorn 1983; Golden 1988b; Goodnick 1992a). Changes in plasma HVA also may be related to response (Golden 1988a; Goodnick 1992b). Bupropion SR was developed with a longer elimination half-life with reduced times for daily dosing. As part of its development, 41 patients (16M, 25F) with a mean age of 44.8 ± 9.6 years and MDD (DSM-III-R) completed eight weeks of 300 mg/day in two doses/day.

Results indicated different responses among bipolar (11), atypical (13), & "typical" (17): dHDRS was 15.6 ± 7.3, 17.1 ± 8.5, & 7.6 ± 9.0 ($F = 5.57$, $p < .01$), and BDI was 21.1 ± 10.2, 16.9 ± 13.9, & 7.3 ± 14.8 ($F = 3.32$, $p < .05$). In a subgroup of 17 for whom blood level results are available, threohydrobupropion levels correlated significantly with dHDRS ($r = -.54$, $p = .025$). Results on relationship of response to bupropion SR and plasma MHPG and HVA will be presented. Bupropion SR, as with IR, appears to have particular benefits in atypical and bipolar depression, with a possible relationship to therapeutic blood concentrations.

NR324 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Hyperactivation of the HPT Axis in Depression: New Evidence

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, Herminia Ombid

Summary:

Previous data from our laboratory have shown that challenge tests can be safely performed in humans with levothryoxine (T4) and triiodothyronine (T3) to produce a pattern of TSH suppression and recovery. Our preliminary findings demonstrated that TSH recovery after T3 suppression was faster (within three to four days) compared with T4 (> 2 weeks). After 50mcg of T3, a two-fold increase in plasma T3 was observed in three groups of patients: 10 normals, six depressed, and four acutely recovered individuals (greater than 50% drop on the HAM-D scale from baseline). Although all groups achieved maximum TSH suppression at 24 hours post T3 administration, the delta TSH was approximately 63% less suppressed in the depressed group, and approximately 50% less suppressed in the acutely recovered groups compared with normals. Normals showed continued maximum suppression at 48 hours when depressed and acutely recovered patients were already closely approaching baseline. Baseline was only approached by normals at 72 hours post T3. The fact that normals tended to achieve greater and longer-lasting TSH suppression is consistent with hyperactivation of the HPT axis in the depressed and acutely recovered groups. Here we present new data regarding the T3 suppression test.

NR325 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Ten-Year Follow-Up of Chronic Depressives

Timothy I. Mueller, M.D., Psychiatry, Brown University, 345 Blackstone Blvd., Providence RI 02906 0; Martin B. Keller, M.D., Andrew C. Leon, Ph.D., David A. Solomon, M.D., M. Tracie Shea, Ph.D., Jean Endicott, Ph.D.

Summary:

Background: The NIMH Collaborative Program on the Psychobiology of Depression has followed subjects with an index episode of major depressive disorder (MDD) since 1978. This poster presents data on time to recovery from index episode in 431 subjects.

Method: The 10-year course of MDD was examined using survival analysis. The predictive value of demographic and clinical variables on the likelihood of recovery was studied using univariate analytic techniques. Somatic treatment was assessed but not controlled by the investigators.

Results: Ninety-three percent (Kaplan-Meier estimate) of probands had recovered from their intake episode of MDD by the 10th year of prospective follow-up. In those ill for the first five years, 38% had recovered within the next five years. Shorter duration of illness prior to intake, being married, and the presence of alcoholism predicted recovery in the group ill for the first five years. Treatment averaged around 100 mg imipramine-equivalents in the chronically ill group.

Conclusion: People continued to recover from MDD for up to 10 years of prospective follow-up despite lengthy prospectively observed episodes of illness. Few demographic and clinical variables predicted recovery. As observed in this naturalistic study, treatment was at a low level despite long episodes of depression.

NR326 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Substance Abuse As an Adverse Outcome of Childhood Depression

Rise B. Goldstein, Ph.D., Psychiatry, Columbia University, 722 W. 168th Street Unit 14, New York NY 10032; Myrna M. Weissman, Ph.D., Priya Wickramaratne, Ph.D., Susan I. Wolk, M.D.

Summary:

Major depression (MDD) and psychoactive substance use disorders (PSUD) co-occur frequently in individuals. However, we have little longitudinal information on the sequence of onsets of MDD and PSUD. We report preliminary data from a re-evaluation of psychiatric status and social functioning in a cohort of children identified over 15 years ago: 204 diagnosed with MDD, 66 diagnosed with anxiety disorders, and 177 with no psychiatric disorder in childhood. Preliminary results indicate that 43.5% of the MDD, 25.0% of the anxious, and 22.9% of the normal children have developed PSUD. In the MDD group, cumulative risk for PSUD was significantly greater among subjects with comorbid conduct disorder. Over the first 10 years of follow-up among individuals 6 to 12 years old at ascertainment, incidence peaked at an average age of 16 and then declined in the MDD, rose steadily in the anxious, and peaked around age 15 but fluctuated thereafter in the normal group. We conclude that PSUD is a common outcome of childhood MDD, that its trajectory of incidence appears to differ from that in anxious and normal children grown up, and that comorbid conduct disorder among depressed children may identify a subgroup at particularly high risk.

NR327 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Impact of Suppression of Thyroxine on Folate Status During Acute Antidepressant Therapy

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.

Summary:

Objective: To examine the possible relationship between thyroid function and folate status given that red cell folate (RCF) has been shown to increase and thyroxine (T4) to decrease with response to antidepressant therapy.

Methods: Tri-iodothyronine (T3) or placebo was given to 16 depressed subjects receiving standard antidepressant treatment and folate levels and mood were measured at baseline and following four weeks of treatment.

Results: T3 but not placebo suppressed T4 up to 40%. Using ANOVA, there was a significant effect of response ($F = 16.51$, $p < .002$) but not treatment group on mean red cell folate levels (RCF; $F = 2.46$, p = ns), and there was no significant interaction ($F = 2.39$, p = ns). The mean change in RCF across the four week trial was significantly greater in responders (62.1 ± 60.9) than nonresponders (–54.8 ± 56.8; $t = -3.97$, $df = 14$, $p = 0.001$) as was the mean percent change in RCF (responders = 14.3% ± 14.7%, nonresponders = –9.6% ± 12.4%; $t = -3.55$, $df = 14$, $p = 0.003$). Percent change in RCF was significantly correlated with percent change in HAM-D ($r = -.75$, $p < 0.001$). Seven of eight responders had increased RCF. Seven of eight nonresponders had decreased or no change in RCF (chi-square = 10.75, $df = 2$, $p = .005$).

Conclusions: RCF increased with response and decreased or did not change with nonresponse. These results suggest that changes in RCF with treatment are not influenced by the suppression of T4. Implications and limitations of the current study are discussed.

NR328 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Brain SPECT Imaging of Serotonin Transporter in Parkinson's Disease Associated with Depression

Amit Anand, M.D., Psychiatry, Yale University, 950 Campbell Avenue, West Haven CT 06516; John P. Seibyl, M.D., Kenneth L. Marek, M.D., Robert B. Innis, M.D., Dennis S. Charney, M.D.

Summary:

Using SPECT imaging with the radioligand [^{123}I]β-CIT, we analyzed midbrain serotonin (5-HT) transporter activity as a measure of 5-HT neuron density (Seibyl 1991). We used V3", the ratio between specific midbrain (midbrain-occipital) binding to nondisplaceable (occipital) binding, as the principal outcome measure. We have previously shown that V3", after establishment of the plateau phase, provides reliable regional outcome measures proportional to the number of 5-HT transporter densities. We analyzed, 24 hours post-injection, midbrain [^{123}I]β-CIT activity, in five age- and gender-matched healthy controls, five PD patients without depression (mean 17 item HAM-D depression rating: 7.2 ± 1.6), and four PD patients with depression (mean HAM-D: 20.2 ± 4.5).

Results: V3"—— Controls: 2.22 ± 0.3, PD without depression: 2.02 ± 0.38, PD with depression: 1.36 ± 0.83. The difference in V3" between controls and PD patients with depression approached significance ($p = 0.06$). Pearson's correlation analysis for HAM-D scores and V3" was –0.67 but was not statistically significant. Midbrain activity did not correlate with striatal activity. These results are consistent with post-mortem (Jellinger 1991) and platelet 5-HT transporter studies in PD patients with depression. Our results indicate that a subgroup of PD patients may have a critical amount of degeneration of 5-HT neurons that makes them much more vulnerable to depression.

NR329 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Prospective Study of Postpartum Mood Disturbance in Fiji

Anne E. Becker, M.D., Psychiatry, Mass General Hospital, Fruit Street, Boston MA 02114; Lee S. Cohen, M.D.

Summary:

Objective: Studies suggest relatively consistent prevalence of postpartum depression across different cultures. The purpose of this pilot investigation was to assess prevalence and potential predictors of postpartum depression in Fiji.

Method: 85 consecutive ethnic Fijian women were recruited during their initial postpartum days at Sigatoka District Hospital. They subsequently underwent translated structured interviews keyed to the mood module of the Structured Clinical Interview for Diagnosis (SCID-P) and indicated perceived social supports on visual analog scales during the first two to five months postpartum; 82 women completed the study.

Results: Only one woman from the sample was noted to have suffered postpartum major mood disorder during the first puerperal months. A subset of 18 women who described symptoms meeting criteria for major depression except for duration (< 2 weeks) was also identified. Compared with women who did not demonstrate such a mood disturbance, these women were more likely to report inadequate social supports ($p < 0.02$) and inadequate assistance with infant care ($p < 0.01$).

Conclusions: The rate of postpartum major mood disturbance appears particularly low in this sample. Traditionally intensive social supports may minimize risk for puerperal illness among ethnic Fijians. Furthermore, perceived inadequate social supports appear to be associated with subsyndromal postpartum mood disturbance in this population.

NR330 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Adjunctive Treatment with High-Dose Thyroxine in Refractory Depression

Michael Bauer, M.D., Psychiatry, Free University, Eschenallee 3, 14050 Berlin, Germany; Rainer Hellweg, M.D., Andreas Baumgartner, M.D.

Summary:

Objective: Since 1982, three open studies have been published describing beneficial effects of treatment with supraphysiological doses of thyroxine (up to 500 μg/day) in previously treatment-resistant, rapid-cycling and non-rapid-cycling bipolar affective disorder. In this study we investigated the efficacy of high-dose thyroxine in patients with refractory major depression.

Method: Patients were given high-dose thyroxine up to 600 μg/day in addition to their previous antidepressant drug regimen during an open eight-week trial.

Results: Preliminary results in 14 patients show an approximately 40% response rate in patients with major depression. High-dose thyroxine was continued in responders. Patients with a good response in the acute depressive phase of treatment also showed an excellent outcome during continuation treatment. In general, thyroxine treatment was well tolerated.

Conclusions: Our data suggest that high-dose thyroxine may be effective in refractory depression, without major side effects.

NR331 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Psychomotor Retardation Attention in Depression

Philippe Baruch, M.D., Psychiatrie, Hop Enfanti-Jesus, 1401 18e Rue, Quebec QC G1J 1Z4, Canada; Sophie Lemelin, B.Ps., Annick Vincent, M.D., Paul Jacques, M.D., Pierre Vincent, M.D.

Summary:

The cognitive component is an essential aspect of the description of depressive psychomotor retardation (slowness of thought and speech, poverty of responses, complaint of poor concentration), but few experimental studies have examined the information-processing disturbances associated with this symptom in depressives. There are some indications, however, in favor of the existence of a global attentional deficit in retarded depressives.

Objective: To specify the attentional disturbance underlying the clinical psychomotor retardation of depressed patients.

Method: Unmedicated major depressives (n = 30) and normal subjects (n = 34) comparable for sex and age were concurrently assessed using the Depressive Retardation Rating Scale (DRRS) and an attentional battery, evaluating selective and divided attention. Data were analyzed following dimensional and categorical approaches.

Results: The depressive episode intensity and the associated anxiety did not correlate with any of the attentional variables. However, significant correlations were observed between the DRRS score and every effortful task, irrespective of the attentional process involved. Results of the categorical analysis contrasting attentional performances of depressives with and without clinical psychomotor retardation argued for the existence of two distinct attentional disturbances: retarded depressives presented a global attentional deficit, whereas nonretarded depressives exhibited a selective attention disturbance.

Conclusions: This study attests to the value of clinical psychomotor retardation in order to group depressives who are not only clinically but also cognitively more homogeneous. Links between clinical retardation and a global attentional impairment disturbing effortful tasks are discussed, and the involvement of a left dorsolateral prefrontal dysfunction is proposed.

NR332 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Safety and Efficacy of Divalproex in Bipolar Disorder: A Retrospective Analysis of Maintenance Treatment

Emalie J. Burks, Ph.D., 6752 Eichelberger, St. Louis MO 63109; Satish Kulkarni, M.D.

Summary:

Objective: To analyze the long-term safety and efficacy of divalproex sodium in the treatment of bipolar disorders.

Method: This is a retrospective analysis of 39 patients diagnosed with bipolar I or bipolar II, treated in a private practice setting. Diagnosis and a divalproex trial longer than 60 days were the selection criteria. Data were gathered through blinded chart review.

Results: The dose was 936mg/d and the length was 286 days. Patients had an average of 6.5 symptoms: depression (82%), labile mood (74.3%), insomnia (59%), racing thoughts (48.7%), irritability (41%), excessive drug/alcohol use (41%), impulsivity (38%), and aggression (35.9%). Forty-six percent received antidepressants concurrently. In the 39 patients reviewed, 85.1% of the symptoms reported were adequately controlled. One patients required inpatient hospitalization. There were 16 side effects, with sedation and weight gain at 12.8% and no discontinuations; 84.6% of patients continued divalproex without an additional antimanic agent. Rehospitalization rates dropped from 0.41/patient to 0.03/patient with divalproex sodium treatment.

Conclusions: The majority of patients analyzed had adequately controlled symptoms of bipolar disorder (85.1%). Divalproex was safe and effective therapy in an outpatient setting for maintenance treatment of bipolar disorders.

NR333 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Seasonal Mood Variations in Late Adolescence

Lois Colle, Ph.D., Psychology, Royal Victoria Hospital, 1025 Pine Avenue West, Montreal Quebec H3A 1A1, Canada; A. Missagh Ghadirian, M.D.

Summary:

Objective: To assess seasonal variations of mood and behavior and to estimate prevalence rates of possible seasonal affective disorder (SAD) in a subgroup of older adolescents.

Method: Ninety-two female and 37 male (mean age 17.6 years) college students in Montreal completed the Seasonal Pattern Assessment Questionnaire (SPAQ) for measurement of seasonal mood variation.

Results: Thirty-five percent of females and 11% of males met the criteria for identifying SAD on the basis of the SPAQ: seasonality scores ℓ 11 along with "moderate" to "severe" problems with the seasonal changes. Females reported a greater degree of change in weight ($p < .006$), appetite ($p < .01$), and energy level ($p < .003$) with the seasons than males. Weight and appetite increased, while energy level decreased during fall/winter. Both sexes reported feeling worst and socializing least in the fall/winter.

Conclusions: Although the small sample size does not justify a definite conclusion, and the use of the SPAQ as a measure of SAD is not fully adequate, the high rate of seasonal changes in mood and behavior in this age group is worth consideration. This high rate could be partly due to the northern latitude of Montreal and to academic/psychosocial factors. This finding requires further exploration.

NR334 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Catecholamine Depletion in Desipramine and Fluoxetine Responders

Pedro L. Delgado, M.D., Psychiatry, Univ of Arizona Sch of Me, 1501 N Campbell Ave, Tucson AZ 85724; Francisco A. Moreno, M.D., Alessandra Buonopane, M.D., Alan J. Gelenberg, M.D., Rebecca L. Potter, M.D.

Summary:

Depletion of plasma trytophan (TRP) causes a transient depressive relapse in 67% of depressed patients treated with selective serotonin (5-HT) reuptake inhibitors (SSRIs), but in less than 25% of patients treated with desipramine (DMI) (Delgado et al., 1991). Brain norepinephrine and dopamine are reduced by inhibiting their synthesis with alpha-methyl-para-tyrosine (AMPT). In a prior pilot study, we showed that 80% of depressed patients having responded to DMI or mazindol had a transient depressive relapse during AMPT depletion, whereas none having responded to an SSRI did (Miller et al., in press). This new study replicates the pilot work in a larger sample using a more rigorously controlled design.

Method: Fifty patients meeting DSM-IV criteria for nonpsychotic, nonmelancholic, unipolar major depression were randomly assigned to a 10-week trial of either DMI or fluoxetine. Those having a therapeutic antidepressant response (predetermined criteria) for ℓ 2 weeks (N = 31; 10 DMI, 21 fluoxetine) received two challenges one week apart in a double-blind, placebo-controlled, crossover fashion. Each challenge had a baseline day, two days of either AMPT 1 gm TID or diphenhydramine (active placebo) 50 mg TID and a follow-up day. Antidepressants were continued throughout

testing. Ratings (Ham-D) and plasma for MHPG and HVA levels were obtained prior to, during, and after testing.

Results: 80% of DMI- and 20% of fluoxetine-responders had a transient depressive relapse during AMPT but not placebo (diphenhydramine) challenge.

Implications: The neurobiological mechanisms underlying antidepressant responses to different drugs involve alterations in the functioning of different neurotransmitter systems. Our results reinforce the importance of changes in both the 5-HT and catecholamine systems for successful antidepressant responses and suggest that disruption of catecholamine neurotransmission may disrupt antidepressant in a small number of fluoxetine-responders.

NR335 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Depression in Parkinson's Disease Is Not Accompanied by Activation of Corticotropin-Releasing Hormone Neurons in the Hypothalamic Paraventricular Nucleus

W.J.G. Hoogendijk, M.D., Netherlands Institute, Meibergdreef 33/1105 AZ, Amsterdam ZO, Netherlands; J.S. Purba, M.D., M.A. Hofman, Ph.D., R.A.I. de Vos, M.D., E.N.H. Jansen Steur, M.D., D.F. Swaab, M.D.

Summary:

Objective: The authors studied the relationship between the number of corticotropin-releasing hormone (CRH) neurons and depression in Parkinson's disease (PD) patients. Depression is frequently encountered in PD. In addition, more than half of the PD patients have a disturbed dexamethasone suppression test (DST). Increased activity of CRH neurons has been implicated in the nonsuppression of the DST. We recently found an increase in CRH neuron number, CRH-mRNA, and vasopressin colocalization in CRH neurons in the paraventricular nucleus (PVN) of depressed patients may be involved in the pathogenesis of depression.

Method: The number of neurons expressing CRH was determined in the PVN of six depressed PD patients with a high score (ℓ 13) on the Hamilton Depression Rating Scale, six nondepressed PD patients, and six controls.

Results: The three groups did not differ in the number of neurons expressing CRH.

Conclusions: Other parameters for CRH neuron activation may be determined to fully evaluate the activity state of CRH neurons, since the activation pattern of these neurons is known to vary in different disorders. The absent increase in the number of CRH neurons in the present study, however, is most likely due to the fact that activation of CRH neurons in the PVN, as we recently observed in idiopathic depression, does not play an essential role in depression in PD.

NR336 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Double-Blind Comparison of Fluvoxamine and Paroxetine in Major Depressive Disorder

Ari Kiev, M.D., Social Psych Research Inst, 150 East 69th Street, New York NY 10021-5704; Alan D. Feiger, M.D.

Summary:

Outpatients (aged 18–65 years) DSM-III-R-defined major depressive disorder were studied in a randomized, double-blind, parallel group, multicentered study. Following a one to two week placebo baseline, patients were randomized to receive either Luvox® (fluvoxamine maleate) tablets, 50–150 mg daily or Paxil® (paroxetine hydrochloride), 20–50 mg daily for seven weeks. Primary efficacy was evaluated by HAM-D (21 item), with CGI, HAM-A, and SCL-56 as secondary efficacy variables. Safety evaluations included vital signs, clinical laboratories, and assessment of adverse events. Sixty patients were randomized to treatment (30 in each group); 20 fluvoxamine patients and 22 paroxetine patients completed the study. Demographically, there were no significant differences between the two groups. Baseline HAM-D scores were comparable for the two groups (fluvoxamine 24.4; paroxetine 24.3). At the endpoint, the mean total daily doses were 102 mg and 36 mg for fluvoxamine and paroxetine, respectively. There was no significant difference between the two treatments in efficacy as demonstrated by a 13.5 point decrease in HAM-D for fluvoxamine and 12.9 point decrease for paroxetine. Secondary and supportive efficacy variables confirmed the HAM-D results. Neither treatment was associated with clinically significant changes in vital signs or laboratory values. The majority of patients in both groups experienced adverse events, although no serious adverse events occurred, and no significant differences were detected between treatments for safety. Six patients (two fluvoxamine; four paroxetine) withdrew early due to intolerance. The most frequently reported events were headache (fluvoxamine 40%; paroxetine 57%), nausea (fluvoxamine 37%; paroxetine 47%), dry mouth (fluvoxamine 47%; paroxetine 27%), somnolence (fluvoxamine 40%; paroxetine 30%) and sweating (fluvoxamine 10%; paroxetine 33%). In conclusion, both fluvoxamine and paroxetine demonstrated comparable efficacy and safety in this depressed outpatient population.

NR337 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Effect of Modified Acute Tryptophan Depletion on Melatonin and Sleep Architecture

Lois E. Krahn, M.D., Psychiatry, Mayo Clinic, 200 1st St SW #W11A, Rochester MN 55905; Peter Y. Lu, M.D., George Klee, M.D., Siong-Chi Lin, M.D., Ralf C. Zimmermann, M.D.

Summary:

Acute tryptophan (TRP) depletion, developed to study the role of serotonin in psychiatric disorders, originally involved an amino acid drink with and without TRP. Because TRP is unavailable, a modified technique was developed using a full-strength and quarter-strength drink. In this double-blind, placebo-controlled study, four male and three female normal volunteers were admitted twice to the research unit where they received three low TRP (160 mg) meals followed by the amino acid drink. Sleep architecture and melatonin (a stable end product of indoleamine synthesis) were selected as biologic markers of serotonin depletion. The Profile of Mood States (POMS) was used to rate behavioral change. Plasma was collected at 14 time points, the POMS was completed every 12 hours, and sleep was monitored with EEG for a baseline and study night during each stay. A two-way repeated-measures analysis of variance (ANOVA) with the Greenhouse-Geisser correction was used to assess changes over time in plasma melatonin, eight sleep variables, and six POMS subscales.

Significant differences existed for reduction in melatonin for drink x time ($F = 5.734$; $df = 14$; $P = 0.0001$; $GG = 0.0307$) and total sleep time ($F = 7.144$; $df = 3$; $P = 0.002$; $GG = 0.016$). These data suggest that the acute TRP depletion as compared with control effectively reduces serotonin, a state theoretically associated with depression. However, corresponding changes in behavioral rating scales and sleep architecture were not found. These observations indicate that the relationship of serotonin to depressive disorders requires further study.

NR338 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Medical Comorbidity in an Adult Outpatient Population with Mood Disorder

Eleanor Lavretsky, M.D., University of S. California, 1937 Hospital Place, Los Angeles CA 90033; George M. Simpson,

M.D., Mina K. Tasik, John M. Murhy, M.D., Michael J. Ilas, M.D., Edmond H. Pi, M.D.

Summary:

Objective: This study was part of the evaluation of an adult outpatient population with mood disorders for comorbidity and treatment outcomes.

Method: Using a questionnaire, data were collected from medical records of all patients registered and receiving treatment in 1994–1995 at a public psychiatric clinic providing care to a central Los Angeles catchment area. Comorbid medical conditions were diagnosed at an internal medicine clinic.

Results: Among 1187 patients registered at the psychiatric clinic, 551 (46.42%) met the DSM-IV criteria for mood disorders. It was found that 373 (67.7%) of those with mood disorders were also treated for one or more medical conditions. Prevalence of three medical conditions—hypertension, diabetes mellitus, and hypothyroidism—was significantly higher than in general population. Hypertension was diagnosed more frequently in patients with major depressive disorder than in bipolar patients and was associated with poor prognosis and treatment resistance.

Conclusion: Chronic medical conditions such as hypertension influence the course and level of functioning in patients with mood disorders and should be considered as risk factors in assessing prognosis.

NR339 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Circadian Variation in the Direction of Mood Switches in Patients with Rapid Cycling Bipolar Disorder

Susana Feldman-Naim, M.D., Psychobiology, NIMH Bldg 10 4S239, 9000 Rockville Pike, Bethesda MD 20892; Ellen Leibenluft, M.D., Erick H. Turner, M.D.

Summary:

Objective: The authors assessed circadian variation in the direction of mood switches in a sample of outpatients with rapid-cycling bipolar disorder (RCBD) on stable medications. We predicted that patients would be more likely to switch from depression into (hypo-)mania during the daytime hours and from (hypo)mania into depression overnight.

Method: Fifteen patients with RCBD completed mood self-ratings twice a day: once shortly after awakening and once at bedtime. Using three months of data for each patient, we performed categorical analyses (McNemar chi square) to study the direction of mood switches between each day's morning and evening rating, and between each evening rating and the subsequent morning ratings.

Results: Switches that occured between the morning and evening ratings were more likely to be from depression into hypomania or euthymia (64.3%) than in the opposite direction (35.6%; $p < 0.0001$). Similarly, switches that occurred between the evening rating and the next morning rating were more likely to be from (hypo)mania or euthymia into depression (65.0%) than in the opposite direction (35.0%; $p < 0.0001$).

Conclusion: Extended wakefulness, exposure to light, increased activity, and/or endogenous rhythms could contribute to the elevation of mood during the course of the day. Sleep, dark, reduced activity, and/or endogenous rhythms could contribute to the tendency to switch into depression overnight. Potential therapeutic implications include the use of light or activity during depression, and of induced sleep or dark exposure during (hypo)mania.

NR340 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Mental Representations and Depression

Kenneth N. Levy, M.A., Psychology, City University, 77 East 12th Street, New York NY 10003; Sidney J. Blatt, Ph.D., Donald M. Quinlan, M.D.

Summary:

Objective: To explore the content and structure of mental representations involved in dependent and self-critical depressive experiences.

Method: Forty male and 51 female subjects were asked, in open-ended questions, to write descriptions of each of their parents. These descriptions were reliably rated for qualitative and structural dimensions using a scoring system developed by Blatt et al. (1992). Subjects also completed Parker's (1982) Parental Bonding Instrument (PBI), a more structured method for assessing mental representations, as well as the Beck Depression Inventory (BDI) and the Depressive Experiences Questionnaire (DEQ).

Results: Depression was significantly related to descriptions of both mother and father as uncaring and overprotective, and as relatively unsuccessful and nonambitious. Self-criticism was significantly related to ratings of mother and father as uncaring and overprotective. For women, but not men, dependency was related significantly to ratings of mother as overprotective, benevolent, and nonpunitive. These results remained significant even after controlling for level of depression.

Conclusions: These findings indicate that mental representations of parents may be a critical aspect in the phenomenology and expression of depression.

NR341 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Attachment Styles and Depression

Kristen Kelly, M.S.N., Nursing, Beth Israel Med Ctr, 77 East 12th Street, New York NY 10003; Kenneth N. Levy, M.A., Sidney J. Blatt, Ph.D.

Summary:

Objective: To investigate the relationship between attachment styles and dependent and self-critical depression in young adults.

Method: One hundred twenty-eight subjects were categorized into four attachment groups: secure, preoccupied, fearful avoidant, and dismissing avoidant, and their degree of correspondence to each of the attachment styles was rated on a 1 to 7 Likert scale. Subjects also completed the Depressive Experience Questionnaire.

Results: Correlational analyses revealed that secure attachment was negatively related to self-critical depression ($r = -.39$, $p < .001$) and associated with efficacy ($r = .22$, p, .01). Both fearful avoidant and preoccupied attachment were associated with both dependent ($r = .25$, $p < .01$ and, $r = .22$, $p < .01$, respectively) and self-critical depression ($r = .29$, $p < .001$ and, $r = .32$, $p < .001$, respectively). Dismissing avoidant attachment was characterized by counter-dependence ($r = -.33$, $p < .01$). A significant MANOVA ($F(15,294) = 2.74$, $p < .001$) found secure subjects scored higher on efficacy and lower in self-criticism than both fearful and preoccupied subjects.

Conclusions: Findings are consistent with the view of Blatt and colleagues that different attachment styles are related to different types of depressive experiences and support Bowlby's view regarding the relationship of avoidant attachment to compulsive self-reliance or counter-dependency.

NR342 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Negative Priming Effect in Depressed Patients

Sophie Lemelin, B.Ps., Psychiatry, Hop Enfant-Jesus, 1401 18ieme Rue, Quebec G1J 1Z4, Canada; Philippe Baruch, M.D.,

Annick Vincent, M.D., James Everett, Ph.D., Pierre Vincent, M.D.

Summary:

Negative priming (NP) tasks have been widely used to investigate distractibility and distractor inhibition processes. A NP deficit has been repeatedly reported in schizophrenics. This deficit leading to a superior performance, it cannot be attributed to generalized deficits and poor motivation. Depressives are also known to suffer from a distractor inhibition disturbance but, to our knowledge, NP effect has not been studied in those patients.

Summary:

Objective: To investigate NP in depressed patients in order to better understand their attentional impairments.

Method: Untreated major depressives (n = 20) and normal subjects (n = 20) were evaluated using a computerized Stroop test. In addition to classical Stroop parameters, this Stroop version allowed for evidence of an NP effect. This effect is seen when the subject must, on the current trial, respond to the color that appeared as the distractor on the previous trial. Using this Stroop version, our group has reported the NP deficit of schizophrenics (Laplante et al., 1992).

Results: Regarding the classical Stroop parameters, as reported in the literature, depressives were slower than normal subjects and presented stronger interference. A repeated ANOVA comparing the two groups in conditions with and without NP revealed a significant Group effect ($F(1, 38) = 18.48$, $p = .0001$), showing the general decrease of depressives' speed, a Condition effect ($F(1, 1) = 4.56$, $p = .04$) attesting the existence of a NP effect, but no significant Group X Condition interaction effect ($F(1, 38) = 0.15$, NS). This last result indicated that the NP effect observed in depressives did not differ from that seen in normal subjects.

Conclusions: Even though depressives exhibit a distractor inhibition distrubance, they are not different from normal subjects regarding their NP effect on the Stroop test. Moreover, these results indicate that cognitive deficits underlying the attentional disturbances are different in depressed and schizophrenic patients.

NR343 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Current Course of Mood Disorders: A Three Year Follow-Up

Alessandro Lenzi, Institute of Psychiatry, Via Rome 67, Pisa 56100, Italy; Fabrizio Lazzerini, M.D., Ilaria Bianco, M.D., V. Milazzo, M.D., S. Raffaelli, M.D., Donatella Marazziti, M.D.

Summary:

A total of 157 patients (all females, mean age: 46.9 ± 15 years) consecutively admitted to the Institute of Psychiatry at Pisa University for an affective or schizoaffective episode during one year, were followed for three years in a naturalistic way after discharge. Forty-seven (30%) of the patients refused to participate in the study; about a half (47%) of these belonged to the bipolar I diagnostic category. In this group a lower frequency of hypertimic temperement was registered.

During the follow-up, three patients committed suicide and three died naturally. The three suiciders were diagnosed as suffering from a depressive episode in bipolar I disorder. Of the remaining 104 patients, 42% had no relapse, 35% had almost three relapses, and 23% had more than three relapses. No differences appeared among the three groups.

In conclusion, recent treatments seem to be able to reduce the length and number of relapses. A hyperthimic temperament seems to be a characteristic of compliant patients. The mortality rate for somatic or accidental causes appears similar to that of the general population, while it is higher for suicide.

NR344 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Do the Antidepressants Have Effects on Quality of Life Independently of Their Antidepressant Actions?

Carmen Lara-Munoz, M.D., Universidad Autonoma De Puebla, 5 Sur 2702-B, Puebla 72420, Mexico; Gerardo Heinze, M.D., Juan Ramon De La Fuente, M.D.

Summary:

Quality of life (QL) has become a matter of concern during the last few years. Depressive illness is a special topic because of the difficulty in distinguishing between how a person feels (affect) and how he feels his life is (QL). There are several scales for the measurement of QL but there isn't an agreement as to which one is the best. Dunbar has developed a scale that can be used with psychiatric patients (DQLS). The unique feature of this self-rating scale is that it evaluates the "self-now" (how the patient feels when he is evaluated) and the "ideal self." We used this scale to evaluate patients with depression in a double-blind trial, imipramine vs. fluvoxamine, besides the Hamilton Depression Scale and other conventional scales for the measurement of the efficacy of antidepressants. We are reporting the results of 49 patients who filled out the DQLS at the beginning of the study and at their last evaluation.

Cronbach's alphas were from .84 to .96; the better was for the "ideal" subscale at the end of the study. The correlations between both subscales were – .26 at the beginning of the study and .35 in the last evaluation. With physical symptoms, there was a negative correlation with the "now" scale at the end of the study (– .42). For the first and last evaluation, the mean of physical symptoms was 35.2 and 8.9, the mean of the "self-now" subscale was 107.6 and 183.3, and the mean of the "ideal-self" subscale was 206.7 and 211.7. We can see that the "ideal-self" doesn't change a lot, but the "now-self" does, being better at the last evaluation.

We haven't disclosed the code so we don't know what the effect of both drugs on depressive symptomatology and QL was. We can say that the DQLS has internal consistency, at least has face and content validity, and is sensitive to change. We are waiting for the disclosure of the code.

NR345 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Depression-Specific Quality of Life Scales Are Flawed

Heinz Katschnig, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18–20, Vienna A1090, Austria; Christian Simhandl, M.D., Murat Serim, M.D., Bahar Subasi, M.D., Ali Zoghlami, M.D., Karin Jaidhauser, M.A.

Summary:

Objective: Available depression-specific quality of life scales, such as the Quality of Life in Depression Scale (QLDS) and the SmithKline Beecham Quality of Life Scale (SBQOL) usually contain a collection of items, which can be interpreted as symptoms of depression. The hypothesis is tested that these depression-specific QoL scales are biased towards measuring severity of depression and are insufficient if a comprehensive evaluation of quality of life is needed.

Method: The QLDS and the SBQOL were used on 71 occasions in inpatients with a DSM-IV diagnosis of major depression, dysthymic disorder, or one of the anxiety disorders, aiming at a wide range of severity of depression. The Beck Depression Inventory (BDI) and the Montgomery Asberg Depression Rating Scale (MADRS) were used alongside the QoL scales in order to measure severity of depression.

Results: Correlation coefficients between the depression measures and the QoL measures were high (BDI and QLDS: .79;

MADRS and QLDS: .79; BDI and SBQO1: .77; MADRS and SBNQOL: .62).

Conclusions: The two depression specific QoL scales, the QLDS and SBQOL, are biased towards measuring severity of depression. Quality of life in depression should be measured by instruments that also evaluate objective functioning in social roles.

NR346 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Tryptophan Depletion: A Potential Predictor of Depressive Episodes

Francisco A. Moreno, M.D., Psychiatry, University of Arizona, 1501 N. Campbell Avenue, Tucson AZ 85724; Alan J. Gelenberg, M.D., Rebecca L. Potter, M.D., George R. Heninger, M.D., Alessandra Buonopane, M.D., Pedro L. Delgado, M.D.

Summary:

Efforts to develop markers to identify people at risk for depression have been fruitless. tryptophan (TRP) depletion lowers brain serotonin and causes depressive symptoms in healthy young men at genetic risk for depression and in depressed patients treated with some antidepressants. This study investigates the sensitivity, specificity, and positive and negative predictive value (PPV and NPV, respectively) of TRP depletion for the prediction of future major depressive episodes (MDE).

Method: 12 subjects with a prior MDE (DSM-IV criteria), in clinical remission and medication-free for at least three months, and 12 age- and gender-matched controls (without personal or family history of any Axis I disorder), received two two-day tests one week apart in a double-blind, controlled (full and 1/4 strength drinks) crossover fashion. Each test included a TRP-free, 15 amino acid drink day and a follow-up day. Hamilton Depression Scale (HAM-D) ratings were obtained prior to, during, and after testing. Follow-up assessments were done at weekly intervals for a month, then at six and 12 months after testing.

Results: Nine of 12 patients and one of 12 controls had an ℓ 6 point increase in HAM-D during TRP depletion (depletion-positive). Five of nine patients and one of one controls who were depletion positive developed a new MDE during follow up. Only one of 14 depletion negative subject has developed a new MDE. These data show that TRP depletion has sensitivity of 86%, specificity of 76%, PPV of 60%, and NPV of 93% for future depressive episodes.

Implications: TRP depletion may be a clinically useful in identifying individuals at risk for furtue MDEs, regardless of previous history.

NR347 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Depression in Medical Outpatients in a City Hospital

Mario I. Rendon, M.D., Psychiatry, Lincoln Medical, 234 149th Street, Bronx NY 10454; Mir M. Akbar, M.D., Faiq A. Hameedi, M.D.

Summary:

Introduction: Various studies have reported high prevalence of depression in medical outpatients. We conducted this survey to determine the prevalence of depression in outpatients at a city hospital in an economically deprived neighborhood of New York City.

Methods: 1209 patients were given Zung Self Rated Depression Scale during National Depression Screening Day over four consecutive years.

Results: Preliminary analysis of the data from 1144 patients who completed the rating scale reveals that 65% of these patients had some depressive symptomatology; 30% of these patients had mild, 24% moderate and 10% had severe depression. Only 19% of the sample was male. Thirty-two percent of the females compared with 24% of the males in this sample reported mild symptoms of depression, while 25% of the females had moderate depression compared with 22% males. Severe depression was reported in 11% of females compared with 8% of the males.

Conclusion: The main findings of this survey are that moderate to severe depression may be more prevalent in medically ill outpatients than in the general population, where the rate has been reported to be between 5%–9% in females and 2%–3% in males. There is some indication that female patients may be more resilient to depression associated with their medical illness compared with males, as male medical outpatients had higher rates of depression proportionately compared with males in the general population.

NR348 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Implication of Substance Abuse Versus Non-Substance Abuse in Bipolar Disorder

Ihsan M. Salloum, M.D., Psychiatry, Univ of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213; Juan E. Mezzich, M.D., Levent Kirisci, Ph.D., Thomas Janoski, Ph.D., Jack R. Cornelius, M.D., Dennis Daley, M.S.W., Miguel R. Jorge, M.D.

Summary:

Objective: The aim of this study was to evaluate the hypothesis that comorbid bipolar and substance abuse disorder patients differ from nonsubstance abusing bipolar patients in terms of patterns of prior episodes of illness.

Method: This was a retrospective investigation conducted at a large metropolitan university hospital. Patients selection included 274 subjects presenting for care over a five-year period (1983 through 1988), who met the DSM-III criteria of bipolar disorder, manic phase, and who were classified into one of four subtypes according to a history of either manic or depressive episodes. These bipolar subtypes included 1) no history of mania or depression (11%), 2) previous episodes of mania only (31%), 3) previous episodes of both mania and depression (46%), and 4) previous episodes of depression only (11%).

Results: Of the subjects selected, 12% had a comorbid DSM-III substance use disorder. The bipolar substance users were similar to the bipolar nonsubstance users on age, ethnicity, marital status, socioeconomic status, and religious affiliation, but differed on gender distribution, with male gender overly represented in the comorbid group (67% vs. 45% of the bipolar-only group) (x^2 = 5.46, df = 1, $p < 0.02$). Logistic regression analysis, controlling for gender, revealed that the comorbid patients were over two times more likely to have a subtype with history of both manic and depressive episodes (odds ratio = – 2.4, $p < 0.05$). On the other hand, the nonsubstance abusing bipolar patients were over two times more likely than the comorbid bipolar to have history of manic episodes only (odds ratio = 2.5, $p < 0.06$).

Conclusions: Substance abusing bipolar patients may differ significantly from nonsubstance abusing bipolar patients in terms of types of prior episodes. Further studies are warranted to elucidate the clinical, etiopathological, prognostic, and treatment significance of these differences.

NR349 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Compliance and Treatment Outcome at Lithium Clinics

Claudia Schumann, A.S.S., Psychiatry, University of Vienna, Waehringer Guertel 18–20, Vienna A1090, Austria; Gerhard Lenz, P.R.O., Anne Berghofer, A.S.S., Prof. Buno Mueller-Oerlinghausen

Summary:

Since the early randomized, double-blind studies, the efficacy of lithium in the treatment of affective disorder is well established. In this study we measured compliance and outcome of lithium treatment in patients of specialized lithium outpatient clinics in order to investigate their influence on the effectiveness of long-term lithium prophylaxis.

All 88 patients of the specialized lithium outpatient clinic of the Universities of Vienna and Berlin who had been put on lithium in 1985 and 1986 for the first time were followed up personally six years later.

At final assessment, 54 patients (61.4%) had dropped out of the initial setting. Drop-out was significantly associated with discontinuation of prophylactic treatment. Just 37.5% of all patients had never stopped prophylaxis during the six-year follow-up period (full compliance). The main reason for discontinuation was resistance to long-term medication. Fully compliant patients showed significant differences in their attitudes toward lithium treatment according the Lithium Attitude Questionnaire.

Treatment outcome was measured by the number and the duration of inpatient episodes. In both variables, full compliant patients had a significantly better treatment outcome than poor compliant patients.

The importance of compliance and the role of specialized lithium clinics for the efficacy of prophylactic treatment are discussed.

NR350 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Treatment of Bipolar Depression: A Survey of Canadian Psychiatrists

Verinder Sharma, M.D., Mood Disorder, London Psychiatric, 850 Highbury Avenue, London ON N6A 4H1, Canada; Dwight S. Mazmanian, Ph.D., Emmanuel Persad, M.B., Karen Kueneman, B.A.

Summary:

*Objective:*This study was conducted to examine how Canadian psychiatrists manage bipolar depression.

Method: A questionnaire was mailed to 1639 active members of the Canadian Psychiatric Association. Respondents were asked to rank order a list of treatment options, and to record subsequent treatment strategies.

Results: Seven hundred and sixty-six questionnaires were returned (46.7%). Most psychiatrists (> 83%) indicated that a combination of psychotherapy and somatic therapy was their preferred approach. For bipolar disorder, depressed, lithium (42%) and selective serotonin reuptake inhibitors (SSRI's) (38.7%) were the preferred treatment strategies, followed by tricyclics (15.9%). If the initial trial of the preferred drug failed, 42% of respondents indicated they would select a drug from another class, 30.8% indicated they would augment the preferred drug, 20% indicated they would select another drug from the same class, and 7.2% indicated they would add another drug to the preferred drug. For substitution, tricyclics were the favored choices. Lithium was the preferred choice for augmentation and addition. The findings for bipolar disorder, NOS, were very similar to those obtained for bipolar disorder, depressed.

Conclusions: These findings indicate that a combination of psychotherapy and somatic therapy is the preferred approach for bipolar depression. Lithium and SSRI's are the favored somatic therapies.

NR351 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Frequency of Atopic Illness and Migraine in Bipolar Patients and Hypertensive Controls

Jonathan Sporn, M.D., Psychiatry, Mass General Hospital, 815 WACC/15 Parkman Street, Boston MA 02114; Gary S. Sachs, M.D., Christine J. Truman, B.A., Una Jain, B.A., Christina D. Demopulos, M.D.

Summary:

Objective: High rates of comorbidity have been reported for bipolar mood disorder, atopic disorders, and migraine headache. These episodic illnesses may have a common etiology or may simply co-occur by chance. This study sought to determine whether the link between these common disorders was greater than chance alone.

Method: A self-report form was given to patients at the MGH bipolar clinic and a hypertension clinic. The first 60 completed forms from each clinic were analyzed using chi square to compare the frequency of asthma, eczema, hay fever, (food or drug) allergies, and migraine headache.

Results: Bipolar patients had significantly ($p < 0.05$) higher rates of co-occurrence of migraine headache, asthma, and eczema. No significant difference between the groups was found for the frequency of hay fever or food/drug allergy.

Conclusions: The present results agree with prior studies indicating a link between asthma, eczema, migraine, and bipolar illness. Further study with psychiatric controls is underway to determine whether the relationship is specific to affective illness and whether the presence of these disorders influences course of illness or treatment response.

NR352 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Antiglucocorticoids in Depression and Schizophrenia

Owen M. Wolkowitz, M.D., Psychiatry, University of California, 401 Parnassus Ave, Box F-0984, San Francisco \A 94143; Victor I. Reus, M.D., Sophia Vinogradov, M.D., Theresa Chan, B.A., Francesca Manfredi, B.A., Elysa Marco, B.A., Ronald Johnson, Ph.D., John Poole, Ph.D., Jonathan E. Litter, M.D.

Summary:

Hypercortisolemia may exacerbate or perpetuate certain symptoms of major depression and schizophrenia, although only open-label trials and case reports have previously evaluated therapeutic effects of antiglucocorticoid drugs. We administered ketoconazole (a cortisol biosynthesis inhibitor, 400–800 mg/d) or placebo, in a double-blind manner, to 20 medication-free patients with major depression for four weeks. Twelve of these patients were eucortisolemic and eight were hypercortisolemic at baseline.

Ketoconazole, compared to placebo, significantly decreased Hamilton Depression (HDRS) and Bunney-Hamburg global depression ratings in the hypercortisolemic but not the eucortisolemic group (Group X Drug: $F = 5.68$, $p < 0.03$). In the hypercortisolemic group, HDRS ratings improved 48% on ketoconazole, compared to 6.6% on placebo. In a separate double-blind study, nine medicated, partially treatment-resistant patients with schizophrenia or schizoaffective disorder ("primarily schizophrenic" subtype) were similarly treated with ketoconazole or placebo. A highly significant reduction in HDRS ratings was observed in the ketoconazole, but not the placebo group (– 32% change vs. + 28% change), ($F = 15.26$, $p < 0.006$). These preliminary results from the first double-blind trials of antiglucocorticoids are consistent with a pathophysiologic role of cortisol in depressive symptoms and should prompt larger-scale trials aimed at developing novel anticortisolemic treatments.

NR353 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Factors Associated with Outcome in Major Depression: A Twelve-Month Prospective Study

Aurelio Garcia, M.D., Mental Health Ctr, Carretera De Vicalvaro 64, Madrid, Spain; Elena Ezquiaga, M.D., Fe Bravo, M.D., Teresa Pallares,

Summary:

Research to identify predictors of recovery has shown widely different results due to several causes: methodological differences in the design, in the diagnostic criteria used, in the diversity of clinical severity of cases, in the treatment carried out, in the periods of follow-up, in the frequent lack of definition in chronicity recurrence and relapse, and in the statistical analysis. It is also possible that the variables under study do not have a predictable capacity of chronicity consistent enough to be replicated.

Summary:

Objective: To identify clinical, psychological, and social variables associated with remission and with incomplete recovery after a 12-month controlled treatment period.

Design: A prospective 12-month study. Initial evaluation and follow-up every three months.

Sample: 90 outpatients consecutively diagnosed with unipolar major depression (DSM-III-R). Index episode of no more than six months.

Statistical analysis: Univariant analysis by chi-square and Mann-Whithney test was performed. Confusion and effect modification was tested by means of a Mantel-Haenszel stratified analysis. Finally, several unconditional logistic models were used.

Results: 59% had recovered, 24% remitted partially, and 17% maintained severe symptomatology. Predictors of outcome were personality disorders, previous episodes, negative evaluation of self, and low social-support satisfaction.

NR354 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Gender Differences in Iatrogenic Sexual Dysfunction in Chronically Depressed Patients Treated with SSRI: A Pilot Study

Lisa A. Piazza, M.D., Psychiatry, NY Hospital-PWC, 300 East 56th Street Apt 17A, New York NY 10022; John C. Markowitz, M.D., James H. Kocsis, M.D., Andrew C. Leon, Ph.D., Laura Portera, B.A., Nina Miller, M.A.

Summary:

Objective: The authors' goal was to determine the baseline prevalence of sexual dysfunction in a population of chronically depressed patients and prospectively measure the incidence of new sexual dysfunction after treatment with sertraline or paroxetine.

Method: 17 women and 11 men with DSM-III-R diagnoses of chronic unipolar depressive disorders underwent assessment of their sexual functioning using the Changes in Sexual Functioning Questionnaire, and severity of depression, using the Hamilton Depression Rating Scale, before and six weeks after treatment with an SSRI antidepressant.

Results: Eighty-eight percent of women with chronic depressive disorders and 27% of chronically depressed men reported baseline difficulty in arousal functioning, which decreased to 54% in women, and increased to 63% in men after six weeks of treatment with SSRI's. Fifty-seven percent of women reported impaired orgasmic function at baseline compared with 64% after treatment. In contrast, men reported a low baseline frequency of orgasmic dysfunction of 18%, which increased to 73% after treatment with an SSRI.

Conclusions: In contrast to men, unmedicated women with chronic depression report a high frequency of arousal and orgasmic dysfunction, and early improvement in arousal functioning after SSRI treatment. Arousal dysfunction reported by depressed women may be a symptom of depression, whereas arousal and orgasmic difficulty in men may be an iatrogenic effect of SSRI treatment. Clinicians must, therefore, take careful sexual histories before initiating pharmacotherapy.

NR355 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

ECT in Patients with Major Depressive Disorder and Low Cardiac Output

Liat Stern, M.D., Psychiatry, Sheba Medical Center, Ramat Gan 52621, Israel; Shmuel Hirschmann, M.D., Leon J. Grunhaus, M.D.

Summary:

The hemodynamic effects of ECT may act synergistically with pre-existing cardiac pathology to increase cardiovascular morbidity and mortality in high-risk individuals. Patients with impaired cardiac output may be at particular risk. Treatment regimens used to control the hemodynamic effects of ECT include drugs such as: beta adrenergic blockers, calcium channel blockers, and anticholinergic agents. Beta adrenergic blockers and calcium channel blockers are not generally recommended in patients with reduced cardiac output, since they may lead to congestive heart failure due to their negative inotropic effects. Anticholinergic agents increase cardiac work load by inducing a rise in heart rate, also a potential detrimental factor in these patients.

Concerning those problems, we suggest an ECT treatment protocol for patients with impaired cardiac output and present three patients, ages 59–78, suffering from resistant major depression with impaired cardiac output (ejection fraction 20%–25%) successfully treated with ECT.

The treatment protocol includes: 1) NPO as of midnight of the previous day. 2) continuous oxygenation during the procedure. 3) monitoring of pulse and blood pressure before and continuously during the entire procedure. 4) monitoring of seizure length clinically and by EEG. 5) succynilcholine 1 mg/kg was used for muscle relaxation. 6) methohexital 0.75 mg/kg as an anesthetic agent. The specific protocol developed for patients with low cardiac output includes: 1) ongoing cardiac medication one hour before ECT. 2) a nitroglycerine 50mg adhesive plaster 30 minutes before ECT. 3) 10mg nifedipine 30 minutes before ECT. 4) 5–15 mg labetalol, 5–10 minutes before the ECT treatment. 5) no use of anticholinergic agents. The patients were successfully treated by ECT, using this protocol. In our discussion, we will address the questions concerning the use of this treatment regimen in patients with decreased cardiac output.

NR356 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Bipolar Spectrum Disorder in Velo-Cardio-Facial Syndrome

Demitri F. Papolos, M.D., Psychiatry, Albert Einstein, 1300 Morris Park Avenue, Bronx NY 10461; Sabine E. Veit, M.D., Sam S. Parsia, B.A., Gianni L. Faedda, M.D., R. Goldberg, M.S., Robert Shprintzen, Ph.D., Bernice Morrow, Ph.D., Raju Kucherpalati, Ph.D., Herbert M. Lachman, M.D.

Summary:

We conducted an assessment of psychiatric illness in patients with velo-cardio-facial syndrome (VCFS), a genetic syndrome that involves over 40 somatic anomalies, learning disabilities, and behavioral disorders, and is associated with a microdeletion on chromosome 22q11. Hemizygosity of one or more genes at the 22q11 locus is likely responsible for the phenotypic anomalies of VCFS. The Diagnostic Interview for Children and Adolescents–Revised or the Standardized Clinical Diagnostic Interview were used to elicit psychiatric symptoms in the sample, which ranged in age between 5 and 25. A clinical interview performed by two research psychiatrists to validate specific symptoms and syndromes served to establish DSM-III-R consensus clinical diagnoses; 64% (16/25) of the VCFS patients studied received consensus clinical DSM-III-R diagnoses of bipolar spectrum disorder (BPD). Many of these cases presented with a rapid-cycling variant of the condition. The high incidence of BPD in this series suggests that a gene deleted

at the 22q11 chromosomal locus is involved in its pathogenesis. One potential candidate gene that is commonly deleted in VCFS is catechol O-methyltransferase (COMT). Our group has recently identified a polymorphism in the COMT gene (158^{met}) that leads to a 3- to 4-fold reduction in enzymatic activity. The studied patients showed a significant association between the low activity allele COMT 157^{met} and the rapid cycling form of BPD.

NR357 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Simplified Accounting of Drug Accumulation

Conrad M. Swartz, M.D., Department Of Psychiatry, ECU School of Medicine, Greenville NC 27858–4354

Summary:

Objective: To account for drug accumulation to determine equivalent daily drug doses at steady-state from knowledge of equivalent single drug doses, and vice-versa. Accordingly, the Accumulation Ratio (AR) was defined as the ratio of the day-mean blood drug level at steady-state to the peak blood drug level after one dose. One use is management of clinical withdrawal from sedatives. *Method:* One-compartment mathematical modeling. *Results:* The AR was found to equal 0.0601 times the half-life in hours, independent of distribution volume, clearance, dosage, and dosing schedule.

Conclusions: By application, although 4 mg alprazolam matches 16 mg clonazepam the first day, the AR reveals that 4 mg/day alprazolam matches 7.7 mg/day clonazepam after three days, because of accumulation. Similarly, 15 mg/day flurazepam matches 2 mg/day lorazepam the first day, but 11 mg/day at steady state. Further, 0.8 mg/day pimozide, costing just $10/month, matches 300 mg/day chlorpromazine.

The AR permits calculation of cumulative toxicity, e.g., exposure to organic chlorine, a carcinogen. Psychotropics with highest chlorine exposure were ranked after calculation: chloral hydrate, ethchlorvynol, chlorpromazine, clomipramine, bupropion, sertraline, and chlordiazepoxide. The AR complements previously-described methods for drug dose prediction and monitoring that were simplified by considering day-mean blood levels.

NR358 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Effects of Double-Blind Treatment with Nefazodone or Sertraline on Re-Emergence of Sexual Dysfunction in Depressed Patients

James M. Ferguson, M.D., Pharmacology Res Co, 448 E 6400 S #350, Salt Lake City UT 84107; Ram K. Shrivastava, M.D., Stephen M. Stahl, M.D., James J. Hartford, M.D., Barbara Nape, R.N., Frances Borian, R.N.

Summary:

Sexual dysfunction (orgasmic dysfunction, erectile and ejaculatory disturbances, and changes in libido) has been reported as a side effect associated with the use of several classes of antidepressants including the SSRIs. This study evaluated the potential for nefazodone to produce sexual side effects in a group of patients who reported sexual dysfunction during treatment of depression with sertraline. Patients with DSM-III-R major depressive episode who were receiving sertraline (100 mg/day) and experiencing sexual dysfunction attributable to sertraline therapy (difficulty with ejaculation/orgasm in men; orgasmic difficulties/inadequate lubrication/swelling in women) were screened for entry into a double-blind (DB) trial of nefazodone versus sertraline. After obtaining informed consent, eligible patients with stable depressive symptomatology were discontinued from sertraline therapy for one week, and then treated with placebo for the next 7 to 10 days. Patients no longer experiencing sexual dysfunction on placebo entered an eight week, randomized, DB trial with nefazodone (starting dose: 200 mg/day, maintenance dose: 400 mg/day) or sertraline (starting dose: 50 mg/day, maintenance dose: 100 mg/day). Patients were assessed weekly for safety and re-emergence of sexual dysfunction and bi-weekly for depressive symptoms. Of the 44 nefazodone and 31 sertraline patients who began DB treatment; 31 nefazodone and 20 sertraline patients completed the eight week study. Six nefazodone- and eight sertraline-treated patients discontinued treatment for adverse events (2 nefazodone and 4 sertraline patients for pyschosexual dysfunction). LOCF analysis of the intent-to-treat patient sample showed both treatments to have similar effects on depressive symptoms, (17-item Hamilton Rating Scale for Depression mean scores: 11.8 at baseline and 9.3 at endpoint for nefazodone; 11.1 at baseline and 9.0 at endpoint for sertraline). However, 71% of sertraline-treated patients experienced significant sexual dysfunction at the end of treatment, compared to only 30% of nefazodone-treated patients ($p < 0.01$). These findings provide evidence that in a select sample of patients with major depression and pre-existing sexual dysfunction attributed to current sertraline treatment, switching to nefazodone therapy resulted in continuation of antidepressant response, but significantly less sexual dysfunction.

NR359 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Double-Blind Comparison of Nefazodone and Fluoxetine in Depressed Patients

Patrice Rioux, M.D., U 320, INSERM, Caen Cedex 14033, France; Yves Kibleur, M.D., Olivier Frachon, Remy von Frenckell, Prof. Edouard Zarifian

Summary:

Background: Nefazodone and fluoxetine are antidepressant drugs marketed in the US and elsewhere. Nefazodone, a $5HT_2$ antagonist and 5HT reuptake inhibitor, down-regulates $5HT_2$ receptors in the frontal cortex when given chronically. Fluoxetine is a selective serotonin reuptake inhibitor.

Objective: The objective of this trial was to investigate the safety and efficacy of nefazodone and fluoxetine in the treatment of patients with mood disorders: moderate to severe nonpsychotic major depressive episode, with or without melancholia.

Method: Flexible doses of nefazodone (200–600 mg/d) or a fixed dose of fluoxetine (20 mg/d) were compared in an eight-week trial in 188 patients who met DSM-III-R criteria for major depressive episode (97%) or bipolar disorder, depressed (3%).

Results: Both treatment groups showed improvement in depressive symptomatology with no significant difference between the two drugs in activity as assessed by HAM-D-17 total score (mean change: – 13.1 fluoxetine, – 13.4 nefazodone) or factor scores, MADRS total score (mean change: – 15.6 fluoxetine, – 15.7 nefazodone), and CGI improvement scale (% responders: 73 fluoxetine, 71 nefazodone). Patients with melancholia also showed improvements on both treatments with no significant differences at endpoint. Treatment resulted in consistent improvement over the eight weeks of therapy for both nefazodone and fluoxetine. The rates of discontinuation for adverse events (10% fluoxetine, 7% nefazodone) were comparable between treatment groups.

Conclusion: The findings of this analysis confirm that nefazodone and fluoxetine both have equal antidepressant activity with a good safety profile.

NR360 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Evaluation of Fluvoxamine in Social Phobia

C. Lindsay DeVane, Ph.D., Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425–0742; Michael R. Ware, M.D., Naresh P. Emmanual, M.D., Olga Brawman-Minizer, M.D., R. Bruce Lydiard, M.D.

Summary:

There is currently no FDA approved treatment for social phobia although data suggest efficacy for several drug classes (beta adrenergic blockers, benzodiazepines, monoamine oxidase inhibitors, and selective ocrotonin reuptake inhibitors (SSRIs). The SSRIs are particularly attractive due to their favorable tolerance and safety profile in the treatment of depression.

We have conducted a single-blind, open-label trial of fluvoxamine to evaluate its efficacy and safety in the treatment of social phobia (DSM-III-R) and to assess physiological changes that may accompany treatment. Fifteen nondepressed patients (baseline HAM-D: 9.6 + / – 4.1), aged 22 to 44 years old (mean = 31.6 yr), entered the study and five males and five females completed a one-week placebo lead-in followed by an active six-week treatment period of flexible dosing (50 to 150 mg/day). A five-minute performance task (public speaking simulation) in which blood was sampled for plasma catecholamines and cortisol preceded and concluded the active treatment period. These data are pending. Preliminary analysis of key rating scales indicated a decrease in the scores (mean + / – -SD) for the total Brief Social Phobia Scale from baseline [BL] (47.3 + / – 12.5) to week 7 [Wk 7] (22.8 + / – 10.8) which averaged 52.0% across completers. The Marks-Sheehan Social Phobia fear scores dropped from 69.3 + / – 32.6 [BL] to 21.6 + / – 20.0 [Wk 7] while the avoidance scores dropped from 37.8 + / – 21.1 [BL] to 10.8 + / – 7.4 [Wk 7].

Fluvoxamine appeared to be effective and well tolerated in completers. Drop outs were due to drowsiness (2), nausea (1), or were lost to follow-up (2).

NR361 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Four Weeks Nonresponse Who Responds at Eight Weeks?

Andrew A. Nierenberg, M.D., Psychiatry, Massachusetts General Hos, 15 Parkman Street WACC 815, Boston MA 02114; Rosemarie Mulroy, B.A., Jonathan E. Alpert, M.D., John J. Worthington III, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Objective: Those patients who fail to respond to fluoxetine by four weeks will sometimes go on to respond after an additional four weeks of treatment. The purpose of this study was to determine if clinically useful predictors could be found that would encourage, or discourage, clinicians to persist with treatment for another four weeks. *Method:* We assessed 101 depressed patients who had either a non response (Hamilton Depression Scale 17 item - HAMD -change ≤ 20%) or a partial response (HAMD change < 40%) after four weeks of open fluoxetine 20 mg daily. Depression characteristics and Axis I comorbidity were evaluated comparing eight week responders and nonresponders using a response criterion of HAMD change ℓ 50%. *Results:* Of the 101 partial and nonresponders after four weeks, 66 patients failed to respond while 35 responded at the end of eight weeks. No differences were found in age, age of onset of depression, duration of depression, or baseline HAMD scores. Furthermore, no differences were found in any Axis I comorbid condition. *Conclusion:* This preliminary study indicates that neither depression characteristics nor Axis 1 comorbid conditions differentiate four-week partial and nonresponders to fluoxetine 20 mg daily who then go on to respond at eights weeks.

NR362 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Effect of Venlafaxine Versus Fluoxetine on the Metabolism of Dextromethorphan

Jess D. Amchin, M.D., Medical Affairs, Wyeth-Ayerst Labs, 555 East Lancaster Avenue, St. Davids PA 19087; Larry Ereshefsky, Pharm D., William M. Zarycranski, Pharm D.

Summary:

Objective: To evaluate the effect of venlafaxine versus fluoxetine on cytochrome P450 2D6 (CYP2D6) as measured by the ratio of dextromethorphan (DM) to its metabolite dextrorphan (DT).

Methods: 28 healthy CYP2D6 extensive metabolizers were randomized to receive either venlafaxine 37.5 mg bid for seven days followed by 75 mg bid until day 28 or fluoxetine 20 mg daily for 28 days. Plasma concentrations for each drug and its active metabolite were assessed. Urinary DM/DT ratios were evaluated at screen and days – 1, 7, 28, and 2 weeks after drug discontinuation (day 42).

Results: 26 subjects completed the study. Steady state drug concentrations were achieved in both groups. Mean DM/DT ratios were as follows:

MEAN DEXTROMETHORPHAN/DEXTRORPHAN RATIOS

	Baseline	Day 7	Day 28	Day 42
Fluoxetine (n=12)	0.014	0.072	0.159	0.077
Venlafaxine (n=14)	0.008	0.011	0.018	0.007

The difference between fluoxetine and venlafaxine DM/DT ratios was statistically significant ($p < 0.05$) at day 7, day 28, and day 42. Furthermore, in a separate analysis comparing percent changes from baseline, DM/DT ratios increased 8.25 times for fluoxetine and 1.95 times for venlafaxine at day 28 ($p < 0.01$).

Conclusions: This in vivo study confirms in vitro data demonstrating venlafaxine's significantly weaker inhibition of CYP2D6 compared to fluoxetine as measured by the metabolism of dextromethorphan, a highly sensitive CYP2D6 marker. These results suggest that clinically significant interactions could occur between fluoxetine and drugs metabolized by CYP2D6, which may not occur with venlafaxine.

NR363 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

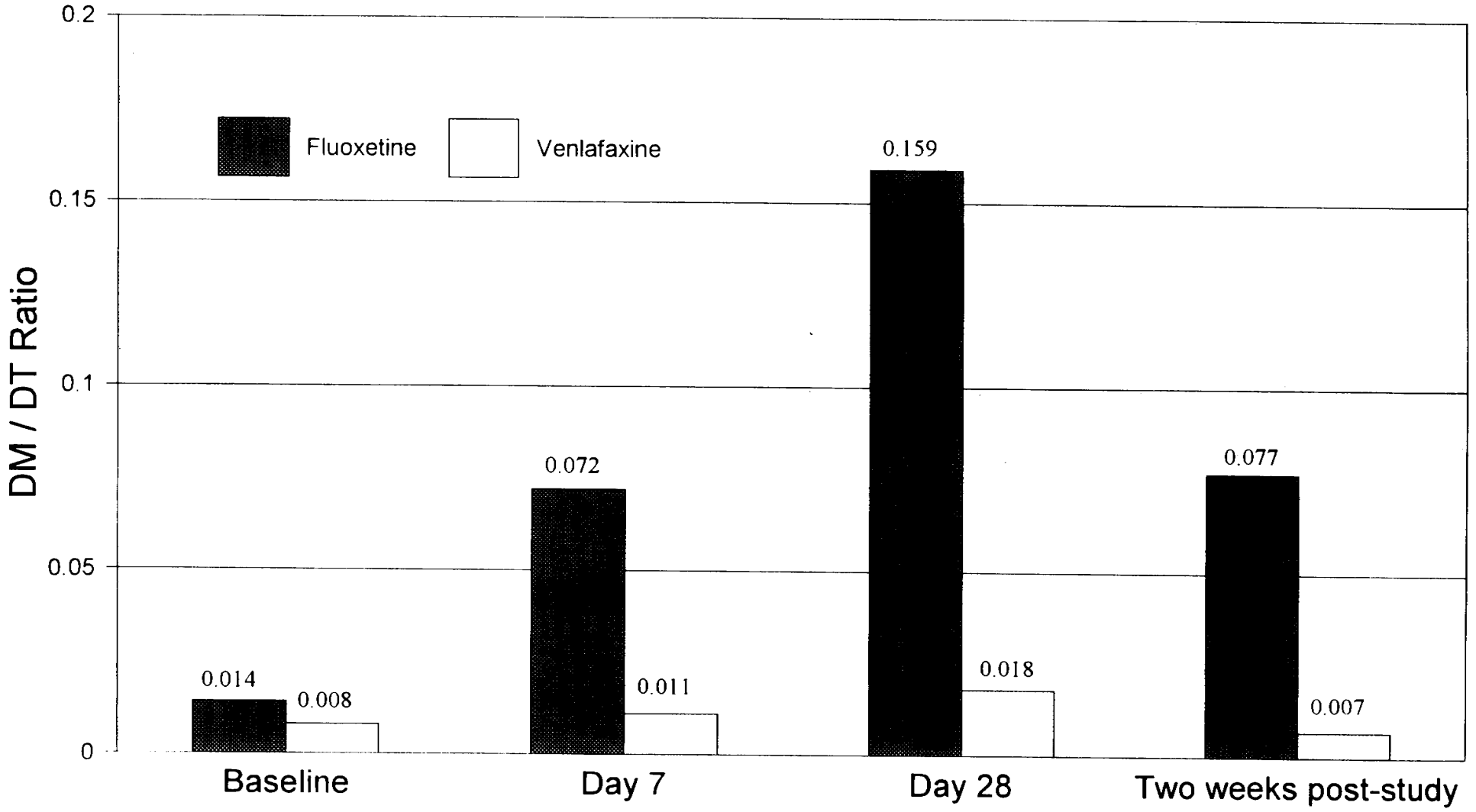
Chart Review: Family Physicians' Prescription of Antidepressants

Marijo B. Tamburrino, M.D., Psychiatry, Medical College Ohio, PO Box 10008, Toledo OH 43699; Rollin W. Nagel, M.A., Denis J. Lynch, Ph.D.

Summary:

The majority of depressed and anxious patients on psychotropic medication receive these prescriptions from family physicians. This study explored antidepressant and anxiolytic prescription patterns of physicians at a Midwestern academic family practice center. Outpatients waiting to see their family physicians completed a demographic survey and gave permission for review of their medical charts. Over 90% (N = 554) of those approached agreed to participate. Approximately 21% (N = 118) of patients had a history of being on antidepressants and 18.9% (N = 105) had been on anxiolytics. Average doses of antidepressants were: amitriptyline, 55 mg (N = 54); desipramine, 65 mg (N = 18); doxepin, 49 mg (N = 30); fluoxetine, 23 mg (N = 32); imipramine, 65 mg (N = 14); nortriptyline, 51 mg (N = 6); protriptyline, 7.2 mg (N = 2); sertraline, 50 mg (N = 5); and trazodone, 107 mg (N = 7). On the charts, there were 105 individuals diagnosed with "depression," one with "dysthymic disorder," and one with "major depression and dysthymic disorder." Fifty-nine individuals received a diagnosis of "anxiety" while 16 persons were diagnosed with "stress." Twelve percent (N = 22) of patients on psychotropic drugs had no psychiatric diagnosis recorded on the chart.

In this study, doses of antidepressants were relatively low, suggesting that family physicians may be undertreating depression. Health care changes will give family physicians even more responsibility for management of psychiatric illnesses in the future. Psychiatrists should be integrated into family practice training pro-


0.2
0.15
0.1
0.05
0
DM / DT Ratio
Fluoxetine
Venlafaxine
0.014
0.008
0.072
0.011
0.159
0.018
0.077
0.007
Baseline
Day 7
Day 28
Two weeks post-study

grams to ensure adequate education on the biological treatment of depression and anxiety.

NR364 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Clozapine and Associated Diabetes Mellitus

Anand P. Popli, M.D., Cleveland VAMC, CWRU, 10000 Brecksville Road, Breckville OH 44141; P. Eric Konicki, M.D., George J. Jurjus, M.D., Matthew A. Fuller, Pharm D., George E. Jaskiw, M.D., Luis G. Ramirez, M.D.

Summary:

Clozapine is an effective therapy for the treatment of refractory psychosis. The common adverse effects associated with clozapine include sedation, sialorrhea, palpitations, seizures, and hematological changes like agranulocytosis. The metabolic effects of clozapine, particularly its effect on weight gain, have received some attention, yet literature on the relation of clozapine to hyperglycemia is limited to two separate case reports. We present a four-case series in which clozapine use was associated with either new onset of diabetes mellitus, or severe exacerbation of preexisting diabetes mellitus. Three of the four patients have been able to continue treatment with clozapine, with improvement in BPRS scores (mean change of 30). The change in glycemic control was not significantly related to weight gain. One of these patients developed diabetic ketoacidosis. In two other patients with pre-existing diabetes and with no weight gain, the loss of glycemic control occurred during a double-blind haloperidol/clozapine trial. One of the patients reverted back to his previous level of glycemic control after discontinuation of clozapine. The exact mechanism of action of clozapine and its effect on glucose control remains to be elucidated. Different hypotheses related to possible mechanisms will be presented.

NR365 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

An Open Trial of Venlafaxine in BPD

Paul J. Markovitz, M.D., Mood & Anxiety Treatment Ctr, 2101 Richmond Rd, Suite 1030, Beachwood OH 44122; Susan C. Wagner, M.A.

Summary:

Introduction: Borderline personality disorder (BPD) is associated with impulsivity, aggression, obsessionality, depression, anxiety, suicidality, and brief psychotic episodes. These behaviors have all been linked to low levels of serotonin in the central nervous system. Venlafaxine, a newer serotonin reuptake inhibitor, has not been studied systematically and evaluated in BPD. We report on such a study with this medication.

Method: 56 patients with DSM-III-R BPD and a Gunderson Diagnostic Interview for BPD score of seven or higher were entered in a 12-week open trial of venlafaxine. Outcome was measured by changes in the Hopkins Symptom Checklist-90R (SCL-90R).

Results: The SCL-90R was reduced from 183.4 ± 32.7 to 71.7 ± 26.8. All subscales of the SCL-90R improved statistically. Presenting behaviors predicting a positive clinical response included self-injury, affective instability, migraines, obsessionality, and fibromyalgia. Predictors of poor response included poor response to prior trials of SRIs, and cigarette usage, which probably results in an increased rate of metabolism of venlafaxine.

Discussion: The data suggest venlafaxine is effective in acutely reducing BPD pathology, and many of the behaviors associated with BPD. The data suggest some comorbid behaviors may help predict an increased likelihood of responding to venlafaxine. Controlled studies are indicated.

NR366 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Flesinoxan in the Treatment of Major Depressive Disorder: A Fixed Dose, Placebo-Controlled Trial

L. DiAnne Bradford, Ph.D., Medical Services, Solvay Pharmaceutics, 901 Sawyer Road, Marietta GA 30062; Carla Prinsze, M.D.

Summary:

The present study reports a Phase II, double-blind, placebo-controlled fixed dose study of flesinoxan, a full serotonin agonist at both pre- and post-synaptic receptors, which has been shown to be safe and effective in generalized anxiety disorder (GAD). The study design included three fixed dose levels of flesinoxan compared with placebo and imipramine as active control in patients with major depressive disorder (MDD). Following a single-blind washout period, patients were randomized to either 0.4 mg/d (n = 63), 1.2 mg/d (n = 58), 4.0 mg/d (n = 60), 150 mg/d imipramine (n = 62), or placebo (n = 126) for a six-week treatment period. Efficacy was assessed by the HAM-D, MDRS, and CGI. Using the ITT-LOCF analysis, 1.2 mg/d flesinoxan showed robust treatment effects on all efficacy parameters which were both statistically significant and clinically relevant, e.g., a four-point difference on the HAM-D and 0.5 point difference on the depressed mood item compared with placebo. Only 12% of the 1.2 mg/d flesinoxan group stopped treatment early (compared with 31% in the imipramine cohort); flesinoxan was remarkably well tolerated with only 1 (2%) patient terminating treatment early because of intolerance (cf: 12(18%) for imipramine. The most commonly reported side effects for the active dose of flesinoxan were nausea (11% cf 10% IMI and 3% PLA) and dizziness (7% cf 11% IMI and 5% PLA). Dry mouth (40% vs 3% PLA), constipation (10% vs 2% PLA), and sweating (10% vs 1% PLA) were also reported for IMI. It is concluded that flesinoxan is extremely well tolerated and may have therapeutic advantages over present therapies, showing efficacy in both MDD and GAD.

NR367 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone in Patients with Developmental Disabilities

Theodore W. Wasserman, M.D., 1345 South 4th St, Philadelphia PA 19147–5932

Summary:

Objectives: Risperidone was evaluated in 40 developmentally disabled adults with a variety of Axis I diagnoses over a period of six or more months.

Results: Equal numbers of the patients live in institutions and in the community. Epilepsy or a history of seizure disorder was diagnosed in one-third of the patients, autistic disorder in 30%. Before starting treatment with risperidone, all patients were receiving neuroleptics (thioridazine in 40%). Transferring patients to risperidone was accomplished in less than one week with no untoward effects and no significant breakthrough behavior (severe breakthrough behavior is seen in many developmentally disabled patients when neuroleptic doses are reduced). The mean risperidone dose was 3–4 mg/day. Risperidone appeared to be effective and safe in this population: aggression, the most common psychiatric symptom in developmentally disabled patients, was reduced; caregivers report that patients are more directable, less irritable, and more in touch with the environment; dysphoric and aggressive features in patients with autistic disorder are improved; no increase in seizure frequency was experienced by patients with epilepsy. Risperidone was generally well-tolerated and fewer than 5% of the patients are taking antiparkinsonian medication.

Conclusion: Risperidone appears to be a potentially useful agent in patients with developmental disabilities.

NR368 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Costs of Treatment with Risperidone and Clozapine

David Thompson, R.N., Mental Health Services, San Diego County, 5352 Van Nuys Court, San Diego CA 92109

Summary:

Objective: A study was conducted to compare the costs of treatment with risperidone and clozapine.

Method: Psychiatric patients who were refractory to conventional neuroleptics were switched to treatment with risperidone or clozapine. Costs associated with psychiatric care of these patients were observed for one year before and after the start of treatment. Information was derived from billing data provided by pharmacies, fee-for-service MediCal, and clinics and hospitals.

Results: Costs associated with psychiatric care were evaluated in 29 patients with schizophrenia and 11 with other psychoses. Twenty patients received risperidone and 20 received clozapine. Before treatment, the average costs of overall psychiatric care were $9,406/patient switched to risperidone and $7,253/patient switched to clozapine. One year after treatment, the average overall costs decreased to $5,360/patient treated with risperidone and increased to $15,085/patient treated with clozapine. The cost differential between treatments resulted from higher clozapine prescription prices and weekly outpatient visits by clozapine patients for blood tests. The average costs of these were $229/month/patient on risperidone compared with $1,043/month/patient on clozapine.

Conclusion: Compared with clozapine, treatment with risperidone is more economical for psychiatric patients refractory to conventional neuroleptics.

NR369 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Double-Blind Comparison of Nefazodone and Sertraline in Highly Anxious Patients with Major Depression

Cal K. Cohn, M.D., 7777 SW Freeway Suite 1036, Houston TX 77074; John P. Feighner, M.D., Steven D. Targum, M.D., Stephen G. Thein, M.D.

Summary:

Background: Although not a specific DSM-III-R diagnosis, major depressive disorder with high levels of anxiety with or without panic attacks, also referred to as mixed anxiety/depression (MAD), is recognized as a commonly occurring syndrome.

Objective: The objective of this trial was to compare the patterns of response between nefazodone (N) and sertraline (S) in patients with symptoms of anxiety associated with major depression.

Method: Flexible doses of nefazodone (100–600 mg/d) or sertraline (50–200 mg/d) were compared in 151 patients (77 N, 74 S) who were highly anxious with a nonpsychotic depression--major depressive episode, moderate or severe, for six weeks. Rating instruments employed were the 17-item Hamilton Depression Rating Scale (HAM-D-17), the Clinical Global Impression (CGI) Scales, and the Hamilton Anxiety Rating Scale (HAM-A).

Results: Baseline scores were as follows: HAM-D-17 total: 24.0 N, 24.1 S; HAM-D Retardation Factor: 7.3 N, 7.4 S; HAM-D Anxiety Factor: 8.6 N, 8.4 S; CGI Severity: 4.3 N, 4.2 S; HAM-A: 24.9 N, 25.3 S. After six weeks of therapy both treatment groups showed reduction in HAM-D-17 total scores (–15.8 N, –16.4 S), Retardation Factor (–4.7 N, –4.9 S), Anxiety Factor (–5.5 N, –5.8 S), CGI Severity (–2.1 for both drugs), CGI Improvement (% responding: 80 N, 87 S), HAM-A scores (–16.9 N, –17.9 S), and in the percentage showing a 50% reduction in HAM-A scores (83 N, 87 S). There were no significant differences in the rate of response between groups on any measure. Seventeen nefazodone-treated patients (20%) and 11 sertraline-treated patients (14%) discontinued for lack of efficacy.

Conclusion: The findings of this analysis confirm that nefazodone and sertraline have antidepressant activity. Both treatment groups also showed improvement on measures of anxiety. Both drugs were safe and well tolerated.

NR370 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Double-Blind Trial of Nefazodone Versus Placebo in Depressed Inpatients

John P. Feighner, M.D., Feighner Res. Institute, 15725 Pomerado Rd, Poway CA 92064-2021; Mary E. Bennett, M.D., Douglas L. Roberts, Jr., M.D., M. Frances D'Amico, M.S., Kathleen O'Brien, M.S.

Summary:

Background: Nefazodone, a $5HT_2$ antagonist and 5HT reuptake inhibitor, down-regulates $5HT_2$ receptors in the frontal cortex when given chronically. While nefazodone has been shown to be an effective drug for the treatment of outpatients with major depressive disorder, its utility in hospitalized patients has yet to be demonstrated. In fact, efficacy in inpatients has been demonstrated for only a few antidepressants.

Objective: The objective of this study was to investigate the utility of nefazodone in the treatment of depressed inpatients.

Method: Flexible doses of nefazodone (100–600 mg/d) and placebo (1–6 tablets/d) were compared for six weeks in 81 inpatients (41 nefazodone, 40 placebo) who met DSM-III-R criteria for nonpsychotic major depression and who required psychiatric hospitalization.

Results: The severity of illness was reflected in baseline values for the Clinical Global Impression (CGI) Severity score (5.0 nefazodone, 4.9 placebo), the 17-item Hamilton Depression Rating Scale (HAM-D-17: 29.7 nefazodone, 29.8 placebo), the Montgomery Asberg Depression Rating Scale (MADRS: 39.0 nefazodone, 38.6 placebo) and the presence of melancholia (98% nefazodone, 93% placebo). At the end of treatment nefazodone was found to be superior ($p \leq .01$) to placebo on the HAM-D-17 (mean change: –13.5 nefazodone, –6.1 placebo), the number of patients exhibiting at least a 50% decrease in HAM-D-17 score (54% nefazodone, 18% placebo), the CGI Improvement (% much or very much improved: 56 nefazodone, 25 placebo) and Severity scores (mean change: –1.6 nefazodone, –0.9 placebo), and the MADRS (mean change: –17.8 nefazodone, –7.7 placebo). Mean modal doses at the end of treatment reached 500 mg with nefazodone and 5.4 tablets with placebo. Five placebo-treated patients (13%) and four nefazodone-treated patients (10%) discontinued for adverse experiences, while 19 (48%) in the placebo group and 12 (29%) in the nefazodone group discontinued for lack of effect.

Conclusion: The results of this study demonstrate that nefazodone is effective in the treatment of severely depressed hospitalized patients.

NR371 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Efficacy of Nefazodone in Continuation Treatment of Depression

Alan D. Feiger, M.D., Feiger Psych Med Ctr, 3555 Lutheran Pkwy Ste 320, Wheat Ridge CO 80033–6022; Robert D. Bielski, M.D., James D. Bremner, M.D., Jon F. Heiser, M.D., Madhukar H. Trivedi, M.D.

Summary:

Background: Patients who have achieved remission from an episode of major depression are at risk of experiencing a relapse or recurrence of the disease in the absence of continuation or maintenance treatment. Although short-term clinical trials are used to establish the efficacy of an antidepressant drug, its therapeutic

benefit ultimately depends on long-term management of depression.

Objective: The objective of this study was to evaluate the safety and efficacy of nefazodone in the prevention of relapse in depressed outpatients, using a double-blind, placebo substitution study design.

Methods: After 16 weeks of single-blind treatment with nefazodone (titrated to 100–600 mg/day) at five study centers, 131 patients responding to treatment and meeting specified remission criteria (HAM-D-17 ≤ 10 on two consecutive visits at least seven days apart) were randomized in a 36-week (nine-month) double-blind continuation trial to either nefazodone (n = 65) or placebo (n = 66).

Results: In the nine months of continuation treatment, the overall rate of relapse was significantly lower ($p < .01$) for patients randomized to nefazodone (1.6%) than for patients randomized to placebo (14%), with relapse defined as HAM-D-17 total score ℓ 18 for two consecutive visits at least seven days apart. A survival analysis of time to relapse showed that, compared with placebo, nefazodone significantly ($p \leq .01$) reduced the probability of relapse. The estimated risk of relapse for patients who continued nefazodone treatment was approximately 1/10th the risk for those patients assigned to placebo treatment. Discontinuation from the trial for lack of effect (based on the investigator's clinical judgment) also occurred less often ($p < .05$) for patients who continued to receive nefazodone (14%) than for patients receiving placebo (29%) during continuation treatment. Survival analysis showed that nefazodone significantly ($p \leq .01$) reduced the probability of discontinuation for lack of effect compared with placebo over the nine-month trial. No nefazodone-treated patient discontinued the study because of an adverse event.

Conclusion: This study shows that nefazodone prevents relapse of depression during continuation treatment, with no or mild adverse events.

NR372 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Clozapine and Change in Body Mass

Frances R. Frankenburg, M.D., Psychiatry, Bedford VA Hospital, 200 Springs Road, Bedford MA 01730; Mary C. Zanarini, Ed.D., Judith Kando, Pharm D., Franca Centorrino, M.D.

Summary:

Objective: Patients being treated with clozapine have been reported to gain weight. We hypothesized that there would also be changes in body mass, which are more directly related to cardiovascular morbidity. We also attempted to determine factors associated with change in body mass.

Methods: Forty-two patients who had been treated with clozapine for at least one year were weighed and measured, and a body mass index (BMI), measured in kg/meter^2, was calculated. Patients were also asked about a series of factors possibly related to change in body mass.

Results: Female patients gained weight and body mass, with a significant increase in BMI from 23.2 to 29.1 kg/m^2 ($p < 0.001$). Males also gained weight and body mass, with a significant increase in BMI from 26.4 to 29.7 kg/m^2 ($p < 0.001$). Stepwise multiple regression analysis showed that factors related to increase in body mass were initial body mass, dose of clozapine, and whether or not the patient stopped smoking.

Conclusions: Both female and male patients treated with clozapine gain significant body mass. This may place them at greater risk for cardiovascular morbidity.

NR373 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone in Patients with Chronic Schizophrenia: Acute Responses and Effects on One-Year Hospitalization Rates

Michael Phillipp, M.D., Psych Clinic, Bezirkskrankenhaus, Prof Buchner Str 22, Landshut, Germany; Risperidone Study Group,

Summary:

Objective: In a multicenter trial, the effects of risperidone on psychopathology, extrapyramidal symptoms, and rates of hospitalization were assessed in patients with chronic schizophrenia.

Methods: The subjects were 254 patients with chronic schizophrenia (DSM-III-R); their mean age was 38 years and mean duration of psychiatric illness was 11 years. After abrupt discontinuation of previous psychotropic drugs, the dose of risperidone was increased from 1 mg to 3 mg twice daily on day 3. From day 14 the dose could be reduced or increased according to each patient's response. The eight-week study was completed by 173 patients. In 63% of the 40 patients who dropped out of the trial during the first two weeks, discontinuation was attributed to the abrupt withdrawal of the previous psychotropic medication.

Results: Mean scores on the Brief Psychiatric Rating Scale and the Clinical Global Impression were reduced significantly from baseline to endpoint ($p = 0.0001$). Of the 79% of all patients who improved their total BPRS scores, 66% showed greater improvement on the negative subscale (anergia cluster) than on the positive subscale (thought disturbances). Severity of extrapyramidal symptoms (mean scores on the Simpson-Angus Scale) was reduced significantly at endpoint ($p = 0.0001$). Hospitalization rates were compared during the year before and after risperidone treatment in 166 patients. The number of psychiatric hospitalizations was reduced by 24% during the year after and the number of days in hospital was increased by 1%. Among the study completers, hospitalizations were reduced by 40% and days in hospital by 23%.

Conclusions: Risperidone was effective and safe in patients with chronic schizophrenia. The results also demonstrate that risperidone can have health economic benefits in the long-term treatment of schizophrenia.

NR374 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone in Schizophrenia: Practical Issues

Alice F. Duncan, M.D., Stokton-On-The-Forest, Stokton Hall Hospital, The Village, York, England; Risperidone Study Group,

Summary:

Objective: To address practical patient management issues associated with risperidone in a multicenter study.

Method: Adult patients with chronic schizophrenia were recruited if they had a relapse, poor response, or unacceptable side effects from other treatments. All patients received risperidone monotherapy for 6–16 weeks. Anticholinergic medication was withdrawn gradually. Routine use of benzodiazepines was discontinued. Response to treatment, side effects, and use of concomitant medication were recorded.

Results: Of 192 patients who entered the study (37 relapsing, 127 men, median age 37 years) 114 completed it. This represented 68% of the relapsing group and 57% of nonrelapsers. Thirty patients withdrew because of adverse effects, 13 due to lack of efficacy. Clinical Global Impression scores improved in 121 patients (63%). Mean Krawiecka score fell from 11.1 ± 5.1 to 7.4 ± 5.5 ($p < 0.0001$). Improvement was noticed within four days of starting risperidone in 63%. Dyskinesia and parkinsonian symptoms improved or responded satisfactorily in 91%. Antiparkinsonian drugs were required by 43% of patients at entry but were stopped or reduced in 76% of these; 36 patients required benzodiazepines (41% were relapsers; 14% were nonrelapsers).

Where used, benzodiazepines improved study completion rate in relapsing patients to 87%.

Conclusion: Risperidone monotherapy was safely and easily achieved and was associated with clinical improvements and reduced extrapyramidal effects in most patients despite reductions in concomitant medications.

NR375 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Health Care Resource Utilization and Costs Before and After Initiation of Risperidone Treatment for Schizophrenia in Saskatchewan

Penny Albright, Ph.D., Janssen Res Foundation, 19 Green Belt Drive, North York Ontario, Canada; Scott Livingstone, M.Sc., David L. Keegan, M.D., Satish Shrikhande, M.D., Jacques Le Lorier, M.D.

Summary:

Objective: A study to assess the role of risperidone in reducing health care costs was conducted in the Province of Saskatchewan, chosen because it maintains a large population-based, computerized health care utilization database.

Methods: Changes in the utilization of health care resources and associated costs were observed a mean of ten months before and ten months after the start of risperidone treatment in 146 patients with schizophrenia. All patients had received at least one prescription for risperidone after unsuccessful treatment with other antipsychotic medications.

Results: During the ten months after initiation of risperidone treatment, hospital admissions decreased by 60%, length of hospital stay by 58%, and physician visits by 27%. Excluding risperidone, the number of prescriptions for antipsychotic medications also decreased; however, the costs for prescriptions increased by 145% with the addition of risperidone. The increase in prescription costs was offset by savings derived from the overall reduction in health care services. Total cost savings during the ten months after the start of risperidone were $7,925 per patient per year.

Conclusions: The results support the role risperidone has in reducing health care services and related costs for patients with schizophrenia.

NR376 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone in the Outpatient Treatment of Chronic Schizophrenia: A Phase IV Multicenter Trial

Guy Chouinard, M.D., Psychiatry, Allan Memorial Hospital, 1025 Pine Avenue West, Montreal PQ H3A 1A1, Canada; Alain Labelle, M.D., Linda Beauclair, M.D., Lili C. Kopala, M.D., Sunny Johnson, Kulbir I. Singh, M.D.

Summary:

Objective: In an eight-week open study, the efficacy and safety of risperidone were assessed in 330 outpatients with chronic or subchronic schizophrenia.

Methods: The dose of risperidone was increased from 2 mg/day on day 1 to 6 mg/day on day 3 and after 14 days could be increased or reduced according to each patient's response; the final mean dose was 6.1 mg/day. Efficacy was assessed by means of the Positive and Negative Syndrome Scale (PANSS), the Clinical Global Impression (CGI) Scale, and the Global Assessment of Functioning (GAF).

Results: Two hundred forty-four patients (74%) completed the study. Patients' scores on the PANSS improved after one week of risperidone and continued to improve for the duration of the study. Total PANSS scores and scores on each of the PANSS subscales were significantly reduced from baseline to treatment endpoint ($p = 0.0001$). A clinical response (ℓ 20% reduction in total PANSS scores) was shown by 37% of the patients after one week and by 77% at endpoint. According to CGI scores, 62% of patients were improved by the end of week 1 and 84% by endpoint. Mean GAF scores were also reduced significantly from baseline to endpoint ($p = 0.0001$). According to scores on the Extrapyramidal Symptom Rating Scale, the patients showed significant reductions in the severity of parkinsonism, dystonia, and dyskinetic movements during the eight-week treatment ($p < 0.0001$). Adverse events were reported by 237 patients; 70% of the events occurred during the first two weeks of treatment.

Conclusion: Our results confirm earlier findings from double-blind studies that risperidone is an effective and safe agent in the treatment of chronic and subchronic outpatients with schizophrenia.

NR377 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Long-Term Safety of Risperidone

Martin B. Brecher, M.D., Janssen Res Foundation, 1125 Trenton-Harbouton Road, Titusville NJ 08560

Summary:

Objective: Studies have been conducted to assess the safety and efficacy of risperidone administered to patients with chronic schizophrenia over a period of up to one year.

Methods: Safety data from three studies are available: 1) a double-blind study of 99 patients who received a mean of 9 mg/day of risperidone over a mean period of 227 days; 2) an open-label study of 265 patients who received a mean of 8.5 mg/day of risperidone for a mean of 184 days; and 3) an open-label study of 107 patients who received a mean of 8.3 mg/day of risperidone for a mean of 206 days.

Results: One patient died (suicide) during treatment with risperidone. No unusual serious adverse events occurred, and, with the exception of myocardial infarction and convulsions, no serious adverse event unrelated to the underlying illness occurred in more than one patient. The two cases of myocardial infarction were reported in men aged 60 + who had risk factors for myocardial infarction. Convulsions associated with hyponatremia were reported in two patients and convulsions associated with head trauma in one. The pattern of adverse events observed in the long-term studies was similar to that observed in the three large double-blind, short-term studies. Severity of extrapyramidal symptoms was similar to that reported in patients receiving the same doses of risperidone in the double-blind short-term studies. No significant electrocardiographic changes or changes in vital signs (except for an increase in mean body weight) were observed in the long-term studies. Increases in prolactin levels were reported; the association of these increases with adverse events is being investigated. Data from other studies still being analyzed will also be presented.

Conclusions: The low incidence of serious adverse events in patients exposed to high doses of risperidone for many months provides strong evidence that risperidone is safe for long-term use.

NR378 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Effects of Clozapine on Aggression: A Randomized-Controlled Study

Eva W.C. Chow, M.D., Clarke Institute of Psychiatry, 250 College Street, Toronto ON M5T 1R8, Canada; Himansu Desai, B.Sc., Alison S. Bury, M.A., Rochelle Roy, R.N., Anne S. Bassett, M.D., Evan J. Collins, M.D.

Summary:

Objective: Many case reports and retrospective studies have described a decrease in violence and in the use of restraint and seclusion with clozapine therapy. The current study examines the

effects of clozapine treatment in a group of aggressive, psychotic patients using a prospective, randomized controlled design.

Method: Fifteen inpatients (10 Male, 5 Female) of a chronic psychiatric hospital with a DSM-III-R psychotic condition (12 schizophrenia, 2 schizoaffective disorder, 1 dementia with psychosis) for whom clozapine was being considered were randomized into clozapine treatment group (N = 9) or the control group (N = 6). Patients in the clozapine treatment group were tapered off their usual medications, and started on clozapine at week 2, while patients in the control group were continued on their usual medications during the study. All patients were assessed using the Positive and Negative Syndrome Scale (PANSS) and the Modified Overt Aggression Scale (MOAS) at baseline and at weeks 6, 10, and 14.

Results: The PANSS scores did not significantly improve over the three months for both groups. However, the MOAS scores at 6 and 10 weeks were significantly reduced from baseline measure in the clozapine treatment group, but not the control group.

Conclusions: Although the sample size is small and the duration relatively short, the results of this study provide further evidence for an anti-aggressive effect of clozapine, and suggest that this effect may be independent from its antipsychotic properties.

NR379 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Depot Versus Oral Neuroleptic Usage in New York State

Leslie L. Citrome, M.D., Clinical Research, Nathan Kline Institute, 140 Old Orangeburg Road, Orangeburg NY 10962; Jerome Levine, M.D., Baerbel Allingham, M.S.

Summary:

Objective: To examine the correlates of prescribing depot neuroleptics within psychiatric hospitals operated by the New York State Office of Mental Health (OMH).

Method: Oral and depot patient groups for the calendar year 1994 for all 21 adult civil inpatient facilities operated by OMH were compared. Patients were placed in the depot group if they were prescribed a depot neuroleptic, regardless of whether they also received oral neuroleptics. A total of 18,543 individual in-patients were identified as having received neuroleptics in 1994. A logistic regression (additive model) was fit using four variables (gender, age, race, and facility) for the probability of receiving depot neuroleptic.

Results: Among facilities, depot utilization ranged from 12% to 39% (mean 28%, standard deviation 8%) of all patients receiving neuroleptics. Differences among facilities were statistically significant ($p < 0.05$). Mean utilization rate for males was 29%, females 26%, whites 22%, blacks 36%, hispanic/others 30%, age under 35 years and between 35 and 65 years 30%, age 65 years or older 16%. Overall, by logistic regression, gender was *not* found to be a statistically significant factor, but blacks and hispanic/others were found to be more likely than whites to receive depot neuroleptics ($p < 0.05$) and those 65 years or older were found to be less likely to receive depot neuroleptics ($p < 0.05$).

Conclusions: Within the New York State psychiatric inpatient population, the percentage receiving depot neuroleptic medication varies significantly by facility, age, and race. This raises the question whether depot neuroleptics are being prescribed rationally and optimally to enhance patient outcome.

NR380 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Tardive Dyskinesia, Clozapine and Treatment Response

Gregory W. Dalack, M.D., Psychiatry, VA Med Ctr, 2215 Fuller Rd 116C, Ann Arbor MI 48105; Lisa M. Becks, B.A., Gina Baslock, B.A., James H. Meador-Woodruff, M.D.

Summary:

Objective: To examine the effect of clozapine treatment on tardive dyskinesia among patients with schizophrenia in a VA outpatient clinic.

Methods: In a retrospective chart review, we examined the relationship among TD, clozapine treatment, and treatment response in patients receiving clozapine at the Ann Arbor VAMC. The 13 subjects were all male, mean age 43.9 ± 6.0 years. Prior to starting clozapine, 12 of the 13 met criteria for refractory illness; one subject had severe and disabling tardive dystonia. Six subjects had a diagnosis of TD at the beginning of clozapine treatment. BPRS and AIMS results were analyzed for subjects grouped by diagnosis of TD (present or absent) at baseline using two-tailed paired t-tests (self as own control).

Results: At baseline, subjects with TD had a BPRS total score of 60.7 ± 3.9 and AIMS score (sum items 1–7) of 12.2 ± 4.1. They received an average clozapine dose of 358 ± 196 mg for 10.3 ± 5.5 months. At follow-up, their average BPRS score was 32.8 ± 10.4 ($t = 5.7$; $p < 0.01$), and AIMS score was 1.8 ± 1.9 ($t = 6.1$; $p < 0.01$). Subjects without TD at baseline also showed a decrease in BPRS scores (baseline 52.0 ± 9.0; follow-up 30.3 ± 8.0; $t = 4.8$; $p < 0.01$) after receiving a mean clozapine dose of 489 ± 258 mg for 17.1 ± 9.8 months. AIMS scores in this group showed no significant change (baseline 1.7 ± 1.3; follow-up 0.71 ± 0.95; $t = 1.62$; p = NS).

Conclusions: The lack of a randomized, double-blind design limits our conclusions. However, our results suggest a clinically and statistically significant effect of clozapine on TD in a group of chronically psychotic patients, and underscore the striking utility of clozapine in those with significant TD.

NR381 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Repeated ECT in Major Depression: Acute Effects on CBF

Michael H. Wiegand, M.D., Psychiatry, Technical University, Ismaninger Street, Munich 81675, Germany; David L. Duncan, M.D., Abbas Alavi, M.D., Mark Stecuer, M.D., William A. Ball, M.D., Laszlo Gyulai, M.D.

Summary:

Objective: Electroconvulsive therapy (ECT) is an effective antidepressant treatment whose mechanism of action has remained unclear. The present study aimed at investigating the immediate responses of cerebral perfusion to electrical stimulation.

Method: Eight patients with major depression (inpatients of the Hospital of the University of Pennsylvania) underwent a series of ECT treatments with unilateral or bilateral electrode placement. Cerebral blood flow during treatment was assessed using ^{99m}Tc-HMPAO SPECT; the tracer was injected simultaneously with the electrical stimulation. In each patient, either two ($n = 4$) or three ($n = 4$) ictal scans were performed.

Results: Unilateral and bilateral stimulation led to different activation patterns, always involving frontal cortical areas. In repeated ECT sessions, a decreased brain perfusion response to electrical stimulation over time was observed.

Conclusion: The decrease of blood flow response over time may correspond to an increasing seizure threshold during a course of ECT treatments, and may be linked to the antidepressant action. The observation of time-related changes in brain function, as demonstrated in the present study, may thus contribute to better understanding of the mechanisms underlying the beneficial clinical effects of ECT and other antidepressant treatments.

NR382 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Meta-Analysis of Treatment Outcome with Risperidone Versus Conventional Neuroleptics

John M. Davis, M.D., Psychiatry, University of IL at Chicago, 1601 W Taylor Street, Chicago IL 60612; Philip G. Janicak, M.D.

Summary:

Objectives: A meta-analysis of the results from controlled comparative studies was performed to assess differences in efficacy between risperidone and conventional neuroleptics in the treatment of schizophrenia and to determine the optimal therapeutic dose range of risperidone.

Methods: Six double-blind, random-assignment studies with sufficient data comparing risperidone with placebo and conventional neuroleptics were included in the meta-analysis (N patients = 1,640). The number of patients responding to treatment (ℓ 20% improvement on a standard rating scale) and mean improvements of each patient were determined. Clinical response was also evaluated in patients receiving low doses (4–8 mg/day) and high doses (10–16 mg/day) of risperidone.

Results: The percentage of patients responding to therapy was higher with risperidone (60%) than with conventional neuroleptics (51%) or placebo (17%). A greater proportion of patients responded to low doses than to high doses of risperidone (64% vs 56%). At all doses evaluated, risperidone was significantly more effective than conventional neuroleptics in treating negative ($p < 0.05$) and symptoms of general psychopathology ($p < 0.01$) and all symptoms combined ($p < 0.01$).

Conclusions: Results of the meta-analysis indicate that risperidone is qualitatively more effective than conventional neuroleptics in treating schizophrenia and that there is a therapeutic window for risperidone dose response in the range of 4–8 mg/day.

NR383 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Effects of Conventional and Atypical Antipsychotic Agents on Cognitive Function in Schizophrenia

Bernd Gallhofer, M.D., Psychiatry, Justus-Liebig University, AM Steg 22, Giessen, Germany

Summary:

Objective: A battery of tests was used to measure the effects of two conventional and two atypical antipsychotics on cognitive function in healthy controls and patients with schizophrenia.

Methods: Five groups of subjects were studied: 16 healthy volunteer controls (used to establish illness-induced impairment) and four groups of 16 schizophrenic patients each who were tested before and after receiving doses of antipsychotics that were chiefly dopamine D_2-receptor blockers (fluphenazine and haloperidol) or serotonin $5HT_{2A}$-receptor blockers (risperidone and clozapine). The patient groups were matched according to BPRS and SANS scores and medical history. The tests included a visuomotor task (maze test), and auditory task (sound discrimination), and a visual version of the Digit Span test.

Results: Untreated patients showed constant impairment of cognitive function. Fluphenazine and haloperidol further impaired function: the more complex the task the more severe the impairment. The maze test demonstrated loss of speed and impaired motor control in patients receiving these conventional agents; this became more marked when the task required frontal strategies. Patients receiving risperidone or clozapine could not be distinguished from the healthy controls in low complexity tasks, and in complex tasks they maintained motor control and used a shorter route than did patients receiving fluphenazine or haloperidol. Sound discrimination was marginally improved by risperidone and clozapine and markedly impaired by fluphenazine and haloperidol. Similar results were elicited by the frontal part of the Digit Span test.

Conclusions: The results appear to reveal a disconnection in the cortico-subcortical system in untreated schizophrenic patients. Antipsychotics that are chiefly D_2 blockers impair cortico-subcortical function, whereas both $5HT_{2A}$ blockers improved functions on most of the tests administered.

NR384 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone As an Adjunct Mood Stabilizer for Bipolar Disorder

S. Nassir Ghaemi, M.D., Aff Dis Prog, Medical College of VA, Box 980710, Richmond VA 23298; Gary S. Sachs, M.D.

Summary:

Objective: We evaluated the outcome of long-term adjunctive risperidone therapy in 12 patients with rapid-cycling, mixed episode, or severe depression variants of bipolar type I disorder unresponsive to maintenance dosages of standard mood stabilizers.

Methods: Twelve patients with bipolar type I disorder and mood instability or severe depression despite adequate doses of lithium or valproate were treated with adjunct risperidone for periods ranging from eight to 72 weeks and evaluated by means of the Clinical Global Impression Improvement (CGI) and the Global Assessment of Function (GAF) scales.

Results: The patients received risperidone for a mean period of 24 weeks at a mean dose of 2.75 mg/day (range, 1–4.5 mg/day). Four patients discontinued treatment, two for lack of efficacy and two because of akathisia or stiffness. Among eight patients given risperidone for more than 15 weeks, four were rated as much improved (CGI = 6) when evaluated at 16, 23, 28, and 44 weeks, respectively, and their mean GAF scores increased from 10 to 15 points. One patient was mildly improved (CGI = 5) at 72 weeks. One was unchanged at 20 weeks and two were mildly or much worse at 64 and 44 weeks, respectively.

Conclusions: The results suggest that adjunct risperidone is effective long-term in patients with bipolar or psychotic mood disorders. Four of eight patients treated for more than 15 weeks maintained good responses to risperidone for periods ranging from 16 to 44 weeks.

NR385 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Bioequivalence of Oral Solution and Tablets of Risperidone in Normal Male Subjects

Rolando Gutierrez-Esteinou, M.D., Janssen Res Foundation, 1125 Trenton-Harbourton Road, Titusville NJ 08560

Summary:

Objective: Since the introduction of the novel antipsychotic risperidone in 1993, the only market formulation available has been in tablet form. An oral solution of risperidone is under development. A study was conducted to investigate the bioequivalence of the market tablet formulation and an oral solution of risperidone.

Methods: In an open-label, randomized, crossover study, a 1-mg market tablet formulation of risperidone was compared with a 1-mg/ml oral solution formulation. Both formulations of risperidone were administered as a single 1-mg dose with a 10-day washout between treatments. Twenty-six healthy male subjects entered the study; 23 completed both formulation treatment periods. Plasma concentrations of risperidone and total risperidone (risperidone plus its active metabolite, 9-hydroxyrisperidone) were determined by radioimmunoassay.

Results: For all key pharmacokinetic values (C_{MAX} and AUCs), the 90% and 95% confidence intervals on the relative bioequivalence of risperidone, 9-hydroxyrisperidone, and total risperidone

were contained within the equivalence range of 80–120% (80–125% for log transformed values).

Conclusion: The results demonstrate that the oral solution is bioequivalent with the market tablet formulation.

NR386 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Clozapine and Quality of Life in Schizophrenia

Marianne S. Goodman, M.D., Psychiatry, NY Hospital- Cornell, 21 Bloomingdale Road, White Plains NY 10605; James W. Hull, Ph.D., Kenneth G. Terkelsen, M.D., Thomas E. Smith, M.D., John F. Clarkin, Ph.D., Donna T. Anthony, M.D.

Summary:

Objective: This study assessed the association between clozapine and quality of life ratings for moderately ill day program patients with psychotic disorders.

Methods: Objective and subjective quality of life was measured using Lehman's Quality of Life (QOL) interview. Patients were divided into clozapine (n = 18) and non-clozapine (n = 49) groups and compared.

Results: There were significant associations or trends between clozapine and subjective levels of satisfaction in housing, work, and health services domains. There was only one significant difference on measures of objective quality of life, with clozapine patients reporting fewer unmet services needs.

Conclusions: This study supports the use of the QOL interview as an outcome assessment measure for intervention studies. In addition, it provides further data suggesting that the greater efficacy of the novel antipsychotic clozapine may be associated with its effects on a wide range of outcome measures such as quality of life.

NR387 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone in Geriatric Patients with Chronic Psychoses and Concurrent Medical Illnesses

Usha P. Joshi, M.D., Pilgrim Psych Center, Box A, West Brentwood NY 11717; Praful M. Joshi, M.D.

Summary:

Objective: A six-month open study was conducted to observe the effects of risperidone in geriatric patients diagnosed with chronic psychoses and concurrent medical conditions.

Methods: The subjects were 47 hospitalized patients demonstrating intolerance or resistance to standard neuroleptics. Their diagnoses were schizophrenia in 13; dementia, organic mental disorders, or mental retardation in 13; bipolar disorder with psychotic features in four; and major depression with psychotic features in one. Treatment with neuroleptics was gradually discontinued and, after a one-week washout period, risperidone was started at 0.5 mg/day and increased in weekly increments of 0.5 mg up to 3 mg/day. Improvements in positive and negative symptoms and cognitive and global functioning were measured after two, three, and six months of treatment by means of the Brief Psychiatric Rating Scale, the MiniMental Status test, and the Global Assessment of Functioning.

Results: Treatment with risperidone at doses of 2–3 mg/day was associated with consistent improvement on all outcome variables and was well tolerated. In 20 patients, clinical improvement led to discharge after six months of treatment. Four patients discontinued treatment; of these, two developed complications and two refused medication. One patient with a history of neuroleptic malignant syndrome with standard neuroleptics tolerated and responded to risperidone treatment. Risperidone was not associated with exacerbation of concomitant medical symptoms.

Conclusions: Risperidone was safe and effective in geriatric patients with chronic psychoses.

NR388 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Use of ECT in California, Revisited: 1984–1990

Barry A. Kramer, M.D., Psychiatry, USC University Hosp, 1500 San Pablo St 3rd Floor, Los Angeles CA 90033

Summary:

Objective: The use of ECT in California was examined from 1984 to 1990 and compared with a previous study examining use from 1977 to 1983.

Methods: Data were collected from legally required reports submitted to the state for all ECT performed.

Results: A total of 18,395 patients (mean = 2627.86 per year) received a total of 107,056 treatments with a mean rate of 0.96 patients/10,000 population. The rate in 1984 (1.15) was similar to the mean rate for 1977–1983 (1.12). This dropped beginning with 1985 to a mean rate of 0.92 for 1985–1990. There were 569 patients (3.1% of total) who were judged to be incapable of giving informed consent and received ECT after a court review. This is similar to the rate of 3% for 1977 to 1983. The number of counties where ECT was available increased to 18 in 1990 from 15 in 1983. The number of facilities providing ECT increased to 83 in 1990 from 62 in 1983. White patients comprised 93.28% of ECT recipients. Three deaths were reported for a rate of 0.28 deaths/10,000 treatments.

Conclusions: ECT has become slightly more accessible in California although availability continues to remain limited geographically and socioeconomically. The frequency of its use has declined somewhat, possibly related to the introduction of bupropion nomifensine, and fluoxetine during the time period reviewed. Other potential causes and implications of ECT's limited availability will also be discussed.

NR389 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Plasma Levels of Sertraline and the Clinical Response in Geriatric Depression

Vinod Kumar, M.D., Psychiatry, Univ of Miami, 4300 Alton Rd Ste 204, Miami Beach FL 33140; Vivian Garcia, B.A., David Loewenstein, Ph.D., Nita Kumar, M.D.

Summary:

Recent reports (Perez et al., 1993, and Norman et al., 1993), suggesting the absence of correlation between fluoxetine and norfluoxetine plasma levels, and clinical outcome are similar to the report of non-correlation between Fluoxamine concentration and clinical response (Kasper et al., 1993). However, we tested the plasma level of 10 geriatric patients, mean age 74 yrs, seven females, three males, dose range 75–200 mg Sertraline. We also measured the global improvement of depression after a semi-structured interview of those patients when they reached a steady state. The plasma levels of Sertraline were done within 24 hrs of the measurement of mood, and blood samples were taken before the morning dose. The plasma levels ranged between 30–158 NG/ML. There was a significant correlation ($r = 0.88$, $P = 0.0007$) between the dose and the plasma level, and a significant correlation ($r = 0.9$, $P = 0.0018$) between the dose and improvement. The correlation almost reached significance ($r = 0.67$, $P = 0.06$) between the plasma levels of Sertraline and improvement.

All of these patients had major depressive disorders and three of them expressed feelings of worthless and occasional suicidal thoughts. We are continuing this study, but note that Sertraline is effective in the treatment of severe major depressive disorders. The measurement of plasma levels may be helpful in the therapeutic drug monitoring.

NR390 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Efficacy of Clinical Management Versus Drug Treatment of Depression in General Practice

Ulrik F.R. Malt, M.D., Psychosomatic, University of Oslo, Rikshospitalet, Oslo 0027, Norway; Ole H. Robak, M.D., Olaf Bakke, M.D., Hans-Peter Madsbu, M.D., Mitchell Loeb, M.Sc., Trond Smedsrud, M.Sc.

Summary:

Objective: To compare the efficacy of clinical management (CM ad modum Fawcett) of depression in general practice with CM combined with active drug treatment.

Method: A consecutive sample of 370 depressed patients in primary care with symptoms of depression persisting for at least two weeks was randomized without a placebo exclusion phase, in a double-blind fashion, to one of three treatment arms for a six-month period: Clinical management + placebo; the selective serotonin reuptake inhibitor sertraline + CM, and the tetracyclic alpha-2 receptor and serotonin 2 + 3 receptor antagonist mianserin + CM. Continuous quality control was achieved by allocating a psychiatrist to each group of six general practitioners.

Results: There were no differences in response rate to the three treatment options in patients with *first* episode of depression. In patients with *recurrent* depression or DSM-III-R melancholia, however, significantly more patients responded to sertraline + CM than the other two treatment options ($p < 0.05$).

Conclusion: This is the first comprehensive clinical treatment study of depression in primary care with a naturalistic design (i.e. consecutive sampling and no placebo exclusion phase). The remission rate of depression following clinical management + placebo in *first episodes* of depression in primary care is higher than previously estimated (77%) and comparable to the remission rate achieved by active drug. The findings question recent guidelines for the treatment of non-melancholic first depressive episodes of depression in primary care and suggest that recurrent depressions are neurobiologically different from first episodes.

NR391 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Tourette's Syndrome

Michael R. Martinez, M.D., Psychiatric Research/MAB, University of Iowa, Quad 2271-University of Iowa, Iowa City IA 52242-1000; Paul J. Perry, Ph.D., Gary R. Gaffney, M.D., Samuel Kuperman, M.D.

Summary:

Objectives: To evaluate the safety and efficacy of risperidone in treating patients with Tourette's syndrome.

Methods: Four patients ranging in age from 7 to 48 years were included in the evaluation. Previous treatment with conventional neuroleptics had either failed or produced undesirable side effects. The patients received risperidone at doses ranging from 0.5–4 mg/day for periods ranging up to 24 weeks.

Results: Symptomatic improvement was shown by all patients after treatment with risperidone. Reductions were seen in the patients' tics, accompanied by improvements in stuttering, mood, classroom behavior, perseveration, obsessive-compulsive symptoms, and extrapyramidal symptoms. Risperidone was well tolerated by all patients. Results of a ten-week parallel-design trial comparing risperidone with clonidine will also be reported.

Conclusions: Treatment with risperidone appears to be safe and effective in reducing the symptoms of Tourette's syndrome.

NR392 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone Treatment in an Academic State Hospital Setting: A Retrospective Study of Outcome

Arnaldo E. Negron, M.D., Psychiatry, RW Johnson Med School, 667 Hoes Lane, Piscataway NJ 08855; Eduardo A. Liederman, M.D., Mohan Parkadavil, M.D., Angel Cienfuegos, M.D., Daniel C. Javitt, M.D.

Summary:

Objective: Risperidone has been found to be more effective than placebo or conventional antipsychotics for the treatment of schizophrenia in controlled clinical trials. We investigated the degree to which this greater efficacy translates into improved outcome for chronic psychotic inpatients of a state hospital.

Methods: Treatment outcome was determined in the 63 patients at the Bronx Psychiatric Center who were started on risperidone during the first year of its availability. Patients' diagnoses were chronic schizophrenia in 42 patients, affective psychosis (schizoaffective disorder, bipolar disorder, and major depression with psychotic features) in 20, and other in one.

Results: Eight (19%) of the 42 patients with schizophrenia were discharged from the hospital, compared with a discharge rate of 12% among all patients and 9% among patients receiving haloperidol during the same period. A higher proportion of schizophrenic patients (19%) than schizoaffective or bipolar patients (5%) were discharged from the hospital. Clinical Global Impression scale scores of the 40 patients hospitalized > 3 months indicated that 27 (67%) were improved (12 moderately, 15 mildly), nine (22%) were unchanged, and four (10%) had deteriorated. Clinical improvement (hospital discharge or improved according to CGI score) was seen in 36 (57%) of the 63 patients; 41% of the patients were discharged or improved their hospital privilege status.

Conclusion: The study results indicate that risperidone shows superior efficacy as evidenced by improved treatment outcome in a state hospital setting.

NR393 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Is Nefazodone an Anticoagulant?

Meena Narayan, M.D., Psychiatry, Yale University, 20 York Street, New Haven CT 06510; George M. Anderson, Ph.D., J. Craig Nelson, M.D.

Summary:

Objective: Nefazodone is an effective antidepressant with 5HT2 antagonistic properties. The platelet 5HT2 receptor mediates its aggregation and shape-change, and 5HT2 antagonists like ketanserin have antiplatelet properties. This study evaluates in vitro the effects of nefazodone on the platelet aggregation.

Method: Platelet-rich plasma (PRP) was prepared from the blood of a healthy, unmedicated control. Platelet aggregation in PRP was induced by ADP (0.5–10 uM) and by 10 uM 5HT + 1 uM ADP. Serotonin-induced (10 uM) platelet shape change was also measured. The IC_{50}s for nefazodone and ketanserin inhibition of 5HT-augmented, ADP-induced platelet aggregation and 5HT induced shape change were determined graphically.

Results: Both nefazodone and ketanserin caused a dose-dependent inhibition of the 5HT augmentation of ADP-induced platelet aggregation. IC_{50}s for ketanserin and nefazodone were 0.067 $\pm$ 0.054 uM and 36 $\pm$ 19 uM, respectively. At concentrations considered to be therapeutic (~ 1–10 uM), nefazodone did not inhibit 5HT augmentation. Similar data were obtained for the inhibition of 5HT-induced shape change.

Conclusions: At concentrations typical of steady-state plasma levels obtained with therapeutic doses in depression, nefazodone did not inhibit either 5HT-augmented, ADP-induced aggregation or 5HT-induced platelet shape change. Nefazodone was much

less potent than ketaserin in inhibiting 5HT2-mediated platelet responses.

NR394 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Optimal Minimum Doses of Trifluoperazine in Acute Schizophrenia

Hector A. Ortega-Soto, M.D., Inv Clinicas, Inst. Mexico Psiquiatr, AV Mex-Xochimilco 101, Mexico DF 14370, Mexico; Elizabeth Brunner, M.D., Rogelio Apiquian, M.D., Pilar de la Torre, B.A., Rosa E. Ulloa, M.D., Arturo Mendizabal, M.D.

Summary:

TFZ efficacy in the treatment of schizophrenia is well documented, but the minimal effective dose is unknown.

Objective: To explore the efficiency of TFZ threshold (minimum extrapyramidal side effects, EPS;TD), subthreshold (no EPS;STD), and conventional doses (CD).

Method: 97 schizophrenics (DSM-IV) free of antipsychotics (two weeks oral or four depot), participated. TD was determined starting with 5 mg/d of TFZ increasing 5 mg/day weekly until EPS appeared (DiMascios's scale), if psychopathology improved--35% in total PANSS--without EPS, the patient continued with STD. Patients on TD were randomized to: group I (TD + 30 mg/day of TFZ) or group II (TD + placebo). The trial lasted six weeks. Subjects received biperiden p.r.n. Comparisons were performed with repeated measures ANOVA.

Results: Twenty patients were in group I, 20 in group II, and 57 received STD; age was similar (overall mean +/– sd; 30.4 +/ – 9.4 years), as were basal PANSS total scores (93.7 +/– 31.8, 98.6 +/– 36.5 and 92.8 +/– 34.5). At the end PANSS scores were similar, however DiMascio's scores were CD > TD > STD ($F[3, 63] = 16.7$; $p < 0.0001$).

Conclusion: CD, TD, and STD are equally effective in the treatment of schizophrenia, but EPS are different.

NR395 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Venlafaxine and Blood Pressure Change Spanning the Ages

Ben Zimmer, M.D., Psychiatry, Allegheny General, 320 E. North Avenue, Pittsburgh PA 15212; Ravi Kant, M.D., Debbie Zeiler, R.N., Mary Brilmyer, R.N.

Summary:

Objective: A young-old differential blood pressure (BP) δ effect of Venlafaxine has been hypothesized. In this study we asked: Is there a differential BP Δ effect of Venlafaxine treatment in a young vs. older depressed population?

Method: Thirty-four depressed patients who sequentially sought treatment in our medical college ambulatory neuropsychiatry program and received Venlafaxine for depression, were compared according to several criteria. Baseline and follow-up BP measures were obtained. Final two clinician mutual consensus CGI scores were assigned.

Results: Sixteen non-geriatric patients (ages 13–65; $\bar{x}$ 37.6 SD 13.74; 9 ♀ 7 ♂) were compared with 18 geriatric patients (65–86; $\bar{x}$ 73.06 SD 5.12; 7 ♀ 11 ♂). Despite a higher mean Venlafaxine dose for the younger group (183.6 mg SD 80.19; $\bar{x}$ 3.7 mos vs 130.5 mg SD 55.6; $\bar{x}$ 6.16 mos), there were no significant systolic BP changes for either group. For the older group there was a 4.7mmHg mean in diastolic BP (76.11 SD 8.62 → 80.83 SD5.3; $p < .0060$). No patient became hypertensive; lower (< 76mmHg) baseline diastolic BP correlated significantly $p < .00005$ with ↑ in diastolic BP in the elderly.

Conclusion: Old-age depressives treated with Venlafaxine were more likely to show minimal diastolic δ when compared to a younger population. Higher baseline diastolic BP (> 76mmHG) seemed to be protective against Velafaxine's diastolic adrenergic BP effect in the elderly.

NR396 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Lithium Carbonate Therapy Is Not a Risk Factor for Osteoporosis

Elie Lepkifker, M.D., Psychiatry, Chain Sheba Hospital, Tel Hashomer 52621, Israel; Theodor B. Rais, M.D., Iris Vered, M.D., Ohad Cohen, M.D., Rueben Ziv, M.D.

Summary:

Lithium treatment in affective patients may affect calcium metabolism by causing parathormone hypersecretion. Such patients might therefore be at increased risk for osteoporosis. The purpose of this study was to evaluate the effect of either short-or long-term lithium therapy on parameters of bone metabolism.

Method Parathyroid function and indices of bone metabolism were assessed in 23 lithium treated affective patients. Ten patients were treated for 5–12 months (group 1) and 13 patients for more than three years (group 2).

In all subjects bone mineral density measurements in the hip and lumbar spine regions were performed using dual energy X-ray absorptiometry. Serum thyroid hormones, PTH, LH, testosterone and urine OH-proline, free cortisol, calcium, and phosphate excretion were measured.

Results: The two groups were matched for sex, weight, calcium intake, lithium levels, and smoking habits. One patient in group 2 had increased PTH levels and urinary OH-proline was elevated similarly in both groups. Bone mineral density and the other parameters were within normal values in both groups.

Conclusion: No effect on bone density after short-or long-term lithium therapy was detected although the data do suggest an increased turnover. Thus, treatment with lithium is not associated with either short- or long-term risk for osteoporosis.

NR397 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Electrical Dose and Seizure Threshold in Bifrontal, Bitemporal and Right Unilateral ECT: Relations to Clinical Outcome and Cognitive Effects

Nicholas J. Delva, M.D., Psychiatry, Queen's University, 72 Barrie Street, Kingston ON K7L 3J7, Canada; James S. Lawson, Ph.D., Martin Rodenburg, M.D., Rita M. Kesteven, Ph.D., James Inglis, Ph.D., Dennis W. Lywood, B.Sc., John J. Waldron, M.B.

Summary:

In a double-blind comparison of three forms (bitemporal [BT], right unilateral [RU], and bifrontal [BF]) of threshold level electroconvulsive therapy (ECT), BF was found to be most and RU least effective, with BT intermediate. Treatment failures occurred only in the RU group. Responders to RU treatment had lower initial seizure thresholds ($\bar{x} = 51$ mC; $p < 0.05$) and longer seizures ($\bar{x} = 56$ s; $p < 0.05$) than nonresponders ($\bar{x} = 100$ mC; $\bar{x} = 39$ s), and were also treated at a greater degree above threshold (at start of treatment, $\bar{x} = 69$ vs $\bar{x} = 31$ mC; $p < 0.10$). BT ECT was effective after RU treatment failure. Cognitive loss was related to electrical dose in the BF group (e.g., correlation between dose and verbal IQ = –0.62; $p < 0.01$) which, however, showed the least intellectual impairment. Changes in seizure threshold during ECT did not predict clinical improvement. BF ECT has advantages of reliable efficacy and ease of administration, while minimizing cognitive impairment. If RU treatment is used, benzodiazepines should be strictly avoided and attention should be paid to seizure threshold, seizure length, and clinical response. Many patients require at least some RU treatments to be given at doses considerably above seizure threshold for a satisfactory outcome. If progress is poor,

consideration should be given to a change to the BF electrode placement.

NR398 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Atypical Neuroleptics Are Less Likely to Produce Hyponatremia

Deborah A. Widmer, M.A., Psychiatry, FD Roosevelt VA Hospital, PO Box 10, Rte 9A, Montrose NY 10548; Cecile E. Sison, Ph.D., Robert G. Stern, M.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D., Benedict J. Connolly, M.A.

Summary:

Objectives: This study tested the hypothesis that hyponatremia in schizophrenic or schizoaffective patients occurs more frequently during treatment with conventional antipsychotic agents than with atypical neuroleptic agents.

Methods: Serum sodium concentrations were compared during treatment with conventional neuroleptics (time period 1) and subsequently during treatment with atypical neuroleptics (time period 2) in patients treated at a VA hospital between 1992–1995. In addition the number of normal (i.e., 143–136 mEq/L), abnormal low (i.e. concentrations < 136 mEq/L), and abnormal high levels (i.e. concentrations > 143 mEq/L) obtained during the two periods were compared across all patients.

Results: Serum sodium concentrations were obtained on 128 occasions during period 1 and 121 occasions during period 2 in 32 patients treated with clozapine. Preliminary results indicate conventional neuroleptics were associated with significantly lower mean serum sodium concentrations and more frequent abnormal low serum sodium concentrations than atypical treatment.

Conclusions: When compared to conventional, atypical neuroleptics appear to be less likely to produce hyponatremia in patients suffering from schizophrenia or schizoaffective disorder. Patients experiencing hyponatremia in association with conventional neuroleptic treatment may benefit from a change to an atypical agent.

NR399 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risperidone for Disturbed Behavior and Tardive Dyskinesia in Developmentally Disabled Adults

Barkat U. Khan, M.D., Gulf Coast Ctr, 5820 Buckingham Road, Fort Myers FL 33905; William M. Glazer, M.D.

Summary:

The agitated, aggressive, or self-injurious behavior of some developmentally disabled persons is often unresponsive to behavior modification programs and manageable only with antipsychotic agents. These, however, are often ineffective and after long-term treatment frequently cause tardive dyskinesia (TD). Twenty-one adults with severe to profound mental retardation (IQ less than 40) were treated with the novel antipsychotic risperidone. All patients had previously received neuroleptics for many years, some since childhood. Risperidone was associated with significant reversal of aggressive, destructive, and self-injurious behavior and TD in 20 patients. Risperidone failed to control behavioral symptoms in one patient but sharply reduced initially severe dyskinetic movements. Most patients required 3 mg to 6 mg of risperidone daily and the maximum dose was 8 mg daily. Four patients given risperidone had complete remission of TD symptoms, while 11 had excellent responses, three had modest responses, and three showed mild improvement in TD symptoms. It is concluded that risperidone is an affective and safe drug in developmentally disabled adults.

NR400 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

In Vivo Comparison of CYP2D6 Inhibition Among SSRIs: Implications for Drug Therapy

Yui Wing F. Lam, Pharm.D., Pharmacology, University of TX Hlth Ctr, 7703 Floyd Curl Drive, San Antonio TX 78284–6620; Larry Ereshefsky, Pharm D., Cara Riesenman, Pharm D., Joseph A. Simpson, M.D.

Summary:

We evaluated the drug interaction potential of four SSRIs using the dextromethorphan/dextrorphan (DM/DP) ratio as a noninvasive probe for CYP2D6. Oral administration of 30 mg DM, followed by an eight-hour urine collection to quantitate DM and DP concentrations, phenotypes individuals as poor or extensive metabolizers (PM, EM, respectively) for CYP2D6 enzyme activity. Three urinary DM/DP determinations over an 11-day period established baseline DM/DP for 32 subjects. Subjects were then randomized to receive one of four SSRIs: fluvoxamine 100 mg, sertraline 100 mg, paroxetine 20 mg, or fluoxetine 60 mg (loading dose to simulate concentrations achieved for 20 mg/day at true steady-state [Cpss] for eight days. Repeat urinary DM/DP was obtained on day 9. Thirty-one Caucasian EM subjects (27.5 ± 7.2 yrs., 74.1 ± 11.5 kg., 10 F & 21 M) completed the study. All subjects were healthy and not taking any drug, caffeine, or tobacco products. Percent change from baseline (average) in DM/DP and the proportion of patients who shift phenotype (EM to PM) were determined. ANOVA indicated highly significant differences in drug interaction potential:

Drug	N	Mean Δ in DM/DP (%) ± SD	EM->PM	PLSD
Fluoxetine	8	.3484 ± 2184	5	p<0.05
Paroxetine	8	.3943 ± 2410	4	p<0.05
Sertraline	7	28 ± 77	0	NS
Fluvoxamine	8	6 ± 92	0	NS

The large changes in DM/DP demonstrate the more potent inhibition of fluoxetine and paroxetine at CYP2D6 and correlate to clinically significant drug interactions with CYP2D6 substrates (e.g. desipramine). Studies are currently underway to evaluate the inhibition potential of other antidepressants, including venlafaxine and nefazodone, at CYP2D6.

NR401 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Can Panic Disorder Patients Treated with More Than Four Milligrams Per Day of Alprazolam Reduce Their Dose?

Mark H.N. Corrigan, M.D., CNS Development, Pharmacia $ Upjohn, 7000 Portage Rd, Kalamazoo MI 49001; Jeffrey M. Jonas, M.D., Therese Kitt, M.D., Susanna Goldstein, M.D., Ann S. Swiontek, Stephen M. Stahl, M.D.

Summary:

This multicenter study investigated the ability of panic disorder patients who required > 4mg/day to reduce their alprazolam dosage following 12 weeks of treatment. Patients who responded to ≤ 4 mg of ALP during the pre-randomization period were excluded from the study. Nonresponders were then treated with doses up to 10mg/day for 12 weeks. At that time they were divided into a *maintained group* (66 patients), or had their *dose reduced by 50%* (63 patients) during an 11-week maintenance period. Patients overall showed improvement in their condition during the study. Based on Kaplan-Meier estimates, the initial response rate was 28.6% at 4 mg, 52.5% at 6 mg, and 88.0% at 10 mg of alprazolam. Overall dropouts were similar between groups. No statistically significant differences in response rates (determined by CGI and/or zero panic attacks) were observed between the maintained dose (75.6%) and 50% dose reduction (68.6%) groups during

the study. More patients in the 50% dose reduction group had treatment emergent signs and symptoms, reflecting the symptoms arising during the time their dosage was decreased. Conversely, more patients in the maintenance group had discontinuation emergent signs and symptoms during taper, perhaps due to their higher dosage. One week following tapering off drug, patients in the maintained group were more likely to be classified as being in remission and less likely to have relapsed. These results suggest that once desired therapeutic effect has been achieved, it may be possible to reduce alprazolam dose. However, there may be long-term treatment benefits to maintaining patients at higher doses.

NR402 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Mood Measures in Normals Treated with Fluoxetine

Robert B. Pohl, M.D., Psychiatry, Wayne State University, 2751 East Jefferson Suite 200, Detroit MI 48207; Richard Balon, M.D., John Deluca, Ph.D., Jennifer Standish, B.A.

Summary:

The SSRIs are effective for a variety of disorders, but their effect on the mood of healthy volunteers is unknown. This ongoing study compares fluoxetine to pemoline and placebo in normals. However, there are no established outcome measures for this purpose. A preliminary analysis was conducted to insure that the main outcome measures, Visual Analog Scales (VAS), were sensitive to change.

Eighteen controls completed seven weeks of double-blind treatment. Six subjects received fluoxetine, five pemoline, and seven placebo. VAS were completed daily, and VAS for each week were averaged. The seven-week scores were then compared after subtracting baseline values.

Subjects experienced greater improvement with fluoxetine compared to either pemoline or placebo on 10 of the 11 VAS: happiness, confidence, energetic, alertness, mental concentration, outgoing, motivation, ability to interact, productivity, and sense of well being. Although the small sample size precluded statistical significance for many comparisons, the effect size for the fluoxetine group was large. For six VAS, the improvement in the fluoxetine group was larger than the standard deviation. Improvement on placebo was usually less than 10% of the SD. These data suggest that VAS are sensitive measures for detecting changes in mood in normal volunteers who receive antidepressants.

NR403 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Melatonin for the Treatment of Sleep Disorders in Major Depression

Ornah T. Dolberg, M.D., Psychiatry, Sheba Medical Center, Ramat Gan 52621, Israel; Shmuel Hirschmann, M.D., Joseph Zohar, M.D., Leon J. Grunhaus, M.D.

Summary:

Insomnia is a frequent complaint among patients with major depressive disorder. Several pharmacological agents have been used for hypnotic purposes in these patients. Commonly used medications are the benzodiazepines. However, concerns exist among clinicians regarding habituation, tolerance, and dependence, especially among the elderly. Melatonin, a hormone secreted by the pineal gland, seems to play a critical role in the synchronization of body rhythms regarding day–night cycles. Several studies have examined the hypnotic effect of melatonin with promising results. However, the use of melatonin in psychiatric disorders, and specifically the use of melatonin as a hypnotic agent in patients with major depression, remains to be studied. Furthermore, none have employed a specific sleep scale to assess the degree of change in sleep and various sleep parameters in the study population. In this study we have attempted to examine the hypnotic effect of melatonin versus placebo in 19 patients with major depressive disorder treated with fluoxetine. Sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI).

Results: No difference was noted on the Hamilton Rating Scale for Depression between those treated with melatonin versus placebo ($p = 0.86$). However, a statistically significant difference was found regarding the improvement in sleep on the PSQI ($p = 0.009$). Further studies are required in order to evaluate the hypnotic effect of melatonin on the sleep of patients with various psychiatric disorders.

NR404 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Risk Factors Distinguishing Fatal and Non-Fatal Suicide Outcome

M. Beatriz Currier, M.D., Psychiatry, University of Miami, 1925 Brickell Ave #D-1913, Miami FL 33129; Victoria Bustamante, M.S., Ana I. Fins, Ph.D., Sherrie L. Baehr, Psy.D.

Summary:

Objectives: A sample of 91 patients with serious life-threatening suicide attempts was compared with 196 adults who completed suicide to identify demographic, psychosocial, psychiatric, and suicide variables which differentiate between a fatal or non-fatal outcome.

Methods: Ninety-one consecutive adult patients whose suicide attempts warranted medical/surgical hospitalization underwent psychiatric consultation which included a clinical interview utilizing *DSM-IV* criteria, the Mini Mental State Exam, medical chart review, and structured inquiry of suicide variables such as method, impulsivity, and prior attempts. The medical examiner's records of 196 consecutive adult victims who completed suicide were reviewed for psychiatric history, suicide variables, and medical history.

Results: The mean age of the suicide victims (52.2 years) was significantly greater ($p < .0001$) than the mean age of the attempters (36.7 years). The most frequent methods accounting for fatal outcome included shooting (50%), hanging (19%), and jumping (7%), whereas the most frequent methods among the non-fatal attempts included overdose (50%), stabbing (14%), and shooting (13%). All the non-fatal attempters restricted the gunshot wounds to the chest and abdomen, whereas in the fatal outcome group 97% of gunshot wounds were to the head. Hispanic patients tended to use more violent methods than African Americans or whites. Depressive disorders, psychotic disorders, and MSA were the most common psychiatric diagnoses among the two groups.

Conclusions: Risk factors found to be significantly associated with fatal suicide outcome include increased age, male gender, history of depression, and use of firearms and hanging. Hispanic patients preferred violent methods, specifically hanging. Risk factors significantly associated with non-fatal outcome included overdose and history of prior suicide attempts. Psychiatric diagnosis was not significantly associated with a particular method.

NR405 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Self-Mutilation: Serotonergic and Clinical Findings

Barbara Stanley, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, Unit 28, New York NY 10032; Ronald M. Winchel, M.D., Michael Stanley, Ph.D., J. John Mann, M.D.

Summary:

Despite the significant morbidity associated with it, self-mutilation has received limited attention in psychiatry. Dulit et al. (1994) found mutilators were at high risk for suicidal behavior and had substantial comorbidity with eating disorders and depression. In an earlier study by our group (Simeon et al., 1992), we found greater impulsivity, aggression, anger, and depression. These

studies suggest that individuals who self-mutilate are at greater risk for other forms of self- (e.g. suicidal behavior) and outward-directed aggression.

Furthermore, while serotonin has been implicated in suicidal behavior, its role in self-mutilation is relatively unexplored. Our earlier work showed a preliminary relationship between serotonergic dysfunction and self-mutilation. The current project extends this work by examining a larger sample.

The purpose of the current study was to investigate further the comorbidity of other forms of self-destructive behavior as well as outwardly-directed aggression in a self-mutilating population compared with suicide attempters and matched controls.

In our current study, we assessed self-mutilating, non-suicidal patients, non-mutilating suicide attempters, and diagnostic controls. We found evidence of serotonergic dysfunction as measured by CSF 5-HIAA (5 hydroxyindoleacetic acid) in both the self-mutilating and the suicide attempters when compared with diagnostic controls. Mutilators had a greater incidence of abuse in their histories, were more aggressive and impulsive than the controls, and were more likely to dissociate.

NR406 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Combined Behavioral and Medicinal Treatment of Insomnia

Milton Kramer, M.D., Sleep Center, Bethesda Hospital, 619 Oak Street, Cincinnati OH 45206; Boris Dashevsky, Ph.D.

Summary:

Residual intractable insomnia remains a serious problem for many profoundly ill psychiatric patients. We report on our effort to treat such a group of patients.

We referred for treatment in a combined behavioral and medicinal treatment program 48 severely psychiatrically ill chronic insomniacs. The patients had an average duration of insomnia of 9.4 years, complained of insomnia nightly, and reported sleeping only 68.6% of the night. Twenty of the patients had been or were being treated for a depression, while an additional 13 had other psychiatric diagnoses. Twenty-four of these patients were taking various psychotropic medications, during treatment. In addition, 18 patients had been treated for pain problems. Patients had failed to respond to medicinal treatments for their insomnia.

Patients were treated individually with progressive muscle relaxation, structured sleep hygiene, stimulus control procedure, and sleep restriction. Thirty-seven of the 48 patients were also treated with hypnotic medications. Patients had an average of 10 treatment sessions.

At six-month follow-up, 72.9% rated themselves as improved compared to 58.3% at two months. Eleven patients had dropped out of the program and were treated as failures. For the remaining patients, sleep efficiency had increased from a baseline of 71.9% to 89.6%, sleep onset had decreased from 67.2 minutes to 26.8, and total sleep time increased from 375.4 to 414.6 minutes.

Profoundly ill psychiatric patients can benefit from the combined use of hypnotic medications and behavioral treatment in improving their sleep. Either treatment alone is unlikely to be succesful.

NR407 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Protective Factors Against Attempted Suicide

Kevin M. Malone, M.D., Neuroscience, NYS Psychiatric Institute, 722 West 168th Street, Box 28, New York NY 10033; Gretchen L. Haas, Ph.D., Shuhua Li, Ph.D., J. John Mann, M.D.

Summary:

Objective: Over 300,000 people a year attempt suicide in the U.S. Prior attempted suicide and hopelessness are the most powerful clinical predictors of completed suicide. We hypothesized that certain "reasons for living" might protect or restrain patients with major depression from otherwise making a suicide attempt.

Method: We studied 98 hospitalized patients with major depression, 49 suicide attempters, and 48 non-attempters. Severity of depression (HAM D), hopelessness (Beck Hopelessness), and Reasons for Living scale (developed by M. Linehan) were measured.

Results: There were no demographic or clinical differences in severity of depression between suicide attempters and non-attempters. Suicide attempters were more hopeless than non-attempters (11.7 ± 6.2 vs 8.5 ± 5.9, $t = 3.1$, $p = 0.002$) and non-attempters had more reasons for living (186.7 ± 40 vs 142.3 ± 40.8, $t = 5.43$, $p < 0.0001$). Reasons for living inversely correlated with hopelessness ($r = -0.62$, $n = 91$, $p < 0.0001$).

Conclusions: Reasons for living including coping beliefs, family responsibilities, fear of social disapproval, and moral objections may counteract hopelessness and protect against suicidal behavior during periods of risk such as major depression, and may account for differences in suicide rates amongst different cultures. Therapeutic efforts to reduce risk of suicide that target reasons for living should be evaluated.

NR408 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Predictors of Suicidal Behavior and Lethality in BPD

Beth S. Brodsky, Ph.D., Neuroscience, NYS Psychiatric Institute, 722 West 168th Street, New York NY 10032; Kevin M. Malone, M.D., Steven P. Ellis, Ph.D., Rebecca A. Dulit, M.D., J. John Mann, M.D.

Summary:

Objective: This study identifies mood and personality characteristics that distinguish suicide attempters (SA) from non-attempters (NA), and low lethality (LL) from high lethality (HL) suicide attempters in individuals with borderline personality disorder (BPD). We predicted that SA's would be more likely than NA's to have major depression and more severe borderline pathology. We proposed that anger and impulsivity would be more predictive of suicidal behavior in BPD patients than other BPD characteristics.

Method: Beck's Suicide Intent and Lethality Scales were administered to 214 inpatients diagnosed with BPD according to structured DSM-III-R personality disorder diagnostic interviews. Statistical analyses compared SA/NA, HL/LL attempters with respect to depression, number of previous suicide attempts, intent to die associated with most lethal attempt, and number and type of BPD criteria endorsed.

Results: SA's were more likely than NA's to endorse the "anger" BPD criterion; no other differences were found between them. HL attempters were more likely than LL to have more previous attempts, higher suicidal intent, and a current diagnosis of major depression.

Conclusions: There is evidence that the anger characteristic of BPD is related to BPD suicidality. BPD patients who make more lethal attempts with higher intent to die have comorbid major depression and have made more previous suicide attempts, contrary to conceptions of BPD suicidality as characterized by numerous low lethality attempts with low intent to die.

NR409 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Rise in Major Depression and Youth Suicide Rates

Paul A. Kettl, M.D., Psychiatry, Penn State University, P.O. Box 850, Hershey PA 17033-0850

Summary:

Over the last 40 years, the youth suicide rate (i.e., in those less than age 25) has more than tripled in the United States. During

the same period, a dramatic rise in the rate of major depression occurred in the same age group. Because half of all suicide victims suffer from depression, we sought to compare existing data on the growth of major depression to the growth in youth suicide rates.

Method: Decade by decade averages for the rates of major depression in those less than age 25 were compared to the ten-year average suicide rate for those age 15–24. The two groups were compared using Pearson Correlation Coefficients to examine if the rise in youth suicide in the United States followed the same curve as the rise in major depression.

Results: Suicide rates for young people followed exactly the same curve as the rise in major depression in the same age group. As rates of major depression rose, so did the youth suicide rates ($r = 0.97$, $p = 0.005$). Suicide rates began to rise after rates of major depression began to rise.

Conclusion: Since World War II, there has been an explosion in youth suicide rates. A variety of social factors have been cited to explain this rise. These data would suggest the growth of major depression should be included in any discussion of factors leading to the rise of suicide in America's youth.

NR410 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Comparison of Recent and Distant Suicide Attempters on Psychopathology and Social Support

Noelle Y.C. Yuen, M.D., Psychiatry, University of Hawaii, 1356 Lusitana Street, 4th Flr, Honolulu HI 96813; Naleen N. Andrade, M.D., Linda B. Nahulu, M.D., George K. Makini, Jr., M.D., George P. Danko, Ph.D

Summary:

Objective: This study evaluated a community sample of adolescents who had made a recent suicide attempt, distant suicide attempt, or no suicide attempt on measures of psychopathology and social support.

Method: 3,598 high school students were surveyed for suicide attempts within the past six months (recent attempters) or more than six months (distant attempters). They were also evaluated for symptoms of depression, anxiety, aggression, substance abuse, and perceived social support.

Results: 11.3% of students reported having made a suicide attempt at some point in their life, 3.9% of them in the six months prior to being surveyed. Recent attempters reported greater symptoms of psychopathology on all measures, and lower perceived family support than distant attempters and nonattempters. Distant attempters, however, reported higher levels of psychopathology and lower perceived family support than students who had never made a suicide attempt.

Conclusions: Data suggest that adolescents who attempt suicide experience high levels of psychiatric symptoms around the time of the suicide attempt and continue to experience elevated levels of psychopathology more than six months after a suicide attempt. Suicide attempters may experience chronically higher levels of psychopathology compared to their nonsuicidal peers.

NR411 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Death Without Warning: First Attempt Completed Suicides Versus Suicides with Prior Attempts

Sara E. Oppenheim, M.A., Neuroscience, NYSPI, 722 West 168th Street, New York NY 10032; Kevin M. Malone, M.D., Thomas M. Kelly, A.C.S.W., J. John Mann, M.D.

Summary:

Objective: About 60% of patients who complete suicide have made no prior suicide attempt, thereby giving no clear clinical warning of future suicide risk. This study compared patients who completed suicide at the first attempt to patients who completed suicide after at least one prior attempt in an effort to detect other predictors of future suicide risk.

Methods: 22 cases of death by suicide without a prior attempt, and 15 cases of suicide with a prior history of an attempt were identified from the medical examiner's office of a large urban catchment area. Clinical data were gathered from family members using the psychological autopsy method.

Results: The first attempt completer group was 12 years older than the reattempt completer group ($p = 0.02$). Those with depression had fewer previous hospitalizations ($p = 0.04$). There were trends for more comorbid alcohol/substance abuse ($p = 0.07$), and cluster B Axis II pathology ($p = 0.06$) in suicides with prior attempts. Low antidepressant prescription rates despite prominent depression, and immediate access to firearms was typical of both groups.

Conclusions: Clinicians should be aware that older depressed patients are more likely to complete suicide on their first attempt. Treatment of depression and removal of firearms should be a priority.

NR412 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Relationships Between Alexithymia and Psychological Traits Associated with Eating Disorders

Graeme J. Taylor, M.D., Psychiatry, Mt. Sinai Hospital, 600 University Avenue #936, Toronto ON M5G 1X5, Canada; James D. Parker, Ph.D., Michael R. Bagby, Ph.D., Michael P. Bourke, M.B.

Summary:

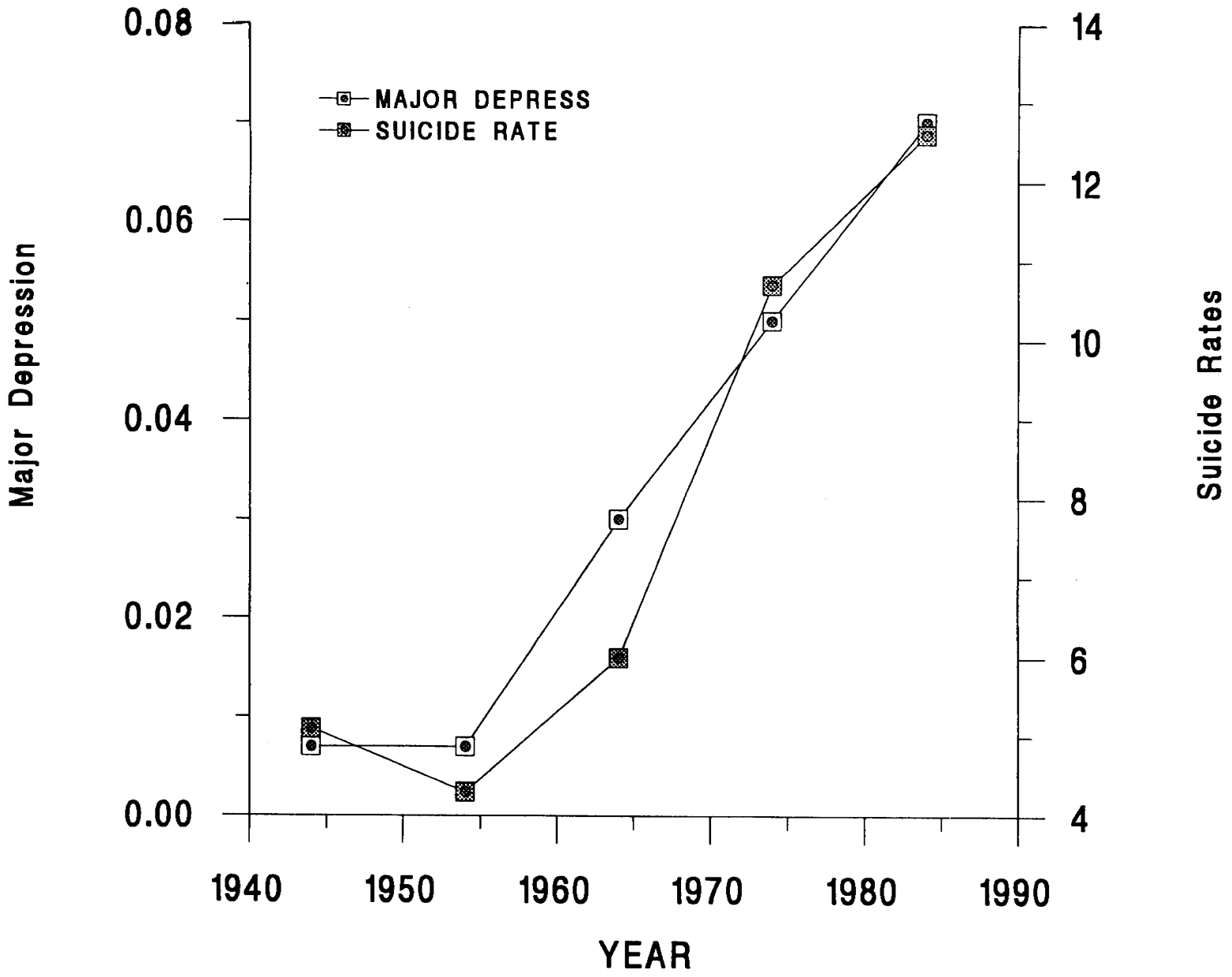
Objective: Several studies have reported high rates of alexithymia among patients with anorexia nervosa or bulimia nervosa. However, there has been little attempt to examine the relationships between alexithymia and other attitudes, behaviors, and psychological traits associated with eating disorders.

Method: The Twenty-Item Toronto Alexithymia Scale (TAS-20) and the Eating Disorder Inventory (EDI) were administered to 48 women with anorexia nervosa at various stages of illness, a comparison group of 30 female volunteers who were matched for age and education, and an unmatched comparison group of 234 university students (118 females, 116 males). Using the TAS-20 cutoff score, rates of alexithymia were calculated for each group. After removal of four items from the TAS-20 to correct for item overlap, the "corrected" TAS-20 was correlated with the eight subscales of the EDI in each sample.

Results: The rates of alexithymia were 68.8% in the anorexic group, 3.3% in the matched comparison group, 16.3% in the male student group, and 11.0% in the female student group. In the anorexic group and in the male students, the "corrected" TAS-20 correlated positively and significantly with the EDI subscales assessing ineffectiveness, interpersonal distrust interoceptive awareness, and maturity fears; correlations were nonsignificant with the subscales assessing perfectionism, drive for thinness, bulimia, and body dissatisfaction. The "corrected" TAS-20 correlated significantly and positively only with interpersonal distrust in the matched comparison group and only with ineffectiveness and interpersonal distrust in the female students.

Conclusions: These data indicate that alexithymia is related to several psychological traits that are characteristic of patients with eating disorders and thought to facilitate the development of the disorders, but is unrelated to attitudes and behaviors concerning abnormal eating and body weight and shape.

MAJOR DEPRESSION (by age 24) vs. SUICIDE RATES (ages 15-24)



NR413 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Fenfluramine and Phentermine in Obese Binge Eaters

Dean D. Krahn, M.D., Psychiatry, University of Wisconsin, 600 Highland Avenue, Madison WI 53792; Roy Blank, M.D., Richard Atkinson, M.D., Laura Olson, Ph.D.

Summary:

Recently, Weintraub et al. (1992) reported that the combination of two weight loss agents with differing methods of action, fenfluramine and phentermine, plus a traditional diet and exercise program resulted in significant, sustained weight loss in obese patients with very few side effects. However, there has been no report on the effect of this treatment on binge eating or mood. As up to 30% of treatment-seeking obese are binge eaters and this group reports more depression than other obese patients, we measured binge eating using the BULIT and depression using the Beck Depression Inventory in 93 consecutive patients at baseline and after three months of open-label treatment. Binge eating declined sharply, with scores on the BULIT decreasing from 78.3 to 63.5. At baseline, a total of 33.4% of subjects scored as subclinical or clinical level binge eaters. After three months of treatment, only 11.8% of these subjects were so classified. At baseline, 16.2% of patients were bingeing at least multiple times per week. At three months, only 1.1% of patients were bingeing at this rate. Mood improved significantly (as expected for obese subjects who are successfully losing weight) on the Beck (10.1 to 7.5, overall; 15.6 to 7.9 in the group who binged at baseline). Thus, these data support the hypothesis that this pharmacologic treatment plus diet and exercise interventions is effective for binge eating behavior and is associated with improved mood.

NR414 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Predictors of Bulimic Behaviors in College Women

Dean D. Krahn, M.D., Psychiatry, University of Wisconsin, 600 Highland Avenue, Madison WI 53792; Candace L. Kurth, Ph.D., Michael J. Bohn, M.D., Laura Olson, Ph.D., Edith Gomberg, Ph.D., Adam Drewnowski, Ph.D.

Summary:

The severity of dieting and bulimic behavior of college women has been extensively described. The prevalence of probable bulimia and at-risk behavior is similar at the beginning and end of the first year. To design appropriate prevention options, we wanted to know what factors present at college orientation predict higher binge/purge behavior at the end of the first year. We predicted that high use of passive coping strategies (PCope), negative attitudes about weight, shape, and control of food intake (Natt), and frequent dieting behaviors (DIET) at entrance to college would result in an increased year-end depression and ineffectiveness (DepIneff) which, in turn, would result in increased binge/purge behavior. We studied over 600 women using the Ways of Coping, SCL-90 depression, and Dieting and Bingeing Severity scales. This model explained 51% of the variance in year-end binge/purge behavior. PCope and Natt at the beginning of the year importantly affected DepIneff at the end of the year (B = 0.21 and B = 0.33, respectively). In turn, DepIneff was linked to binge/purge behavior (B = 0.33). DIET at the start of college did not importantly influence depression and ineffectiveness at the end of the first year (B = .01) but had a large direct effect on year-end binge/purge behavior (B = .56). Baseline Natt also had a direct effect on binge/purge behavior at the end of the year (B = .15), but PCope had little direct effect (B = .03). It appears that passive coping and negative attitudes about weight, shape, and control of food intake predispose freshman women to a sense of depression and ineffectiveness, which combines with the independent effects of frequent dieting to result in binge/purge behaviors.

NR415 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Eating Disorder Symptomatology in Major Depressive Disorder

Maurizio Fava, M.D., Psychiatry Mass Gen Hosp Bldg ACC815, 15 Parkman Street Ste 815, Boston MA 02114; Melissa Abraham, B.A., Nancy E. McLean, B.A., Joel A. Pava, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: To assess eating disorder symptomatology in depressed outpatients before and after antidepressant treatment.

Method: We studied 151 depressed outpatients (87 women and 64 men; mean age: 40.7 ± 10.7) participating in a clinical study involving open treatment with fluoxetine 20 mg/day. Diagnosis of MDD was made with the SCID-P, and all subjects had a 17-item Hamilton Rating Scale for Depression (HAM-D-17) score ℓ 16 at baseline. All subjects filled out the Eating Disorder Inventory (EDI) before treatment, and a total of 139 completed it after treatment. The EDI includes eight subscales: drive for thinness, bulimia, body dissatisfaction, ineffectiveness, perfectionism, interpersonal distrust, interoceptive awareness, and maturity fears.

Results: Mean baseline HAM-D-17 was 19.7 ± 3.2; after treatment the mean was 9.1 ± 6.3. Severity of depression was significantly positively related to interoceptive awareness, ineffectiveness, and body dissatisfaction after adjusting for age and body mass index. Patients with comorbid eating disorders had significantly higher scores on all but three subscales of the EDI as compared to those without these disorders. Depressed patients with comorbid anxiety disorders scored significantly higher on drive for thinness, ineffectiveness, maturity fears, and interoceptive awareness subscales, and had significantly lower scores on interpersonal distrust than those without anxiety disorders. All EDI subscales showed a statistically significant decrease following treatment with fluoxetine.

Conclusion: Eating disorder symptomatology, as measured by the EDI, appears to be related to both severity of depression and presence of comorbid eating and anxiety disorders, and to change with antidepressant treatment.

NR416 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

A Pilot Study of Paroxetine in the Treatment of Patients with Bulimia Nervosa

Teresa A. Pigott, M.D., Psychiatry, University of Texas, 301 University Blvd., Galveston TX 77555; Brent A. Sunderland, M.D., Lawrence Horn, M.D., Suzanne Bernstein, B.S., Billinda Dubbert, M.S.N., Virginia Smolka

Summary:

Objective: Bulimia nervosa is an eating disorder characterized by recurrent binge and purge episodes. Both tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) have been shown to be effective anti-bulimic agents; however, there are relatively few reports of the use of selective serotonin reuptake inhibitors (SSRIs) in bulimia. Since SSRIs such as paroxetine lack the anticholinergic side effects and weight gain associated with TCAs or MAOIs, they may represent a useful alternative in patients with bulimia nervosa. In this pilot study, we evaluated the safety and efficacy of paroxetine in the treatment of bulimia.

Method: In the present study, ten patients meeting DSM-III-R criteria for bulimia nervosa were enrolled in a 12-week, open-label study of paroxetine 20 mg/day. Therapeutic efficacy was assessed by serial self-report measures of binge and purge behaviors and changes from baseline in Clinical Global Impression (CGI) scores.

Results: Repeated measures ANOVA revealed significant reductions in the frequency of binge ($F = 3.12$, $P < 0.004$) and purge ($F = 2.87$, $P < 0.008$) behaviors and in CGI scores ($F = 3.40$, $P < 0.005$) during paroxetine treatment. Paired t-tests of maximum

decreases from baseline also revealed significant reductions ($P < 0.05$) in the frequency of binge (63% reduction) and purge (54% reduction) behaviors during paroxetine administration. Paroxetine was associated with only mild side effects and a slight, but nonsignificant, decrease in body weight.

Conclusion: Although further controlled studies are needed, data from this pilot study suggest that paroxetine may be efficacious in patients with bulimia nervosa.

NR417 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Effects of a High-Carbohydrate Diet on Serotonin Turnover and Mood in Obese Women

Dana L. Hirsch, B.A., 5 Winthrop Drive, Rye Brook, NY 10573; H. Keith H. Brodie, M.D., Richard S. Surwit, Ph.D.

Summary:

Objective: The purpose of this study was to determine if a high-carbohydrate diet would elevate serotonin metabolism, as measured by 24-hour urinary excretion of 5-HIAA in overweight women. Depression in these women was also assessed.

Method: 29 women were studied. All were 25% above ideal body weight, non-exercisers, and free of interfering disease. Subjects were fed 1,000 calori daily diets consisting of 65% carbohydrates, 20% proteins, and 15% fats. Subjects collected refrigerated 24-hour urine samples three times during the study at Week 0, 3, and 6. All samples were analyzed by HPLC for 5-HIAA. The subjects also completed Beck Depression Inventories pre- and post-intervention at Weeks 0 and 6.

Results: Post intervention, all 29 women's urinary 5-HIAA dropped [3.68 ± 2.28 mg./24-hours to 2.55 ± 1.20 mg./24-hours ($p < 0.05$)] as did their Beck Depression scores [8.07 ± 8.60 to 3.66 ± 5.56] indicating a mood improvement [$p < 0.01$].

Conclusions: Past studies have shown that when healthy individuals ingest carbohydrate-rich meals, their serotonin turnover as measured by urinary 5-HIAA increases, elevating their mood and decreasing their appetite. In our study, although the subjects became less depressed, their urinary 5-HIAA decreased reflecting the possibility of a decrease in serotonin turnover, resulting in no decrease in appetite. This abnormal nutrient-neurotransmitter response may be causally related to the obesity of our subjects who lacked the ability to elevate serotonin turnover given a high-carbohydrate diet and were thus unable to diminish their appetite in the process. This finding has etiological implications for obesity.

NR418 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

The Relationship Between Dietary Restraint, Exercise Dependence and Training Patterns

Julian P. Morrow, Ph.D., Psychology, Iona College, 715 North Avenue, New Rochelle NY 10801; Jerry L. Johnson, Ph.D.

Summary:

Excessive or pathological patterns of exercise have been documented in both anorexia and bulimia nervosa. Eating disorders have been reported to occur with surprisingly high frequency in female recreational athletes and certain sports have a high prevalence of participants who meet diagnostic criteria for eating disorders. One characteristic consistently associated with exercise pathology in eating disorders is an inflexible pattern of exercise, instead of multi-sport cross-training. In this study, amateur athletes, selected from first-time participants in the New York City Marathon (n = 112) and the Iron Man Triathlon (n = 116), were examined with The Exercise Salience Scale (TESS), a measure of "exercise dependence," and a number of additional measures of eating and exercise patterns. Female marathoners scored higher on the TESS ($\bar{x}_f = 62$ vs. $\bar{x}_m = 59$, $p < .05$) and dietary restraint scores were correlated with TESS scores for both genders (r's = .30 and .31). Marathoners who reported running only, with no other form of exercise, received scores on the TESS that were twice as high as cross-trainers. Triathletes, who are cross-trainers by virtue of their sport, received scores that were significantly lower than the marathoners as a group ($\bar{x} = 47$, $p < .01$), despite the high level of exertion required by their sport. These data suggest that in well-conditioned recreational athletes flexibility in athletic activity is associated with considerably less pathological use of exercise. These data have substantial treatment implications for patients with eating disorders, suggesting that promotion of flexibility in exercise may be a helpful intervention strategy.

NR419 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Eating Disorders in African-Americans

Xenia Johnson, M.D., Psychiatry, Med University of SC, 171 Ashley Avenue, Charleston SC 29425; William H. Carson, Jr., M.D.

Summary:

Objective: The authors reviewed the literature published since 1980 concerning eating disorders in African Americans.

Method: The review began with a computerized literature search. Further sources were located through citations from articles identified in the original search.

Results: The authors synthesized the contents of the articles reviewed using the categories of anorexia, bulimia, and eating disorders. Racial heritage used African American or Black.

Conclusions: The literature on eating disorders in African Americans supports the following: 1) The number of articles written about eating disorders in African Americans has stayed fairly constant (an average of 13 articles/five year period). 2) The predominate eating disorder described in African Americans is obesity. 3) The predominate DSM-IV Axis I eating disorder in African Americans is bulimia. 4) Young African-American girls have a greater drive for thinness than white girls. 5) Despite much study in the area of eating disorders, there are no strong hypotheses to explain the relatively low prevalence of eating disorders in African Americans.

NR420 Tuesday, May 7, 3:00 p.m.-5:00 p.m.

Eating Behavior, Serotonin and Tryptophan Depletion

Barbara E. Wolfe, Ph.D., Psychiatry, Beth Israel Hospital, 330 Brookline Avenue, Boston MA 02215; Eran D. Metzger, M.D., David C. Jimerson, M.D.

Summary:

Objective: CNS serotonin is thought to be important in post-ingestive satiety. This pilot study investigated the hypothesis that decreased serotonin synthesis following acute tryptophan depletion (ATD) challenge would result in increased test meal intake.

Method: Subjects included 11 healthy, medication-free, normal-weight women, age 20 ± 1 years (SD). In a double-blind, randomized design, controlling for menstrual cycle phase, subjects received on separate days capsules containing a TRP-free amino acid mixture or lactose placebo. Food intake was measured six hours later using a single-item, frozen yogurt test meal. Hunger, satiety, and fullness were assessed using 100 mm analog scales.

Results: Hunger ratings prior to the test meal, and fullness and satiety ratings following the meal, were not significantly different on active and placebo days. Test meal food intake was significantly greater on the active study day than on the placebo day (257 ± 74 vs 224 ± 58 grams, $p < .05$). For subjects reporting equivalent post-meal fullness ratings on both study days, increase in test meal size on the active day was significantly inversely correlated with the placebo-adjusted ATD-induced decrease in plasma tryptophan concentration ($p < .005$).

Conclusions: These preliminary results suggest that ATD challenge may be valuable in assessing serotonin-mediated satiety responses in patients with eating disorders.

NR421 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Informed Consent in Schizophrenia Research

Debra A. Pinals, M.D., Exp. Therapeutic, NIMH, 9000 Rockville Pike, Bldg. 10, Bethesda MD 20892; Anil K. Malhotra, M.D., Alan F. Breier, M.D., David Pickar, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to understand the pertinent issues of informed consent and its context in the history of research. In addition, a technique for improving informed consent practice will be discussed.

Summary:

Objectives: This study was conducted to 1) measure the degree to which schizophrenics and healthy controls understand consent forms for research and 2) develop a method to improve the informed consent process in clinical research.

Methods: Data were collected over six months on a research ward for all subjects (18 schizophrenics and 14 healthy controls) participating in any of four studies: MRI, ketamine infusion, neuroleptic treatment, or lumbar puncture. Controls did not participate in the latter two. After reading consent forms, subjects answered fill-in and multiple-choice questionnaires regarding risks, purpose, and procedures described in the consent documents. Prior to signing consent forms, answers were reviewed with subjects, and were later scored by a psychiatrist who was blind to information about the subject.

Results: There were no significant differences between scores for controls and schizophrenics on fill-in (Ctl = 76%, Scz = 67%; $t = 0.84$, $p = 0.41$) or multiple choice (Ctl = 89%, Scz = 87%; $t = 0.19$, $p = 0.85$) MRI questionnaires, although scores for fill-in type questions were significantly lower for both subject groups ($t = -2.34$, $p = 0.03$). Subject numbers limited data analysis of the questionnaires for the other three studies, but similar trends were seen.

Conclusions: Schizophrenics and controls showed no significant differences in their degree of understanding of research consent forms. Questionnaires regarding the content of consent documents, especially fill-in type questions, may help investigators obtain consent that is truly informed. Sample questionnaires and responses will be provided for discussion.

References:

1. Schacter D, Kleinman I, Prendergast P, et al.: The Effect of psychopathology on the ability of schizophrenic patients to give informed consent. *J of Nervous and Mental Disease* 182:360–362, 1994.

2. Applebaum PS, Roth LH: Competency to consent to research: a psychiatric overview. *Arch Gen Psychiatry* 39:951–958, 1982.

NR422 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Quetiapine, an Atypical Antipsychotic: Results From a Multiple Fixed Dose, Placebo-Controlled Study

Lisa A. Arvanitis, M.D., Director CNS Clinical Res, Zeneca Pharmaceuticals Gr, 1800 Concord Pike, Wilmington DE 19897; Barbara G. Miller, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should demonstrate an understanding of the typical pharmacologic profile and the clinical efficacy and side effect profile of 'Seroquel' (quetiapine), an atypical antipsychotic agent.

Summary:

Quetiapine, ICI 204, 636, a dibenzothiazepine with affinity for multiple brain receptors, is a new atypical antipsychotic agent intended for the treatment of schizophrenia. Phase II clinical trials in patients with acute exacerbation of schizophrenia showed that quetiapine was effective in treating positive and negative symptoms and was well tolerated. The atypical profile of quetiapine was supported by the lack of induction of extrapyramidal symptoms (EPS) and the lack of sustained elevations in plasma prolactin levels. In two multicenter, placebo-controlled trials, the incidence of EPS was no greater than with placebo, and no acute dystonic reactions were noted. Similarly, plasma prolactin levels were no greater with quetiapine than with placebo. A six-week, multicenter, randomized, double-blind, placebo-controlled trial evaluated the efficacy, safety, and optimal dose range of quetiapine in patients with acute exacerbation of schizophrenia (DSMI-IIR). Overall, 361 patients in the US and Canada received one of five fixed doses of quetiapine (75, 150, 300, 600, or 750 mg daily), haloperidol (12 mg daily), or placebo. Patients were assessed weekly using the BPRS, CGI, and SANS for efficacy and the Simpson Scale for EPS. At end point, significant differences ($p < 0.05$, ANCOVA) in mean changes from baseline were identified in quetiapine, haloperidol, and placebo for BPRS total score, BPRS positive symptom cluster, and the CGI Severity of Illness scores (quetiapine 150–750 mg/day), and for SANS summary score (quetiapine 300 mg/day). Overall, quetiapine showed a maximal clinical effect at 300 mg/day and was well tolerated. There was no difference between quetiapine at any dose across the dose range, and placebo with regard to EPS as assessed by the Simpson Scale, use of concomitant anticholinergic medications, and motor system adverse events. No acute dystonic reactions were noted. Additionally, there was no difference between quetiapine, at any dose across the dose range and placebo with regard to plasma prolactin levels. These results provide further evidence that quetiapine is effective in the treatment of the positive and negative symptoms of schizophrenia at doses of 150 to 750 mg/day and is well tolerated. The lack of induction of EPS or sustained elevations in plasma prolactin levels further support quetiapine's atypical profile.

References:

1. Saller CF, Salama AI: 'Seroquel': biochemical profile of a potential atypical antipsychotic. *Psychopharmacology* 112:285–292, 1993.

2. Goldstein JM, Litwin LC, Sutton EB, Malick JB: 'Seroquel': electrophysiological profile of a potential atypical antipsychotic. *Psychopharmacology* 112:293–298, 1993.

NR423 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Regional Shape and PET Analysis of Corpus Callosum in Patients with Schizophrenia and Schizotypal Personality Disorder

Jack E. Downhill, Jr., M.D., Psychiatry, Mt. Sinai Med Ctr, One Gustave Levy Place, New York NY 10029; Tse-Chung Wei, Ph.D., M. Mehmet Haznadar, M.D., Jacqueline Spiegel-Cohen, M.S., Larry J. Siever, M.D., Monte S. Buchsbaum, M.D.

Educational Objectives:

At the end of this presentation the participant should be able to understand the nature of the procedures used to analyze the anatomical and functional characteristics of the corpus callosum and be able to recognize how two patient groups: schizophrenics and schizotypals, differ from normals.

Summary:

Genetic and CT imaging studies have suggested that patients with schizotypy may be intermediate in severity between normals and patients with schizophrenia. This study examines this hypothesis with comparison of the size, shape, and relative metabolic activity of the corpus callosum between the groups.

Subjects were 13 patients with schizotypal personality disorder (SPD) (1 female, 12 male, mean age = 43.3 SD = 13.6), 27 patients with schizophrenia (7 females, 20 males, mean age = 38.3, SD = 14.3), and 31 healthy volunteers (8 females, 23 males, mean age = 41.2, SD = 12.3). Patients with SPD were recruited from the outpatient clinics and were assessed with the Schedule for Affective Disorder and Schizophrenia. Patients with schizophrenia were evaluated with the Comprehensive Assessment of Symptoms and History scale. All patients met DSM III-R diagnostic criteria for their respective disorders. All subjects were screened for neurological illnesses and concurrent substance abuse or dependency.

Thin section MRI and PET data were obtained for each subject. A realigned mid-sagittal slice was used for all analyses. PET data were coregistered with MRI and pixel-by-pixel t-tests were performed. A new analytical technique of pixel-by-pixel chi-square analysis was performed comparing the shape of the CC in the three groups. ANOVAs of 31 evenly spaced areas of the CC was also performed.

In the coregistered PET, the CC was clearly visualized as an area of relatively low metabolic rate. Exploratory pixel-by-pixel t-tests did not reveal significant areas of different metabolic rate among the three groups. The chi-square analysis showed decreased area in the genu and splenium in schizophrenics compared to normals. Schizotypals had a smaller difference in the splenium only. A region on the superior edge of the callosum just medial to the genu was narrower in schizotypals compared to both normals and schizophrenics. ANOVAs comparing individual areas showed a significantly smaller area in schizophrenics in area 5 in the genu ($F = 3.192$, $p = .047$) and areas 27 ($F = 3.202$, $p = 0.47$) and 29 ($F = 3.719$, $p = 0.29$) in the splenium. Schizotypals were intermediate in value between schizophrenic and normal in two of the three significantly different regions: 5 and 29.

Decreases in regional areas of the CC in schizophrenics and schizotypals suggest deficits in interhemispheric communication and may be related to observed cognitive deficits. The anatomy of the CC in SPD appears to be on a continuum between schizophrenia and the normal state.

References:

1. Raine A, Harrison, Reynolds GP, Sheard C, Cooper JE, Medley I: Structural and functional characteristics of corpus callosum in schizophrenics, psychiatric controls and normal controls. *Arch Gen Psychiatry* 47:1060–1064, 1990.

2. Denenberg V, Kertesz A, Cowell P: A factor analysis of the human's corpus callosum. *Brain Research* 548:126–132, 1991.

NR424 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Anticipation in a Large Representative Sample of Schizophrenia

Anne S. Bassett, M.D., Psychiatry, University of Toronto, 1001 Queen Street West, Toronto ON M6J 1H4, Canada; Janice Husted, Ph.D., William G. Honer, M.D., Susana B. Correia, Alison S. Bury, M.A., Joseph Berg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand what genetic anticipation is, what possible ascertainment biases need to be taken into account and what the clinical and genetic implications are, stemming from the demonstration of anticipation in a representative sample of schizophrenia and related disorders.

Summary:

Anticipation is the younger age at onset or increased severity of a genetic disorder in successive generations. Previously we reported this phenomenon in a sample of familial schizophrenia. The current study investigated whether anticipation was present in a large representative sample. The sample, originally collected by Penrose, comprised all pairs of relatives hospitalized with any mental illness in Ontario (7,935 subjects); raw data are available for contemporary analyses. Anticipation in relative pairs with schizophrenia (SZ), schizoaffective (SA), and affective disorders (AD) was studied using the Wilcoxon test. Mean age at first hospitalization (AFH) was 13.41 years younger for offspring than parents, if both had SZ ($z = -8.68$, $p = .0001$, $n = 167$). When one subject had SZ and the relative had SZ, SA, or AD, AFH was 15.56 years younger for offspring than parents ($z = -12.74$, $p = .0001$, $n = 419$). To address possible bias due to fertility effects, aunt/uncle-niece/nephew pairs were examined. Aunts/uncles had AFH 8.46 years older than nieces/nephews if both had SZ ($z = -10.13$, $p = .0001$, $n = 164$), and 10.91 years older if one relative had SZ, SA, or AD ($z = 14.24$, $p = .0001$, $n = 364$). A positive control, Huntington disease (HD), also showed significant anticipation. These results support the finding of anticipation in schizophrenia. Recent results in other disorders, e.g. HD, indicate unstable DNA as a molecular mechanism for anticipation. Replication of anticipation in a representative sample supports the likelihood that expansion of unstable DNA may be a causal genetic event in schizophrenia.

References:

1. Bassett AS & Honer WG: Evidence for anticipation in schizophrenia. *Am J Hum Genet* 54:864–870, 1994.

2. Penrose LS: Survey of cases of familial mental illness. *Eur Arch Psychiatry Clin Neurosci* 240:315–324, 1991.

NR425 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Quality of Life Outcomes for Olanzapine and Haloperidol Treatment for Schizophrenia and Related Psychotic Disorders

Dennis Revicki, Ph.D., Health Research, Medtap International, 2101 Wilson Blvd. Suite 802, Arlington VA 22201; Laura A. Genduso, RPh, Susan L. Hamilton, M.S., Christophe Martin, M.D., Joe Reblando, B.S., Pierre V. Tran, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the use of a disease-specific scale in quality of life research for schizophrenia and the results in one large clinical trial.

Summary:

Objectives: To evaluate the effect of treatment with olanzapine and haloperidol on quality of life (QOL) outcomes.

Methods: 1996 patients with DSM-III-R diagnosis of schizophrenia, schizophreniform disorder, or schizoaffective disorder participated in a randomized, double-blind clinical trial. Patients were from 174 academic and community centers in 17 countries. A total of 1270 patients had baseline Quality of Life Scale (QLS) scores and 811 had baseline and six-week QLS scores. Treatment was with either olanzapine 5 to 20 mg/day or haloperidol 5 to 20 mg/day for 52 weeks. BPRS total scores, PANSS positive and negative scores, CGI Severity scores, and Quality of Life Scale (QLS) total and subscale scores were measured.

Results: During the acute treatment phase, the olanzapine treatment group had significantly greater improvements in BPRS total

(p = .015), PANSS negative (p = .032), and CGI Severity (p = .029), QLS total (p = .013), intrapsychic foundations (p = .005), and interpersonal relations (p = .022) compared with the haloperidol treatment group scores during the acute phase. The improvements in QLS total and intrapsychic foundations scores were maintained over the 52-week trial.

Conclusion: Olanzapine was significantly more effective in reducing severity of psychopathology and in improving quality of life. This superior QOL performance was especially evident in the QLS domains of interpersonal relations and intrapsychic foundations.

References:

1. Schiz Bull 10:388–398, 1984 Med Care 31:247–263, 1993.

NR426 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Late-Life Schizophrenia in the United States and the United Kingdom

Philip D. Harvey, Ph.D., Psychiatry, Mt. Sinai School of Med., One Gustave Place, New York NY 10029; Noam Trieman, M.D., Michael Davidson, M.D., Julian Leff, M.D., Janel Lombardi, M.D., Peter Powchik, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate the homogeneity of schizophrenia across cultures and that aging related changes in schizophrenia are similar around the world.

Summary:

Recent research has suggested that many geriatric schizophrenic patients with a chronic course of illness manifest substantial cognitive impairments. While these impairments may be a result of a disease-specific neurodegenerative process, they may also be influenced by correlates of the illness, including long-term institutional care. These concerns would be obviated if similar results were found across different cultures and care systems. This study performed a cross-national comparison of geriatric schizophrenic patients in care in the US and the UK. Geriatric chronically hospitalized schizophrenic patients over the age of 70 who met formal criteria for schizophrenia and who had an early age (< 45) of onset were collected from New York (n = 87) and London (n = 136) long-term psychiatric centers. All patients were assessed with the Mini-Mental State Examination (MMSE) and assessments of adaptive functioning. The US patients had a longer total stay in psychiatric care (39.3 vs 24.8, t(221) = 5.20, p < .001), but were essentially the same age (81.1 vs 80.8). The two samples had remarkably similar MMSE total scores (10.5 vs 10.7, t = –.16). US patients had more impairments in social skills, but were less impaired in personal self-care skills than the UK patients. Scores on hostility and belligerence did not differ across the two groups. These data indicate that severe cognitive impairments are present in geriatric schizophrenic inpatients in both the US and the UK, suggesting that previous findings across US sites were not specific to American systems of care. In addition, there were several differences in adaptive functioning across the samples, possibly related to differences in patterns of care or criteria for discharge. Our findings underscore the homogeneity of schizophrenia across cultures and suggest that aging related changes in schizophrenia are similar around the world as well, at least in chronically hospitalized patients.

References:

1. Davidson M, Harvey PD, Powchik P et al.: Severity of symptoms in geriatric chronically institutionalized schizophrenic patients. *American Journal of Psychiatry*, 152:197–207, 1995.

2. Leff JP, Thornicroft G, Coxhead N, and Crawford C: The TAPS Project. 22: A five-year followup of long stay psychiatric patients discharged to the community. *British Journal of Psychiatry* (Supplement). 165 (Supplement 25):13–17, 1994.

NR427 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Platelet Aggregation is Increased in Alzheimer's Disease

Steven Sevush, M.D., Psychiatry, University of Miami, 1400 NW 10th Ave. Suite 702, Miami FL 33136; Wenche Jy, Ph.D., Richard S. Mallia, B.A., Lawrence L. Horstman, Luciano Kolodny, M.D., Yeon S. Ahn, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to explain about platelet serotonin levels and how they may be diminished in AD.

Summary:

Objectives: Platelet serotonin levels have recently been reported to be diminished in Alzheimer's disease (AD) (Kumar et al., 1995). The cause of this phenomenon is unknown. In the present study, we examined the possibility that altered platelet serotonin levels in AD patients might result from subclinical activation of platelet aggregation, a process known to be associated with lowering of platelet serotonin concentration.

Methods: 50 patients with NINCDS probable AD and 20 age- and sex-matched normal controls served as the study group. All subjects were free of both vascular disease and platelet-activating medication. In addition, groups were matched for frequency of cigarette smoking. Flow cytometry was used to measure calcium-activated platelet aggregation (Ca^{++}-PA) in platelet rich plasma (Wenche, 1992). Analysis of variance was used to compare Ca^{++}-PA between groups.

Results: Mean values of Ca^{++}-PA were significantly higher (F = 11.02, p = .001) in AD patients (0.36 ± 0.27) than in controls (0.16 ± 0.06).

Conclusions: These data represent the first report of elevated platelet aggregation in AD, supplementing previous reports of diminished platelet serotonin in these patients. Potential causes of this phenomenon might include activation resulting from subclinical damage to cerebral blood vessel walls or from elevated levels of amyloid precursor protein, a known activator of platelet aggregation.

References:

1. Kumar AM, Sevush S, Kumar M, Ruiz J, Eisdorfer C: Peripheral serotonin in Alzheimer's disease. *Neuropsychobiology* 32:9–12, 1995.

2. Adams GA: Platelet aggregation. The Platelets: Physiology and Pharmacology 1–14, 1985.

NR428 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Depressed Mood and the Incidence of Alzheimer's Disease

Davangere P. Devanand, M.D., Psychiatry, New York State P.I., 722 W 168th Street Box 72, New York NY 10032-2603; Mary Sano, Ph.D., Ming-Xin Tang, Ph.D., Yaakov Stern, Ph.D., Richard Mayeux, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should learn about the relationship between depression and cognitive impairment, and about the implications of depressed mood being associated with a moderately increased risk of developing Alzheimer's disease in the community elderly.

Summary:

A total of 1,070 elderly individuals were identified as part of a community registry for dementia in North Manhattan, New York. Of the 1,070 subjects, 218 met criteria for dementia at baseline evaluation. In the 852 subjects without dementia, depressed mood was more common in individuals with greater cognitive impairment. A total of 478 of these subjects without dementia were followed annually for one to five years (mean 2.54, SD 1.12 years of follow-up). Cox regression analyses showed that depressed mood (item from the 17-item Hamilton Rating Scale for Depression, HRSD) at baseline was associated with an increased risk for incident dementia (RR = 2.94; 95% confidence interval [CI], 1.76 to 4.91, $p < .001$), and 93.4% of the incident dementia cases met diagnostic criteria for Alzheimer's disease. This effect remained after adjusting for age, gender, education, language of assessment, Blessed Memory Information and Concentration test scores, and Blessed Functional Activity Scale scores (RR = 2.05; 95% CI, 1.16 to 3.62, $p < .02$). Similar results were obtained when the total HRSD score was used as the "depression" variable, using the same covariates.

Depressed mood moderately increased the risk of developing dementia, primarily Alzheimer's disease. Whether depressed mood is a very early manifestation of Alzheimer's disease, or increases susceptibility through another mechanism, remains to be determined.

References:

1. Alexopoulos GS, Meyers BS, Young RC et al.: The course of geriatric depression with "reversible dementia": a controlled study. *Am J Psychiatry* 150:1693–1699, 1993.

2. Jorm AF, Van Duijn CM, Chandra V et al.: Psychiatric history and related exposures as risk factors for Alzheimer's disease. *Int J Epidemiology*20:S43–S47, 1991.

NR429 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

The Cost of Delirium in the Surgical Patient

Kathleen N. Franco, M.D., Psychiatry, Cleveland Clinic, 9500 Euclid Avenue Desk P57, Cleveland OH 44195; Joseph A. Locala, M.D., David Litaker, M.D., David L. Bronson, M.D., Ziad Tannous, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe a systematic method of screening for delirium, understand the variety of additional costs which result from this complication and ways in which interventions can reduce its incidence in the surgical population.

Summary:

Objective: To identify the added cost of treating delirium in the patient undergoing elective surgery.

Methods: Five hundred consecutive patients were evaluated prior to their elective surgery, assessing cognitive functioning, medical conditions, medication usage, and other information regarding their health status. Patients were assessed for delirium with the TICS and CAMS on postoperative days 1 through 4. Medical record review provided laboratory, radiological, and pharmaceutical information. Cost information was collected through the hospital data base and analyzed using the Student t-test.

Results: Of the 500 patients assessed, 57 (11.2%) developed delirium during the study. Those patients who developed delirium had a mean length of stay (LOS) of 6.0 days, while those patients who did not stayed 4.5 days ($p = .001$). Total charges for patients with delirium were $4,311.82 greater on average ($p = 0.013$). The mean direct cost for the delirious group was an added $1,433.61 ($p = .014$). Likewise, the non-direct costs were greater by $912.95 ($p = .006$). The professional contribution margin was higher for the non-delirious group ($2,959.54 versus $1,858.75; $p = .021$). Hospital net income was an added $1,295.08 for the non-delirious patient ($p = .004$). Routine care costs were significantly greater for the delirious patient by $307.00 ($p = .001$). In addition, pathology labs ($p = 0.008$) and pharmaceutical supplies ($p = 0.045$), total technical fees ($p = 0.015$), and consulting physician fees ($p = 0.009$) were significantly higher in the delirious patient.

Conclusion: Delirium is an extremely costly disorder to the patient in terms of morbidity and mortality, as well as to the medical facility. Increased length of stay, increased charges to third party payors, and a reduced return to physicians and hospitals occur when delirium develops. It is believed by presurgical assessments and effective interventions that length of stay and costs may be reduced, as well as bringing greater physical, emotional, and cognitive health to patients hospitalized for elective surgery.

References:

1. Francis J, Martin D, Kapoor WN: A prospective study of delirium in hospitalized elderly. *JAMA* 263:1097–1101, 1990.

2. Thomas RI, Cameron DJ, Faks MC: A prospective study of delirium and prolonged hospital stay. *Arch Gen Psychiatry* 45:937–940, 1988.

NR430 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Glucose Metabolic Rate in the Frontal and Temporal Lobes in Alzheimer's Disease

Lina S. Shihabuddin, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Leonart Abel, Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., N. Pandit, M.D., Deborah B. Marin, M.D.

Educational Objectives:

At the conclusion of this presentation the audience would have a clearer idea on the progression of pathology in different brain areas in Alzheimer's disease and would appreciate the input of functional imaging on diagnosis and prognosis of this debilitating disease.

Summary:

To assess regional metabolic change in lateral and medial temporal cortex in early Alzheimer's disease MRI and PET scans with FDG were done on 33 patients (16 males and 17 females, mean age 70.6, range 54–89). We also identified 32 age- and sex-matched controls from our sample of 80 normal subjects, ages 21–87. All subjects were evaluated with DSM-III-R criteria for dementia of the Alzheimer type. The Clinical Dementia Rating (CDR) Scale and the Mini-Mental State Examination (MMSE) were used to assess the degree of impairment. Ten subjects were diagnosed with questionable AD (MMSE 25.6, SD 2.2), and 23 subjects met criteria for probable AD (MMSE 20.9, SD 4.37) at the time of the scan. None of the subjects met criteria for any major psychiatric diagnosis at the time of the scan. Nineteen subjects had a CDR of 0.5 (10 questionable, 9 probable), 10 subjects had a CDR of 1.0, and five had a CDR of 2.0. We obtained PET scans with fluorodeoxyglucose uptake during a serial verbal memory task and coregistered high resolution magnetic resonance images. PET scans are obtained using our GE 2048 head scanner with measured resolution of 4.5 mm in plane and 5.0 mm axially. We obtain 15 slices at 6.5 mm intervals in two sets so as to cover the entire brain. For MRI, we use the GE Signa 5x system with the SPGR sequence (repetition time of 24 ms, echo time of 5 ms, flip angle 40 degrees), for contiguous 1.2 mm thick axial slices, with a 256 x 256 pixel matrix in a 23 cm field of view. PET Scans are reconstructed with a blank and transmission image attenuation correction. For accurate anatomical analysis, we coregister every PET with MRI using our own version of the surface-fit Pelizzari et al. method (1989). Metabolic rate was assessed

only for MRI-coregistered pixels segmented as gray matter to minimize contribution of CSF and white matter locations. The cortical surface revealed decreases in total frontal metabolic rate in probable AD patients but not in questionable patients. Examination of the different segments of the frontal lobe, revealed the effect to be most prominent in the anterior frontal cortex. In the temporal cortex, the metabolic rate decreased in probable AD patients while it increased in questionable patients. These findings suggest that the disease process in Alzheimer's starts in the temporal lobe with a compensatory increase in the metabolic activity without affecting the frontal lobe and then progresses, with a decline in activity appearing in both the temporal and frontal lobes.

References:

1. Buchsbaum MS, Kessalak JP, Lynch G et al.: Temporal and hippocampal metabolic rate during an olfactory memory task assessed by positron emission tomography in patients with demential of the Alzheimer's type and controls. *Arch Gen Psychiatry*, 48:840–847, 1991.

2. Grady CL, Haxby JV, Schapiro MB et al.: Subgroups in dementia of the Alzheimer type identified using positron emission tomography. *J Neuropsych Clin Neurosci* 2:373–384, 1990.

NR431 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Apolipoprotein E Epsilon 4 Allele Vascular Disease and Dementia

Deborah B. Marin, M.D., Psychiatry, Mount Sinai Med Center, Box 1230 1 Gustave Levy P1, New York NY 10029; Richard C. Mohs, Ph.D., Lawrence Altsteil, M.D., David M. Greenberg, M.D., Melinda S. Lantz, M.D., Kenneth L. Davis, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the relationship between APOE4 and peripheral arterial disease, cerebrovascular disease, vascular dementia, and primary degenerative dementia in the very old.

Summary:

Introduction: The association between the apolipoprotein E epsilon 4 allele (APOE4) and Alzheimer's disease has been demonstrated in several studies. The relationships between APOE4 and peripheral and central nervous system vascular diseases are less certain. This study investigated the relationship between APOE4 and peripheral arterial disease, cerebrovascular disease, vascular dementia, and primary degenerative dementia in the very old.

Methods: 619 nursing home residents with mean age of 85.1 years were included. ICD-9 criteria were used for diagnoses. Ischemic heart disease and peripheral arterial disease were grouped as peripheral symptomatic atherosclerosis.

Results: 25% of the sample had cerebrovascular disease, 30% had peripheral symptomatic atherosclerosis, 4.5% had vascular dementia, and 32% had primary degenerative dementia. The APOE4 allele was significantly more frequent in primary degenerative dementia individuals than in individuals without this diagnosis (38% vs 22% $p < .0001$). Individuals with peripheral symptomatic atherosclerosis, cerebrovascular disease, or vascular dementia did not have a greater frequency of the APOE4 allele when compared to individuals without these diagnoses.

Conclusion: The association between APOE4 and primary degenerative dementia is replicated in this sample of very old. The relationship between APOE4 and each of the vascular diseases was not significant.

References:

1. Jarvik GP, Wijsman EM, Kukull WA, et al. Interactions of apolipoproteinE, genotype, total cholesterol level, age, and sex in prediction of Alzheimer's Disease: A case-control study. *Neurology;* 45: 1092–1096, 1995.

References:

2. Betard C, Robitaille Y, Gee M, et al. ApoE allele Frequencies in Alzheimer's Disease, Lewybody dementia, and Vascular Dementia. *Neuroreports* 5: 1893–1896, 1994.

NR432 Wednesday, May 8, 9:00 a.m.-10:30 a.m.

Recognizing Risk for Postoperative Delirium

Joseph A. Locala, M.D., Psychiatry, Cleveland Clinic Foundati, 9500 Euclid Avenue Desk P57, Cleveland OH 44195; Kathleen N. Franco, M.D., David Litaker, M.D., Ziad Tannous, M.D., David L. Bronson, M.D., Joy Frame, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe a systematic method of screening for delirium, identify significant risk factors for this complication, appreciate its link to increased morbidity and costs, and understand basic components of a clinical intervention to reduce the incidence of delirium in surgical populations.

Summary:

Objective: To identify patients at high risk for postoperative delirium using factors present at preoperative evaluation.

Methods: 500 consecutive patients about to undergo major, elective surgery were seen for preoperative medical evaluation and assessed using standardized instruments measuring cognitive and functional status. Information on comorbid conditions, past medical problems, current medication usage patterns, and data on health habits were obtained by history. Patients subsequently underwent evaluation for confusion on postoperative days 1 through 4 using medical record review for reports of confusion, disorientation, or agitation by medical staff and through direct patient interviews focusing on cognitive function. Multivariate regression techniques were used to identify preoperative factors most closely associated with the subsequent development of delirium.

Results: Compared with those who developed no signs of confusion, the 56 (11.2%) patients experiencing this complication were more often 70 years or older (RR = 3.1 [1.75, 5.55]), or had pre-existing cognitive impairment (RR = 3.1 [1.73, 5.43]), greater functional impairment (RR = 1.57 [1.27, 1.94]), and a previous history of acute confusion (RR = 4.1 [1.98, 8.37]). In a multivariate model, previous delirium (RR = 4.08 [1.85, 9.0]), age > 70 (RR = 3.2 [1.67, 6.0]), and pre-existing cognitive impairment (RR = 2.16 [1.15, 4.0]) remained predictive of delirium. In addition, alcohol use (RR = 6.53 [1.5, 28.1]), and use of narcotic analgesics preoperatively (RR = 2.7 [1.37, 5.3]) were also significantly associated with this complication.

Conclusion: Acute confusion in the postoperative setting can be predicted preoperatively using easily obtainable clinical indices. Although risk recognition should allow for strategies aimed at reducing the incidence of this complication, many of the factors identified in this sample could not be modified. These data suggest that the use of elective major surgical procedures in high risk patients should be considered carefully in a risk-benefit equation, especially when non-surgical or more conservative management alternatives exist. Continuous endpoints such as the number of days of recognized postsurgical delirium may be more useful than dichotomous ones at determining the effect of these surgical alternatives or medical interventions applied to high risk individuals in the future.

References:

1. Marcantonio ER, Goldman L, Mangione CM et al.: A clinical prediction rule for delirium after elective noncardiac surgery. *JAMA* 271:134–139, 1994.

2. Dyer CB, Ashton CM and Teasdale TA: Postoperative delirium; A review of 80 primary data-collection studies. *Arch Intern Med* 155:461–465, 1995.

NR433 Wednesday, May 8, 12 noon-2:00 p.m.

Impact of Interventions to Prevent Delirium

Martin G. Cole, M.D., Psychiatry, St. Mary's Hospital Ctr., 3830 Lacombe Avenue, Montreal QU H3T1M5, Canada; Francois J. Primeau, M.D., Jane McCusker, M.D.

Summary:

Objective: To determine the effectiveness of systematic interventions to prevent delirium in hospitalized patients.

Methods: Two databases, MEDLINE and CINAHL, were searched for relevant articles published in January 1966 to May 1995, and January 1982 to May 1995, respectively. The bibliographies of identified articles were searched for additional references. Ten reports were located that met the following three inclusion criteria: original research, published in English or French and controlled trial (nonrandomized or randomized) of a systematic intervention to prevent delirium in hospitalized patients. The quality of the studies was independently assessed according to the criteria for intervention studies proposed by the Evidence-Based Medicine Working Group. Information about study design, patient population, sample size, diagnostic criteria, interventions, and results was systematically abstracted from each report and tabulated. Absolute risk reduction and relative risk reduction (RRR) for delirium were calculated for each study.

Results: Eight trials involved surgical patients and two involved elderly medical patients; most studies had serious methodological limitations. Among surgical patients, RRR's ranged from –26% to 93% and were not related to the type or timing of the intervention or the personnel involved. Among elderly medical patients, RRR's ranged from –6% to 14%.

Conclusion: Interventions to prevent delirium among surgical patients may be effective but further trials are necessary.

NR434 Wednesday, May 8, 12 noon-2:00 p.m.

Environmental Strategies Are Instituted in Response to Behavioral Challenges in Patients with Delirium

David J. Meagher, M.D., Psychiatry, St. Itas, Portrane, Co Dublin, Ireland; Donal O'Hanlon, M.D., Edmond O'Mahony, M.D., Patricia Casey, M.D.

Summary:

Purpose: To examine the pattern and frequency of implementation of environmental strategies and the use of psychotropic medications in the management of patients with delirium in an acute hospital setting.

Methods: The study involved 46 consecutive referrals to a consultation psychiatry service, each of whom met ICD-10 criteria for delirium. Patients were subdivided into hyperactive, hypoactive, and mixed subtypes and assessed regarding severity of delirium, the use of psychotropic medications prior to consultation, and the implementation of environmental measures in their management.

Results: Mean age was 60.1 years. Thirty percent were of the hyperactive subtype, 24% hypoactive, and 46% mixed. Psychotropic medications were given to 56.5% prior to consultation and this was significantly associated with severity of delirium and in particular with hyperactive delirium subtype. Of eight environmental strategies, only four were instituted in over 50% of the patients prior to consultation. The application of these strategies was associated with overall severity of delirium, agitation, mood lability, and sleep-wake cycle disturbance, but not with severity of disorientation or disturbed perception/thinking.

Conclusion: Simple environmental manipulations (such as limiting staff changes, minimizing noise levels, and involving relatives in re-orientation) are frequently overlooked in the management of delirium. This study suggests that environmental strategies are instituted in response to behavioral challenges rather than to limit the core features of delirium.

NR435 Wednesday, May 8, 12 noon-2:00 p.m.

Focal Anatomic Substrates in Late-Life Depression

Anand Kumar, M.D., Psychiatry, University of Pennsylvania, 3615 Chestnut Street, Philadelphia PA 19104; David S. Miller, M.D., Patricia Cowell, Ph.D., Warren Bilker, Ph.D., Jin Zhisong, M.S., Laura L. Swan, B.A.

Summary:

The purpose of our study was to examine MRI determined volumetric measures of the frontal and temporal lobes in subjects with late life major depression (LLD) and to compare them to similar indices obtained from non-depressed controls. Our study groups were comprised of 41 subjects who met DSM-IV criteria for major depressive disorder (14 M, 27 W, Mean age = 74.4 SD = 6.6), and 31 non-depressed healthy controls (7 M, 24 W, Mean age = 70.5 SD = 6.4). The depressed subjects had Hamilton Depression Scale Scores of 15 or greater without any clinical evidence of dementia. They had several stable comorbid medical disorders and were free of other central nervous system disease. Axial spin echo images were acquired on all subjects using a GE signa scanner with head coil. The 5mm thick, contiguous slices were obtained using a repetition time (TR) of 3000 msec and echo time (TE) of 30 and 80 msec in planes parallel to the canthomeatal line. The neuroanatomical boundaries used in the image analysis have been previously described (Cowell et al. *J Neurosci* 1994). Frontal and temporal lobe volumes normalized using total brain and intracranial volumes were used for comparison between groups. The two groups differed significantly on most normalized measures of frontal and temporal lobe volumes after correcting for age using linear regression ($P < 0.05$). These data demonstrate that focal neuroanatomical abnormalities occur in LLD and provide further evidence for a structural basis to depression occurring in late life.

NR436 Wednesday, May 8, 12 noon-2:00 p.m.

The Role of Medications in the Developmental of Postoperative Delirium

Joseph A. Locala, M.D., Psychiatry, Cleveland Clinic Foundati, 9500 Euclid Avenue Desk P57, Cleveland OH 44195; David Litaker, M.D., Kathleen N. Franco, M.D., David L. Bronson, M.D.

Summary:

Objectives: To identify associations between pre- and postoperative medications and the development of postoperative delirium.

Methods: The medications of 500 patients without evidence of existing delirium who were scheduled for major elective surgery at the Cleveland Clinic were recorded at a preoperative medical assessment. Medications administered on the day of surgery after return from the recovery room were also documented. Patients were visited daily on postoperative days 1 through 4 and assessed for the presence of delirium using a standardized screening process. Univariate comparisons and multivariate regression techniques were used to identify both pre- and postoperative medica-

tions associated with the subsequent development of postsurgical delirium.

Results: In univariate comparisons with patients who did not subsequently develop delirium, the 57 (11.4%) who did were using narcotic analgesics ($p < 0.01$) and benzodiazepines ($p = 0.02$) more often at the time of preoperative consultation. Similarly, those developing delirium also received benzodiazepines ($p < 0.01$) and antipsychotic medications ($p = .02$) more often in the immediate postoperative period (initial 24 hours). In a multivariate model, those receiving preoperative narcotic analgesics (RR = 2.65 [1.33–5.25]), postoperative benzodiazepines (RR = 2.93 [1.20–7.14]), or post-operative antipsychotic agents (RR = 6.67 [1.3, 34.2]) were all significantly more likely to experience delirium after surgery. No significant associations were observed between postoperative use of antihistamines, narcotics, antidepressants, or anticholinergic agents and subsequent delirium.

Conclusions: Medications have long been recognized to play a significant role in the development of acute confusional states. While antihistamines and anticholinergic medications have been implicated in the development of postoperative delirium, their association as potential causative agents may have led to subsequent avoidance and substitution of other medications. These data suggest the need for cautious use of psychoactive medications in the perioperative period in order to lower the incidence of this common postsurgical complication.

NR437 Wednesday, May 8, 12 noon-2:00 p.m.

Evaluation of a Risk Assessment System for Postoperative Delirium

Kathleen N. Franco, M.D., Psychiatry, Cleveland Clinic, 9500 Euclid Avenue Desk P57, Cleveland OH 44195; Joseph A. Locala, M.D., David Litaker, M.D., Joy Frame, R.N., David L. Bronson, M.D., Ziad Tannous, M.D.

Summary:

Objectives: To validate a previously reported delirium risk scoring system in a different population.

Methods: 500 consecutive patients undergoing major, elective surgery were enrolled at preoperative medical consultation. Risk for delirium was ascertained for each individual using a scoring method based on age, history of alcohol use, abnormal preoperative laboratory values, type of surgery, and assessment of functional and cognitive status with standardized instruments. Development of delirium was determined on postoperative days 1 through 4 by daily cognitive re-assessment and medical record review for comments by medical staff indicating confusion, agitation, or disorientation. Sensitivity and specificity for this delirium risk score were calculated at two scoring cutpoints along with receiver operator characteristic (ROC) curve values to evaluate the performance of this scoring system in our patient sample.

Results: 56 (11.2%) patients developed delirium with preoperative risk stratified as follows:

Risk Level (Score)	Low (0)	Low/Med.(1)	Med./High(2)	High (>2)
Delirium Absent (%)	188 (94)	187 (92)	56 (73)	12 (65)
Delirium Present (%)	12 (6)	17 (8)	21 (27)	6 (35)

Delirium scores > 2 yielded a sensitivity of 47.4% and specificity of 85%. Sensitivity improved to 77% with a score > 1, but specificity fell to 42.4%. The area under the ROC curve was 0.69, differing significantly from that reported in the original sample ($p = 0.007$).

Conclusions: Although the delirium scoring system performed well in the original validation and derivation sets, it did not generalize to a sample selected in a similar fashion at a different site. Its lack of generalizability may be related to differences in patient demographics, surgical practices, burden of comorbid illness, or surgical disease severity. These results suggest that systems used to stratify preoperative risk for delirium should be applied cautiously, but remain useful in elevating clinical awareness of a frequently underdiagnosed postsurgical complication.

NR438 Wednesday, May 8, 12 noon-2:00 p.m.

Postpartum Psychiatric Morbidity

Rafia O.S. Ghubash, Ph.D., Psychiatry, UAE University, Faculty of Medicine Box 17666, Al Ain, U. Arab Emirates; Prof. M.T. Abou-Saleh, Ph.D.

Summary:

Background: There have been very few studies of the prevalence of post-partum psychiatric illness outside western Europe and North America. This prompted us to study its prevalence in a UAE sample and examine psychosocial risk factors that contribute to its occurrence.

Method: A series of 134 women were prospectively studied post-partum on the third day, first week, eighth week, and 30th week after delivery. An assessment was made using the Edinburgh Post-natal Depression Scale, the Self-Reporting Questionnaire, and the Present State Examination. Socio-demographic and obstetric data were also collected.

Results: The prevalence of post-partum psychiatric illness was 17.8% in the first week, 22.2% at week 8 and 12.8% at week 30. The occurrence of psychiatric illness was significantly associated with increased number of children, poor marital relationship, being divorced/previously married, living with own family, presence of past psychiatric history, and an alcoholic member in the family.

Conclusion: The findings are similar to studies in Western Europe and North America except for the emergence of more specific social risk factors.

NR439 Wednesday, May 8, 12 noon-2:00 p.m.

Duration of Delirium: A Prospective Study

Peter J. Manos, M.D., Psychiatry, Virginia Mason, 1100 9th Avenue, Seattle WA 98111-0900; Rae Wu, M.D.

Summary:

Objective: We wished to produce a complete frequency distribution of the duration of delirium in a large number of patients, plot the data as a "survivorship" curve for delirium, and examine differences between postoperative and medical patients and between demented and non-demented patients. We wished to study mortality as well.

Methods: The senior author entered into the study a series of 94 consecutive patients with delirium and followed the patients closely throughout their hospital course. Patients were telephoned for follow-up after discharge.

Results: The rates of disappearance of delirium appeared log linear for approximately two weeks, but rate of resolution for medical patients was slower than for postoperative patients. The mean and median duration of delirium for medical patients were 13.2 and 8 days; for postoperative patients, 7.6 days and 6 days. Combined mortality over three and half years was 46.8%. Demented patients had longer average durations of delirium than non-demented patients but differences were not statistically significant because of large variance.

Conclusions: Populations of delirious patients may be characterized by the shape of the delirium survivorship curve. Postoperative patients may have shorter deliria than medical patients. Mortality is high for both groups.

NR440 Wednesday, May 8, 12 noon-2:00 p.m.

Valproate Treatment of Behavioral Disturbances Associated with Dementia

Meena Narayan, M.D., Psychiatry, Yale University, 20 York Street, New Haven CT 06510; J. Craig Nelson, M.D.

Summary:

Objective: Behavioral problems are present in more than 50% of patients with dementia. Neuroleptics are used extensively in these patients despite their relatively low efficacy and significant side effects. Valproate (VPA) is a non-neuroleptic treatment reported to be efficacious, but clinical data with this drug are sparse. This study evaluates the role of VPA in patients with behavioral disturbance and dementia.

Methods: Charts of consecutive patients with dementia and behavioral problems treated with VPA were retrospectively reviewed. Target symptoms were identified and change was rated using a Global Improvement Scale.

Results: Seventeen patients with a mean age of 78 years were identified. The most common target symptoms resulting in hospitalization were agitation, restlessness, and combativeness. The mean final dose of VPA required was 1838 (250–4000mg) with a mean level of 60 ± 22ug/ml. In eight of the 17 patients, VPA was added to an ongoing neuroleptic which had been ineffective. After the addition of VPA, nine of the 17 patients were much improved, one patient was very much improved, five patients were minimally improved, and two patients were unchanged.

Conclusions: VPA is a helpful agent for managing behavior symptoms of dementia either alone or when added to a neuroleptic.

NR441 Wednesday, May 8, 12 noon-2:00 p.m.

Psychiatric Morbidity in Epilepsy: The Role of Anticonvulsants

Bettina Schmitz, M.D., Psychiatrie Klinikum, Abteilung, Rudolfvirchow Eschenallee, Berlin 314050, Germany; Mary J. Robertson, M.A., Michael R. Trimble, M.D.

Summary:

In a retrospective study we investigated the role of anti-epileptic drugs (AED) for the development of schizophrenia-like psychosis and major depression in patients with epilepsy.

Method: We studied 25 patients with epilepsy and psychosis, 25 patients with epilepsy and major depression, and 50 consecutive non-psychiatric epilepsy patients with respect to biological and social data. The AED regime at onset of the psychiatric disorder was recorded in detail.

Results: With respect to AED there were only few significant differences between groups: polytherapy as well as treatment with phenytoin was more frequent in psychotic patients as compared to depressive and non-psychiatric patients. Patients with depression were rarely treated with valproate, as compared to both psychotic and non-psychiatric patients. Patients with schizophrenia-like psychoses or depression suffered more frequently from focal epilepsies arising from the temporal lobe than non-psychiatric controls. Schizophrenic patients had an early age of onset of epilepsy and a severe epilepsy. These patients were also characterized by social dependency and professional failure. Depressive patients were significantly older than schizophrenic patients and controls. They did not differ from non-psychiatric controls with respect to social variables and severity of epilepsy.

Conclusions: In this study, polytherapy was positively linked with schizophrenia-like psychosis, and treatment with valproate was negatively linked with depression. These retrospective results are unlikely to reflect a simple etiological relationship between AED and psychiatric morbidity in epilepsy. Polytherapy might only be the consequence of severe epilepsy, a major risk factor for psychiatric complications. Our data suggest however, that valproate might have prophylactic antidepressive properties in epilepsy patients.

NR442 Wednesday, May 8, 12 noon-2:00 p.m.

Neurologic Status in Combat and Sexual Abuse PTSD

Tamara V. Gurvits, M.D., VA Research Service, 228 Maple Street Second Floor, Manchester NH 03103; Daphne Simeon, M.D., Mark W. Gilbertson, Ph.D., Alexandra C. Tarhan, Ph.D., Natasha B. Lasko, Ph.D., Roger K. Pitman, M.D.

Summary:

Objective: This project replicated the neuropsychiatric study of combat-related post-traumatic stress disorder (PTSD) and extended it to non-combat, child-abuse-related PTSD. We tested the hypothesis that subjects with PTSD would have more neurologic impairment and compromised developmental histories, independent of gender or nature of traumatic experience.

Method: The first group comprised 25 PTSD and 16 non-PTSD, male Vietnam combat veterans (VNV). The second group comprised 12 PTSD and 11 non-PTSD, female survivors of childhood sexual abuse (CSA). Each subject underwent a videotaped neurologic examination of 58 neurologic soft signs (NSSs), each scored on a predefined 0–3 scale, and a standardized neuropsychiatric history.

Results: Mean NSS scores (and SDs) were: VNV-PTSD 29.0 (10.2) vs. VNV-non-PTSD 17.3 (6.4), $t(39) = 4.1$, $p < .001$; CSA-PTSD 29.0 (14.4) vs. CSA-non-PTSD 14.0 (5.0), $t(33) = 3.3$, $p = .005$. Numbers of subjects in each group with a compromised developmental history (i.e., attention deficit, learning disability, and/or enuresis) were: VNV-PTSD 15/25 (60%), VNV-non-PTSD 3/14 (21%), $p = .02$; CSA-PTSD 7/12 (58%), CSA-non-PTSD 3/10 (30%), $p = .18$.

Discussion: The results indicate that subtle neurologic impairment is common to different kinds of chronic PTSD. The compromised developmental histories in PTSD subjects raise the possibility that pre-existing neurologic impairment represents a risk factor for the development of this disorder.

NR443 Wednesday, May 8, 12 noon-2:00 p.m.

SPEM Abnormalities in Gilles de la Tourette's Syndrome and OCD

Stefano Pallanti, M.D., Institute for Neuroscien., Vle Ugo Bassi 1, Florence 50137, Italy; Leonardo Quercioli, M.D., Gaetano Zaccara, M.D., Graziamo Armetoli, Ph.D.

Summary:

Objective: Eye movement abnormalities have been reported in several neurological and psychiatric disorders. Recently, low gain and increased anticipatory saccades have been documented in OCD patients. To our knowledge there are no research about SPEM in Gilles de la Tourette's syndrome (GTS).

Method: We investigated eye movements through oculographic method in both GTS (n = 6), a rare neuropsychiatric disorder clinically related to the OCD spectrum, and OCD (n = 16) DSM-IV patients, compared to 22 healthy subjects.

Results: OCD and GTS patients showed worse eye tracking (increased frequency of intrusive saccades, $p < .01$; reduced pursuit gain measured as typical matching target velocity, $p < .001$) as compared with control sample. No significant differences were found between GTS and OCD oculographic variables, however, a nonsignificant reduced SPEM gain was recorded in GTS patients.

Conclusion: Correlation between eye movement abnormalities and clinical features, treatment response, and clinical subtype are discussed.

NR444 Wednesday, May 8, 12 noon-2:00 p.m.

Carbamazepine Induces Escape From Dexamethasone Suppression Across Mood Disorder Subtypes and Panic Disorder

Gabriela Cora-Locatelli, M.D., NIH, 10908 Rampart Way, Silver Spring MD 20902-4764; Mark A. Frye, M.D., Timothy A. Kimbrell, M.D., Kirk D. Denicoff, M.D., Terence A. Ketter, M.D., Robert M. Post, M.D.

Summary:

The Dexamethasone Suppression Test (DST) is a common test performed in patients with affective and anxiety disorders. DST escape (non-suppression) indicates state dependent neuroendocrine dysregulation characterized by increased CSF corticotropin releasing factor and subsequent hypercortisolemia. Persistent DST escape in clinically remitted patients has been associated with development of hypomania/mania and poor therapeutic outcome (i.e., relapse.) A review evaluating DST escape vs. non-escape was conducted to assess differences in escape rates by diagnostic categories and carbamazepine therapy.

Ninety-four inpatients (BP I = 29, BP II = 16, UP = 17, and panic disorder = 32) hospitalized at the NIMH from 1979–1987 had DSTs on placebo (n = 88) or carbamazepine, CBZ (n = 39). Thirty-three patients had DST testing on/off CBZ. DST escape was defined as a cortisol level greater than 5.0 mcg/dL at 8AM, 4PM, or 11PM the day after a 1 mg 11p.m. dexamethasone dose.

Although only 28% of BP I patients on placebo escaped, 88% escaped on CBZ. Similarly, 26% of BP II patients escaped on placebo, and 82% on CBZ. While only 13% UP patients and 34% of panic patients escaped on placebo, 100% of patients in these two groups escaped on CBZ. Regarding on/off CBZ DSTs, all patients who escaped on placebo escaped on CBZ. In addition, of the patients who initially did not escape on placebo, 83% of BPI, 67% of BP II, and all UP and panic patients later escaped on CBZ.

All diagnostic categories significantly increase DST escape rates on CBZ. The etiology of the mechanism remains to be clarified. Healthy volunteers on CBZ can inappropriately potentiate ACTH responsiveness to CRH. Also, CBZ, cortisol, and dexamethasone all induce cytochrome P 450 3A/4, thereby altering pharmacokinetic profiles of all of these compounds and any subsequent testing of the HPA axis. Regardless of primary diagnosis, DST escape rates may not necessarily be indicative of poor therapeutic outcome, particularly if the patient is currently on CBZ. Further studies will help determine whether CBZ induction of DST escape is a pharmacokinetic or neuroendocrine mediated and whether this is related to drug response.

NR445 Wednesday, May 8, 12 noon-2:00 p.m.

Nerve Growth Factor Plasma Levels in Schizophrenic Patients: A Preliminary Study

Giuseppe Bersani, 3rd Psychiatric Clinic, Via Del Corallo 25, Rome 00185, Italy; Angela Iannitelli, Paolo Maselli, Francesco Angelucci, Enrico Alleva, Luigi Aloe

Summary:

Nerve Growth Factor (NGF) is the best known neurotrophic factor of the neurotrophin family. More recently, it was observed that NGF has an essential role in neuronal development in the first phases of ontogenesis and seems to take part in the modulation of response to stress, of psychical rather than physical type, in the human species.

The aim of our study is to verify the possible differences in NGF plasma levels between schizophrenic patients and controls that could be linked to a possible alteration of primitive development of the CNS and/or to specific psychopathological characteristics of schizophrenia. The sample examined was made up of 24 male inpatients, with diagnosis of schizophrenia according to DSM-III-R criteria (average age = 30; S.D. = 7.93), compared with 29 controls (average age = 23.28; S.D. = 4.65). The method utilized was ELISA (sensitivity < 1 pg/ml).

The differences between mean NGF plasma levels in schizophrenic patients (14.83 pg/ml; S.D. = 10.75) and controls (32.70 pg/ml; S.D. = 17.03) was highly significant. The lower levels found in schizophrenic patients might correspond to specific developmental characteristics of the CNS of these patients. In the future, the evaluation of the role of neuroleptic in the release of NGF will be of great interest.

NR446 Wednesday, May 8, 12 noon-2:00 p.m.

Role of Serotonin Receptors in Alcoholism

Marc M. Ansseau, M.D., Psychiatric Unit, Chu Sart Tilman B-35, B-4000, Liege 00028, Belgium; William Pitchot, M.D., Valerie Barbier, M.D.

Summary:

Objective: Several preclinical evidence support the hypothesis of a serotonergic dysfunction in alcohol preference. In humans, some studies have demonstrated a serotonergic hypoactivity in alcoholism. The serotonergic abnormalities observed in alcoholics could be related to impulsive-aggressive and suicidal behaviors. In 1989, Coccaro et al., studying the prolactin (PRL) response to fenfluramine, reported that the strongest behavioral correlate of a reduced serotonergic function was the dimension of irritable impulsive aggression. However, little is known about the role of 5-HT1A receptors. Recently, we showed a blunted cortisol and temperature response to flesinoxan, a highly potent and selective 5-HT1A full agonist, in depressed inpatients with a history of suicidal behavior compared to nonattempters. Therefore, the objective of the present study was to assess the role of 5-HT1A receptors in alcoholism and its relationship with suicidal behavior.

Methods: Ten male inpatients meeting DSM-III-R criteria for alcohol dependence were included in the study. They were subgrouped into suicide attempters (n = 5) and nonattempters (n = 5) and completed the Past Feelings and Acts of Violence (PFAV) scale. All patients were assessed more than three weeks after the last reported use of alcohol and antidepressants. All patients had a flesinoxan 1 mg challenge test with assessment of cortisol and temperature responses to iv flesinoxan at times - 30, 0, 15, 30, 60, 90, and 120 min. The patients were compared to age-matched male controls.

Results: Mean delta cortisol responses to flesinoxan were significantly lower in alcoholics compared to controls: 10.9 ± 14.2 μg/l ($F = 9.9$, $p = 0.005$). There was also a difference between alcoholic patients and controls for the delta temperature responses, but only at a trend level:0.42 ± 0.24°C vs 0.65 ± 0.31°C ($p = 0.07$). A significant effect of suicide class on delta temperature values was apparent among the patients with a history of alcohol dependence: mean delta temperature values, 0.24 ± 0.16°C in alcoholic patients with a history of suicide attempt vs 0.61 ± 0.15°C in alcoholics without a history of suicidal behavior ($F = 13.8$, $p = 0.006$). Hormonal and temperature responses to flesinoxan were not correlated with PFAV scores.

Conclusion: The results of the present study support the implication of the serotonergic system, and particularly of 5-HT1A receptors, in the control of self-directed aggressive behavior in alcoholism.

NR447 Wednesday, May 8, 12 noon-2:00 p.m.

Low Serum Cholesterol, Suicide and Serotonin

Marc M. Ansseau, M.D., Psychiatric Unit, Chu Sart Tilman B-35, B-4000, Liege 00028, Belgium; Beatrice Hild, M.D., William Pitchot, M.D.

Summary:

Objective: In a recent article, Golier et al. reported a relationship between low cholesterol levels and history of medically serious suicide attempt in male psychiatric patients, confirming the results of epidemiologic studies in the general population demonstrating an increased mortality from suicide in patients with low cholesterol levels. Engelberg suggested that a lowering of plasma cholesterol concentrations could induce a decrease of cerebral serotonin activity leading to poor impulse control. Indeed, animal studies provided some evidence supporting this hypothesis. However, until now, studies performed in human did not demonstrate a link between blood cholesterol and serotonin function. In fact, in view of the excellent mechanisms of adaptation of the brain cell to extracellular fluctuations of cholesterol levels, this hypothesis could be too simplistic. Therefore, the objective of the present study was to test the relationship between cholesterol levels and central 5-HT1A receptors, using hormonal and temperature responses to flesinoxan, a 5-HT1A potent and selective full agonist.

Methods: 20 DSM-IV major depressive inpatients were included in the study: 13 males and 7 females with a mean age (± SD) of 42.2 years (± 9.6). The flesinoxan 1 mg challenge was performed after a drug-free period of at least three weeks, with injection of flesinoxan 1 mg and measurement of cortisol and temperature responses at times - 30, 0, 15, 30, 60, 90, and 120 min. Cholesterol levels were measured on admission.

Results: There was no correlation between delta peak cortisol and serum cholesterol concentrations ($r = -0.12$, $p = 0.61$) as well as between delta peak temperature and serum cholesterol concentrations ($r = -0.13$, $p = 0.60$).

Conclusion: These results do not support the hypothesis of a relationship between blood cholesterol and serotonin function. Therefore, the association between low serum cholesterol and suicide could be linked with dysfunctions in other neurotransmitter systems such as the catecholaminergic system and not only in the serotonergic function. In fact, low serum cholesterol levels and decreased serotonergic activity could be both independent "biological markers" whose association could induce suicidal or aggressive behaviors.

NR448 Wednesday, May 8, 12 noon-2:00 p.m.

CSF Monoamine Metabolites and the Weather in Humans

Timothy D. Brewerton, M.D., Psychiatry, MUSC, 171 Ashley Ave, Charleston SC 29425-0002; Michael J. Norden, M.D., Richard J. Lewine, Ph.D., S. Craig Risch, M.D.

Summary:

Objective: Seasonal variations in neurotransmitter function have been reported in humans, but studies have involved small sample sizes and have not examined possible relationships with climatological (meteorological) variables.

Methods: We compared cerebrospinal fluid (CSF) concentrations of the major monoamine neurotransmitter metabolites (5-HIAA, HVA, & MHPG) in 188 healthy controls (80 men, 108 women) and several meteorological variables for the *day prior* to LP (photoperiod, percent [of total possible] sunshine, temperature (max, min, mean), barometric pressure, relative humidity, amount of precipitation and skycover).

Results: Results revealed significant differences across the year for CSF 5-HIAA and HVA, but not MHPG, in the total group. CSF 5-HIAA was correlated with temperature (max: -0.15, $p < 0.007$; min: -0.2, $p < 0.006$; mean: -0.18, $p < 0.02$), relative humidity (-0.2, $p < 0.007$) and percent sunshine (0.19, $p = 0.008$). When analyzed by sex, the inverse relationship between CSF 5-HIAA and temperature was seen in men (max: -0.32, $p = 0.004$; min: -0.25, $p < 0.03$; mean: -0.31, $p = 0.006$) but not women. Relative humidity was correlated with CSF 5-HIAA (-0.22, $p < 0.03$) and HVA (-0.28, $p = 0.003$) in women but not men. In men, CSF HVA was significantly correlated with percent sunshine (0.3, $p = 0.007$). CSF MHPG was not significantly correlated with any of the variables.

Conclusions: These data confirm previous seasonal variations in serotonin and dopamine metabolites and highlight possible underlying mechanisms involving sex, the amount of light available, temperature, and relative humidity. The extent to which weather changes result in alterations in behavior requires further investigation.

NR449 Wednesday, May 8, 12 noon-2:00 p.m.

Neuroendocrine Profiles in Psychiatric Disorders: Markers of Diagnosis or of Syndromes?

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: Abnormal responses to endocrine tests have been described in a number of different psychiatric disorders. We investigated whether the use of multiple endocrine tests could result in better diagnostic specificity.

Method: Hormonal responses to 8 a.m. and 11 p.m. TRH tests, dexamethasone suppression test (DST), and apomorphine test were evaluated in 152 unmedicated inpatients with DSM-IV major depressive disorder ($n = 93$), schizophrenia ($n = 36$), or schizoaffective disorder ($n = 23$), and in 27 hospitalized healthy controls.

Results: A factorial correspondence analysis (FCA) separated the neuroendocrine profiles of the diagnostic groups. The depressed group was characterized by chronobiological dysregulation of the thyroid axis (blunted 11 p.m. ΔTSH: maximum increment in thyrotropin (TSH) above baseline after TRH, and blunted $\Delta\Delta$TSH: difference between 11 p.m.-ΔTSH AND 8AM-ΔTSH), and normal responses to apomorphine. The schizophrenic group was characterized by a functional alteration of the hypothalamic-pituitary dopamine receptors (blunted apomorphine-induced growth hormone and cortisol stimulation and prolactin suppression) and normal thyroid function. The schizoaffective group showed abnormalities found both in schizophrenic and in depressed groups. Further FCAs performed on the schizophrenic group showed that abnormal responses to apomorphine characterized the psychotic dimension, whereas the disorganized dimension was associated with normal responses to apomorphine. Depressive features were associated with normal responses to apomorphine and with chronobiological dysregulation of the thyroid axis.

Conclusions: These results suggest that multiple neuroendocrine measures distinguish different diagnostic groups more clearly than single tests. However, the endocrine abnormalities appear more linked to psychiatric syndromes than to nosological entities.

NR450 Wednesday, May 8, 12 noon-2:00 p.m.

Clinical and Pathophysiologic Implications of Structural Brain Abnormalities in Schizophrenia

Todd Lafargue, M.D., Psychiatry, NYU Medical Center, 423 East 23rd Street, New York NY 10010; Luigi Arena, M.D., Michael P. Sanfilipo, B.S., Eric D. Peselow, M.D., Henry Rusinek, Ph.D., Adam Wolkin, M.D.

Summary:

Temporal and frontal gray matter reductions along with ventricular enlargement in schizophrenia are commonly reported in magnetic resonance imaging (MRI) studies. Whether these abnormalities result from a separate or combination of neurodevelopmental

and neurodegenerative processes remains unclear. However, a growing body of post-mortem and imaging findings are lending increasing support for a neurodevelopmental pathophysiological mechanism. In addition, heterogeneity of symptomatology further complicates the interpretation of cerebral differences in schizophrenia. Indeed, no consistent relationship has been demonstrated between structural abnormalities and phenomenological subtypes.

Objective: The purpose of the present structural MRI study is to further characterize the nature of brain abnormalities in schizophrenia. The relationship of these findings to possible pathophysiologic mechanisms and to negative syndrome schizophrenia will also be addressed.

Method: High resolution coronal T1-weighted MR images were obtained in 72 male, schizophrenic patients and 31 normal controls.

Results: Schizophrenics had significant temporal and frontal gray matter deficits compared to controls, while high negative symptom schizophrenics evidenced a reduction in frontal white matter.

Conclusion: Differing cerebral structural abnormalities in schizophrenia may be related to the variety of patient phenomenological subtypes, and allow further speculation regarding hypothesized pathophysiologic processes underlying the illness.

NR451 Wednesday, May 8, 12 noon-2:00 p.m.

Menstrual Cycle Changes in Laterality and Emotion

Alexandra A. Bowers, B.A., Psychiatry, Yale University, CMHC 34 Park University, New Haven CT 06519; Margaret Altemus, M.D., Bruce E. Wexler, M.D.

Summary:

Hormones play an important role in the development and aging of the brain, in gender related differences in brain organization and function, and in normal and abnormal changes in mood. The repetitive nature of the menstrual cycle allows a unique opportunity to study effects of endogenous endocrine changes on the brain. In this and a previous study we used fused dichotic word tests to study both lateralized cerebral activation and the perception of emotion-evoking words throughout the cycle. In these tests subjects receive two words simultaneously, one in each ear, but are aware of hearing only one word from each pair. The number of times they hear the right ear word rather than left ear word is an index of relative left hemisphere activation and function. The number of times they hear the emotionally positive or negative word in special stimulus pairs consisting of an emotion-evoking and a neutral word, reflects the degree of unconscious perceptual sensitivity to emotion. Previously we tested women before and after menstruation and found a premenstrual decrease in the normal right ear - left hemisphere perceptual advantage (REA) and in perceptual awareness of positive words. In this study 30 women were tested during each of the four weeks of their cycles. ANOVA showed a main effect of week ($p = .03$), with the REA lower during the premenstrual week than during each of the subsequent weeks ($p = .03, .05, .06$). Differences among other weeks did not approach significance ($p = .29–.85$). Also in replication of the previous study, women heard fewer positive words premenstrually than during subsequent weeks ($p = .04, .09, .10$). This is the first replication of cycle-related changes in brain organizational state. This and replication of the premenstrual decrease in perceptual sensitivity to positive emotion have clinical implications for premenstrual disorder and cycle-related onset of affective disorders.

NR452 Wednesday, May 8, 12 noon-2:00 p.m.

Physostigmine and Cognition in Personality Disorder

Ann M. Callahan, M.D., Psychiatry, Mt. Sinai School of Med, 130 West Kingsbridge 116A, Bronx NY 10468; Antonia S. New, M.D., Andrea Bergman, Ph.D., Vivian Mitropoulou, M.A., Barbara A. Cornblatt, Ph.D., Larry J. Siever, M.D.

Summary:

There is increasing evidence that schizophrenia may encompass a spectrum of disorders, which lie on a continuum ranging from mild personality traits to severe psychotic disorders. Schizotypal personality disorder (SPD) appears to be a manifestation of symptomatology within this spectrum. SPD subjects show similar yet less severe attentional and cognitive impairment than patients with schizophrenia, and therefore may be more amenable to pharmacologic interventions to induce changes in neuropsychological functions. SPD patients show impairments in working memory as measured by the DOT test ($p < 0.05$), attention as measured by Continuous Performance Task-Identical Pairs Version (CPT-IP) ($p < 0.01$), and verbal learning as measured by the California Verbal Learning Test (CVLT) ($p < 0.05$). We investigated changes in these cognitive functions following a physostigmine infusion in subjects with SPD and obsessive-compulsive personality disorder (OPD). Improvement in visuospatial performance and attention but not verbal learning was observed in SPD subjects following physostigmine (data collection is ongoing and updated results will be presented). These preliminary data raise the possibility that deficits in attention and working memory in SPD patients may be amenable to pharmacologic manipulation with cholinergic agents.

NR453 Wednesday, May 8, 12 noon-2:00 p.m.

Blockade of NMDA Receptor Modulates C-FOS Expression in Cortex and Limbic Regions

Andrea De Bartolomeis, M.D., Neuroscience, University Med School, "FedericoII" Via Pansini, Naples 80131, Italy; Luigi Aloj, M.D., Giovanni Muscettola, M.D., David Pickar, M.D., Alan F. Breier, M.D.

Summary:

Objective: Ketamine, a dissociative anesthetic, provides an interesting pharmacological tool to explore the putative role of glutamate system in pathophysiology of schizophrenia. In vivo studies with PET have demonstrated a specific pattern of metabolic activation by ketamine in prefrontal cortex of schizophrenic patients compared to normal controls. We attempted to investigate by means of in situ hybridization histochemistry the anatomical pattern of cortical and subcortical c-fos gene expression in an animal model of NMDA receptor blockade after subconvulsant and subanesthetic dose of ketamine.

Methods: Sprague-Dowley rats were injected with subanesthetic (12–50mg/kg, i.p) doses of ketamine-HCl or with equal volume of 0.9% NaCl, and sacrificed 30 minutes or three hours after the injection. Coronal section (12 μm) were cut through the brain and processed for in situ hybridization using synthetic oligodeoxyribonucleotides for the protoncogene c-fos, DA receptor D1 and D2 and for the dopamine transporter (DAT).

Results: Computer-assisted analysis of the film autoradiograms demonstrated a significant increase of c-fos gene expression in prefrontal cortex ($p < 0.002$) and other cortical and mesolimbic regions, as well as modulation of the gene expression for DA markers in rats treated with subanesthetic dose of ketamine.

Conclusions: NMDA receptor blockade by non-competitive antagonist significantly activates c-fos in discrete cortical and mesolimbic regions of rat brain and partially mirrors the metabolic activation observed in humans.

NR454 Wednesday, May 8, 12 noon-2:00 p.m.

Quantitative EEG Topographic Maps: Testing Individual Patient's Maps Against a Data Base

James S. Lawson, Ph.D., Psychiatry, Queen's University, Kingston Ontario K7L 3N6, Canada; Susan J. Adams, M.D.,

Donald W. Brunet, M.D., Magarita Criollo, M.D., Howard Galin, M.A., Duncan J. MacCrimmon, M.D.

Summary:

Objective: To develop a sufficient inferential statistical method to test individual topographic maps against a database.

Method: The database comprised 477 healthy subjects age 14–79 years, 273 males, 204 females ascertained at four North American sites. Four patients (head injury, Huntington's, major depression, and schizophrenia) were individually compared with the database. There were 20 channels in the 10/20 configuration referenced to linked ears. Data expressed as log power were collected in the frequency range 0.4–23.8 Hz. Each channel was assigned a Cartesian coordinate (x, y) so that the response surface could be expressed as

$$\log V^2 = \sum_i \sum_j b_{ij} x^i y^j$$

producing 20 computable parameters b_{ij}. These were entered into a mathematical graphics program generating a 3-dimensional surface which exactly reproduced the original data. The b_{ij} were used to test if the individual surface was significantly different from those of the database in various respects after adjusting for age, sex, and site.

Results: Significant differences from the database were demonstrated in all subjects:

Head injury:	lateral asymmetry
Huntington's:	generalised abnormalities
Major depression:	hypo-occipitality
Schizophrenia:	bilateral posterior abnormalities

Conclusions: The model demonstrated topographic map abnormalities in two neurological patients. It also identified the more subtle abnormalities occurring in two functional psychiatric patients. The model can be extended to encompass the frequency dimension and to allow covariate control of drug regimen.

NR455 Wednesday, May 8, 12 noon-2:00 p.m.

mRNA Expression of Serotonin Receptors in Lymphocytes

Donatella Marazziti, M.D., Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy; Irma Nardi, M.D., Massimo Pasqualetti, M.D., Lionella Palego, Ph.D., Alessandra Rossi, M.D.

Summary:

Besides the many functions of serotonin (5-HT) in the central nervous system, this neurotransmitter exerts certain effects at the level of the immune system. Little is known about the subtypes of 5-HT receptors mediating the immunomodulation processes. Therefore, the authors investigated the presence of 5-HT receptors of type 1A (5-HT_{1A}), as labeled by the specific ligand ^{3}H-8 hydroxy-2-(di-N-propylamino) tetralin (^{3}H-8-OH-DPAT) in saturation experiments and the expression of the mRNA encoding them, in human peripheral blood mononuclear cells (PMBC). The results showed that the [^{3}H]-8-OH-DPAT failed to label the 5-HT_{1A} receptor (approximate K_D: 2–5 nM). The RNase protection experiments revealed the presence of a protection fragment of the expected size, 158 nt, in the sample in which total PBMC RNA was hybridized to the 5-HT_{1A} riboprobe. The lack of a receptor in the presence of its specific mRNA might be explained by the fact that the receptor is not expressed, because the translation process of the mRNA is blocked, or it is internalized or masked somehow in normal conditions, only to become "active" under particular conditions (stress?, disease?, neuroendocrine challenges?). Future studies should explore whether dissociation between binding and mRNA expression is also present in lymphocytes from patients with mood or anxiety disorders, where a dysfunction of the 5-HT_{1A} receptors has been reported.

NR456 Wednesday, May 8, 12 noon-2:00 p.m.

Fenfluramine Versus Clomipramine Challenge

Linda M. Nicholas, M.D., Psychiatry, University North Carolina, CB# 7160, Chapel Hill NC 27599–7160; David F. Naftolowitz, M.D., Amy D. Heine, M.S., R. David Ekstrom, M.S., Manuel E. Trancer, M.D., Robert N. Golden, M.D.

Summary:

Fenfluramine (FEN) and clomipramine (CMI) have used as pharmacologic challenge agents in studies of 5-HT function. We compared the characteristics of these two 5-HT challenge tests in a randomized, double-blind, crossover design. Twelve healthy subjects were administered standard oral FEN, intravenous CMI, and placebo challenges, each separated by a four-week period. Placebo-corrected maximum changes from baseline in plasma hormone levels and in self-reports of nausea were calculated. Differences in placebo-corrected FEN and CMI challenge tests were analyzed using signed rank tests.

Prolactin responses did not differ significantly ($p = 0.18$) between challenge tests, although prolactin rises occurred later following FEN challenge and peaks may not have occurred for all subjects prior to IV discontinuation. Cortisol and nausea responses were significantly greater for CMI compared to FEN ($p = 0.02$ and 0.01, respectively). These results suggest that FEN and CMI may have different effects on various components of the 5-HT system.

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

NR457 Wednesday, May 8, 12 noon-2:00 p.m.

Diurnal Rhythm of of CSF Neurohormones in Major Depression: Comparison with Healthy Volunteers and Effects of ECT

Mitchel A. Kling, M.D., Psychiatry, Baltimore VA Med Ctr, 10 North Greene Street, Baltimore MD 21201; Thomas D. Geracioti, Jr., M.D., Michael D. De Bellis, M.D., Samuel J. Listwak, B.S., Debbie Hu, M.S.W., E.H. Oldfield, M.D., Philip W. Gold, M.D.

Summary:

The neurohormones corticotropin-releasing hormone (CRH), oxytocin (OT), and norepinephrine (NE) have been implicated in some of the symptoms of mood disorders, and their cerebrospinal fluid (CSF) levels have been examined in these disorders by single time point lumbar puncture (LP). However, preclinical studies have shown that the levels of these neurohormones undergo significant circadian variation in experimental animals; thus, single-time point LP's may provide an incomplete view of CSF neurohormone secretion. To further study the potential relevance of CSF CRH, OT, and NE to normal physiology and to the pathophysiology of major depression, we examined their levels using hourly sampling over a 30-h period in 8 healthy volunteers and in six medication-free patients with DSM-III-R major depression; three underwent repeat studies following electroconvulsive therapy (ECT). CSF was sampled continuously for 30 h via an epidural catheter placed in a low lumbar interspace and connected to a peristaltic pump that removed CSF at a constant rate of 6 ml/h (1 ml q 10 min). CSF CRH and OT were measured by RIA in a 2-ml aliquot representing the 30th–50th min of collection for each hour. CSF NE was measured by HPLC-EC in a 1-ml aliquot representing the last 10 min of each hour. The presence of 24-hour trends was tested by cosinor analysis.

Significant ($p < 0.05$) diurnal variation was found in healthy volunteers for all three mediators. CSF CRH showed peak levels

around 2200 h and lowest levels around 0730 h, a pattern nearly opposite to that of plasma cortisol levels. CSF OT and NE showed peak levels during the late morning (1030 h and 1155 h, respectively) with lowest levels in the early morning (around 0430 h for both).

Depressed patients had elevated mean 24-hour urinary free cortisol (UFC) excretion. 30-h mean CSF IR-CRH in depressed patients was similar to that in controls, although variability was greater. Thus, 1/6 depressed patients had a 30-h mean CSF CRH level exceeding that of the highest control subject, while one patient had a mean level below the lowest control subject. The mean amplitude and phase of the CSF IR-CRH rhythm were similar to controls. CSF NE levels in depressed patients showed significant ($p < 0.001$) diurnal variation with a peak at about 1 pm; 30-hr mean levels were slightly but not significantly increased. The 30-hour mean CSF IR-OT level and diurnal rhythm in the depressed patients were similar to controls.

Each of the three patients restudied after ECT showed clinical improvement in depression as well as a reduction in Hamilton Depression scores (38–17, 38–4, and 30–21, respectively). Mean UFC excretion and plasma cortisol levels also declined. CSF IR-CRH showed a significant ($p < 0.05$) reduction in each of these patients following ECT treatment by paired t-test. A significant ($p < 0.05$) fall in CSF NE was also seen in each of the three patients. No consistent effects on CSF OT were seen following ECT treatment.

The significant fall in CSF CRH and NE following ECT suggests that the depressed state is associated with a relative increase in CRH and NE secretion into the CSF. These data further suggest that, in contrast to CRH and NE, CSF OT is not systematically altered either in association with depression and its attendant hypercortisolism, nor with ECT-induced improvement. The lack of change in CSF OT with ECT suggests that ECT is not associated with a global alteration in CSF neurohormone patterns. The preservation of the diurnal rhythm of CSF OT in depressed patients suggests that circadian rhythm disturbances in depression may be confined to systems directly involved in its pathophysiology rather than being due to a global alteration of circadian timekeeping.

NR458 Wednesday, May 8, 12 noon-2:00 p.m.

Discrepancy in Imipramine and Paroxetine Bindings

Mihaly Arato, M.D., Psychiatry, Hiete-Opni, Nyeki Ut 10-12, Budapest 27 1281, Hungary; George Bagdy, Ph.D., Deirde E.M.CookeM.D., Ilona Ozoroczy, M.B.

Summary:

Objective: The parameters of the tritiated imipramine binding (IMIB) of platelets and brain tissues have been postulated as an index of central serotonergic mechanisms in clinical research. Reduced IMIB has been described, although with some inconsistency, in depression, OCD, and suicide. Paroxetine, a selective serotonin (5HT) reuptake inhibitor with higher affinity to 5HT receptors, seemed to be a more specific and pure ligand than IMI. We have found, however, remarkable differences between IMIB and paroxetine binding (PARB) in several research studies.

Results: The Bmax value of IMIB in the frontal cortex showed marked hemispheric asymmetry (higher value on the right side). Using the same tissue samples IMIB did show the same right-left difference, while PARB was not different in the two hemispheres. Treatment with Moclobemide, a selective, reversible MAO-A inhibitor antidepressant, has resulted in significant decrease in IMIB, but not in PARB. The delta IMIB and PARB did not correlate. Both the Bmax and Kd values of IMIB were significantly lower in children with autistic disorder (AD) compared with controls. There were no differences, however, in the parameters of PARB and 5HT contents of platelets. Collecting control data, we have repeatedly sampled healthy volunteers for the measurement of serotonergic indices. Women showed consistently higher Bmax values of PARB compared with men. There was no gender difference in IMIB and 5HT content.

Conclusions: All these findings suggest that parameters of IMIB and PARB reflect different characteristics of a complex, 5HT-related binding site mechanism.

NR459 Wednesday, May 8, 12 noon-2:00 p.m.

The Influence of ECT on Olfactory Memory

Pinkhas Sirota, M.D., Abarbanel Men Hlth Ctr 6A, 15 Keren Kayemet, Bat-Yam, Israel; Tanya Mosheva, M.D.

Summary:

Memory impairments post-ECT are well known and documented in the psychiatric literature. The present study was designed to answer the question of whether ECT affects olfactory memory. Twenty-three patients——12 schizophrenic patients and 11 major depressive disorder patients, and 14 control subjects participated in the study. Eugenol, geraniol, vanilin, and isoamyl acetate were dissolved in Lubinol (heavy odorless-tasteless) mineral oil. Subjects were presented with the eugenol bottle and were asked to remember its odor. One hour later all four bottles were presented to the subjects who were asked to identify the bottle containing eugenol. This procedure was performed three more times: after the first ECT, the third ECT, and the sixth ECT. The clinical improvement post the third ECT and drugs was significantly better than in those with only ECT ($p < 0.05$). The improvement in olfactory memory paralleled the clinical improvement, especially post the third ECT after 120′ ($p > 0.040$).

Conclusion: No difference in olfactory memory was found between patients treated with ECT and controls.

NR460 Wednesday, May 8, 12 noon-2:00 p.m.

Proton MRSI in Schizophrenia

Raymond F. Deicken, M.D., Psychiatry, DVA Medical Center, 4150 Clement Street 116-N, San Francisco CA 94121-1598; Zhou Ling, M.D., Faith Corwin, M.A., Sophia Vinogradov, M.D., George Fein, Ph.D., Michael W. Weiner, M.D.

Summary:

Objective: The objective of this study was to determine if N-acetyl-aspartate (NAA), a putative neuronal marker, is reduced in the frontal and temporal lobes in schizophrenia utilizing proton magnetic resonance spectroscopic imaging (MRSI).

Methods: Nineteen schizophrenic patients (15 males and 4 females) and 12 age-matched controls (6 males and 6 females) were studied. All subjects underwent proton MRSI using a 1.5T Siemens Magnetom VISION MRI/MRS system. Sagittal, coronal, and transverse images were obtained for proper positioning of MRSI slices. Proton MRSI was performed with two-dimensional PRESS volume selection in the frontal and temporal lobes. A single voxel was selected in comparable locations for each subject in the right and left frontal and temporal lobes. After spectral processing, concentration estimates were obtained for NAA, choline, and creatine.

Results: For the frontal lobes, NAA values in schizophrenics were lower in the left side compared to the right ($p = .008$). For the temporal lobes, NAA values in the schizophrenics were lower bilaterally ($p = .018$) and creatine values higher bilaterally ($p = .04$). These results support the notion of reduced neuronal density in the left frontal lobe and bilaterally in the temporal lobes.

NR461 Wednesday, May 8, 12 noon-2:00 p.m.

Drug Effect on Regional Proton MRS in Schizophrenia

Carolyn Heimberg, M.D., Psychiatry, University of Arkansas, 2200 Fort Roots Drive 116F2, North Little Rock AR 72114–1706; Richard A. Komoroski, Ph.D., William B. Lawson, M.D., David W. Cardwell, M.D., Craig N. Karson, M.D.

Summary:

Proton (^{1}H) magnetic resonance spectroscopy (MRS) is a technique for measuring the concentrations of amino acids such as creatine (CRE), choline (CHO), N-acetylaspartate (NAA), and inositol (INO) in brain in living subjects. Previous reports have suggested that patients with schizophrenia may have reduced NAA concentrations in temporal and frontal cortex. We sought to examine this issue and whether atypical antipsychotic treatment was reflected by changes in the proton spectrum.

Nineteen male patients (ages 25–67) with schizophrenia and 20 male controls (ages 34–54) participated. Localized stimulated-echo (STEAM) ^{1}H MRS was performed on a GE Signa MRI system using the automated PROBE/SV routine. Voxels of 2 × 2 × 2 cm^3 were examined in left temporal cortex, caudate nucleus, and frontal lobe. NAA, CHO, and INO were ratioed to the CRE peak.

In the temporal cortex, schizophrenics tended to have reduced NAA concentrations (1.30 ± .11 vs. 1.19 ± .17, p ± .064), and a reduced INO concentration (.82 ± .14 vs. .67 ± .16, p ± .035). No obvious effect of atypical agents was found. As NAA concentration may indicate the neuronal number in a brain region, these results are consistent with the notion that schizophrenic patients have reduced neuronal numbers in temporal cortex.

NR462 Wednesday, May 8, 12 noon-2:00 p.m.

Anterior Paralimbic Hypometabolism in Patients with Unipolar Depression in Remission

Timothy A. Kimbrell, M.D., NIH, 3408 Robey Terrace Apt #202, Silver Spring MD 20904; Terence A. Ketter, M.D., Mark S. George, M.D., Robyn M. Stein, M.D., Aimee Danielson, B.A., Robert M. Post, M.D.

Summary:

Objective: Previous functional neuroimaging studies suggest that medication free euthymic mood disorder patients have abnormal resting paralimbic rCBF as well as blunted paralimbic rCBF activation with mood induction. In this study we report rCMRglu in patients with unipolar depression in remission compared to healthy controls.

Methods: Eleven medication free patients with unipolar depression in remission (HAM-D < 12 day of scan) and thirty-three age and gender-matched healthy controls were studied with positron emission tomography and 18-Fluorodeoxyglucose while performing an auditory continuous performance task with eyes patched. Statistical parametric mapping was used to compare absolute and normalized rCMRglu in these remitted patients and controls.

Results: Remitted patients had non significantly lower global CRMglu (7.68 ± 0.70 mg/100g/min) than the control group 7.77 ± 0.85 mg/100g/min). Remitted patients compared to controls had decreased rCMRglu (normalized greater than absolute) in right medial temporal lobe, thalamus, posterior left temporal lobe, bilateral posterior association cortex, and left dorsolateral prefrontal cortex ($p < 0.005$). Remitted patients compared to controls had increased normalized but not absolute rCMRglu in the right lateral temporal lobe and bilateral occipital lobe ($p < 0.005$).

Conclusion: These data suggest that the decreased paralimbic activity observed in depressed unipolar patients persists even when patients have recovered. These areas of dysfunction could either represent the residue of prior episodes or a component of the predisposition to affective disorder.

NR463 Wednesday, May 8, 12 noon-2:00 p.m.

Increased Basal Ganglia, Thalamic and Anterior Cingulate Glucose Metabolism in Women Compared to Men

Timothy A. Kimbrell, M.D., NIH, 3408 Robey Terrace Apt #202, Silver Spring MD 20904; Terence A. Ketter, M.D., Mark Willis, Mark S. George, M.D., Paul J. Andreason, M.D., Robert M. Post, M.D.

Summary:

Objective: Gender differences have been noted in healthy subjects' resting rate of cerebral glucose metabolism and in regional cerebral blood flow during neuropsychological activation. Such studies may reveal regional gender differences in brain activity in health which could aid in understanding cerebral dysfunction in psychiatric illness (such as mood disorders) which have gender differences in prevalence. We analyzed regional cerebral metabolic rate of glucose of utilization (rCMRglu) during an auditory continuous performance task in healthy volunteers to further explore this issue.

Method: Thirty-one healthy females (average age = 34.5) and thirty-one healthy males (average age 36.4) were studied. Menstrual cycle for the women volunteers was not controlled. All subjects had normal physical exams, laboratory screens, and had no personal or first-degree relative history of psychiatric disorder. 18-Fluorodeoxyglucose positron emission tomography studies were obtained with eyes covered while performing an auditory continuous performance task. A between-group analysis using statistical parametric maps was performed for both absolute and normalized rCMRglu.

Results: Women had non significantly higher global CMRglu (7.63 ± 1.09 mg/100g/min) compared to men (7.32 ± 1.09 mg/100g/min) ($p = 0.3$). Women compared to men had higher absolute and normalized rCMRglu in bilateral basal ganglia, left thalamus, left anterior cingulate, and left temporal lobe ($p < 0.005$). Women compared to men also had lower rCMRglu (normalized but not absolute) in right dorsolateral prefrontal cortex and the left occipital lobe ($p < .005$). Both the extent and degree of women's metabolic increases were greater than the decreases.

Discussion: The non significantly higher global CMRglu in women parallels previously reported trends of higher cerebral metabolism in women. The increase in anterior cingulate metabolism is also consistent with previous reports. The increase in left thalamus and left temporal lobe have not been reported. Subject task and data analysis may account for some variability in gender differences across studies.

NR464 Wednesday, May 8, 12 noon-2:00 p.m.

Characteristics of White Matter in Late-Life Depression: Brain Volumes and Clinical Characteristics

Hillel T. Grossman, M.D., Psychiatry, Tufts University School of Med, 750 Washington Street, Boston MA 02111; Eric D. Caine, M.D., Leena Ketonen, M.D., Christophe Cox, Ph.D., Heather Booth, M.S., Jeffrey M. Lyness, M.D.

Summary:

Objective: This study compares a prospective sample of elderly with major depression with community dwelling normal elderly on brain volumes and clinical characteristics.

Methods: Subjects were 37 prospectively identified inpatients and 37 community recruited controls (mean ages 69 vs 70). Procedures included SCID-R, medical history, and physical exam.

Cerebrovascular risk factor scores (CVRF) were calculated according to American Heart Association criteria. Medical burden was measured with the Cumulative Illness Rating Scale. MRI was obtained at 1.5T, yielding 5mm, interleaved axial sections. Images were analyzed on Macintosh Quadra workstations, using a modified version of NIH Image. All brain volumes were divided by intracranial volume to correct for head size. The association between brain volumes and clinical characteristics was assessed using multiple analysis of covariates.

Results: There were significant group differences in mean education (11 vs 16), CIRS, MMSE (26 vs 29). The depressed group had smaller mean volumes of: Total gray ($p < .05$); Total white, total intermediate anterior white, total intermediate posterior white, gray: white ratio, and total hyperintensity (all $p < .01$). There were no lateralizing findings. When age, sex, education, CVRF, and CIRS scores were controlled in the regression analysis all group differences retained significance.

Conclusions: Late-life depression is associated with a loss of both gray and white matter relative to normal controls. The WM loss is more prominent and is concentrated in white matter subserving the posterior frontal, temporal, and parietal regions. WM hyperintensity volumes are more prominent in the depressed as well. Similar to many studies of normal aging, we did not find measures of cerebrovascular risk or medical burden to be predictive of white matter or hyperintensity volumes.

NR465 Wednesday, May 8, 12 noon-2:00 p.m.

Effects of Aging and Gender on Regional Brain Glucose Metabolism in Healthy Individuals

Erin A. Hazlett, Ph.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Richard C. Mohs, Ph.D., Lina S. Shihabuddin, M.D., Tina Ciaravolo, B.A., Jacqueline Spiegel-Cohen, M.S.

Summary:

The present study examined regional brain metabolism during a memory task in 70 right-handed healthy adults using state-of-the-art quantitative imaging methodology involving co-registered PET/MRI scan data. Ten subjects (5 females, 5 males) in each decade of life from age 20 to 87 participated and were screened by history, psychiatric interview, physical exam, and laboratory testing. PET with ^{18}F–2-deoxyglucose scans were obtained with our GE 2048 head scanner with measured resolution of 4.5 mm in plane and 5.0 mm axially. A task based on the principles of the California Verbal Learning Test (CVLT) was developed for PET scanning and administered to the subjects during the FDG uptake period. For MRI, scans were done on our GE Signa 5x system with a SPGR sequence (repetition time of 24 ms, echo time of 5 ms, flip angle 40 degrees) for 124 contiguous 1.2 mm thick slices. Ten PET slices were co-registered with MRI for anatomical accuracy. Next, a new cortical peel technique was used to calculate mean relative glucose metabolic rate (GMR) for four separate areas of the cortex in each lobe of the brain. GMR was assessed only for MRI co-registered pixels which were segmented as gray matter. A 7(Decade) × 2(Gender) × 4(Lobe) × 4(Segment) × 2(Hemi) ANOVA with Huynh-Feldt correction revealed a significant Decade × Lobe × Segment interaction ($F = 1.61$, $p < .05$). Regression analyses indicate that relative GMR declines significantly with age in all four frontal lobe regions (superior, mid, inferior, and precentral); parietal lobe is spared with the exception of the angular gyrus; three of the four temporal lobe regions decline (superior, mid, inferior temporal but not posterior); the entire occipital lobe is spared. Performance on the CVLT declines significantly with age ($R = -.33$, $p < .01$). The ANOVA also revealed a significant Gender × Lobe × Segment interaction ($F = 2.69$, $p < .05$). Pairwise comparisons showed that compared to males, females have significantly higher relative GMR in superior and middle prefrontal and superior parietal cortex. There were no gender differences in memory performance and no gender differences with aging. Studies have shown varying degrees of aging- and gender-related regional GMR differences which may be explained by differences in sample size, scanner resolution, and activation task.

NR466 Wednesday, May 8, 12 noon-2:00 p.m.

Thalamic Metabolic Rate in Schizophrenia

Monte S. Buchsbaum, M.D., Psychiatry, Mt. Sinai Med Ctr, One Gustave Levy Place, New York NY 10029; Erin A. Hazlett, Ph.D., M. Mehmet Haznedar, M.D., Tse-Chung Wei, Ph.D., Jacqueline Spiegel-Cohen, M.S.

Summary:

Magnetic resonance imaging and positron emission tomography with F-18 flurodeoxyglucose (FDG) were used to study size and metabolic rate in the thalamus in 18 schizophrenia patients who were either never medicated ($n = 17$), or off medications ($n = 11$) for at least two weeks, and 24 age- and sex-matched normal volunteers. During the FDG uptake period, all subjects performed a modified version of the California Verbal learning Test. PET (30 slice, 3–4M counts/slice, 4.5 mm FWHM) and MRI images (TR 24, TE 5, flip angle 40 degrees, 1.2–mm intervals) were coregistered. The MRI was differentiated and thalamus edges outlined for each hemisphere by tracers without knowledge of diagnosis who used with radial morphing program to conform all slice outlines to the average of the normal group. Proportional z-axis interpolation then yielded an exactly uniform volume for statistical parametric mapping in three dimensions. Using t-values yielding $p < 0.05$, two tailed, we visualized a 3D cluster in the region of the medial dorsal nucleus within the 3D images of the thalamic surface. This cluster of pixels was an area (diameter about 1.2–1.5 × larger than the FWHM resolution) where patients had lower relative metabolic rates than controls. Using resampling methods, we drew 5,000 samples of $n1 = 18$ and $n2 = 24$ from a population of 46 similarly traced controls and observed the frequency of pixel clusters of at least this size to occur in less than one such sample in 20. Volumetric and shape measures of the thalamus were also obtained. General methods for 3D morphing and aligning postmortem thalamic images with MRI will be demonstrated.

NR467 Wednesday, May 8, 12 noon-2:00 p.m.

Patterns of Connectivity Assessed by Metabolic Rate During a Memory Task in Humans: A PET Study

M. Mehmet Haznedar, 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., Melissa Biren, B.S., Tse-Chung Wei, Ph.D., Philip D. Harvey, Ph.D.

Summary:

The California Verbal Learning Test (CVLT) is used to measure different memory functions: overall recall, rate of learning, recognition memory, recall errors, and serial versus semantic clustering. Semantic clustering possibilities of the CVLT involve a broad range of cognitive processes. Higher levels of memory performance reflect the attentional and mental tracking aspects of executive abilities and may involve Brodmann areas 32 and 24. These features of the CVLT make it an appropriate tool to explore attention, memory and cognitive disturbances in a variety of neuropsychiatric illnesses. Seventeen right handed, healthy volunteers performed a modified CVLT or rested during uptake of 18F-deoxyglucose. PET images (resolution 4.5mm) corresponding to 34% and 41%, of the head height (Matsui and Hirano) were picked for each individual. These PET images were morphed to the average normal contour, co-registered MRI were used to locate structures for each level. Pixel to pixel correlations were done, using the

structures which are implicated in memory and attentional mechanisms; the cingulate gyrus, medial temporal cortex, and prefrontal cortex as reference points. The same coordinates were applied to both scans. At 41% of the head height the left anterior cingulate gyrus showed a correlation with both prefrontal cortices ($p < 0.05$) as tested by a population random resampling method. Resting condition did not produce any significant correlations. The left medial temporal cortex showed direct correlations with right prefrontal cortex ($p < 0.03$), left insular cortex ($p < 0.05$), left caudate and putamen ($p < 0.03$) at the activation condition and during resting the activity correlated only with the right medial temporal cortex ($p < 0.03$). A similar correlation pattern was observed at the 34% of the head height. These maps support the role of the cingulate gyrus and medial prefrontal region in memory and attention processes in humans.

NR468 Wednesday, May 8, 12 noon-2:00 p.m.

Anterior Cingulate Gyrus Volume in Autistic Disorder

M. Mehmet Haznedar, M.D., Psychiatry, Mount Sinai, 1 Gustave Levy Place Bex 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Andrea Solimando, B.S., Michael Metzger, B.S., Tina Ciaravolo, B.A., Eric Hollander, M.D.

Summary:

Autism is a developmental disorder with multiple etiologies. It is suggested that dysfunction in the limbic system, resulting in the disturbance of information acquisition, is one of the mechanisms responsible for the illness. In postmortem studies of autistic individuals, limbic structures, including the hippocampus, amygdala, and the anterior cingulate gyrus, show cytoarchitectural changes, increased cell densities, but no significant cell loss. The same studies showed no differences in the basal ganglia. In the current study, we measured the volume of the anterior cingulate gyrus, caudate nucleus, and the putamen, on the magnetic resonance imaging (MRI) scans of seven patients with autistic disorder, and seven sex- and age-matched controls. The diagnosis of autistic disorder was established by using the Autism Diagnostic Interview in six of the cases. In one case, clinical interviews by the experts were used. The patient group was compromised of relatively high functioning young adults: two women, five men, all right handed (mean age = 24.3 SD = 10.7). The control group consisted of two women and five men all right handed (mean age = 26.4, SD = 9.1). All subjects were screened for other neuropsychiatric illnesses and all but one autistic individual were free of psychoactive medications at the time of the MRI scanning. MRI acquisitions were done with GE Signa 5x system with TR 24, TE 5, flip angle 40 degrees, for 124 1.2 mm slices. The structures were outlined starting with the appearance of the cingulate sulcus bilaterally on the axial plane at 28% of the head height, until the disappearance of the corpus callosum at the 54% of the head height (Matsui and Hirano) consecutively. The relative volumes of these structures were measured and corrected for brain volume. The results show a significantly smaller right cingulate gyrus ($T -2.18$, $p = 0.05$, $dbf = 12$).

NR469 Wednesday, May 8, 12 noon-2:00 p.m.

Reduced Basal Ganglia Volumes in Trichotillomania Measured Via Morphometric MRI

Richard L. O'Sullivan, M.D., Psychiatry, Mass General Hospital, Bldg 149 13th Street, Charlestown MA 02129; Scott L. Rauch, M.D., Hans C. Breiter, M.D., Igor Grachev, M.D., Lee Baer, Ph.D., David Kennedy, Ph.D.

Summary:

A morphometric MRI study compared volumes of brain structures in 10 female subjects with trichotillomania (repetitive hair-pulling) versus 10 female normal controls matched for age, handedness, and education. Three dimensional MRI scans were blindly normalized and segmented using well-characterized semi-automated intensity and differential contour algorithms by signal intensity-frequency histograms. Consistent with a priori hypotheses, left putamen and left lenticulate volumes were found to be significantly smaller in trichotillomania subjects as compared with normal matched controls. This is the first report of structural brain abnormalities in trichotillomania. Results are discussed in terms of putative relationships between trichotillomania, Tourette syndrome, and obsessive-compulsive spectrum disorders.

NR470 Wednesday, May 8, 12 noon-2:00 p.m.

Visual Functional Abnormalities Occur in Striate and Peristriate Regions in Alzheimer's Disease Despite Relatives Pathological Sparing

Marc J. Mentis, M.D., L.N.S., NIH, 9000 Rockville Pike, Bethesda MD 20892; Gene E. Alexander, Ph.D., Terri Strassburger, M.D., Pietro Pietrini, M.D., Jack S. Krasuski, M.D., Mark Schapiro, M.D.

Summary:

Motor vehicle accidents, failure to recognize people/places, etc., are Alzheimer's disease (AD) symptoms commonly caused by memory loss, drug side effects, or visual processing abnormalities. The latter are usually assumed to result from "high level" dysfunction in parieto-temporal lobes, areas that have more neurofibrillary tangles than striate or peristriate cortex. We systematically varied visual input during positron emission tomography (PET) scanning (with 150 water), and compared the regional cerebral blood flow (rCBF) response in all visual cortical areas between an AD group (21 patients) and an age- and sex-matched healthy control group (19 patients). A recti-linear grid of red light emitting diodes imbedded in each eyepiece of a pair of goggles was flashed alternately between left and right eyes during the PET scan. Five scans were performed on each subject, one scan at each of 0, 1, 4, 7, and 14 Hz alternating flash frequencies. Both the striate and peristriate cortex had significantly smaller rCBF response patterns in the AD group, and this effect was more marked at high frequencies. Failure to clinically evaluate the visuospatial contribution to AD symptoms may result in management errors i.e., inappropriate medication changes.

NR471 Wednesday, May 8, 12 noon-2:00 p.m.

Abnormal Brain Perfusion During Opioid Dependence: SPECT Imaging with TC-99M-HMPAO

Lukas Pezawas, M.D., Allgemeine Psychiatry, University Klinik F. Psych, Waehringer Guertel 18–20, Vienna 1090, Austria; Gabriele Fischer, M.D., Karin Diamant, M.D., Corinna Schneider, M.D., S. Schindler, M.D., Siegfried Kasper, M.D.

Summary:

The aim of this study was to describe abnormalities in brain perfusion in pure opioid dependent patients (DSM-IV 304.00). Twenty-one opioid dependent patients were included and Tc-99m-hexamethyl-propylene-oxime (Tc-99m-HMPAO) brain single photon emission computed tomography (SPECT) was performed to evaluate regional cerebral blood flow (rCBF). Cerebral computed tomography (CCT) was administered to 17 patients in order to assess the possible effects of substance abuse on brain morphology. Drug history was evaluated with Europe-Addiction Severity Index (ASI). Present drug consumption was screened by urine samples with EMIT. Thirteen patients were undergoing a detoxification treatment and eight patients a methadone maintenance program. Just before imaging all subjects were examined in order to detect withdrawal symptoms with Wang's withdrawal scale. No subject showed withdrawal symptoms. Normalized rCBF-values

in corresponding regions of interest (RIO) in both hemispheres were compared. Significantly higher left sided rCBF-values were found in the pre- and postcentral gyre ($p = 0.001$), the mesiotemporal ($p = 0.003$), superior temporal ($p = 0.003$), and inferior parietal cortex ($p = 0.007$). This study shows changes in brain perfusion during opiate dependence.

NR472 Wednesday, May 8, 12 noon-2:00 p.m.

SPECT Correlates of Depressive Symptoms in Patients with Dementia of Alzheimer's Disease

Igor I. Galynker, M.D., 46 Valley Ln, Chappaqua NY 10514; Silviu M. Burcescu, M.D., J. Paul Teusink, M.D., Fukiat Ongseng, M.D., Howard Feinstone, M.D., Dragos Serseni, M.D., Eamon Dutta, M.D., Naomi Vilkas, B.A., Richard N. Rosenthal, M.D.

Summary:

Objective: The purpose of the current study was to establish if differences exist in regional cerebral blood flow (rCBF) between depressed and nondepressed groups of patients with dementia of Alzheimer's type (DAT) when these patient groups are matched for negative symptoms (NS).

Method: Seventeen patients with the diagnosis of DAT, were administered the Hamilton Rating Scale for Depression (HRSD), Scale for the Assessment of Negative Symptoms (SANS), the Positive and Negative Symptom Scale (PANSS), and the Mini-Mental Status Examination (MMSE). Each patient underwent a SPECT scan using Tc-99m HMPAO and an ADAC 1 head SPECT camera. Images were analyzed by two raters who were blind to the patients' identities. Transaxial images were displayed on a computer terminal. Cortical and subcortical regions of interest (ROIs) were symmetrically defined in each hemisphere. Cerebellar ROIs were selected in the middle portion of each cerebellar hemisphere. Cortical-to-cerebellar perfusion ratios were established quantitatively. The subjects were divided into two groups——a depressed group (HRSD > 15) and a control group (HRSD < 15)——and statistical analyses were performed using SYSTAT 5.2 software package.

Results: There was no significant difference between the subject groups in MMSE, SANS, or PANSS scores. The subjects in the depressed group had significantly lower rCBF in the posterior parietal cortex bilaterally in two adjacent sections (Mann-Whitney, $p < .05$), in the occipital cortex bilaterally ($p < .05$), and in the right caudate nucleus ($p < .05$).

Conclusions: Symptoms of depression in DAT are associated with decreased rCBF in posterior parietal and occipital cortices bilaterally and in the right caudate nucleus. No decreased perfusion in the frontal cortex was noted between the two groups matched for NS. These results differ from those reported for patients with depression when the NS severity was not taken into account.

NR473 Wednesday, May 8, 12 noon-2:00 p.m.

Structural Brain Changes in Chronic Cocaine and Heroin Abuse

Thomas E. Schlaepfer, M.D., Psychiatry, The Johns Hopkins Hosp, 600 N Wolfe St/Meyer 3–166, Baltimore MD 21287; Eric Lancaster, B.A., Patrick E. Barta, M.D., Godfrey D. Pearlson, M.D.

Summary:

It has been established, that prolonged and frequent cocaine abuse may lead to biochemical and vascular cerebral insults that eventually may cause functional and structural abnormalities affecting predominantly the fronto-temporal areas (Pascual-Leone A et al., *Neurotoxicology* 12:393–400, 1991).

The purpose of this study was to test the hypothesis that chronic abuse of cocaine and/or heroin leads to structural changes in the brain and to quantify these changes. Eighteen substance abusers (2 cocaine, 1 heroin, 15 cocaine and heroin, mean age 36.7 ± SD 6.4 years) and 18 age-, sex- and race-matched controls underwent Magnetic Resonance Imaging (MRI) on a 1.5 Tesla Signa scanner. All subjects in the substance abuser group had an abuse history of more than seven years. Contiguous, 5mm thick axial slices were acquired with simultaneous T_2 and proton sequences. Scan parameters were TR = 2500ms, TE = 20ms/80ms. In order to enhance contrast two images were calculated for each slice: T_2 minus proton weighted images were used to assess cerebrospinal fluid (CSF) volume, T_2 plus proton weighted images were used for assessment of gray and white matter volumes. Using point counting as an unbiased stereological volume estimation method, we calculated overall CSF, gray and white matter volumes, and gray and white matter volumes in the frontal lobe.

Cocaine and/or heroin abusers had less gray matter volume overall with a clear accentuation in the frontal lobe; their CSF volume was higher than in the group of healthy controls. This study is consistent with findings of neuropsychological frontal lobe dysfunctions in chronic cocaine abusers (Strickland TL et al. *J Neuropsychiatry Clin Neurosci* 5:419–27, 1993).

NR474 Wednesday, May 8, 12 noon-2:00 p.m.

The Effects of ECT on Cerebral Glucose Metabolism

Mark E. Schmidt, M.D., Clinical Pharm Rm4N212, NIMH, 9000 Rockville Pike Bldg. 10, Bethesda MD 20892; Michael Henry, M.D., John A. Matochik, Ph.D., Bradley S. Folley, B.S., William Z. Potter, M.D.

Summary:

Although electroconvulsive therapy (ECT) is a highly effective treatment for mood disorders, the mechanisms by which ECT ameliorates such disorders are unknown. We undertook a study of cerebral glucose metabolism (CMRglu) during ECT using ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET).

Methods: Six patients (4 F, 40 ± 6 yrs) with a major depressive episode (1 BPI, 4UP) underwent FDG PET scans before and 5–7 days after completing bifrontal ECT. Four volunteers that had undergone repeat PET scans served as controls for habituation to PET scans. PET images were analyzed by regions of interest (ROIs), and pixel by pixel following stereotactic normalization.

Results: Global CMRglu was lower in the post-ECT PET scan and was lower in 21/60 regions, most in frontal cortex (all $p < 0.05$). Decreases in CMRglu correlated with change in Hamilton Depression scores ($r = -0.81$). Controls also showed decreases during the second scan, although not nearly as much as the patients.

Conclusions: These data are consistent with reports of reduced cortical blood flow following ECT. Interestingly, decreases occurred in some of the same cortical areas reported to be less active in depressed patients. Additionally, decreases may correspond with the anticonvulsant effects of ECT.

NR475 Wednesday, May 8, 12 noon-2:00 p.m.

EEG and Provoked Potential Brain Mapping in ADHD

Karl G. Sieg, M.D., Suite B206, 501 Goodlette Rd., North, Naples FL 33940–5664; Gary G. Gaffney, M.D., Kevin D. Schockley, M.S., Teri O'Donnell

Summary:

Objective: This study was conducted to compare quantitative EEG and auditory evoked potentials in ADHD children with those of normal controls.

Method: Electrophysiologic data were collected from 22 children with ADHD and 20 age- and sex-matched normal controls. For each subject, a minimum of 80 seconds of EEG was collected with at least 16 two-second artifact free epochs derived for FFT spectral analysis. The Donchin protocol was utilized to generate auditory evoked potential tracings which were averaged for non-target and target paradigms.

Results: Analysis of FFT EEG data revealed significant increases in frontal delta activity in ADHD subjects versus controls. With respect to the evoked potentials, ADHD subjects demonstrated several differences upon comparison, including greater N200 and P300 amplitudes in response to non-target stimuli at Cz. Target stimuli elicited P300 components of smaller amplitude in ADHD subjects at Cz and Pz while N2 components were of greater amplitude at all locations. Latencies were significantly increased in the N200 and P300 components during the discriminating conditions.

Conclusions: These findings are consistent with other studies demonstrating EEG and evoked potential alterations in ADHD children. Our data support existing evidence which suggests deficits in selective attention in ADHD.

NR476 Wednesday, May 8, 12 noon-2:00 p.m.

MRI and SPECT in Very Early Alzheimer's Disease

Godfrey D. Pearlson, M.D., Department of Psychiatry, Johns Hopkins Hosp, Meyer 3–166/600 N. Wolfe St, Baltimore MD 21287–7362; Thomas E. Schlaepfer, M.D., Patrick E. Barta, M.D.

Summary:

In an initial study (Pearlson et al., *Arch Gen Psychiatry* 49:402–408, 1992) we compared 26 patients with moderately severe AD (mean Mini-Mental State score, 19/30) to 16 screened normal control subjects using quantitative MRI measures of mesial temporal atrophy and SPECT assessment of regional cerebral blood flow (rCBF). Both SPECT and MRI abnormalities were detected, which when combined yielded 100% diagnostic discrimination. Severity of structural and functional measures correlated with severity of various cognitive deficits, and both types of changes accorded with areas known to be affected neuropathologically. More recently, in an Alzheimer's Association-funded study in the PI's Lab, detected similar significant differences between minimally impaired elderly patients at-risk for AD (mean Mini-Mental State score 26) and controls, again revealed highly significant changes in both SPECT rCBF and in volumes of mesial temporal regions on MRI. Findings again are consistent with the argument that as in HD, pathological changes in AD may potentially be detectable, not only very early in the course of the disease, but years before clinical disease onset. This hypothesis is reinforced by a recent study (Small et al., *JAMA* 273:942–7, 1995).

NR477 Wednesday, May 8, 12 noon-2:00 p.m.

Constant Observation in a General Medical Hospital

Michael Blumenfield, M.D., Psychiatric Institute Rm. N314, Valhalla NY 10595; Jane Milazzo, R.N., Barbara Orlowski, Ph.D.

Summary:

Constant observation (CO) in a general hospital is important from clinical, legal, and economic perspectives. The literature cites costs of between $1,000 and $240,000 per hospital per year. Liability issues and lack of clear policy guidelines for CO compound difficult clinical problems with these patients.

A chart review was conducted of 120 patients on CO over ten months at a 665–bed tertiary care hospital. A multiple regression analysis determined the best predictors for the cost of sitters. Correlations (two-tailed) of variables with the cost of sitters was also analyzed.

Organic mental syndrome (41.7%), no mental illness (21.7%), and mood disorders (15%) were the most common categories of patients who were put on CO. The economic cost averaged $3,280 per CO patient per admission with a range of $144 to $68,500. The projected yearly cost for CO at this hospital was $472,303.

Higher costs were predicted by combativeness ($p = .0013$), absence of alcohol use ($p = .0046$), and anxiety ($p = .029$). Significant correlations with increased cost were shown by: HIV status ($r = .21$, $p = .02$), number of suicide attempts ($r = .22$, $p = .04$), auditory hallucinations ($r = .22$, $p = .02$), combativeness ($r = .2$, $p = .03$), dangerousness ($r = .27$, $p = .004$), disorientation ($r = .2$, $p = .03$), and disruptiveness ($r = .19$, $p = .05$).

NR478 Wednesday, May 8, 12 noon-2:00 p.m.

Jumping and Other Suicides in a General Hospital

Richard T. White, M.B., Psychiatry, Royal Prince Alfred Hosp., Missenden Road, Camperdown, Sidney 2050, Australia; Robert J. Gribble, M.B., Melissa J. Corr, M.B., Matthew M. Large, M.B.

Summary:

Suicide in the nonpsychiatric wards of general hospitals indicates severe patient distress, is a source of anguish to families and to hospital staff, and in certain cases, may be preventable.

We describe 14 subjects who jumped from our general hospital between 1980 and 1995. Nine died. There was only one other successful suicide, by hanging, during the study period. The total ($n = 15$) suicide rate of 1.4 per 100,000 admissions is much lower than the last published series ie 3.3 per 100,000 by Glickman in 1980.

We postulate three clinical subgroups: the acutely psychotic with suicidal preoccupation ($n = 2$), the acutely delirious ($n = 4$), and the chronically medically ill ($n = 9$). In the first subgroup there were two psychotic depressives, one being in the puerperium. Factors appearing frequently in the third subgroup were: pain, dyspnea, transient confusion, poor prognosis, and recent adverse news. When we compared the hospital jumpers with 30 nonfatal jumpers who attended our emergency department, the medical and psychiatric profiles differed in the frequency of medical illnesses, advancing age, male gender, and absence of pre-existing psychiatric illness. Proximity and ease of access to balconies and windows appear highly relevant to the prevention of general hospital suicide.

NR479 Wednesday, May 8, 12 noon-2:00 p.m.

Psychiatric Illness in Medical Inpatients Increases Medical Re-Hospitalizations and Outpatient Visits at Four-Year Follow-Up

Stephen M. Saravay, M.D., Psychiatry, Long Island Jewish MC, 270–05 76th Avenue, New Hyde Park NY 11042; Eliot Goldman, Ph.D., Susan Hirsch, A.C.S.W., Jonathan Schor

Summary:

Medical/surgical inpatients with psychiatric disorders have longer hospital stays and use more health care resources during hospitalization. Two studies show more frequent medical rehospitalizations after discharge. We report on a third prospective study in which psychological distress was associated with increased medical rehospitalization and outpatient visits after discharge.

Medical records at the Long Island Jewish Medical Center were reviewed four years after discharge from the index admission of a convenience sample of 239 medical inpatients 18–70 years of age who had received psychological tests from 11/1/90 to 8/15/91. A two-tailed alpha value of 0.05 was used to determine significance. Scores for depression (BDI) correlated with more rehospi-

talizations (r = .26, p < .01) and ER visits (r = .43, p = .06) while cognitive impairment (MMSE) correlated with days rehospitalized (r = .26, p < .01) for patients with fewer than 10 rehospitalizations. For all patients, social work ratings of guardedness (r = .18, p = .04) and hostility toward staff (r = .21, p = .02) correlated with more frequent rehospitalizations, while ratings of noncompliance (r = .25, p = .03) were associated with more outpatient visits. Any psychiatric treatment in the year before the index admission correlated with more direct hospital admissions (r = .36, p < .01). These findings suggest the potential importance of diagnosing and planning effective treatment for psychiatric problems in hospitalized medical inpatients to reduce excessive postdischarge utilization of medical resources.

NR480 Wednesday, May 8, 12 noon-2:00 p.m.

A Diagnostic Aid for Detecting (DSM-IV) Psychiatric Disorders in Primary Care

Myrna M. Weissman, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, Unit 14, New York NY 10032-2603; Mark Olfson, M.D., Patricia Conolly, M.D., David V. Sheehan, M.D.

Summary:

WITHDRAWN

NR481 Wednesday, May 8, 12 noon-2:00 p.m.

Health Complaints Attributed to Dental Amalgam: A Study of 99 Patients and 272 Comparison Subjects

Ulrik F.R. Malt, M.D., Psychosomatic, University of Oslo, Rikshospitalet, Oslo 0027, Norway; Per Nerdrum, Ph.D., Bjorn Oppedal, D.D.S., Roger Gunderson, M.D., Martin Holte, M.D., Jostein Lone, D.D.S.

Summary:

Objective: The physical and mental symptomatology of 99 self-referred patients complaining of multiple somatic and mental symptoms attributed to dental amalgam fillings were compared with patients with known chronic medical disorders seen in alternative (n = 93) and ordinary (n = 99) medical family practices and patients with dental amalgam fillings (n = 80) seen in an ordinary dental practice.

Method: The assessments included written self-reports, a 131-item somatic symptom checklist, and the General Health Questionnaire.

Results: The self-reports suggested that 62% of the dental amalgam sample suffered from a chronic anxiety disorder and 47% from major depression compared with 14% in the two clinical comparison groups and none in the dental control sample. Symptoms suggesting somatization disorder were found in 29% of the dental amalgam sample compared with only one subject in the 272 comparison subjects. One third of the dental amalgam patients reported symptoms of chronic fatigue syndrome compared with none in the dental control sample and 2% and 6%, respectively, in the two clinical comparison samples.

Conclusion: Self-referred patients with health complaints attributed to dental amalgam are a heterogeneous group of patients who suffer multiple symptoms and frequently have mental disorders. There is a striking similarity with the multiple chemical sensitivity syndrome.

NR482 Wednesday, May 8, 12 noon-2:00 p.m.

Postpartum Depressive Symptoms Are Associated with Decreased Prevalence of Breastfeeding

Veronika Solt, M.D., Psychiatry, Columbia University, 5141 Broadway, Allen Pavilion, New York NY 10034; Carmello Colon, M.S.W., Andrea K. Gondocs, M.D., Alec Roy, M.D.

Summary:

Breast-feeding is recognized as the preferred form of infant nutrition since breast-fed infants have lower rates of infections and hospital admissions than their bottle-fed counterparts. In the United States, only half of the mothers initiate breast-feeding. Many speculate that the increasing number of women in the labor force, early discharge of mothers from hospitals, lack of appropriate counseling, and encouragement by physicians are important contributing factors.

As postpartum depressive symptoms are often manifested by functional impairment, disrupting the mothers' capacity to care for their newborn child, we hypothesized that women who show depressive symptoms are less likely to breast-feed their baby.

Women who returned for their six-week postpartum visit were asked to complete the Edinburgh Postnatal Depression Scale (EPDS) and were asked whether they were breast-feeding their baby.

EPDS scores ranged from 0 to 22. Nineteen (26.4%) of the 72 women scored 12 or above (positive). Women who were found positive were referred for further assessment. Breast-feeding was significantly less frequent (p < 0.034) among those women with depressive symptoms (EPDS score 12 or above) compared with the group with scores less than 12 (4 out of 19 vs 26 out of 53).

In this study, postpartum depressive symptoms were associated with lower prevalence of breast-feeding among women six weeks postpartum. Therefore, we speculate that postpartum depressive symptoms may be additional contributing factors to the low frequency of breast-feeding. Screening and appropriate referral for counseling may prevent further deterioration of the mood disorder and its adverse effects on the mother-child relationship.

NR483 Wednesday, May 8, 12 noon-2:00 p.m.

Incidence of Delirium in Patients Referred by Primary Care Physicians for Evaluation of Depression

Michael N. Valan, M.D., Psychiatry, CA Pacific Med Ctr, 2340 Clay St 7th Floor, San Francisco CA 94115; Donald M. Hilty, M.D.

Summary:

This study reviewed the initial consultation question made by referring physicians and compared it with the principal diagnoses made by the consulting psychiatrist.

A retrospective chart review was conducted of 208 consecutive psychiatric consultations that were provided to medical/surgical patients in a community hospital. The charts were reviewed and screened to determine the reason the consultation was requested by the primary care provider and the subsequent diagnosis made by the consulting psychiatrist. Of the 208 psychiatric consultations reviewed, 74 were made for evaluation and treatment of depression. Of these 74, 17 (23%) were subsequently given a diagnosis of delirium by the psychiatrist. Characteristics exhibited by the patients referred for depression but then diagnosed with delirium included advanced age of greater than 70 years (14 of 17), hip fracture (5 of 17), use of opiates for analgesia (12 of 17), the presence of psychomotor slowing on mental status examination (13 of 17), living alone prior to admission (10 of 17), and psychiatric history of depression (3 of 17).

Primary care providers are sensitive to psychiatric symptoms but often misinterpret their underlying etiology. With managed care putting increased responsibility on primary care providers to manage complicated patients, these physicians will need increased training in the recognition and treatment of comorbid psychiatric disorders in medically ill patients. Delirium is a common syndrome found on medical/surgical services and is often underrecognized and misdiagnosed. This study illustrates the difficulty in distinguishing between delirium and depression. Specific patient characteristics may increase the difficulty in distinguishing between delirium and depression.

NR484 Wednesday, May 8, 12 noon-2:00 p.m.

Relationship Between Dental Status and Dental Anxiety

Bogdan P. Radanov, M.D., Psychiatry, Murtenstr 21, Berne 3010, Switzerland

Summary:

Objective: To analyze the relationship between dental status and dental anxiety

Method: The study included 164 patients (90 women, 74 men, mean age = 46.3 ± 13.9) who came for a regular dental-hygiene check-up. In order to assess dental status, D3.4MFS-/D3.4MFT index and Bleeding-on-Probing-Index (BOP) were applied. Dental anxiety was assessed using dental anxiety rating, while state and trait anxiety were analyzed by the State-Trait Anxiety Inventory. The hypothesis was: higher levels of dental anxiety lead to avoiding check-ups and necessary treatment, the consequence of which is worsening of dental status.

Results: No significant correlation was found between dental anxiety and dental status. In contrast, significant correlation could be found between patients' age and D3.4MFS-/D3.4MFT index. In addition, a significant correlation was found between dental anxiety and trait anxiety.

Conclusion: These results suggest that dental anxiety is a rather nonspecific phenomenon but an aspect of anxiety proneness (i.e., high trait anxiety).

NR485 Wednesday, May 8, 12 noon-2:00 p.m.

Alzheimer's Disease and Its Lewy Body Variant

Myron F. Weiner, M.D., Department of Psychiatry, UT Southwestern Med Ctr, 5323 Harry Hines Blvd. F5.400, Dallas TX 75235-9070; Richard C. Risser, M.S., C. Munro Cullum, Ph.D., Charles White III, M.D., Roger N. Rosenberg, M.D., Sam Speciale, Ph.D.

Summary:

Objective: To compare clinical findings in Alzheimer's disease (AD) and the so-called Lewy body variant (LBV) of AD.

Method: We analyzed available data on the clinical features of 55 AD and 24 LBV patients who underwent postmortem examination.

Results: The proportion of men in the LBV group was significantly larger than in the AD group (2/3 vs. 1/3) and the LBV group was slightly taller. There was an increased prevalence of hallucinations, delusions, and depressed mood in LBV cases compared with AD cases, but no significant differences in age of onset, duration of illness, cognitive impairment, overall severity of illness, or neuropsychological findings. LBV patients more frequently experienced extrapyramidal side effects (EPS) of neuroleptics, but otherwise did not have increased EPS. The cerebrospinal fluid (CSF) concentration of homovanillic acid (HVA) was significantly lower in the LBV patients, even when correction was made for height.

Conclusions: LBV may be suspected in elderly male dementia patients who otherwise meet criteria for AD but who manifest significant psychiatric symptoms, neuroleptic-induced extrapyramidal symptoms, and low (< 40 ng/ml) levels of CSF HVA.

NR486 Wednesday, May 8, 12 noon-2:00 p.m.

Testosterone, Mood and Psychotropic Medication

Catherine L. Woodman, M.D., Dept of Psych, Univ of Iowa Hosp and Cli, Iowa City IA 52242; W. Rockwell Williams, P.A.

Summary:

Issues related to aging are increasingly important as more people are living to be older and there are more treatment options available for medical disorders associated with aging. Not many decades ago, the discomforts associated with menopause were accepted as a physiological process, but now hormone replacement therapy is routinely used to ameliorate these symptoms. There is a debate among endocrinologists about whether such a condition involving testosterone occurs in males, beginning around age 50, and whether such a condition has serious physical and psychological effects. Patients with low free testosterone are noted to have 1) loss of libido and/or impotence, 2) depression, fatigue, and lack of zest; 3) headaches, as well as insomnia, lack of attention, arthritic pain, weight gain, low back pain, irritability, and formication. A number of these overlap with signs and symptoms of depression. This preliminary study looks for a relationship between low testosterone levels and mood disorders.

Methods: The charts and medication profiles for 173 outpatients who have received testosterone over that past three years were reviewed. The average age of the subjects was 63.2 years (range 25–85) and all were male. All subjects were on testosterone replacement secondary to low free testosterone. Treatment is through the endocrinology clinic, and all subjects were referred with chief complaints of change in libido or problems with impotence.

Results: Of the 173 probands, 68 (39%) were on psychotropic medication. The current prevalence of affective disorders in the general male population is between 7%–12%, so this is substantially elevated compared to normals; 78% of subjects were on psychotropic medication prior to testosterone treatment.

Conclusions: In this study subjects with low free testosterone have an increased prevalence of mood and anxiety disorders compared with the general population. As most subjects were on psychotropic medication prior to testosterone replacement therapy, it is unclear whether low free testosterone precipitated a mood disorder or if psychotropic medication has caused a decrease in testosterone. Evidence for and against each hypothesis will be discussed.

NR487 Wednesday, May 8, 12 noon-2:00 p.m.

Delirium Risk Factors in the Elderly: A Meta-Analysis

Michel Elie, M.D., Psychiatry, St. Mary's Hospital, 3830 Lacombe Avenue, Montreal PQ H3T 1M5, Canada; Martin G. Cole, M.D., Francois J. Primeau, M.D., Francois Bellavance, Ph.D.

Summary:

Objective: To identify through systematic literature review (meta-analysis) the risk factors associated with the development of delirium (D) in hospitalized geriatric patients.

Methods: First, Medline/Current Contents databases were screened for relevant articles published from 1966 to 1994, and from bibliographies of identified articles additional papers were selected. Second, the reports were screened by two investigators and retained only if meeting the five following criteria: 1.) original research in French or English; 2.) prospective study; 3.) patients over age 50; 4.) minimum of one risk factor (RF) identified; 5.) accepted definition of D. Third, the methodology of each study was graded according to specific criteria for RF studies. Fourth, RF were identified and tabulated.

Results: 21 articles were retained after meeting all of the above criteria. Among these studies, eight were done on medical patients, eight on surgical patients, two on medical and surgical patients, and three on psychiatric patients. A total of 955 subjects with delirium were studied. Forty-four different risk factors were identified, the five most common being cognitive impairment, increasing age, medical illness, male sex, and multiple medication use. Methodological weaknesses were present in many studies.

Conclusion: Despite the methodological limitations, certain RF for D seem to be consistent and could help identify high-risk patients.

NR488 Wednesday, May 8, 12 noon-2:00 p.m.

Acute Administration of the Nicotinic Agonist ABT-418 Improve Learning in Alzheimer's Disease

Paul A. Newhouse, M.D., Dept of Psych, Univ of VT College of Med, 1 South Prospect Street, Burlington VT 05401; Alexandra Potter, B.S., June Corwin, Ph.D., Robert H. Lenox, M.D.

Summary:

Studies of the neurochemical pathology of Alzheimer's disease (AD) and Parkinson's disease (PD) reveal a severe and specific loss of central nicotinic cholinergic receptors. We and others have shown that acute nicotine improves some aspects of cognitive functioning in AD patients. However, nicotine has disadvantages, and new selective nicotinic agonists (cholinergic channel activator; CCA) have been developed to produce nicotinic stimulation with reduced side effects and problems. Three doses (6 mg, 12 mg, and 23 mg) of the novel CCA ABT-418 were administered continuously for six hours in a double-blind, placebo-controlled study to six subjects with NINDS-ADRDA diagnosed AD (four female, two male, mean age 70.2). Cognitive testing and behavioral ratings were completed before drug administration, two and six hours post administration, and two hours after withdrawal of drug. Testing consisted of a computer administered battery that focused on the domains of attention, new learning, recognition, response bias, and psychomotor speed. Behavioral and physiological measures were collected at regular intervals.

At six hours after ABT-418 administration began there was a significant dose-related improvement in short-term recall ($p < .03$) accompanied by a significant ($p < .006$) decrease in recall failure on the selective reminding task. Recall consistency also showed dose-related improvement. Strong trends ($p < .09$) were seen for improvements in spatial memory hits, improvements in response bias on a recognition memory task, and speeding of reaction time. Improvement was seen on tasks that the nicotinic antagonist mecamylamine impaired in prior studies. Behavioral and physiological effects were modest suggesting a larger therapeutic index than nicotine. We conclude that acute stimulation of CNS nicotinic receptors with the selective CCA and nicotinic agonist ABT-418 may have positive effects in AD. (Supported by Abbott Laboratories, NIMH R29–46625, and GCRC M01–00109.)

NR489 Wednesday, May 8, 12 noon-2:00 p.m.

Estrogen Effects on Cognitive Impairment in Women

M. Martin Costa, Ph.D., Psychiatry, UC San Francisco, 359 America Avenue, Sunnyvale CA 94086; Victor I. Reus, M.D., Owen M. Wolkowitz, M.D., Francesca Manfredi, B.A., Morton Lieberman, Ph.D.

Summary:

Estrogen use may be associated with enhanced cognitive functioning in post-menopausal women, but few studies have longitudinally examined this relationship. We report the results of a retrospective, one-year, longitudinal study examining cognitive functioning in female estrogen and nonestrogen users as part of a multisite study of Alzheimer's and other cognitive impairments. Estrogen users and nonestrogen users were compared on the MMSE and Blessed-Roth Dementia Rating Scale (BRDRS) at baseline and one-year follow-up. Age, education, and baseline cognitive ratings did not significantly differ between groups. At time 2, nonestrogen subjects showed significant cognitive deterioration on both cognitive measures (both $p < .0005$). Estrogen users showed no significant deterioration from baseline levels on either cognitive rating; further, BRDRS ratings were significantly higher ($p < .01$) than nonestrogen BRDRS ratings at time 2, with trend level differences ($p < .07$) on the MMSE. When estrogen users were matched with nonestrogen users on baseline cognitive ratings, all results were replicated with similar significance levels. Age and education did not significantly differ between groups.

Our preliminary findings suggest that estrogen may act as a significant buffer against deterioration in Alzheimer's and other cognitive impairments, an effect not necessarily accounted for by initial level of functioning.

NR490 Wednesday, May 8, 12 noon-2:00 p.m.

Control-Related Intervention in the Treatment of Nursing Home Residents with Mild to Moderate Depression

Jules Rosen, Geriatrics, WPIC, 3811 O'Hara Street, Pittsburgh PA 15213; Joan C. Rogers, Ph.D., Robert S. Marin, M.D., Avner Shahar, M.D., Benoit H. Mulsant, M.D., Charles F. Reynolds III, M.D.

Summary:

Depression has been reported to occur in up to 50% of nursing home residents with approximately one-third experiencing syndromal major depressive episodes (MDE) and the remainder with a "subsyndromal" depression. In a community nursing home, 31 cognitively intact residents with either MDE (mild and moderate severity) or subsyndromal depression were identified through structured diagnostic evaluation. A social activities intervention of two-months duration, based on the theory that "loss of control" over daily activities contributes to depression in long-term care, was initiated. The nature of the activity as well as the frequency and duration of each session was determined by the residents. Following termination of the treatment program, the participants were reassessed after two months of returning to the routine in the nursing home. For all participants, the pre- and post-treatment GDS scores were 18.4 ± 6.0 and 16.1 ± 6.2 ($p < 0.05$), whereas the Hamilton Depression Rating Scale (HDRS) scores did not show a significant change. Fourteen residents (45%) were "signifi-

cantly improved" following intervention according to independently obtained global ratings. For the residents who were "significantly improved," HDRS scores declined from 12.4 ± 2.9 to 9.2 ± 2.9 ($p < 0.001$), and pre- and post-treatment GDS scores were 20.1 ± 4.7 and 15.4 ± 6.6 ($p < 0.02$). At two-month follow-up, both rating scale scores significantly worsened, suggesting that the treatment effect did not persist for these residents. The concept of subsyndromal depression, the use of the GDS and HDRS as measures of change in mildly depressed patients, and "control-related milieu interventions" for the treatment of depressed nursing home residents will be discussed.

NR491 Wednesday, May 8, 12 noon-2:00 p.m.

Personality and Disability in Geriatric Depression

Robert C. Abrams, M.D., Psychiatry, New York Hospital, 21 Bloomingdale Road, White Plains NY 10605; Lisa A. Spielman, Ph.D., George S. Alexopoulos, M.D., Ellen J. Klausner, Ph.D.

Summary:

Objective: Personality disorders may contribute to the persistence of impairments in functional capacity or activities of daily living (ADL), in treated elderly depressives. This paper focuses on the implications of personality dysfunction and residual depression for disability in geriatric patients recovered from acute major depression.

Method: The subjects were 47 elderly patients treated for major depression who were judged by their clinicians to be in remission from the acute episode. Subjects completed measures of personality disorders, depression, and ADL, as well as mediating measures of cognitive functioning, recent stress, and socioeconomic status. Correlational and logistic regression analyses tested the hypothesis that symptoms of personality disorder predict greater deficits in ADL functioning after recovery.

Results: Correlations revealed significant inverse relationships between ADL and scores for the avoidant and dependent personality disorders (r's = –.297 and –.337, respectively). Subjects were then dischotomized using a median split of the ADL score. The resulting dependent variable was subjected to logistic regression, with mediating variables, depression, and total personality disorder scores entered as independent variables. A significant model resulted ($x^2 = 23.734$, df = 7, $p < .01$), with gender, socioeconimic status, and total personality disorder scores contributing significantly. The interaction of depression and personality disorder scores was also significant (Wald = 4.075, $p < .05$). For this model, effects were stronger at low levels of residual depression (Hamilton < 10).

Conclusion: Personality disorder symptoms may adversely influence ADL functioning in remitted elderly depressives; personality dysfunction and low-grade residual depression appear to interact in predicting poor adherence to basic self-care tasks. However, the disabling effects of personality are overwhelmed in patients with more severe depression. These findings point out an important group at risk for ongoing disability despite the remission of severe affective symptoms. Practical psychotherapeutic interventions may need to address both personality and functional capacity.

NR492 Wednesday, May 8, 12 noon-2:00 p.m.

Depression and PET Imaging in Alzheimer's Disease

David L. Sultzer, M.D., Psychiatry, UCLA, 760 Westwood Plaza, Los Angeles CA 90025–1759; Jeffrey L. Cummings, M.D., Michael E. Mahler, M.D., M. Andrew Berisford, Ph.D., Mark A. Mandelkern, M.D., Charles H. Hinkin, Ph.D.

Summary:

Objective: A heterogeneous group of depressive symptoms occur in patients with Alzheimer's disease (AD). This study examined the relationship between specific clusters of depressive symptoms and regional brain function in AD.

Method: 25 patients with probable AD underwent structured assessment for three types of depressive symptoms. Subjective mood disturbance (depressed mood, anxiety, guilt) and objective signs of behavrioral retardation (emotional withdrawal, blunted affect, motor retardation) were measured on the Neurobehavioral Rating Scale. Neurovegetative symptoms (sleep/appetite disturbance, somatic symptoms) were measured on the Hamilton Depression Scale-Neurovegetative subscale. Regional cerebral metabolic activity was measured using ^{18}F-fluorodeoxyglucose PET imaging.

Results: Greater subjective mood disturbance was associated with low metabolism in the medial parietal lobule (r = .53), angular gyrus (r = .52), posterior cingulate (r = .51), and inferotemporal regional (r = .55). In contrast, behavioral retardation scores and neurovegetative symptom scores were not significantly correlated with absolute metabolic rate in any brain region. Subjective mood symptoms were more severe in patients with low relative parietal metabolism and high relative frontal metabolism. Behavioral retardation, however, was greater in those with high relative parietal metabolism and low frontal metabolism.

Conclusions: Distinct clusters of depressive symptoms are based on different pathophysiologic mechanisms in AD. Subjective mood symptoms are associated with dysfunction in heteromodal association and limbic regions of the parietal and temporal cortex, whereas behavioral retardation and neurovegetative symptoms may be more nonspecific manifestations of illness.

NR493 Wednesday, May 8, 12 noon-2:00 p.m.

Risperidone in the Treatment of Elderly Psychiatric Patients

Stephen M. Aronson, M.D., University of Michigan, 18101 Oakwood Blvd, Derborn MI 48123; Venkataramana S. Lingam, M.D., K.A. Hasanat, M.D.

Summary:

Objective: Recent reports have demonstrated the effectiveness of risperidone in the management of elderly psychiatric patients. These patients pose a pharmacologic challenge because of poorly understood age-related pharmacodynamic changes, sensitivity to side effects, and interactions with concomitant medications. Many treatments for behavioral symptoms in dementia are inadequate in elderly patients with chronic Axis I disorders. We sought to determine the role of risperidone in the treatment of elderly psychiatric patients resistant to treatment with conventional neuroleptics.

Methods: The records of hospital inpatients and nursing-home residents aged 65 years and over who had received risperidone were reviewed. Their diagnoses included dementia, schizophrenia, bipolar disorder, major depressive disorder with psychotic features, and schizoaffective disorder.

Results: After treatment with risperidone, symptoms were ameliorated in many patients and they became more manageable, and in most patients Clinical Global Impression scale scores improved. Risperidone was well-tolerated.

Conclusions: The results indicate that risperidone is an effective agent in several neuropsychiatric disorders in the elderly. Further longitudinal data on risperidone in the treatment of behavioral disturbances in dementia among geriatric patients in different treatment settings are being collected and will be presented.

NR494 Wednesday, May 8, 12 noon-2:00 p.m.

Risk of Depression in Caregivers of Alzheimer's Disease Patients

Marc Cantillon, M.D., The Wien Ctr, Mt. Sinai Med Ctr, 4300 Alton Road, Miami Beach FL 33140; Dylan G. Harwood, M.A., William Barker, M.S., Marina Bravo, M.S.W., Deborah A. Hurwitz, M.S.W., Ranjan Duara, M.D.

Summary:

Purpose: To determine the risk of depression in caregivers of Alzheimer's disease (AD) patients.

Methods: CES-D scores of 620 primary caregivers of family members diagnosed with AD were analyzed. We compared risk for depression by level of cognitive impairment in the patient (Folstein MMSE), patient gender, patient psychiatric features (diagnoses of depression or psychosis), caregiver level of education, caregiver gender, and caregiver ethnicity.

Results: Caring for male patients, regardless of caregiver gender, was associated with significantly elevated CES-D scores (males = 16 ± 11 vs females = 13 ± 10)(mean ± SD)($p = .005$). Female caregivers evinced the highest depression scores (females = 15 ± 10 vs males = 11 ± 9)($p = .002$). Diagnosis of patient psychosis was the greatest predictor of elevated CES-D scores (16 ± 10 vs 13 ± 10)($p = .0004$). Significantly elevated scores were also observed in the caregivers of patients diagnosed with depression (14 ± 10 vs 13 ± 10)($p = .01$). Other associations were not significant. Overall, 37% of caregivers presented with CES-D scores ℓ 16.

Conclusion: Our findings support the association between caregiving and caregiver depressive symptomatology. Caring for a patient with depression or psychosis was significantly related to increased risk for depression. Overall, female spouses evinced the highest rates of depressive symptomatology.

NR495 Wednesday, May 8, 12 noon-2:00 p.m.

The Clinical Presentation of Vascular Depression

George S. Alexopoulos, M.D., Psychiatry, NYH-WD, Cornell UMC, 21 Bloomingdale Road, White Plains NY 10605; Barnett S. Meyers, M.D., Robert C. Young, M.D., Tatsuyuki Kakuma, Ph.D., Mary E. Charlson, M.D., David A. Silbersweig, M.D.

Summary:

Clinical and neuroimaging findings suggest that vascular lesions may predispose or precipitate depression in a considerable percentage of elderly patients. This study examined the clinical presentation of late-onset depression associated with vascular risk factors. Two groups of consecutively recruited geriatric patients (60 years and older) with major depression (by RDC) were studied. The first group (N = 33) had onset of depression after the age of 59 and one or more risk factors for vascular disease identified with the Cumulative Illness Rating Scale-Geriatrics (CIRS-G). The second group (N = 32) consisted of geriatric patients with onset of depression earlier than 60 years of age and no vascular risk factors. Subjects with "vascular depression" had greater cognitive impairment (Mattis Dementia Rating Scale) and disability (Philadelphia Multiphasic Assessment Instrument) than patients without vascular risk factors (ANCOVA with age as covariate $F(2,63) = 13.16$, $P < 0.0006$ and $F(2,63) = 15.87$, $P < 0.0002$ respectively). Logistic regression of specific neuropychological test scores showed that fluency ($P < 0.04$), visual recognition ($P < 0.002$), and language comprehension ($P < 0.02$) were more impaired in depressed patients with vascular risk factor than in depressives without vascular risk factors. The two groups had comparable severity of depression (total HAM-D). Principal component analysis of behavioral ratings identified two factors that jointly accounted for 58% of the variance in discriminating the two groups; retardation/agitation 31%, guilt/lack of insight 27%. These findings suggest that late-onset depression occuring in the context of vascular disease is associated with cognitive impairment, disability, psychomotor retardation, and the relative absence of depressive ideation, and agitation. Studies are needed to examine the relationship of location and volume of vascular lesions to behavioral and cognitive abnormalities of depression.

NR496 Wednesday, May 8, 12 noon-2:00 p.m.

Life Review Group Therapy in Degenerative Dementia

Rhoda R. Frankel, M.A., Psychiatry, UIC Psych Institute, 1601 West Taylor Street, Chicago IL 60612; Karen S. Carlisle, M.S.W., Rajiv P. Sharma, M.D., Lawrence W. Lazarus, M.D.

Summary:

Objective: This study examines the effects of structured life review group psychotherapy on well-being, self-esteem, and social functioning of retirement home residents with degenerative dementia (Study II), comparing results with previously reported Study I. (APA 1992)

Method: Participants with mild to moderate dementia (Folstein scores 22 to 25, ages 81 to 99) completed standardized self-assessment instruments to determine self-esteem and psychological and social functioning levels before/after a six-week group process (Self-Esteen Scale, Rosenberg, 1965; Affect Balance Scale, Bradburn, 1969).

Results: Data analysis showed increased self-esteem in three of seven in Study II (five of six, Study I) and increased positive affect in six of seven in Study II (three of six, Study I). This format limits group membership to eight for maximum participation. Content analysis of audio/videotapes of all sessions indicates participants may experience a sense of capability, mastery, control, and satisfaction in the tasks of reminiscing, reviewing, reevaluating, and reintegrating lifetime memories.

Conclusions: Similar results were obtained in both studies. This group process may provide critical opportunities for supportive interaction and relatedness among peers, contributing to increased adjustment/social functioning levels by shifting the focus from disability and dysfunction to rediscovered strengths, coping mechanisms, and adaptation.

NR497 Wednesday, May 8, 12 noon-2:00 p.m.

Efficacy of Clozapine Versus Chlorpromazine in Geriatric Schizophrenia

Evelyn M. Howanitz, M.D., Psychiatry, FDR VA Hospital, Montrose NY 10548; Moris Pardo, M.D., Peter Litwin, M.D., Robert G. Stern, M.D., Kathleen M. Wainwright, R.N., Miklos F. Losonczy, M.D.

Summary:

Objective: We conducted a 12-week, double-blind, comparison study to assess the efficacy of clozapine (CLOZ) vs. chlorpromazine (CPZ) in a group of elderly schizophrenic inpatients.

Method: 42 patients age 55 or older (mean 66.5 years) were enrolled and randomized to CLOZ or CPZ. All subjects were assessed at baseline and at four-week intervals with the PANSS, CGI, AIMS, and EKG. All subjects entered a titration phase followed by a stable dose phase, with a maximum dosage of 300 mg CLOZ or 600 mg CPZ.

Results: 34 subjects completed a minimum of seven weeks of stable dose of medication (21 CLOZ 13 CPZ); four subjects completed less than five but more than two weeks of stable dose of medication (one CLOZ, three CPZ). There were four dropouts prior to week 2 (two CLOZ, two CPZ). The mean baseline PANSS scores for CLOZ subjects was greater than that for CPZ but the difference was not statistically significant. At the conclusion of the study both groups improved compared to baseline, at a statistically

significant level. There was no significant difference in PANSS scores comparing positive and negative symptoms for each group from baseline to the study's conclusion. The mean CGI scores reflecting severity of illness also demonstrated improvement in both groups over time.

Conclusion: These results suggest both CLOZ and CPZ are effective treatments for psychosis and behavioral disturbances in geriatric schixophrenia. CLOZ was slightly more efficacious in symptom reduction, but not at a statistically significant level.

NR498 Wednesday, May 8, 12 noon-2:00 p.m.

Telemedicine Evaluation of Geriatric Depression

Beverly N. Jones, M.D., Psychiatry, Bowman Gray School of Med, Medical Center Blvd, Winston-Salem NC 277157; Lyn Exum, M.A., Mary McFarlane, Ph.D.

Summary:

Objective: To determine the reliability of telemedicine interviews in the assessment of geriatric depression.

Method: Consecutive admissions to a geriatric psychiatry unit were offered the opportunity to participate in a psychiatric interview using low-cost, PC-based videoconferencing equipment. Seven patients completed the interview. A psychiatrist administered the mood disorders section of the SCID using the telemedicine system to see and hear the patient while a face-to-face rater simultaneously observed the participant and completed SCID ratings. Paired t-test analyses of the summary ratings and of individual items were made. Participants completed a satisfaction questionnaire, which compared the telemedicine interview to traditional face-to-face interview. Descriptive analysis of the satisfaction ratings was made.

Results: Paired t-test analysis of summary ratings yielded t = −0.725 (p > = 0.47) leading to acceptance of the null hypothesis of equal ratings. Paired t-test analyses of 12 individual SCID items yielded t values less than the critical t value, (all p values > = .05) indicating agreement between the two raters. The average satisfaction rating of the telemedicine interview was 2.76, where 3.0 indicated acceptance, confidence, and comfort equivalent to a traditional face-to-face interview.

Conclusions: These preliminary results indicate high reliability between telemedicine and face-to-face ratings of geriatric depression. Participants' ratings of satisfaction and comfort indicate that telemedicine assessment of geriatric depression is acceptable to patients.

NR499 Wednesday, May 8, 12 noon-2:00 p.m.

Late-Life Depression, Vascular Diseases and Brainstem-Evoked Response Abnormalities

Balkrishna Kalayam, M.D., Psychiatry, NY Hospital-Cornell, Med., 21 Bloomingdale Road, White Plains NY 10605-1504; George S. Alexopoulos, M.D., Robert C. Young, M.D., David A. Silbersweig, M.D., Frank E. Musiek, Ph.D.

Summary:

Vascular disease is associated with major depression and with BAER wave V abnormalities. Behavioral abnormalities similar to major depression are seen in patients with vascular lesions of the ponto-mesencephalic region. BAER latency change for wave V produced by increased stimulation (Δ Latency V) has been used to detect clinically silent brainstem lesions. Findings are reported from a study of geriatric depressives (N = 53) and control subjects (N = 23) examined for differences of BAER Δ Latency V.

Methods: Unipolar nondemented geriatric depressives and elderly control subjects were assessed for BAER, and for depressive symptoms, vascular disease, and cognitive performance using clinical rating instruments.

Results: Grouping by depression and by vascular disease based on clinical ratings showed longer Δ Latency V in depressives compared with controls (p < .008; ANCOVA), and in subjects with vascular disease compared with subjects without vascular disease (p < .008; ANCOVA). Depressives with vascular disease had greater Δ Latency V compared with depressives without vascular disease (p < .0002; ANCOVA), control subjects with vascular disease (p < .009; ANCOVA) and control subjects without vascular disease (p < .0001; ANCOVA). The interaction of depression and vascular disease was correlated with Δ Latency V (R = .443; p < .0001).

Discussion: The findings suggest that clinically silent brainstem lesions are associated with both major depression and vascular disease in geriatric patients, and BAER wave V latency change can identify a subgroup of patients for further studies that examine differences in the course and outcome of illness. (supported by MH 01051 and MH 49762)

NR500 Wednesday, May 8, 12 noon-2:00 p.m.

Geriatric Patients with Manic Only Episodes: Characterization of Unipolar Mania

Isabelle Paquette, M.D., Psych/Geriatrics, Hosp Louis H Lafontaine, 7401 Hochelaga Street, Montreal PQ H1N 3M5, Canada; Jean-Francois Ricard, M.D., Maryse Charron, M.D., Carole Murphy, M.D., Rosita Punti, M.D., Claude Richer, M.D., Arthur Amyot, M.D., Michelle Rochon, M.D., Jacques Garant, M.D., Luiza Dumitrescu, M.D., Hugues Cormier, M.D., Marie-Claire Baril, M.D., Luiz Dumitrescu, M.D.

Summary:

Objective: Interest in geriatric mania has fostered attempts to identify subgroups of patients according to age at onset or clinical features of bipolar disorder. Although the existence of a manic-only course is acknowledged, few have addressed the subject, and the rationale for a specific subgroup is challenged. By providing a longer time frame to study, elderly patients are well suited for attempts to delineate this clinical entity. This study aimed to characterize unipolar mania in an elderly sample.

Method: Sixty-one subjects were recruited over a three-year period and charts studied retrospectively. All patients were discharged with a diagnosis of mania/hypomania after age 65. Information gathered included family history, neurological conditions, and cognitive impairment. For each subject, every hospitalization was reviewed, with an emphasis on manic episodes.

Results: Ten of the 61 patients followed a manic-only course (mean: 5, 2 episodes). The number of manic episodes was comparable, but onset of mania was earlier in the unipolar group (age span 26–68). Family and medical history were similar, as were most clinical characteristics of manic episodes.

Conclusion: Although sample size hampered significance of comparisons, our results suggest further characterization and subtyping of the course of illness in elderly bipolar patients is worthwhile.

NR501 Wednesday, May 8, 12 noon-2:00 p.m.

Screening for Depression in Primary Care Elderly

Tamson K. Noel, M.S., Psychiatry, UR Med Ctr, 300 Crittenden Blvd., Rochester NY 14642; Jeffrey M. Lyness, M.D., Christophe Cox, Ph.D., Deborah A. King, Ph.D., Yeates Conwell, M.D., Eric D. Caine, M.D.

Summary:

Objective: Depressive symptoms and syndromes in later life are a major public health problem. Most older persons with clinically significant mood symptoms do not present to mental health professionals, but do see their primary care providers. A validated

screening instrument might aid in the recognition of depressions. However, many prior studies did not use well, validated measures of psychopathology as their diagnostic "gold standard," and focus on the elderly was rare. To address these issues, we examined the test characteristics of the Center for Epidemiologic Studies Depression Scale (CES-D) in a group of older primary care patients.

Method: One hundred thirty patients age > 59 years attending three primary care internists' offices were enrolled in the study using stratified sampling on the CES-D to increase the number of patients with depressive syndromes. Subjects completed the CES-D and the Structured Clinical Interview for DSM-III-R (SCID); DSM-IV proposed criteria for minor depression were also evaluated based on the SCID data. Descriptive statistics and receiver operating curve (ROC) analyses were performed.

Results: Mean (SD) age was 71.0 (6.8) years, and 76 (58.5%) of the subjects were female. The mean (SD) CES-D score was 12.9 (9.3), with a range of 0–43. Based on the SCID, 12 patients had current major depression, 10 had minor depression, two had major depression in partial remission, eight had major depression in full remission, and one had bipolar depression. For current major depression, the CES-D's ROC demonstrated excellent properties, with the area under the curve (AUC) = 0.95. The greatest accuracy was achieved at a CES-D cut-off of 21, yielding a sensitivity of 92% and a specificity of 87%. The CES-D was less useful for minor depression (AUC = 0.73) or any depressive diagnosis (AUC = 0.85).

Conclusions: In older primary care patients, the CES-D is a useful screening instrument for affective illness, although its discriminatory power is greatest for major depression.

NR502 Wednesday, May 8, 12 noon-2:00 p.m.

Perceived Adequacy of Psychiatric Consultation and Expertise in Nursing Homes

William E. Reichman, M.D., Copsa Inst for Alzheimers, Disease & Related Disorder, UMDNJ-CMHC 671 Hoes Ln, Piscataway NY 08854; Andrew C. Coyne, Ph.D., Soo Borson, M.D., Barry W. Rovner, M.D., Kenneth M. Sakauye, M.D., Paul R. Katz, M.D.

Summary:

Purpose: Psychiatric symptoms frequently complicate the care of nursing home residents. This study examined the perceived adequacy of psychiatric consultation and staff mental health expertise, as reported by directors of nursing in long-term care facilities.

Method: A one-page questionnaire was sent to 2,150 skilled nursing home facilities in New York, New Jersey, Pennsylvania, Louisiana, and Washington. Directors of nursing rated the availability and competency (0-none, 4-a lot) of their medical directors, aides, nurses, staff physicians, and consultants to manage disruptive behavior. Availability of psychiatric consultation and its helpfulness was also assessed.

Results: Of the 2,150 surveys mailed, 729 were completed and returned (29.4%). Of the responding facilities, 31.7% were rural, 42.2% were suburban, and 26.1% were urban in location. Thirty-eight percent of residents were reported to be in need of an evaluation provided by a psychiatrist. Surveys showed that 83.2% of the nursing homes reported having a consulting psychiatrist available, with only 48.3% reporting that they had an adequate level of consultation. In those facilities in which a psychiatrist was available to consult, the adequacy of the consultation varied by the specific function provided.

Conclusions: The majority of nursing homes surveyed reported a significant need for psychiatric consultation and improvement in the abilities of their staffs to manage disruptive behavior. When a psychiatrist is available, diagnostic clarification and medication recommendations are viewed as adequate in the majority of facilities. However, psychiatrists are not viewed ad being adequately helpful in nonpharmacologic management, staff education, management of staff stress, and assisting with conflict between residents' families and the nursing home staff.

NR503 Wednesday, May 8, 12 noon-2:00 p.m.

Putamen Volume and Age at Onset in Geriatric Mania

Robert C. Young, M.D., Psychiatry, Ny Hosp-Cornell Med Ctr, 21 Bloomingdale Road, White Plains NY 10605–1504; J. Phillipe Bocksberger, M.D., George S. Alexopoulos, M.D., Mony J. De Leon, Ed.D., Balu Kalayam, M.D., Charles Elkin, M.D.

Summary:

Volumes of basal ganglia nuclei may be smaller in geriatric manic patients than in same-age controls (Bocksberger et al., 1996). We examined relationships between basal ganglia morphology and age at onset of illness in such patients. Psychiatric inpatients aged 60 or older with manic disorder by RDC were studied. Intermediate T2-weighted axial images were obtained using a 1.5 Tesla magnetic resonance scanner. Volumes of caudate and putamen nuclei and cerebral hemispheres were determined by a systematic sampling stereologic method. In 27 patients, age at onset of illness (17 to 82 years), but not index age, was significantly negatively correlated with left and right putamen volume ($r = -0.53$, $p < .01$, and $r = -0.39$, $p < .05$, respectively), and with left and total putamen volume corrected for cerebral hemisphere volume ($r = -0.42$, $p < .03$, and $r = -0.38$, $p < .05$, respectively). These preliminary findings suggest a modest negative association between putamen volume and age at onset of illness in geriatric mania. Further examination of basal ganglia morphology and clinical features in this heterogeneous population is warranted. (Supported by MH2522, MH49762, and MH00192.)

NR504 Wednesday, May 8, 12 noon-2:00 p.m.

Characterization of Geriatric Mania According to Age of Onset

Rosita Punti, M.D., Geriatrics, Louis-H. Lafontaine, 7401 Hochelaga, Montreal PQ H1N 3M5, Canada; Maryse Charron, M.D., Isabelle Paquette, M.D., Carole Murphy, M.D., Claude Richer, M.D., Jacques Garant, M.D., Arthur Amyot, M.D., Michelle Rochon, M.D., Marie-Claire Baril, M.D., Luiza Dumitrescu, M.D., Hugues Cormier, M.D.

Summary:

The prevalence of mania is estimated at 5%-10% in geropsychiatric patients referred for treatment of affective illness. A number of these patients develop their first manic symptoms after age 65 and are classified as having late-onset mania.

Objective: In this retrospective study, we attempted to identify clinical characteristics and differences between early-onset and late-onset mania in a geropsychiatric population.

Method: The data were obtained restrospectively from medical records of patients hospitalized in the last three years.

Results: All 58 patients were over age 65 and received a diagnosis of manic or hypomanic episode at the time of discharge. Of these, 41 had their first episode before age 65 (early-onset) and 17 had their first episode after 65 (late-onset). The two groups were comparable in severity of the manic episode and pharmacological treatment. In contrast to most previous studies, no differences were observed in family history for mood disorders. Patients with late-onset mania had more cardiovascular disease. Apart from pressure of speech and flight of ideas, which were more prevalent in late-onset mania, other manic symptoms, psychosis, confusion, and cognitive impairment were similar in both groups.

Conclusion: Late onset-mania appears to be a subgroup of bipolar disorder with many similarities to early-onset mania.

NR505 Wednesday, May 8, 12 noon-2:00 p.m.

Aging Effects on Motor and Cognitive Skill Learning

Charles Peretti, M.D., Inserm UR 405, Hop Universitaires, Clinique Psychiatrique BP 426, Strasbourg 67091, France; Jean M. Danion, M.D.

Summary:

The aim of the present research was to investigate the ability of older subjects to acquire a cognitive and a motor skill, as assessed by repeated testing on the Tower of Toronto (TT) puzzle. The TT puzzel is a four-disk variant of the Tower of Hanoi.

We investigated the component parts of the cognitive skill with reference to the ACT theory of skill acquisition (Anderson, 1987). Two groups of 20 subjects participated in the study, a group of older adults (67.0 ± 5.1 years) and a group of younger adults (24.7 ± 2.4 years). A computerized version of the TT puzzle was used. Subjects were asked to solve three blocks of eight consecutive trials each. The study yielded three main findings: 1) The older subjects exhibited an intact motor skill acquisition. 2) Their overall performance on cognitive skill was impaired, but the acquisition rate was identical to that of younger subjects. This indicates that older and younger subjects learned similarly and that cognitive skill learning was intact. 3) Defective performance on cognitive skill was probably due to a problem-solving deficiency. This finding was supported by the demonstration that, when they have been matched to younger subjects with regard to problem solving, older subjects did not exhibit any significant performance deficit.

NR506 Wednesday, May 8, 12 noon-2:00 p.m.

The Need to Change Laboratory Lithium Reference Ranges to Avoid Geriatric Iatrogenesis

Hilary T. Hanchuk, M.D., Psychiatry, UMDNJ RWJ Med School, 667 Hoes Lane/CMHC COPSA, Piscataway NJ 08855–1392; Galina Staroselsky, M.D.

Summary:

Though the use of lithium carbonate for bipolar disorder is well established, the safe use of this medication in the older patient is not as well understood. The application of guidelines on the use of lithium carbonate for adult patients may lead to frequent neurotoxic reactions in the older patient. Here we present five cases where physicians guided by the standard therapeutic serum lithium ranges on laboratory printouts increased lithium dosing that resulted in severe adverse consequences for the patient.

In most of the cases the patients were more clinically stable and side-effect free on lower lithium levels. We also present data from a retrospective review of all elderly bipolars (22 patients over five years) treated in our geriatric psychiatry outpatient clinic describing the effective lithium dose and serum level range for this population. Physicians not experienced in the use of lithium for the geriatric patient at times may change dosing trying to achieve printed laboratory ranges of serum lithium levels. In our experience, to help prevent neurotoxicity in the elderly patient, the printed reference therapeutic and toxic ranges of serum lithium levels on laboratory printouts must change. Printed laboratory information on serum lithium levels should include age-based ranges and possibly a reminder that achieving an adult therapeutic lithium level in not more important than clinical outcome.

NR507 Wednesday, May 8, 12 noon-2:00 p.m.

The Comprehensive Observational Psychiatric Screening Assessment in Dementia: Nursing Home Application of a New Behavioral Scale

Hilary T. Hanchuk, M.D., Psychiatry, UMDNJ RWJ Med School, 667 Hoes Lane/CMHC COPSA, Piscataway NJ 08855; Jessica M. Berlet, M.D., Robert Hamer, Ph.D., David Epstein, M.S., Anmolsingh Roopa

Summary:

We developed a structured instrument, the Comprehensive Observational Psychiatric Screening Assessment in Dementia (COPSAD), to assist in the assessment and documentation of behavioral disorders suffered by cognitively impaired patients. A patient's behavior may be transitory, not observed by the physician, and denied by the patient. Care providers are frequently distressed and rarely trained in psychometric assessment. Many existing scales are time consuming and chart-space consuming and difficult to execute and interpret. The COPSAD is a one-page assessment battery whose information is organized in a user-friendly and efficient manner though remaining thorough (seven categories, each with 20 items with four global parameters per category), < 15 minutes to complete, scored in < 30 seconds, and interpreted in < 1 minute. It has also proved flexible, useful in a clinician's interview, or completed by caregivers themselves after a brief instruction. Though used in an outpatient environment (where validity and reliability issues were addressed), here we present its use in a nursing home. The McCarrick Care Center staff completed a COPSAD in addition to a Dementia Signs and Symptoms Scale (DSS) on its population (123 patients, 82% female, average MMSE 10, and average age 85), once a month, during each shift for three months. The DSS was chosen since it was the most thorough and similar instrument available at the time of our instrument's development. The batteries were completed 655 times each, and Pearson correlation coefficients of the most analogous subscales were high, though all 17 staff members completing the scales preferred the COPSAD over the DSS due to speed and ease of completion. Hence, we have found the COPSAD a useful and efficient instrument to document behavioral disorders in a nursing home population.

NR508 Wednesday, May 8, 12 noon-2:00 p.m.

Reduced Frequency of Self-Reported Anticholinergic Side Effects to Nortriptyline in the Elderly

Nunzio Pomara, M.D., Geriatric Psychiatry, Nathan Kline Institute, 140 Old Orangeburg Road, Bld37, Orangeburg NY 10962; Hla Tun, M.D., Dennis Deptula, Ph.D., Rajkumar R. Singh, M.D., Feliciano B. Leviste II, M.D., Thomas B. Cooper, M.A.

Summary:

Objective: The considerable morbidity associated with the development of TCA-induced peripheral anticholinergic side effects in the elderly prompted us to examine the relationship between age and frequency of anticholinergic side effects (dry mouth, constipation, and urinary retention) during treatment with nortriptyline (NT), a TCA still widely prescribed in the elderly.

Method: Seventy-eight medically healthy and cognitively intact outpatients (ages 21–81, mean 50; 33 male/45 female) who met RDC and DSM-III criteria for major depression participated in a six-week, double-blind, parallel trial of NT versus placebo. Plasma NT levels were maintained within the therapeutic range. Subjects were characterized as young (< 55 years; n = 45, mean 39) or elderly (ℓ 55 years; n = 33, mean 66). The subjective symptoms were elicited weekly using the Treatment Emergent Symptoms Scale (TESS).

Results: NT treatment was associated with a significant increase in the frequency of dry mouth and constipation. An increase in the frequency of dry mouth was reported by the young throughout the six weeks of treatment but by the elderly only on week 3-week 5. Only younger subjects reported a significant increase in the frequency of constipation on week 3-week 5. There were no significant baseline differences between these age groups in the severity of symptoms, and also no relationship between reported side effects and plasma NT levels.

Conclusions: Contrary to expectations, the elderly reported anticholinergic side effects less frequently than the young in response to comparable plasma NT levels. These findings, which need to be replicated, may be due to age-related reductions in anticholinergic sensitivity or age-related alterations in the ability to discern/report changes in the internal milieu, and they highlight the need for more objective measures of anticholinergic side effects.

NR509 Wednesday, May 8, 12 noon-2:00 p.m.

MRI Brain Ventricular Volumes 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., Jian Hu, M.D., Manzar Ashtari, Ph.D., Peter M. Aupperle, M.D., Houwei Wu, M.D., Bernhard Bogerts, M.D., Simcha Pollack, Ph.D.

Summary:

Structural brain changes have been implicated in geriatric depression, especially in those patients whose onset of depression began in late life.

Objective: To compare brain ventricular volumes in elderly depressives and normal controls.

Methods: Elderly DSM-III-R unipolar depressives (n = 40) and controls (n = 48) participated in an MRI study (Magnetom, Siemens 1.0 T). Brain images were obtained in the coronal plane through the whole head in 3.1 mm contiguous slices (63 slices) (FLASH; TR = 40 msec; TE = 15 msec). For volumetric analysis, images were input onto a SUN workstation via 1.25 cm magnetic tape. Original images were reformatted into a standardized position (GE MrX software). Anatomic guidelines for structure delineation were established. Volumetric measurements were completed by the same operator (JH) under blinded conditions using a menu-driven, semiautomated, computer mensuration system with patients and controls in random order. Test-retest and interrater reliability (HW) ranged from .87 to 1.00. Measurements included whole brain, ventricular system subdivisions (lateral ventricle structures [body, frontal horn, occipital horn, temporal horn] and third ventricle), total ventricular volume, and ventricle/brain ratio (VBR).

Results: Multivariate analysis of variance (MANOVA) covarying for age, height, gender, and whole brain volume revealed significantly greater third ventricle volume in depressives as compared with controls ($p < .05$). Late-onset depressed patients (n = 24; first episode > age 60 years) demonstrated significantly greater volumes of the lateral ventricle: right body ($p < .01$), right occipital horn ($p < .04$), left temporal horn ($p = .05$); total ventricular volume ($p = .03$); and higher VBR ($p = .03$) as compared with early-onset (n = 16) depressed counterparts. Ventricular volumes correlated significantly with age, age at onset, cognitive ratings, depression severity, and qualitative ratings of ventricular enlargement.

Conclusions: Findings support the notion that structural brain changes contribute to late-onset geriatric depression.

NR510 Wednesday, May 8, 12 noon-2:00 p.m.

Plastic Cortical Changes As Indicators of Pain Memories in Phantom Limb Pain Patients

Wolfgang Larbig, M.D., Dept Med Psychology &, Behavioral Neurobiology, Gartenstrasse 29, 72074 Tuebingen, Germany; Pedro Montoya, Ph.D., Herta Flor, Ph.D., Neils Birbaumer, Ph.D.

Summary:

Objective: According to previous data from our laboratory demonstrating that the magnitude of phantom limb pain (PLP) is significantly correlated with the amount of cortical reorganization, it was suggested that plastic changes as indicators of activated pain memories may contribute to the origin and maintenance of PLP. The purpose of the present experiment was to examine cortical activity associated with the processing of pain-related stimuli in PLP patients.

Method: On the basis of a standardized pain interview, 18 amputees were assigned to either a PLP group (n = 11) or a pain-free group (n = 7). Amputees and matched healthy controls (n = 13) were presented 40 pain-related, 40 body-related, and 40 neutral adjectives in pseudorandom order at their individual perception threshold. Subjects' task was to name the presented words. EEG was recorded from 11 recording sites.

Results: Analyses of variance revealed significant group effects for the early and late visual evoked potentials (VEPs). Pain-free amputees showed reduced N100 amplitudes, whereas PLP patients displayed significantly enhanced LPC-amplitudes (500–800 ms). VEP components were unaffected by word type.

Conclusions: Altered early and late VEP components suggest that PLP patients are characterized by a more elaborated somatosensory pain memory. (Supported by the German Research Society)

NR511 Wednesday, May 8, 12 noon-2:00 p.m.

Comparison of the Human Interstitial Nuclei of the Anterior Hypothalamus with the Sexually Dimorphic Nucleus of the Preoptic Area of the Rat

William M. Byne, M.D., Psychiatry, Mt. Sinai, One Gustave Levy Place, New York NY 10029; E.M. Kemether, M.D., Inna Markhasima, M.D.

Summary:

The first and third interstitial nuclei of the human anterior hypothalamus (INAH1 and INAH3, respectively) have each been conjectured as being the homologue of the sexually dimorphic nucleus of the preoptic area (SDN-POA) of the rat.

Objective: To address the issue of homology by using immunocytochemistry to compare the neurochemical content of the SDN-POA with that of INAH1 and INAH3.

Method: Immunocytochemistry was used to examine the distribution of somatostatin (SS), neuropeptide Y (NPY), tyrosine hydroxylase (TH), and leu enkephalin (Enk) in the autopsied human hypothalamus. The distribution of these markers in the human was compared with their previously described distribution in the rat hypothalamus.

Results: INAH3 exhibited a moderate density of NPY-positive fibers, while INAH1 exhibited very few. Both INAH1 and INAH3 were essentially negative for SS, TH, and Enk.

Conclusions: INAH1 and INAH3, like the SDN-POA, are positive for NPY but essentially negative for the other markers employed in this study. The fact that the SDN-POA and INAH3 both display a moderate density of NPY-positive fibers while INAH1 displays a low density favors INAH3 as the better candidate for homology with the SDN-POA.

NR512 Wednesday, May 8, 12 noon-2:00 p.m.

Writes with the Right Hand, but Throws with the Left: An Indicator of Pathology in Males?

P.S.B. Sarma, M.D., Psychiatry, Finch University Health Sci., 3333 Greenbay Road, North Chicago IL 60064

Summary:

Right-handed males have more specialized cerebral hemispheres than left-handed males as well as females in general (NAGAE 1985). Several studies of handedness have found that writing and throwing a ball elicit relatively extreme responses, with most individuals claiming to use one hand for the two actions exclusively (particularly those who write with the right hand). So, if there is a dissociation for hand preference (for writing and throwing) in boys who write with the right hand, it might be due to some noxious effect on the development of the brain. If such is the case, it should be reflected in their academic functioning.

In a preliminary test of this hypothesis, the author surveyed the total population of third and fourth graders in an urbal school district for self-reported mixed handedness (writes with on hand but throws with the other). Among the fourth grade boys who were mixed handed, the right-handed writers (RHW) scored significantly lower on study skills (normal curve equivalent scores in the California Achievement Test) than the left-handed writers (LHW). Among the girls there was no significant difference (SARMA, 1989).

A new sample of mixed-handed boys was identified in grades six to eight in two middle schools, and the recent California Achievement Test scores were examined.

The RWH and LHW groups did not differ significantly in age (mean age 12.0) or in ethnic background (50% Hispanic). The RHW (16) obtained Spelling scores below 30 (one S.D. below the mean) significantly more frequently ($X^2 = 6.53$, df 1, $P < 0.025$) than the LHW (16). 62% of the RHW scored below 30 in Reading, Language or Spelling, whereas only 35% of the LHW did so. On re-examination of the old data from the third and fourth graders, a similar distribution was seen (42% of RHW vs 18.5% of LHW).

Conclusions: The findings support the inclusion of such mixed handedness (writes with the right hand but throws with the left) as a minor neurological sign in boys. Further studies are needed to understand this association.

NR513 Wednesday, May 8, 12 noon-2:00 p.m.

Psychiatric Disorders in Patients with Intracranial Neoplasm

Thania V. Quesada, M.D., Psychiatry, University of Miami, 1611 NW 12th Avenue, Miami FL 33136; M. Beatriz Currier, M.D., Florinda S. Calderon, M.D., Vijaya L. Uppu, M.D., Ana I. Fins, Ph.D.

Summary:

Fourteen consecutive adult patients with newly diagnosed intracranial neoplasm (ICN) admitted to Jackson Memorial Hospital neurosurgical service underwent structured clinical interview for DSM-IV (SCID-IV) to determine the prevalence of psychiatric comorbidity and identify demographic, psychosocial, neurological, and tumor variables significantly associated with ICN. The Mini Mental State Examination and a structured frontal-subcortical examination that tested for abstraction, complex problem solving, perseveration, and sequencing were also administered. When applicable, the Hamilton Depression Scale, Young Mania Scale, and the Delirium Rating Scale were used. Patients also completed the Brief Symptom Inventory (BSI).

The sample consisted of equal number of affected men and women. Mean age was 53.0 years. Twelve patients had primary ICN and two patients had metastatic tumors. Twelve were supratentorial, one was infratentorial, and one was both supratentorial and infratentorial. Tumor types included: 10 gliomas, two meningiomas, and two metastatic tumors. Fifty-seven percent (8/14) of patients had a psychiatric diagnosis, including dementia (N = 5), delirium (N = 4), substance abuse disorders (N = 2), and depressive disorders (N = 1).

Psychiatric comorbidity is common in patients with ICN (57%). Dementia and/or delirium accounted for 75% of the psychiatric diagnosis (9/12). Demographic, psychosocial, and tumor variables such as tumor type and location did not identify patients at risk for psychiatric comorbidity.

NR514 Wednesday, May 8, 12 noon-2:00 p.m.

Comparison of Patients with Suicidal Plans During the Acute or Chronic Post-Stroke Period

Yasuhiro Kishi, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive # 2887 JPP, Iowa City IA 52242; Robert G. Robinson, M.D., J. Todd Kosier, M.A.

Summary:

Of 301 acute stroke patients, 6.6% developed suicidal plans during the initial in-hospital evaluation (acute-onset suicidal plans) and 11.3% of patients developed suicidal plans at 3, 6, 12 or 24 month follow-up (delayed-onset suicidal plans). The development of both acute- and delayed-onset suicidal plans was strongly related to the existence of depressive disorders: 20 of the 36 (55.6%) with suicidal plans had major depression at the initial evaluation versus only 16 of 117 (13.7%) of those without suicidal plans, $x2 = 25.3$, $p = .0001$. The suicidal groups were also more likely to have a history of stroke: 13 (36%) versus 15 (12.9%), Fisher's $p < .01$. Acute-onset suicidal plans were also related to premorbid alcohol abuse: of the acute-onset group five (27.8%) had a history of alcohol abuse, only 11 (9.4%) of the nonsuicidal group and none of the delayed-onset patients (Fisher's $p < .03$). Acute-onset suicidal patients had more anterior lesion locations and delayed-onset suicidal patients had more posterior stroke lesions. Delayed-onset suicidal plans were associated with greater physical impairment ($p = .06$). These data suggest that the etiology of these two types of suicidal plans may be different, with acute-onset related to biological and delayed-onset related.

NR515 Wednesday, May 8, 12 noon-2:00 p.m.

Postconcussional Disorder: DSM-IV Criteria

Lawrence A. Labbate, M.D., Psychiatry, Walter Reed AMC, Borden Pavillion, Washington DC 20015; Deborah L. Warden, M.D., Andres M. Salazar, M.D., Anthony D. Pridgen, B.S.

Summary:

Objective: To determine the incidence and time course of the proposed DSM-IV postconcussional disorder (PCD) among patients with mild to moderate closed traumatic brain injury (TBI).

Method: Seventy-eight active duty service members (76 men, mean age 27 ± 7) who sustained moderate TBI defined as post-traumatic amnesia greater than 24 hours and recovery to Ranchos Los Amigos level 7 (oriented and cooperative) within 90 days of injury were enrolled in an ongoing outcome study. Patients were administered a Present State Exam modified for use with head-injured patients. Questions correlating with DSM-IV PCD criteria were culled. Patients were evaluated at baseline (N = 78), two months (N = 63), six months (N = 47) and 12 months later (N = 31). Dizziness and vertigo symptoms are only partially represented at the time of this analysis.

Results: At baseline, 44/78 (56%) patients met criteria for PCD, and this was associated with a history of TBI ($X^2 = 6.5$, $p = .01$). PCD was as follows over time: two months 14/63 (22%); six months 17/46 (37%); 12 months 9/31 (29%). PCD was not associated with past TBI at times other than baseline. PCD was associated with current major depression at baseline and all periods of follow-up: baseline ($X^2 = 29$, DF = 1, $p < 0.0001$); two months ($X^2 = 46$, DF = 1, $p < 0.0001$); six months ($X^2 = 39$, DF = 1, $p < 0.0001$); one year ($X^2 = 22$, DF = 1, $p < 0.0001$). PCD was also associated with generalized anxiety disorder at all time periods ($p < 0.0001$) except for at six months when there was a trend ($p < 0.1$). The most common symptoms (> 25% at each point) were

tiredness or exhaustion, sleep disturbance, and irritability. Inappropriate sexual behavior was extremely uncommon (N = 1).

Conclusion: PCD by DSM-IV criteria appears to be common, and there is considerable overlap with generalized anxiety disorder and major depression. The diagnostic criteria may need to be more stringent.

NR516 Wednesday, May 8, 12 noon-2:00 p.m.

Selective Attention, Illness Duration and Symptoms

Janet L. Tekell, M.D., Psychiatry, VA Hospital, 7400 Merton Minter, San Antonio TX 78284; J. Arturo Silva, M.D., Charles L. Bowden, M.D.

Summary:

Objective: Selective attention deficits, as measured by the Span of Apprehension Task (SAT), have been noted in schizophrenic patients at various stages of illness. We measured SAT performance in a chronic veteran psychiatric population upon admission to the hospital. Performance was compared with several clinical measures to more clearly define clinical correlates of these neurocognitive deficits in a psychiatric population with a long duration of illness.

Methods: We are currently conducting investigations of hospitalized decompensated schizophrenic patients; bipolar manic patients; nonmanic, nonschizophrenic patients, and healthy volunteers. Concurrent with the SAT, we are obtaining measures of illness severity as measured by the BPRS and GAF, negative symptoms as measured by the Negative Symptom Assessment (NSA), and executive functioning as measured by the EXIT25.

Results: Preliminary data analysis of 60 subjects and controls shows no correlation between the SAT and duration of illness (mean duration = 19 years). SAT performance (reaction time) was correlated with BPRS scores ($r = .3574$ $p = .005$), negative symptoms ($r = .5406$ $p < .001$), and executive functioning ($r = .5969$ $p < .001$).

Conclusion: These findings replicate several earlier studies in a more chronic population of patients. In addition, this is the first time that SAT performance has been examined in relation to executive functioning utilizing the EXIT25.

NR517 Wednesday, May 8, 12 noon-2:00 p.m.

Comparative Effects of Nefazodone and Fluoxetine on Sleep in Outpatients with Major Depressive Disorders

A. John Rush, M.D., Mntl Hlth, University of TX SW Med Ctr, 5959 Harry Hines Ste 600, Dallas TX 75235–7200; Christian Gillin, M.D., Roseanne Armitage, Ph.D., H. Moldofsky, M.D.

Summary:

Sleep disturbances are prevalent in major depressive disorders (MDD). Most antidepressants, including selective serotonin reuptake inhibitors (SSRIs), significantly prolong REM latency, suppress total REM time, and may also increase both awake time and light nonrestorative sleep. By contrast, small, open trials indicated that nefazodone, a 5-HT_2 antagonist that also inhibits 5-HT reuptake, did not prolong REM latency, but did improve sleep continuity. The present study evaluated the effects of nefazodone and fluoxetine on sleep EEG in a larger sample of patients with MDD.

Methods: This multisite, randomized, double-blind, eight-week, acute-phase treatment trial compared nefazodone (n = 60) with fluoxetine (n = 62) in outpatients with nonpsychotic MDD and insomnia complaint. Sleep EEG was recorded at baseline (while patients were symptomatic, but unmedicated) and at weeks 2, 4, and 8 of treatment.

Results: Nefazodone and fluoxetine were equally effective in reducing depressive symptoms, according to the Hamilton Rating Scale for Depression (HRS-D) total score. Nefazodone also significantly decreased the HRS-D sleep factor score in contrast to fluoxetine. Objective sleep EEG measures indicated that nefazodone increased sleep efficiency, reduced Stage 1 sleep, and awake and movement time, whereas fluoxetine had the opposite effect. Fluoxetine also prolonged REM latency and suppressed REM sleep, while nefazodone did not. In fact, nefazodone significantly increased total REM time. Subjective sleep quality (patient report and clinician ratings) was improved with nefazodone, but unchanged with fluoxetine.

Conclusion: Compared with fluoxetine, nefazodone was associated with more "normal" objective and subjective sleep characteristics. The differential effects on REM sleep and REM latency suggest that nefazodone and fluoxetine may have somewhat different spectra of action. Research supported by Bristol-Myers Squibb Company.

NR518 Wednesday, May 8, 12 noon-2:00 p.m.

Apathy Syndrome After Head Injury and Treatment Outcomes

Ravi Kant, M.D., Psychiatry, St. Frances Med Ctr, 400–45th Street, Pittburgh PA 15201

Summary:

Introduction: Emotional and motivational changes are commonly seen after closed head injury (CHI). No information is available in literature about the prevalence or treatment outcomes of apathy after head injury. In conducted a study in a head injury clinic to estimate the prevalence of apathy after head injury and response to treatments in a clinical population.

Methods: Apathy Evaluation Scale (AES) and Beck Depression Inventory (BDI) were used at initial evaluation and follow-up visits in patients with CHI. Family members completed the informant version -AES-I. Of the 83 patients 73.5% were male, mean age 38 ± 12.27, mild CHI in 74.7%. Ten patients were treated for apathy syndrome with methylphenidate (9) or amantadine (1). Cut off score for AES was 34 and BDI was 11.

Results: Of the 83 patients, nine (10.84%) met AES criteria for apathy without depression and the same number were depressed without apathy. Fifty (60.24%) were both depressed and apathetic, while 15 (18.07%) were neither. Family members rated patients significantly higher on AES ($p < .000001$). Young age ($p < .04$) and higher severity of injury ($p < .01$) correlated with apathy. AES scores significantly improved after treatment in 10 patients ($p < .004$). Similar change in AES-I scores was noted ($p < .01$). BDI scores did not change much ($p > .227$).

Conclusion: Apathy is a frequent symptom after CHI that needs to be recognized. It responds well to dopaminergic agents. It appears to be an independent entity, but may coexist with depression.

NR519 Wednesday, May 8, 12 noon-2:00 p.m.

Clinical Features of Recurrent Catatonia

Andrew J. Francis, Jr., M.D., Psych and Behav Sciences, Suny Hlth Sciences T-10, Health Sciences Center T-10, Stony Brook NY 11794; Krishna Divadeenam, B.A., George Bush, M.D., Georgios Petrides, M.D.

Summary:

Objectives: Consistency of symptom profiles across episodes of catatonia has not been examined. A standardized examination and rating scale [Bush-Francis Catatonia Rating Scale (BFCRS), *Acta Scand Psychiat*, in press] systematically tests 23 motor signs of catatonia, permitting symptom analysis of recurrent illness.

Methods: Patients from the emergency room or inpatient unit were prospectively examined using the 23-item BFCRS both on initial presentation and during a later episode of catatonia.

Results: To date, five cases have been identified, with a variable interval (avg 10.7 mo, range 4.5–20) between the initial and recurrent episode. All five met DSM-IV motor criteria for catatonia (293.89) and research criteria of more than 2 BFCRS signs. There were three females and two males, (avg age 32.8, range 25–42), whose diagnoses included schizophrenia, bipolar disorder, or conversion disorder. They showed 9.6 (range 7–15) catatonic signs in the first episode and 9.6 (range 4–14) in the second. Of the 23 individual BFCRS motor signs, an average of 16.6 (range 13–21) showed concordance (+ + or – –) between the two episodes.

Conclusions: The BFCRS facilitates systematic study of catatonia. Catatonia is recurrent in some cases with consistent motor symptoms across episodes.

NR520 Wednesday, May 8, 12 noon-2:00 p.m.

Standardized Assessment of Psychiatric Symptom Severity Enhances the Prediction of Length of Stay on an Intensive Rehabilitation Unit

Cori Salvit, B.S., Psychiatry-6K, Beth Israel Med Ctr, First Avenue At 16th Street, New York NY 10003; Christian Miner, Ph.D., Mary Focseneanu, M.D., Richard N. Rosenthal, M.D., Igor I. Galynker, M.D.

Summary:

Purpose: The purpose of this preliminary study was to investigate whether psychiatric symptom severity contributes to length of hospital stay (LOS) on an intensive rehabilitation service. Admissions to this unit included patients with common medical and surgical illnesses such as fractures, CVAs, tumors, deconditioning, etc.

Methods: 38 consecutive admissions to an intensive rehabilitation service were assessed at admission and prior to hospital discharge by means of the Functional Independence Measure (FIM). Though subjects had no history of psychiatric illness, they were also administered the Hamilton Rating Scale for Depression (HRSD), the General and Positive Symptom Severity subscales of the Positive and Negative Symptom Scale (PANSS-g, PANSS-p), and the Scale for the Assessment of Negative Symptoms. Setwise hierarchical multiple regression techniques were used to determine the contribution of psychiatric symptom severity to the prediction of LOS. Statistical significance testing was performed by Fisher's protected t procedure.

Results: When LOS was regressed on FIM-at-admission, age, and gender (Set I), about 26% of the total outcome variance was accounted for [$R^2 = .262$; $F = 3.91$, $df = (3, 33)$, $p < .05$], with gender the only significant individual predictor, indicating that males had longer LOS than females [$\beta = .41$; $T = 2.67$, $p < .05$]. The addition of FIM-at-discharge to this set of predictors added negligibly (< 1%) to the proportion of variance accounted for, and this measure was dropped from further study. When HDRS, PANSS-g, and PANSS-p (Set II) were added to the model, total LOS variance accounted for increased to $R^2 = .402$ [$F = 3.36$, $df = (6, 30)$, $p < .05$] with these three psychiatric measures independently contributed a unique (semi-partial) increment I = .140 [$F = 3.50$, $df = (3, 30)$, $p < .05$.]. Of the three predictors in Set II, only PANSS-g yielded a significant result by the protected t test [$\beta = .46$; $T = 2.42$, $p < .05$]. Finally, the five SANS subscales (Set III) together added I = .163 a nonsignificant contribution perhaps owing to the larger number of variables in this set. Overall, the three sets combined yielded an $R^2 = .565$; $F = 2.95$; $df = (11, 25)$, $p < .025$], with gender, PANSS-g, and the SANS. Attention subscale affording significant ($p < .05$) contributions to LOS outcome variance. A regression model consisting of these three predictors alone yielded $R^2 = .42$ [$F = 7.96$, $df = (3, 33)$, $p < .001$].

Conclusions: Study results suggest the apparent utility of standardized psychiatric evaluation in medical rehab patients, especially in light of the failure of functional independence assessment to predict LOS.

NR521 Wednesday, May 8, 12 noon-2:00 p.m.

Maintenance ECT for Intractable Parkinson's Disease

Steven P. Wengel, M.D., Psychiatry, 600 South 42nd Street, PO Box 985575, Omaha NE 68198–5575; William J. Burke, M.D., William H. Roccaforte, M.D., Ronald Pfeiffer, M.D., Stephen R. Paige, Ph.D.

Summary:

Objective: Subjects with intractable Parkinson's disease without depression or dementia received ECT in two phases to investigate the effects of long-term ECT on motor performance.

Method: The initial treatment phase consisted of twice-weekly treatments, which were continued until treatment effects plateaued or side effects supervened. A maintenance phase followed with ECT given every three to four weeks. Subjects were monitored with twice-monthly neurological examinations, including the Schwab and England, and the Unified Parkinson's Disease Rating Scales. Detailed diaries noting number of 15-minute intervals spent "on," "off," or asleep were kept by subjects' caregivers.

Results: Four subjects consented to participate, although one patient dropped out after two treatments because of emergent psychosis. Motor rating scale scores did not change during the course of the study. Data from subjects' diaries demonstrated a statistically significant decrease in the number of hours spent "off" in the five days following maintenance ECT treatments compared with the subsequent 10 days and the five days prior to maintenance ECT treatments. All subjects reported improved motor function, and two subjects asked to continue ECT after completion of the study.

Conclusion: ECT may be a useful adjunct for patients with Parkinson's disease, although its effects may be short-lived.

NR522 Wednesday, May 8, 12 noon-2:00 p.m.

Differential Retention of Emotional Material in Patients with Schizophrenia

Kirsten Fleming, Ph.D., Psychiatry, UCI, 101 City Drive, Route 88, Orange CA 92668; Jeff Moenter, B.A., Rimal B. Bera, M.D., Dan Carreon, M.D., Steven G. Potkin, M.D.

Summary:

Objective: The goal of this study was to determine how patients with schizophrenia encode emotionally laden material, which may rely on different neuronal networks than recall for neutral stimuli.

Method: 13 DSM-IV diagnosed, neuroleptic-medicated, schizophrenic patients (SC) and 10 normal controls (NC) participated. All subjects were administered three 15-item word lists for three trials each. The words were either positive, negative, or neutral in valence (e.g. laugh, temper, square, respectively) and were matched for concreteness, emotionality, and pleasantness. An immediate and 24-hour delayed recall was assessed.

Results: Overall, the NCs recalled significantly more words than the SCs at both time periods: $F(2, 21) = 11.1$, $p = .003$. Post-hoc analyses showed that at immediate recall SCs recalled more emotional words than neutral words ($p = .08$ for positive; $p = .001$ for negative), whereas the NCs recalled approximately equal number of emotional and neutral words. At the 24-hour delay, the SCs continued to recall more negative words than neutral words ($p = .02$). In contrast, the retention pattern for the NCs changed

in that their recall for emotional words was better than for the neutral stimuli ($p = .05$).

Conclusions: SCs may encode emotionally laden material differently than NCs.

NR523 Wednesday, May 8, 12 noon-2:00 p.m.

Dopamine Receptor Gene Polymorphism in OCD

Humberto Nicolini, Institute of Mexicano PSIQ, Calz Mexico-Xochimilco 101, Mexico DF 14370, Mexico; Beatriz Camarena, B.Sc., Francisco Paez, M.D., Karen Herrera, M.D., Juan Ramon De La Fuente, M.D.

Summary:

We conducted an allelic association study of the dopamine receptor gene polymorphism (DRD4) in obsessive-compulsive disorder (OCD). Sixty-one patients with OCD and 48 controls with no psychiatric diagnosis were genotyped.

OCD patients were subtypified according to different clinical variables. DRD4 alleles were not significantly different in OCD patients subtypified by age of onset, severity, and family history. However, those OCD patients with tics had a significant difference in prevalence and frequency of the DRD4 allele number 7 (R7). Also, there was a significantly higher frequency of the genotype DRD4-44 among OCD patients without tics. This results suggest that tics in OCD distinguish different genetic subtypes of the disorder.

NR524 Wednesday, May 8, 12 noon-2:00 p.m.

Dopaminergic Genes and Personality Disorders

Kenneth Blum, Ph.D., Pharmacology, University of TX Hlth Sci Ctr, 7703 Floyd Curl Drive, San Antonio TX 78284; Nancy L. Schnautz, M.D., Eric R. Braverman, M.D., Daniel Matthews, M.D., L. Fischer, B. Williamson, A. Eisenberg, M. Sherman, J. Seals, John G. Cull, Ph.D., D.E. Comings, W. Walsh, T.H. Chen, R. Wood

Summary:

Objective: To assess polymorphisms of the dopamine D_2 receptor (DRD_2), dopamine transporter (DAT_1), and the dopamine β hydroxylase (DβH) genes with impulsive-aggressive-violent and schizoid/avoidant behaviors in adolescent and adult probands.

Method: Eleven adolescents (ages 12–19) with impulsive-aggressive violent behavior and an abnormal brain electrical activity (> 2.5SD) were genotyped for DRD_2 and DAT_1 polymorphisms. Secondarily, we genotyped 109 schizoid/avoidant probands DRD_2 and DAT_1 and DβH genes and 162 screened controls.

Results: Six of 11 (56%) had DRD_2 A_1 allele, all (100%) had the VENT 10 dAT_1 gene. DRD_2 A_1 allele genotype in 11 subjects compared with "super" controls (1/30 or 3.3%) yielded significant association ($X^2 = 14.9$, df = 1, $p < 0.0006$), DAT_1 10 gene compared with literature controls (34/91 or 37.4%) yielded statistically significant association ($X^2 = 15.6$, df = 1, $p < 0.0006$).

We found the DRD_2 A_1 allele associated with schizoid (12/24 or 50%) and avoidant personality disorders (10/18 or 53.16%) probands (score > 84 on the Millon Clinical Multi-Axial Inventory) as compared with DRD_2 A_2 allele ($X^2 = 9.7$, df = 1, $p < 0.00002$). In schizoid/avoidant subjects DRD_2 A_1 alleles associated when compared with "super" controls ($X^2 = 18.6$, df = 1, $p < 0.00002$). The DAT_1 480 bp (VENT 10 gene repeat) associated with schizoid/avoidant behaviors (16/17 or 94.1%) when compared with controls ($X^2 = 18.4$, df = 1, $p < 0.00002$). The DβH B_1 allele also associated in schizoid/avoidant probands (14/18 or 78%) compared with screened controls ($X^2 = 5.7$, df = 1, $p < 0.02$).

Conclusions: These findings may have relevance in terms of early identification of these tendencies and possible strategic treatment of both adolescent and adult personality disordered probands.

NR525 Wednesday, May 8, 12 noon-2:00 p.m.

Brain Electrophysiological Abnormalities As a Function of the Dopamine D2 Receptor A1 Allele and Comorbid Substance Use Disorder

Kenneth Blum, Ph.D., Pharmacology, University of TX Hlth Sci Ctr, 7703 Floyd Curl Drive, San Antonio TX 78284; Eric R. Braverman, M.D., John G. Cull, Ph.D., B. Brenner, J. Gill, Mark Zedar

Summary:

Objective: To assess contribution of dopamine D_2 receptor allelic variance and comorbid substance use disorder (SUD) to brain electrophysiological abnormalities.

Method: Of the 137 patients in this study, 79 were genotyped for the dopamine D_2 receptor gene allelic variance (DRD_2 A_1 and A_2 alleles) in accord with Blum, *et al.* (1990); were 58 experimental controls. A Nicolett BEAM™ (brain electrical activity mapping) was used to assess: total brain abnormalities, total spectral abnormalities, evoked potentials (EP) (AER, and VER), and P300. Substance use disorders were assessed using *DSM-IV* criteria.

Results: 52% of the experimental subjects carried the DRD_2 A_1 alleles. The percent prevalence is significantly different when compared with our "super normal" controls (DRD_2 A_1) with a prevalence of 4% or one out of 30 [$^2 = 21.6$, df = 1, $p < 0.0000033$]. Weighted linear trend revealed significant worsening effect of event-related potentials in the presence of the DRD_2 A_1 allele and comorbid SUD (11.05). Duncan's Range Test showed SUD with or without DRD_2 A_1 allele significantly worsened the EPs, suggesting the role of both genetics and the environment.

Conclusions: Results suggest the presence of the DRD_2 A_1 allele and comorbid SUD (with or without the A_1 allele) are significant risk factors in subjects possessing an abnormal EP, a finding in agreement with other work showing association of the DRD_2 A_1/A_1 genotype and prolonged P300 latency (Blum, *et al.* 1994).

NR526 Wednesday, May 8, 12 noon-2:00 p.m.

Complex Segregation Analysis of Schizophrenia

Aida P. Ruiz, Psychiatry, University of Chile, Avenida La Paz 1003, Santiago, Chile; Mauricio Arcos, Rafael Blanco, Jaime Santander, M.D., Adriana San Martin

Summary:

Objective: Genetic epidemiologic studies have provided evidence that genetic factors contribute to familial aggregation of schizophrenia. However, the precise mode of inheritance has not been elucidated. Most such studies correspond to reports of Caucasian populations. The present study was performed in Santiago, Chile, whose population stems from the admixture of Amerindians and Spaniards.

Method: The sample consisted of 44 randomly ascertained schizophrenic probands (22 males and 22 females) with ages ranging between 20 and 48. Extended pedigree information was thus obtained. The diagnosis was made according to DSM-III-R criteria. Both probands and relatives were interviewed using a structured interview (CIDI) and the DSM-III-R Checklist. Complex segregation analysis was carried out using the computer program POINTER.

Results: The nontransmission model (Q = H = O) was rejected as was the recessive single locus (H = 0, Z = 1). The multifactorial, the single codominant, the nonmajor locus component, the nonpoligenic component transmission model and the nontransmission of a major effect could not be rejected.

Conclusions: The most likely model that fits the data of the present study is that of a mixed model with a substantial environment component (93.12%). The frequency of the major gene was estimated at 0.000155. Our results are similar to those previously reported in ethically different populations.

NR527 Wednesday, May 8, 12 noon-2:00 p.m.

A Family Study of Dyslexia

Gail A. Edelsohn, M.D., Director Child & Adol Psy, Jefferson Medical College, 1201 Chestnut St Rm 1501, Philadelphia PA 19107–4192; Wade H. Berrettini, M.D., Eric Richardson, Rachel Lashever, B.A., Jodi Langfeld, B.A.

Summary:

Objective: The purpose of this research was to determine whether tests of phonological encoding skills could detect this subtype of dyslexia in multiplex families.

Method: Eight multiplex dyslexia families who responded to advertisements were clinically evaluated with these instruments: Adult Reading History Questionnaire (Pennington), Wilson Language Training Screening Questionnaire, Wilson Nonsense Word Reading (for individuals older than 17 years), Woodcock Reading Mastery Test (Word Attack and Word Identification (for individuals 17 years and younger).

Results: The mean score for adults on the Wilson nonsense reading test was 0.876 +/– .126 while on the regular word reading test was 0.711 +/– .194. The mean grade adjusted score for children on the Word Attack subtest was 0.702 +/– .228 indicating profound deficits in reading nonsense words. The mean score for children on the Word Identification subtest was 0.563 +/– .278. The correlation of adult regular and nonsense reading scores ($r = .808$) was significantly different from that of children ($r = .294$), $c = 2.37$, $p < .02$). The proportion of regular words correctly identified by adults was significantly different from that of nonsense words correctly read by adults $T = 6.982$, $p < .0001$.

Conclusions: The use of nonsense words is an efficient way to detect dyslexia in compensated adults.

NR528 Wednesday, May 8, 12 noon-2:00 p.m.

The Nature of Traumatic Memories Following Adult and Childhood Trauma

Bessel A. van der Kolk, M.D., Trauma Ctr, 227 Babcock Street, Brookline MA 02146; Jennifer Burbridge, M.A., Joji Suzuki, B.A., Rita E. Fisler, Ed.M.

Summary:

Since trauma arises from an inescapable stressful event that overwhelms people's coping mechanisms, it is uncertain to what degree the results of laboratory studies of ordinary events are relevant to the understanding of traumatic memories. Clinical observations suggest that "memories" of trauma tend to, at least initially, be experienced primarily as fragments of the sensory components of the event: as visual images, olfactory or auditory sensations, or intense waves of feelings.

Subjects: 28 recent adult trauma victims (AT) (physical, sexual assaults, accidents) and 34 adults who were physically or sexually assaulted as children (CT).

Instruments: Traumatic Antecedents Questionnaire (self-rating version) (TAQ [S]), Dissociative Experiences Scale, & The Traumatic Memory Inventory (TMI, van der Kolk & Fisler, 1995), a 60-item, structured interview about the retrieval of a traumatic memory and a memory of a significant, but nontraumatic, event.

Results: All subjects, regardless of age at which the first trauma occurred, reported that they initially "remembered" the trauma in the form of somatosensory or emotional flashback experiences; only 20% of the At, and none of the CT, had a narrative memory of when the event first occurred. None had olfactory, visual, auditory, or kinesthetic reliving of nontraumatic events. Currently, most subjects continue to experience their trauma in sensorimotor modes, but most are able to *tell* about what happened to them. AT had significantly more auditory reliving ($x^2 = 5.5$, $df = 1$, $p < .02$).

Conclusions: Traumatic memories, regardless of the age at which the trauma occurs, are initially retrieved in the form of dissociated mental imprints of sensory and affective elements of the traumatic experience. Over time, subjects report the gradual emergence of a personal narrative that can be properly referred to as "explicit memory."

NR529 Wednesday, May 8, 12 noon-2:00 p.m.

Depression As a Predictor of Return-to-Drinking Using Categorical Diagnosis and Symptom Scores

Shelly F. Greenfield, M.D., Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Roger D. Weiss, M.D., Lisa Bello, B.A., Jacqueline Michael, M.S.W., John Kelly, B.A., Larry Muenz, Ph.D.

Summary:

Objective: Using categorical diagnosis and symptom scores we investigated whether depression at the time of entry into treatment for alcohol dependence is a predictor of return-to-drinking.

Method: We recruited 70 subjects who met DSM-III-R criteria for alcohol dependence during inpatient admission. After detoxification we administered the SCID-III-R to diagnose major depression and the Beck Depression Inventory (BDI) to assess symptoms of depression. We used the Time Line Follow Back (TLFB) interview to measure alcohol use each month for one year following discharge. We defined return-to-drinking as at least one drink in any 30-day period of follow-up. Using the Cox-proportional hazard model we analyzed the effect of depression on return-to-drinking during the first seven months of follow-up.

Results: Diagnosis of depression was predictive of return-to-drinking (hazard = 2.04, $p = .03$). High initial BDI scores showed a greater probability of return-to-drinking that did not reach statistical significance (hazard ratio = .174, $p = .084$).

Conclusions: Depression at time of entry into treatment is predictive of return-to-drinking during the first seven months of follow-up. Our data suggest that diagnosis rather than symptom score may be a more useful measurement of initial depression in this population.

NR530 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

P50 and Stimulus Change in Schizophrenia

Nashaat N. Boutros, M.D., Dept of Psych, West Haven VAMC, 950 Campbell Avenue, West Haven CT 06516; Patricia Tueting, Ph.D.

Summary:

Objective: The goal of this study was to examine the differences in brain responses to stimulus change in the early phases of information processing, between patients with chronic schizophrenia and normal volunteers.

Methods: Evoked potentials (EPs) were collected in three EP paradigms designed to study the effects of stimulus change on the amplitude of the P50 EP. Twelve healthy volunteers were compared to 12 age- and sex-matched patients with chronic schizophrenia. Pairs of clicks (S1-S2) identical in pitch and two nonidentical pair conditions (1000/1500 and 1000/500 Hz) were used.

Results: The degree of attenuation of S2 was decreased in the schizophrenia patients when the identical pairs were used ($F = 3.524$, $p = 0.07$). Normal volunteers reacted to change of S2 in the nonidentical pairs with decreased attenuation of S2. In

schizophrenia patients, S2 attenuation was increased with nonidentical pairs. This increased attenuation of S2 occurred whether the high-low ($F = 4.757$, $p < 0.05$) or the low-high ($F = 6.683$, $p < 0.02$) condition was used.

Conclusions: These preliminary data suggest that the two groups react differently to stimulus change. The data also suggest that this difference in response occurs in the early phases of information processing.

NR531 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Treatment Resistance in First-Episode Psychosis

Jane I. Edwards, M.A., EPPIC, Locked Bag 10, Parkville Victoria 3052, Australia; Dana Maude, M.A., Patrick D. McGorry, Ph.D.

Summary:

Objective: Brief Psychiatric Rating Scale (BPRS) data collected in the Aubrey Lewis Unit follow-up sample (n = 130) suggest that approximately 7% of patients with first-episode psychosis experience psychotic symptoms at discharge, three months, and 12 months. Drawing on that information, this paper outlines the issues involved in definition and treatment of early resistance and prescribes the development of two new clinics within the Early Psychosis Prevention and Intervention Centre (EPPIC) targeting the "prolonged recovery" group.

Method: The Treatment Resistant Early Assessment Team (TREAT) identifies early psychosis patients who have not remitted within three months of entering EPPIC and provides a consultancy service to case managers and psychiatrists/psychiatric registrars regarding assessment and treatment options. Systematic Treatment of Persistent Positive Symptoms (STOPP) is a psychological therapy that draws on a number of perspectives—cognitive-behavioral, cognitive, and psychodynamic—with the aim of providing an integrated psychotherapy of the person experiencing persistent symptoms.

Results: Data are presented describing the profile of patients attending each clinic, and research in progress is outlined.

Conclusions: Early identification and specialized treatment of individuals falling in the "treatment resistant" category may assist in alleviating symptoms and have the potential to change the course of the illness.

NR532 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Cognitive Correlates of Specific Types of Communication Disturbances in Schizophrenia

Nancy M. Docherty, Ph.D., Psychiatry, Kent State University, 118 Kent Hall, Kent CT 44242; Ralph E. Hoffman, M.D., Keith A. Hawkins, P.S.D., Jaak Rakfeldt, Ph.D., Donald M. Quinlan, M.D., William H. Sledge, M.D.

Summary:

Objective: This study examined the cognitive underpinnings of different types of schizophrenic communication disturbances.

Method: Speech samples from 48 schizophrenic and 24 bipolar outpatients and 23 nonpsychiatric controls were rated for six types of communication disturbances using the Communication Disturbances Index (CDI). Scores were compared between diagnostic groups, and associations of CDI ratings with performance on tests of working memory, sustained attention, general cognitive functioning, and positive and negative symptoms were examined.

Results: Measures of working memory were associated with four of the six types of communication disturbances in the schizophrenic group, even when general cognitive functioning and severity of illness were statistically controlled for in the comparisons. Weaknesses in sustained attention and prominent negative symptomatology also were related to some types of communication failures in this group. These associations were present only in the schizophrenic group.

Conclusions: Deficits in working memory and sustained attention are factors in some but not all types of schizophrenic communication disturbances. These associations appear to be diagnostically specific.

NR533 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Prepulse Inhibition, Habituation and Communication Disturbances in Schizophrenia

Nancy M. Docherty, Ph.D., Psychiatry, Kent State University, 118 Kent Hall, Kent OH 44242; Anthony Hebert, B.A.

Summary:

Objective: Failures of sensorimotor gating and habituation mechanisms have been hypothesized to underlie cognitive disorganization in schizophrenia. We examined relationships between inhibitory failures of the startle response, communication disturbances, and affective reactivity of communication disturbances in schizophrenia.

Methods: Fifteen schizophrenic outpatients each provided two speech samples: one of affectively negative topics and one on affectively positive topics. These were analyzed using the Communication Disturbances Index (CDI). A language reactivity score was computed for each subject by subtracting CDI ratings in the affectively positive condition from CDI ratings in the affectively negative condition. We also separately measured prepulse inhibition (PPI) and habituation of the eyeblink component of the startle response to repeated acoustic stimuli. We compared CDI ratings and language reactivity scores with levels of PPI and habituation.

Results: PPI was associated with baseline CDI ratings, $r = .54$, $p < .03$, but not with language reactivity scores, $r = -.12$, *ns*. Habituation was not associated with CDI ratings, $r = -.16$, *ns*, but was associated with language reactivity scores, $r = .56$, $p < .03$.

Conclusions: Failures of sensorimotor gating may be related to stable communication disturbances in schizophrenia, and failures of habituation may underlie exacerbations of language symptoms in response to negative affect.

NR534 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Race and Substance Abuse in Schizophrenia

William B. Lawson, M.D., Psychiatry Service 116/NL, N Little Rock VA Med Cent, 2200 Ft Roots Drive, North Little Rock AR 72114

Summary:

Racial differences in substance abuse patterns have been reported in the general population. More than half of schizophrenic patients may be substance abusers, yet racial differences in abuse patterns have not been examined. Such studies may be clinically significant, since black schizophrenics tend to have more symptoms and may be more likely to develop tardive dyskinesia. Drugs such as cocaine are risk factors for worsening symptoms and abnormal involuntary movements.

We studied 109 black and 34 white DSM-IV-positive schizophrenia veterans in a program for patients with concomitant schizophrenia and substance abuse disorders (the PAT program). Black schizophrenic veterans were significantly more likely to be abusers of cocaine but not of other drugs of abuse or alcohol ($p < 0.002$). Whites scored higher on the MAST. No signification differences were seen between black and white schizophrenic substance abusers in age, education, or employment status. Whites showed longer duration of use of hallucinogens and noncocaine stimulants. No racial differences were seen in positive or negative symptoms, degree of depression, number of suicide attempts, or duration of psychiatric or substance abuse hospitalizations. Black

patients were more likely to stay longer in the PAT program. Whites showed a trend to more alcohol-related arrests. Black patients were more likely to have tardive dyskinesia but not acute extrapyramidal reactions.

Previously reported racial differences in schizophrenia may be a consequence of differences in usage of drugs of abuse.

NR535 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Sources of Diagnostic Uncertainty Among Chronically Psychotic Cocaine Abusers

Andrew L. Shaner, M.D., Psychiatry, VA Medical Center, 11301 Wilshire Blvd B151Z, Los Angeles CA 90073; Jody M. Racenstein, M.A., Lisa J. Roberts, M.A., Thad A. Eckman, Ph.D., John W. Tsuang, M.D., Douglas E. Tucker, M.D.

Summary:

Diagnostic uncertainty among psychotic drug abusers is a major obstacle to treatment and research. This study developed and tested a diagnostic algorithm to record uncertainty and specify alternate diagnoses. A total of 165 patients with chronic psychoses and cocaine abuse were evaluated using the SCID, urine toxicology, hospital records, and collateral interviews. The algorithm was applied allowing key SCID items and diagnostic criteria to be designated as provisionally met (or uncertain). For these items, interviewers specified the source of uncertainty and proceeded with SCID items that would be asked in both the "met" and "not met" conditions. In 30 cases (18%), the algorithm produced a definitive diagnosis, including 21 cases of schizophrenia, six of schizoaffective disorder, and three of psychostimulant-induced psychotic disorder. In the other 135 cases, a definitive diagnosis could not be reached because of one or more sources of diagnostic uncertainty, including insufficient abstinence (78%), poor memory (24%), and inconsistent reporting (20%). Thus, it was frequently difficult to distinguish schizophrenia from chronic substance-induced psychoses, despite the use of structured interviews. Clinicians facing such diagnostic dilemmas may conclude prematurely that psychotic symptoms are, or are not, substance induced. Instead, clinicians should initiate concurrent treatment of both psychosis and substance abuse in uncertain cases.

NR536 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Clozapine in Tardive Dyskinesia

George J. Jurjus, M.D., Psychiatry, Cleveland VAMC, 10000 Brecksville Road, Brecksville OH 44141; P. Eric Konicki, M.D., Anand P. Popli, M.D., Ken Y. Kwon, M.D., George E. Jaskiw, M.D.

Summary:

Tardive dyskinesia (TD) is the most serious long-term side effect of antipsychotic drugs. To date there are few effective treatments for it. There have been limited reports that clozapine, an atypical antipsychotic drug, may reduce the severity of pre-existing TD. We tested that hypothesis. We reviewed the medical records of 97 schizophrenic patients treated openly with clozapine at the Cleveland VAMC. These patients (mean age 52) were treated with clinically indicated doses of clozapine (mean daily dose = 410mg) for a mean duration of 14.9 months. Typical antipsychotic drugs were stopped six weeks after starting clozapine.

The Abnormal Involuntary Movement Scale (AIMS) was administered before clozapine treatment and every three months thereafter. Thirteen of the patients had TD at baseline according to the research criteria of Schooler and Kane. Seven patients had total remission of their dyskinetic movements, four showed partial remission, and two failed to improve on clozapine treatment. The reduction in the total AIMS score was highly significant (baseline = 12.9, last assessment = 4.4, $p < 0.0001$). "Area specific" improvements were also significant for all seven areas, greatest for the face ($p < 0.0006$) and least for the neck and shoulders ($p < 0.02$).

Our data suggest that clozapine may suppress pre-existing TD. Further studies are needed to determine whether clozapine has an active therapeutic effect on TD or a passive effect resulting from discontinuation of neuroleptic treatment.

NR537 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neurologic Soft Signs in Schizophrenia

Jeong-Ho Chae, M.D., Psychiatry, Keyo Hospital, CPO Box 8551, Seol 100685, South Korea; In-Ho Paik, M.D., Kyu-Hang Lee, M.D., Chung Kyoon Lee, M.D.

Summary:

Many studies have demonstrated greater frequency of neurologic soft signs (NSS) in patients with schizophrenia than in controls. However, factors associated with chronicity, institutionalization, individual differences, and neuroleptic medication make it difficult to interpret these results. We report on our ongoing study of NSS and their relationship to neuroleptics and institutionalization in schizophrenia. NSS were examined with a standardized instrument, Neurological Evaluation Scale–Korean Version (NES-K) in 11 neuroleptic-naive patients with schizophrenia, 17 neuroleptic-treated patients, and 14 chronically institutionalized patients. Scores of total items ($p = 0.002$), sensory integration ($p = 0.014$), sequencing of complex motor acts ($p = 0.015$), and other ($p = 0.009$) functional areas of NES-K were significantly different among three groups. Posthoc analysis showed that scores of total items ($p = 0.005$) and sensory integration areas ($p = 0.01$) of NES-K were significantly higher in the institutionalized patients than in the neuroleptic-naive group. But scores for motor coordination, sequencing of complex motor act, and others categories were not different in the institutionalized and neuroleptic-naive patients. These findings suggested that neuroleptic treatment or chronic institutionalization might partially affect NSS, especially the sensory integration area, in patients with schizophrenia. However, the NSS of motor coordination and sequencing of complex motor act areas could be biological trait markers of schizophrenia independent of confounding variables.

NR538 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neuroleptic Dosing in Asian and Hispanic Outpatient Schizophrenic Patients

John M. Herrera, Ph.D., Psychiatry, Mount Sinai, c/o 2105 Hill Drive, Grandview WN 98930; John J. Sramek, Pharm.D., Sigfried Ruiz, M.D., Peter Chu, M.D.

Summary:

Recent studies suggest that minorities may have higher plasma levels due to ethnic variations in pharmacokinetics under standard neuroleptic treatment and would be at increased risk for extrapyramidal side effects and more likely to be treatment noncompliant. The study examined the prescribing pattern of antipsychotic medication to Asian and Hispanic schizophrenics in outpatient psychiatric programs developed to meet their treatment needs. A computer search was conducted of registered clients in a Hispanic and Asian outpatient clinic in order to identify all "schizophrenia" diagnosed patients, and for purposes of comparison, a third sample of consecutively drawn "schizophrenia" diagnosed outpatients registered in the clinic proper were selected. All outpatient medical records (n = 152) were secured and select biodemographic, psychiatric history, and neuroleptic-dosing patterns extracted and quantified. Neuroleptic doses were converted to chlorpromizine (CPZ) equivalents and also corrected for body weight to a standard of 68kg. One way analysis of variance (ANOVA) procedures were utilized to compare both the actual and standardized neuroleptic

doses across the three samples, and these analyses revealed a significant main effect for both actual ($p < .05$) and standardized dose ($p < .05$). With regard to the former, secondary analysis yielded significant differences between the General sample compared with the Hispanic ($p < .05$) and Asian ($p < .05$) samples, which did not differ significantly from each other. These results were similar with the standardized dose comparisons. The presentation will review these and related findings and implications for the development of cross-cultural treatment.

NR539 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neuroleptic Dosing in Hispanic and Asian Inpatient Schizophrenic Patients

John M. Herrera, Ph.D., Psychiatry, Mount Sinai, c/o 2105 Hill Drive, Grandview WN 98930; John J. Sramek, Pharm.D., Jasmine Collazo, M.D., Raymond Tam, M.D.

Summary:

The study is the second in a series examining the prescribing of antipsychotic medication to schizophrenics in cross-cultural clinical programs. A computer search identified all "schizophrenia" diagnosed patients treated over a one-year period in an inpatient Hispanic and Asian psychiatric unit. A second computer search was completed in order to identify a sample of Anglo patients from the general inpatient psychiatry services who were matched to the Hispanic and Asian samples (admission date). All medical records ($n = 130$) depicting the inpatient experience were secured for extraction and quantification of select biodemographic, psychiatric history, and neuroleptic-dosing patterns. The medication variables included type of neuroleptic drug used, the maximum dose, the stabilized dose (i.e., neuroleptic dose at discharge), and the dose associated with first report of extrapyramidal symptoms. Neuroleptic doses were converted to chlorpromazine equivalents and also corrected for body weight to a standard of 68 kg. One way analysis of variance (ANOVA) procedures were utilized to compare both actual and standardized neuroleptic CPZ across the three samples, and these statistical comparisons were completed for both maximum and stabilized dose. The analysis with maximum dose revealed a significant main effect for both actual ($p < .05$) and standardized CPZ ($p < .05$). Similar results were also found for stabilized dose with both actual ($p < .05$) and standardized CPZ ($p < .05$). Examination of the direction of mean differences for both medication-dosing variables using both CPZ comparisons revealed that the General sample was prescribed significantly larger doses of antipsychotic medication than either of the two ethnic minority samples. The presentation will review these and related findings and their implications for the development of cross-cultural treatment settings.

NR540 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Predictors of Treatment Response and Outcome in First Episode Schizophrenia

Amy R. Koreen, M.D., Psychiatry, Long Island Jewish, Hillside Division, Glen Oaks NY 11004Jeffrey A. Lieberman, M.D., Jose Alvir, D.P.H.

Summary:

To examine potential clinical and biological predictors of treatment response and outcome in first-episode schizophrenia, analyses of treatment response and outcome and their relationship to baseline clinical and biologic measures were done on 118 acutely ill, first-episode schizophrenics. Baseline clinical and biological assessments were completed and patients entered into standardized treatment. Patients were followed prospectively for up to five years with regular follow-up assessments. Eighty-seven percent of the patients responded by year one, with a median time to treatment response of nine weeks. Predictors of treatment response included gender, mode of onset, duration of illness prior to treatment, and plasma homovanillic acid (pHVA). Thus females, patients with acute onset, and patients with higher pHVA responded more quickly. Diagnosis was predictive at a trend level, with schizoaffectives responding faster. Predictors of outcome also included growth hormone (GH). Higher GH was predictive of a worse relative and absolute outcome. These and other analyses will be presented.

NR541 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Psychosocial Outcome of a First-Episode: Schizophrenia Cohort Followed Up to Five Years

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., Stephen H. Geisler, M.D., Jose Alvir, D.P.H., Margaret Woerner, Ph.D., Jeffrey A. Lieberman, M.D.

Summary:

Objective: To determine five-year psychosocial outcome in first episode schizophrenia.

Method: A cohort of 118 patients admitted for their first episode of psychosis was followed for up to five years. Subjects were evaluated for social adjustment using the Social Adjustment Scale and for symptomatology with the Schedule for Affective Disorders and Schizophrenia and the Scale for Assessment of Negative Symptoms.

Results: Social and leisure functioning at two years demonstrated no impairment in 20%, mild impairment in 37%, moderate in 24%, and severe in 19%. At five years, no impairment in role performance social functioning showed in 27%, mild impairment in 23%, moderate in 27%, and severe in 23%. Role performance at two years showed no impairment in 27%, mild in 18%, moderate in 27%; and severe 28%. At five years, no impairment in role performance was seen in 38%, mild in 27%, moderate in 23%, and severe impairment in 12%. Other data will be available at a future time.

Conclusion: The data demonstrate a high percentage of social and work and role performance impairment. Overall, there since the first psychotic episode appears to be essentially stable to some improved psychosocial functioning. Though the majority incur some impairment, there appears to be a smaller sample that has good, unimpaired social outcome.

NR542 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Prevalence and Severity of Acute Extrapyramidal Side Effects in Patients Treated with Clozapine, Risperidone or Conventional Antipsychotics

Carl H. Miller, M.D., Psychiatry, Insbruck University, An Ic Hstrasse 35, Innsbruck 6020, Austria; Daniel S.G. Umbricht, M.D., Jeffrey A. Lieberman, M.D., Fritz Mohr, M.D., Wolfgang Fleischhacker, M.D.

Summary:

Acute extrapyramidal side effects (EPSE) are a common phenomenon in treatment with conventional antipsychotic drugs. Clozapine has nearly no propensity to cause EPSE. For risperidone, multicenter trials also indicate fewer EPSE.

The ongoing trial compares the prevalence and severity of EPSE in patients treated with clozapine or risperidone or conventional antipsychotic drugs for at least three months. To examine the prevalence of EPSE, the Barnes Akathisia Scale and the modified version of the Simpson Agnus Dyskinesia Scale were used. Additionally, the van Putten Scale and the Mini-Dotes were administered to assess subjective side effects. We have examined 50 patients (19 patients treated with clozapine, nine patients

treated with risperidone, and 22 treated with conventional antipsychotics). The mean age of our patients is 36.14 ± 9.15 years. The mean dose of antipsychotic drugs, calculated in chlorpromazine equivalents (CPZE), is in the clozapine group 836.84mg/d CPZE, in the risperidone group 188.8 mg/d CPZE, and in the group with conventional antipsychotics 535.91 mg/d CPZE. The prevalence of akathisia is 10.5% in the clozapine group, 11.1% in the risperidone group, and 22.7% in the group treated with conventional neuroleptics. The prevalence of rigidity and cogwheeling are 0% in the clozapine group versus 11.1% in the risperidone group. The highest prevalence of rigidity we found in the group with conventional neuroleptics with 31.8%; 18.2% of the group treated with conventional antipsychotics had cogwheelrigidity. Further results will be presented and discussed.

NR543 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Efficacy and Safety of Three Doses of Sertindole Versus Three Doses of Haloperidol in Schizophrenic Patients

Dan L. Zimbroff, M.D., N. Hills Behavioral Med Assoc., 974 West Foothill Blvd., Upland CA 91784–1492; Randall J. Mack, B.S., Joanne Zborowski, B.S.N., David D. Morris, Ph.D., Terri B. Sebree, B.S., Bruce A. Wallin, M.D.

Summary:

Sertindole is a novel antipsychotic with 100-fold greater selectivity for dopamine D_2 receptors within the limbic pathways of the brain over the nigrostriatal pathway. D_2 blockade within the latter is thought responsible for the unwanted extrapyramidal syndrome (EPS) seen with currently available antipsychotics. Discovered and patented by H. Lundbeck (Copenhagen) and under development by Abbott Laboratories in the United States and Canada, sertindole also demonstrates $5HT_2$ and α_1 antagonist activity.

Objective and Method: This landmark Phase III placebo-controlled, double-blind study (M93-113) assessed the dose-response profiles of three doses of sertindole and three doses of haloperidol in 497 schizophrenic patients. Following a single-blind placebo lead-in period, patients were randomly assigned to receive placebo, sertindole 12, 20, or 24 mg/day or haloperidol 4, 8, or 16 mg/day for eight weeks.

Results: All active treatment groups were effective in treating psychosis as demonstrated by significant improvement over placebo for PANSS, BPRS, and CGI scores. The 20 mg sertindole and 8 mg haloperidol groups showed the greatest response. Only sertindole 20 mg was effective in the treatment of negative symptoms as indicated by the PANSS negative symptom subscale and total SANS. Sertindole and placebo were clinically and statistically indistinguishable in EPS profiles. In contrast, all haloperidol doses caused significantly more EPS than either sertindole or placebo.

Conclusion: Sertindole is effective in the treatment of the positive and negative symptoms of schizophrenia without producing EPS.

NR544 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Two Open-Label, Long-Term Safety Studies of Sertindole

David G. Daniel, M.D., Washington Clinical Research, 6404-P Seven Corners Place, Falls Church VA 22044; Peter J. Schmitz, M.S., Jerry A. Staser, B.A., Kathryn L. Holgate, B.S.C., Terri B. Sebree, B.S., Matthew W. Cravets, M.A.

Summary:

Discovered and patented by H. Lundbeck (Copenhagen) and under development by Abbott Laboratories in the United States and Canada, sertindole is a selective antipsychotic with relatively strong affinities for D_2, $5HT_2$, and α_1 receptors. Demonstrating a 100-fold greater selectivity for D_2 receptors within the VTA (limbic) over the SNC (motor) pathway in the brain, sertindole is hypothesized to produce minimal or no extrapyramidal syndrome (EPS). Sertindole also exhibits relatively low affinity for muscarinic and histaminic receptors.

Objective and Method: The long-term safety of sertindole was assessed in two multicenter, open-label studies (M92–795 and M93–061) during which 1070 patients diagnosed with schizophrenia or schizoaffective disease took 4 to 24 mg sertindole once daily for up to two years. Most patients had participated in previous double-blind studies. Assessments included movement rating scales together with adverse event monitoring, routine laboratory tests, and ECGs. Efficacy was assessed using the Clinical Global Impression Scale (CGI).

Results: Patients were maintained for more than one year at sertindole doses ranging from 4 mg/day to 24 mg/day. Improvement in CGI was demonstrated, with the majority of improvement achieved in the first two months. All parameters indicated that sertindole produced minimal EPS, confirmed by lack of use of anti-EPS medications. There was no agranulocytosis or clinically significant elevation in LFTs or prolactin. A total of 191 patients received concomitant valproate, carbamazepine, paroxetine, fluoxetine, or sertraline.

Conclusion: Sertindole, in monotherapy or in combination with a number of psychiatric medications, appears both effective and well-tolerated in the long-term treatment of the manifestations of psychosis without EPS.

NR545 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Brain Imaging to Determine the Effects of Sertindole in Schizophrenic Patients

Steven G. Potkin, M.D., Irvine Med Ctr, UCI Medical Center, 101 City Drive South Route 88, Orange CA 92668–2901; Joanne Zborowski, B.S.N., Joseph C. Wu, M.D., Randall J. Mack, B.S., Terri B. Sebree, B.S., Bruce A. Wallin, M.D.

Summary:

Sertindole, discovered and patented by H. Lundbeck (Copenhagen), and under development by Abbott Laboratories in the United States and Canada, is a new compound with a selective antagonistic activity at D_2, $5HT_2$, and α_1 receptors. Sertindole selectively antagonizes mesolimbic dopamine neurons.

Objective: Study M93-098 was a large, Phase III, double-blind, placebo-controlled, fixed-dose, randomized, eight-week trial of the efficacy and safety of two doses of sertindole (20mg and 24mg) and haloperidol (16mg) in hospitalized schizophrenic patients. Sertindole's effect on specific brain metabolism was also measured.

Method: Brain imaging with positron emission tomography (PET) of 10 patients participating at the UCI Medical Center were obtained during the placebo lead-in phase and at Week 5. 18-F deoxyglucose (FDG) PET scanning was conducted while subjects performed the degraded stimulus version of the Continuous Performance Test (CPT). Analysis of these data was combined with data collected from patients treated with clozapine, placebo, and haloperidol in a similar manner.

Results: Statistically significant decreases were seen in the metabolic activity of the basal ganglia while on sertindole therapy. In contrast, haloperidol increases basal ganglia metabolism and clozapine has no effect. The cortical areas affected by sertindole are associated with attention, working memory, processing of emotional content, and the negative symptoms.

Conclusion: The PET data presented here suggest that brain metabolism of sertindole-treated patients is consistent with a metabolic profile of a psychotic drug with atypical antipsychotic properties and a low incidence of extrapyramidal symptoms.

NR546 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Radioreceptor Binding Profile of Olanzapine

Frank P. Bymaster, M.S., CNS Research, Lilly Research Labs, Lilly Corporate Center, Indianapolis IN 46285; David T. Wong, Ph.D., David L. Nelson, Ph.D., David O. Calligaro, Ph.D.

Summary:

Objective/Method: The interaction with multiple receptors may be involved in the atypical antipsychotic activity of clozapine. Thus, the binding profile of the atypical antipsychotic olanzapine was compared to clozapine and haloperidol using receptor binding assays.

Results: Olanzapine had high affinity for dopamine D_2-type receptors (D_2, D_3, D_4) and clozapine had high affinity for D_4. Olanzapine had moderate affinity for D_1 receptors and, similar to clozapine, lower affinity for D_5 receptors. Haloperidol had high affinity for D_2-type receptors, but lower affinity for D_1-type receptors. Olanzapine, like clozapine, had high affinity for serotonin $(5HT)_{2A, 2B, and 2C}$ receptors; whereas haloperidol had low affinity for $5HT_2$ receptors. Olanzapine and clozapine had high affinity for muscarinic receptor subtypes, particularly m_1. Clozapine had high affinity for α_1- and α_2-adrenergic receptors, but olanzapine and haloperidol had high affinity for histamine H_1 receptors. In addition, olanzapine and clozapine had high affinity for histamine H_1 receptors. The binding profile of olanzapine was comparable in human, rat tissue, and clonal cell lines.

Conclusions: We conclude that olanzapine has a broad binding profile quite similar to that of clozapine and distinctly different from that of haloperidol. The interaction with multiple receptors subtypes probably contributes to its clozapine-like antipsychotic activity.

NR547 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Course of Primary and Secondary Negative Symptoms in a Controlled Trial with Olanzapine

Gary D. Tollefson, M.D., Clinical Invest & Regula, Eli Lilly Co Lilly Corp C, Drop Code 0538, Indianapolis IN 46285; Todd Sanger, Ph.D., Charles M. Beasley, Jr., M.D.

Summary:

Schizophrenia includes multiple psychological domains e.g., "negative" symptoms. Distinguishing between primary (disease-specific) and secondary negative symptoms is a challenging, but important question. These analyses explored whether primary negative symptoms are enduring or, alternatively, appear so due to the therapeutic limitations of conventional neuroleptics. It was double-blind, placebo- and comparator-controlled trial of subjects 18 to 65 years old with DSM-III-R schizophrenia. Initial BPRS was ℓ 24 (scale of 0 to 6). The acute six-week trial randomized 335 subjects to: placebo, olanzapine (5, 10, or 15 [$\pm$ 2.5] mg daily), or haloperidol (15 $\pm$ 5 mg daily). A total of 139 subjects completed the acute phase. LOCF analyses of mean baseline to endpoint SANS change indicated OLZ-low and OLZ-high treatment groups were significantly superior to placebo; OLZ-H was also superior to the HAL treatment group. Analyses of the Simpson-Angus and Barnes Akathisia Scales demonstrated both OLZ and PLCBO endpoint scores had improved. Conversely HAL-treated subjects had a significant score worsening. A path analysis, after controlling for baseline status and favorable changes in secondary negative symptoms with OLZ, revealed OLZ-H exhibited a statistically significant reduction in primary negative symptoms. These differences occurred in the context of comparable OLZ and HAL positive symptom change. Conventional drugs, the by-product of D-2 receptor screening programs, may possess pharmacologic limitations. OLZ has a unique pharmacology exhibiting 5-HT2:D2 ratio ℓ 1, D4, D3, D1, 5HT-6, and muscarinic affinity, blockade of NMDA receptor antagonist effects, etc. This may explain its superior performance.

In summary, this trial demonstrated that both primary and secondary negative symptoms were significantly improved by OLZ relative to haloperidol or placebo.

NR548 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Childhood-Onset Schizophrenia: A Double-Blind Clozapine Trial

Sanjiv Kumra, M.D., Child Psychiatry, Mental Health, Bldg. 10, Rm 6N240, 10 Center, Bethesda MD 20892; Leslie K. Jacobsen, M.D., Judith L. Rapoport, M.D.

Summary:

The first double-blind controlled trial of an atypical neuroleptic in children and adolescents has just been completed at the NIMH. Clozapine is an atypical neuroleptic that has superior efficacy for severely ill, treatment-refractory, adult patients with schizophrenia. In this study, the authors examined the efficacy and safety of clozapine for children and adolescents with the onset of psychosis by age 12. Twenty-one patients with a DSM-III-R-defined diagnosis of schizophrenia, who were nonresponders to at least two different neuroleptics (age 14.0 +/– 2.3 years, male 11, female 10) participated in this double-blind, parallel-group comparison of clozapine and haloperidol. The outcome was assessed by weekly standardized behavioral ratings.

We found a marked therapeutic response favoring clozapine treatment. Clozapine was superior to haloperidol on all measures of psychosis (p values from 0.04 to 0.002). Both positive and negative symptoms improved. However, toxicity, particularly seizures and neutropenia, were major concerns. In summary, the judicious use of clozapine for severely ill schizophrenic children and adolescents who are nonresponders to typical agents is warranted. Due to possibly increased toxicity of this drug in pediatric populations, patients must be carefully monitored for adverse effects.

NR549 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Gamma Aminobutyric Acid and the Pathophysiology of Schizophrenia: A Neurodevelopmental Perspective

Daniel P. Van Kammen, M.D., 7180 Highland Drive, Pittsburgh PA 13206–1297; Frederick Petty, M.D., Mary E. Kelley, M.S., Gerald L. Kramer, B.A., Jeffrey K. Yao, Ph.D., John A. Gurklis, Jr., M.D.

Summary:

Objective: Recent autopsy studies indicate that gamma-aminobutyric acid (GABA) function is decreased in brain areas that involve the well-described structural changes observed with CT and MRI in schizophrenia. These structural brain changes have been reported to be associated with negative symptoms, poor premorbid functioning (i.e., a putative neurodevelopmental disorder), and with decreased dopamine and serotonin turnover.

Methods: In 52 drug-free, physically healthy male patients with schizophrenia (DSM-III-R, age range 23–49 years) plasma GABA, brain CT scans, CSF monoamine metabolites, and clinical assessments were obtained. Plasma GABA was also obtained in 14 healthy male control subjects.

Results: Lower plasma GABA levels were independently associated with larger ventricle brain ratios, lateral prefrontal atrophy, lower CSF HVA and 5HIAA, more affective flattening, and poor premorbid school functioning, accounting for 48%–50% of the variance. The plasma GABA levels of the drug-free schizophrenic patients were not significantly different from the normal controls.

Conclusions: Although several reports have indicated that these measures are inter-related, their relationships with plasma GABA

were independent of each other. The presence of these relationships without a difference in GABA levels from controls suggests changes in neuronal circuits that include GABA neurons. Our data support the hypothesis that GABA is involved in the pathophysiology of schizophrenia, consistent with a putative neurodevelopmental etiology.

NR550 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Spontaneous Dyskinesia and Psychiatric Disorders

Wayne S. Fenton, M.D., Research, Chestnut Lodge, 500 West Montgomery Avenue, Rockville MD 20850; Crystal R. Blyler, Ph.D., Richard Jed Wyatt, M.D., Thomas H. McGlashan, M.D.

Summary:

Objective: Abnormal involuntary movements resembling tardive dyskinesia have been described among patients with schizophrenia never exposed to neuroleptic medications. To examine the specificity of spontaneous dyskinesia we compared the prevalence of abnormal movements in patients with schizophrenia to patients with other psychiatric disorders treated in the preneuroleptic era.

Method: Extensive case records of patients from the Chestnut Lodge Follow-up Study who had never received neuroleptic medications were screened, and descriptions of abnormal movements recorded verbatim for blind rating. The prevalence of abnormal movements in six body areas was compared among 97 patients with a research diagnosis of schizophrenia and 119 patients with other diagnoses.

Results: Patients with and without schizophrenia were comparable in age and duration of illness at index admission (mean year 1954). Abnormal oral/facial, eye, and upper extremity movements were significantly ($p < .01$) more prevalent among patients with schizophrenia. The records of 14% of patients with schizophrenia, but 3% of patients with other disorders, documented oral/facial dyskinesia with sufficient detail to consider their presence nearly certain ($p = .001$).

Conclusions: These data suggest that spontaneous oral/facial and upper extremity dyskinesias are relatively specific to schizophrenia and may be intrinsic to the pathophysiology of the disorder.

NR551 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

MRI of Brain Iron in Tardive Dyskinesia

George Bartzokis, M.D., Psychiatry, UCLA, 300 UCLA Medical Plaza Ste2200, Los Angeles CA 90024; Keith Nuechterlein, M.D., Stephen R. Marder, M.D., Mace Beckson, M.D., Jim Mintz, Ph.D., Kenneth Dery, B.A.

Summary:

A pilot MRI study (Bartzokis et al., 1990) and postmortem data indicate that increased caudate iron levels may be involved in the pathophysiology of tardive dyskinesia (TD). Forty-seven male schizophrenic subjects (DSM-III-R diagnosis) and 28 matched normal control subjects participated in the study. The patients were evaluated with the Abnormal Involuntary Movement Scale (AIMS) and TD was diagnosed using the Schooler and Kane (1982) criteria. Basal ganglia T_2 relaxation time was evaluated with a 1.5 Tesla instrument using a Carr Purcell Meiboom Gill dual spin-echo sequence (TR = 2500, TE = 20, 90) with two signals averaged, 3 mm slice thickness. Because of skewness, a logarithmic transformation of age and medication exposure was performed.

Analysis of covariance, controlling for age, showed caudate T_2 to be a significant discriminator among the three groups (no-TD, TD, and normal controls; $F = 5.2$, $df = 2, 71$, $p = .008$). The TD group had the shortest caudate T_2 (age-adjusted mean: 66.9 ms), the no-TD group had the longest (68.5 ms), and the normal control group had an intermediate caudate T_2 (67.7 ms), confirming pilot study results.

A logistic regression model that included three variables showed two of the variables to be significant independent predictors of TD [caudate T_2 (= .03) and medication exposure ($p = .05$)], while age was found to have no additional independent predictive value. Although T_2 values estimated with a single high-field instrument have limited specificity for tissue iron (Bartzokis & Marder, 1995), the data support the hypothesis that basal ganglia iron levels may be involved in the pathophysiology of TD.

NR552 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Performance on the Stroop Color Naming Test and Signal Detection Accuracy During Auditory P300 Paradigms in Schizophrenic Patients

Edward L. Merrin, M.D., VAMC 116N, 4150 Clement Street, San Francisco CA 94121; Monica Quesada, B.A., Thomas C. Floyd, M.A., Raymond F. Deicken, M.D., Sophia Vinogradov, M.D.

Summary:

Objective: Novel nontarget stimuli elicit P300s with different latencies and topography than do targets. Novel stimuli also impair target detection accuracy, more so in schizophrenics than controls. Wisconsin Card Sort Test performance and clinical ratings were correlated with P300 amplitude but not with effects of novels on detection accuracy. We hypothesized that the Stroop Color Name Test, a measure of selective attention, would predict vulnerability to this performance decay in schizophrenics.

Method: Thirteen medicated DSM-IV schizophrenics (11 men, two women, aged 43 ± 5) responded with finger lifts to targets during oddball and novel paradigms. Neuropsychological tests, including the Stroop, were also administered. Relationships between the Stroop score and rates of false positive and negative responses were assessed by repeated measure MANCOVA.

Results: Lower Stroop scores were associated with higher error rates (main effect; $F(1, 11) = 6.38$, $p = .028$), increased errors in the novel paradigm (paradigm x stroop interaction; $F(1,11) = 5.83$, $p = .034$), and longer reaction times in the novel paradigm ($r = -.69$, $p = .01$). However, they were not correlated with physical characteristics of P300s.

Conclusion: The Stroop may be a direct measure of the cognitive demands of P300 paradigms and is sensitive to behavioral deficits in schizophrenic patients. However, the systems responsible for this function are apparently not involved in P300 generation.

NR553 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Concurrent Use of Clozapine and Sodium Valproate in the Maintenance Therapy of Chronic Schizo-Affective Patients: A Retrospective Analysis

Michael J. Reinstein, M.D., Psychiatry, University Hospital, 116 North Kedzie, Chicago IL 60615; Kathleen D. Colombo, R.N., Lynn Jones, R.N., Sangarapillai C. Mohan, M.D.

Summary:

Objective: The relative maintenance efficacy of clozapine and sodium valproate cotherapy were compared with clozapine monotherapy in a population of chronic schizoaffective patients in order to determine the best pharmacological regimen to reduce hospital recidivism for psychiatric stabilization purposes.

Method: 114 patients between the ages of 23–77 diagnosed as schizoaffective according to DSM-IV criteria were identified at a long-term care facility that was judged to provide a consistently high level of clinical care. A retrospective time-samples design was used to determine individual responses to medication regimens. Main outcome measures were hospital recidivism rates

and hospital days per year on each medication regimen. Facility and doctor's office records and hospital charts were reviewed for each patient to determine medication regimens and number of hospitalizations/hospital days required for psychiatric stabilization purposes/per medication regimen. Analysis of variance was conducted between the various pharmacological regimens.

Results: Initial results of this study suggest that concurrent clozapine/sodium valproate maintenance therapy is more effective than clozapine monotherapy in reducing hospital recidivism rates for psychiatric stabilization purposes in this population of chronic schizoaffective patients.

Conclusion: Concurrent use of clozapine and sodium valproate may be of benefit in the maintenance therapy of chronic schizoaffective patients.

NR554 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Relationship Between Neuropsychological Performance and Psychopathology in Schizophrenia

Myung A. Lee, M.D., Psychiatry, SUNY at Buffalo, 462 Grider Street, Buffalo NY 14215; Herbert Y. Meltzer, M.D.

Summary:

Objective: The relationship between psychopathology and cognitive deficit in schizophrenia (SCH) has not been clearly deliberated. Therefore, we examined this relationship.

Methods: 193 patients meeting DSM~III~R criteria for schizophrenia or schizoaffective disorder were administered (after at least five days of a drug-free period), neuropsychological tests, including measures of attention (Digit Symbol Test (WAIS~R), Consonant Trigram], verbal fluency [Controlled Word Association, Category Instance Generation], recall memory [Verbal List Learning (VLL) ~ Immediate Recall (VLL~IR) and Delayed Recall (VLL~DR)], and executive function [Wisconsin Card Sorting Test (WCST), Wechsler Intelligence Scale for Children~Revised (WISC~R) Mazel, and psychopathology ratings based on the Scale for the Assessment of Positive Symptoms (SAPS) and Negative Symptoms (SANS). Spearman rho correlations were calculated and $p \leq 0.005$ was chosen as the basis for statistical significance.

Results: The SANS total global score was significantly negatively correlated with WCST-category (rho = ~0.30), Controlled Word Association (rho = ~0.26), Category Instance Generation (rho = ~0.30), Digit Symbol Test (rho = ~0.25) and VLL~IR (rho = ~0.36) and DR (rho = ~0.32), and positively with WCST~perseverative error (rho = 0.21). Among the subscales of SANS, Affective Flattening, Alogia, and Attention, but not Anhedonia and Avolition were significantly correlated with neuropsychological performance. The SAPS total global score was also significantly negatively correlated with neuropsychological performance. The SAPS total global score was also significantly negatively correlated with WCST~category (rho = ~0.26), WISC~R (rho = ~0.29), and Digit Sympbol Test (rho = ~0.23), and positively with WCST~perseverative error (rho = 0.22).

Conclusion: These results suggest that both negative and positive symptoms of SCH are related to neuropsychological performance. The results also suggest a diffuse brain dysfunction that gives rise to both psychopathology and cognitive deficit in SCH.

NR555 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Empirical Evaluation of Alternative Models of Schizophrenic Symptoms

Leonard White, Ph.D., Clinical Neuroscience Ctr, Pilgrim Psychiatric Center, Box A, Building 23-5, W. Brentwood NY 11717; Lewis A. Opler, M.D., Jean-Pierre Lindenmayer, M.D., Morris Bell, Ph.D., Professor Sonia Dollfus, Carol Cayton, M.D.

Summary:

The Positive and Negative and Syndrome Scale (PANSS) was conceptualized as a method for evaluating three syndromes of schizophrenic symptoms. The scale also provided for the derivation of five subscales containing items comparable to those of the Brief Psychiatric Rating Scale. Based upon exploratory factor analysis of the PANSS, four-, five-, and six-factor models of schizophrenic symptom structure have been proposed. This study used confirmatory factor analysis to determine which of 12 alternative factorial models of the PANSS provided the best fit for symptoms of schizophrenia. A large (N = 1233) and diverse sample was obtained by pooling data across five centers. Test of the equality of the correlation matrices of 30 PANSS items across centers found uniformly high fit indices (CFI = > .955), indicating equivalence across samples. All 12 models evaluated failed to meet criteria for a good fit to the data. The best fitting alternative was the modified five-factor model of Lindenmayer et al. (1995) (Robust CFI = .831). Since the lack of fit was not attributable to either poor reliability, small sample size, or low variance, we conclude that modifications in the PANSS are required if the scale is to be used to generate an adequate structural model for the symptoms of schizophrenia.

NR556 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Longitudinal Course of the Offspring of Schizophrenics: Neurological and Cognitive Functioning in the First Seven Years

Stephen L. Buka, Sc.D., Mat Child Health, Harvard Public Health, 677 Huntington Avenue, Boston MA 02115; Jill Goldstein, Ph.D., Larry J. Seidman, Ph.D., William S. Kremen, Ph.D., Daniel Koren, M.A., Lisa R. Denny, B.A., Ming T. Tsuang, M.D.

Summary:

We are completing a prospective study of a prenatal cohort to investigate the interactive effects of a genetic predisposition to schizophrenia and PPCs on the lifetime development of offspring. The study sample was drawn from the National Collaborative Perinatal Project and includes 17,741 pregnancies followed prospectively with systematic assessments of mental, motor, sensory, and physical development through age seven.

We present preliminary data on the neurological and cognitive function of 78 offspring of psychotic parents and 140 offspring of matched normal control parents. Chi-square and t-tests were calculated to determine whether measures of neurologic abnormality and attention at age seven were elevated among the high-risk offspring. Compared to control offspring, high-risk offspring have an approximately 1.6 greater rate of neurologic abnormality (n.s.); and statistically higher rates of abnormal scores on the Bender Gestalt Test (relative risk = 1.9) and the Tactile Finger Recognition Test (relative risk = 2.4). Behavior ratings and results of intelligence testing indicate significantly more attentional problems among the high-risk offspring (relative risk = 1.8; $p < .05$).

Results provide preliminary support for the hypothesis that a genetic predisposition to schizophrenia places one at higher risk for neurologic and attentional deficits by age seven. Implications and plans for adult follow-up of this cohort are discussed.

NR557 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Sex and Negative Symptom Dimension in Relatives of Schizophrenic Probands

Farooq Amin, M.D., Psychiatry, Houston VAMC, 2002 Holcombe Blvd. RM 6C-316, Houston TX 77030; Jeremy M. Silverman, Ph.D., Christopher Smith, M.A., Dianna Densmore, M.S., Larry J. Siever, M.D.

Summary:

Objective: Male schizophrenic patients frequently manifest more severe negative symptoms than female patients, raising the possibility that a sex-related mechanism might be involved in the expression of these symptoms. However, the assessment of negative symptoms can be confounded by various artifacts such as withdrawal in response to severe psychotic symptoms, side effects of neuroleptic medications, demoralization, and socioeconomic deprivation, etc. Since male schizophrenic patients are generally believed to have an earlier onset of illness with a less favorable response to antipsychotic treatment, it is conceivable that the observed greater severity of negative symptoms in males might be due to these confounding factors. To clarify this issue we examined the milder continuum of the negative dimension of schizophrenic symptoms in the first-degree relatives of schizophrenic probands, a population that is characterized by attenuated symptoms of schizophrenia, especially the negative dimension of symptoms.

Method: As part of a family study, Positive and Negative Syndrome Scale (PANSS) assessments were done in 53 nonpsychotic, first-degree relatives of schizophrenic probands. All relatives were physically healthy as determined by a medical history, physical examination, and routine lab tests. Axis I psychotic disorders had been excluded by using a face-to-face structured interview supplemented by an interview with an informant for each relative.

Results: Male relatives scored significantly higher on PANSS negative subscale compared with females, while there was no sex difference in the severity of PANSS positive or general subscales. Furthermore, male relatives scored significantly higher than females on Chapman Physical Anhedonia and Chapman Social Anhedonia scales, which are independently derived measures of negative schizophrenic dimension. On the other hand, males and females did not differ on Chapman Perceptual Aberration scale, which is an independently derived measure of positive schizophrenic dimension.

Conclusions: Our results are consistent with the accumulating evidence that the negative dimension of schizophrenic symptoms is manifested more severely in males than in females.

NR558 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Is Diurnal Variation in Plasma HVA Due to Its Renal Excretion?

Farooq Amin, M.D., Psychiatry, Houston VAMC, 2002 Holcombe Blvd. RM 6C-316, Houston TX 77030; Adriana E. Stroe, M.D., Aqeel Hashmi, M.D., Dianna Densmore, M.S., Thomas Kahn, M.D., Peter Knott, Ph.D.

Summary:

Background: A pattern of diurnal variation in plasma concentrations of homovanillic acid (HVA), a major dopamine (DA) metabolite, is well documented with a peak during early morning and a trough during early afternoon. Although generally believed to be related to changes in brain DA metabolism, this diurnal variation can also be explained by changes in renal excretion. Since cardiac output and renal plasma flow may be a major determinant of the renal excretion of organic anions such as HVA, it is plausible that the nocturnal rise in plasma HVA may be due to a decrease in organic anion excretion. If diurnal variation in HVA is due to renal mechanisms, a similar variation would also be observed for plasma 5-hydroxyindolacetic acid (5-HIAA), a serotonin metabolite, that is handled by the kidney in a similar manner to HVA.

Methods: To investigate this we examined simultaneously measured plasma concentrations of HVA and 5-HIAA in two groups of normal subjects. Blood samples were collected at 9:00 am, 11:00 am, 12:30 pm, and 20:00 pm in study-1 (n = 8), and at 9:30 am, 10:00 am, and 10:30 am in study-2 (n = 18). All subjects were physically healthy and free of major psychiatric disorders. Before each study subjects observed a low monoamine diet for 72 hours, fasted overnight for 14 hours, avoided smoking and strenuous activity in the morning, and reported to the medical centers at 8:15 am.

Results: Repeated Measures ANOVA suggested a statistically significant decline in plasma HVA concentrations over time in study-1 ($F = 14.52$, $df = 3, 21$, $p < 0.0005$) as well as in study-2 ($F = 18.31$, $df = 2, 34$, $p < 0.0005$). On the other hand, plasma 5-HIAA did not significantly change over time in either study-1 ($F = 0.66$, $df = 3, 21$, p = NS) or study-2 ($F = 1.36$, $df = 2, 34$, p = NS). Furthermore, plasma MHPG (methoxy-hydroxy-phenyl-glycol), which is an indicator of noradrenergic metabolism that contributes most of plasma HVA derived from periphery, did not change over time in either of these two studies.

Conclusions: Our data suggest that the diurnal variation in plasma HVA is neither due to renal mechanisms nor to variations in noradrenergic metabolism. The results are consistent with the view that the diurnal variation in plasma HVA is related to brain DA metabolism.

NR559 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Quality of Life in Schizophrenic Patients Treated with Risperidone

Jose L. Ayuso-Gutierrez, M.D., Clinical R & D, Janssen Research, Avenida De Europa, 19, Alcobendas, Madrid 28100, Spain; Demetrio Barcia, M.D., Maria L. Herraiz, M.D., Antonio F. Fernandez, M.D.

Summary:

A total of 980 schizophrenic patients according to ICD-10 criteria were included in an open-label, post-marketing surveillance study to evaluate quality of life, safety, and efficacy of risperidone during a six-month period. The doses ranged from 0.5 mg/day up to a maximum of 12 mg/day (average dose at the endpoint was 5.4 mg/day). Psychopathology was evaluated by the Brief Psychiatric Rating Scale (BPRS) and the Clinical Global Impression Scale (CGI). Quality-of-life assessments included the Quality of Life Scale (QLS, Heinrichs *et al.*) and the Global Assessment of Functioning (GAF). Safety was evaluated by spontaneous reports and the UKU subscale for neurological side effects. Twenty-four patients were excluded from the statistical analysis due to protocol violation. A total of 167 patients dropped out due to inefficacy (n = 50), lost for follow-up (n = 40), side effects (n = 38), and other reasons (n = 39). Risperidone produced a significant reduction in the mean scores of the scales used to assess clinical efficacy (BPRS and CGI) and a significant increase in the scales used to evaluate quality of life and impairment (QLS and GAF) in the assessments after one, three, and six months of treatment. The reduced severity of EPS was reflected in the number of patients who needed antiparkinsonian drugs: 415 at baseline and 84 at the end of the six-month period.

Overall, risperidone was well tolerated. Treatment had to be stopped because of adverse events in only 4% of patients. The most common adverse events reported were insomnia (3.7%), sexual dysfunction (3.1%), anxiety (2.5%), and weight gain (1.9%). The safety and efficacy findings of this open study are consistent with those of previous controlled trials with risperidone (Marder *et al.*). The improvement observed in the quality-of-life and impairment scales (QLS and GAF) shows that the efficacy and safety profile of risperidone is also backed by an improvement in the patients' quality of life.

NR560 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Dose Reduction in Schizophrenia

Scott Badgett, M.A., Psychiatry, Bronx VAMC, 130 Kingsbridge Road, Bronx NY 10468; Robert J. Hitzemann, Ph.D., Gail Burr,

R.N., Kathy Piscani, R.N., Ede Frecska, M.D., Jack Hirschowitz, M.D.

Summary:

Objective: This study explored the relationships between dose reduction and clinical status in 28 very chronic schizophrenic patients who were on high doses of antipsychotic drugs (> 20 mg haloperidol).

Method: Subjects were inpatients at V.A. and affiliated hospitals in the New York City area. At baseline, subjects were stabilized on 20 mg/day of haloperidol. In a double-blind fashion, doses were reduced, increased, and unchanged for roughly 1/2, 1/4, and 1/4 of patients, respectively. We report here on changes in positive, negative, and general symptoms as measured by the PANSS and extrapyramidal side effects as measured by the Modified Simpson Dyskinesia Scale after stabilization on adjusted doses and up to six-month follow-up.

Results: The main finding was a strong correlation between dose reduction and symptom reduction ($r = 0.58$, $df = 28$, $p = 0.001$), indicating that patients whose doses were reduced were more likely to show improvement in positive symptoms. A number of patients were lost to follow-up for various reasons, including exacerbation of symptoms. Of those who were followed for six months ($n = 15$), the significant relationship between lower dose and symptom reduction was maintained ($r = 0.60$, $df = 15$, $p = 0.03$).

Conclusion: Many patients who had been maintained on high doses of haloperidol had clear improvement when their doses were reduced on average by 10 mg/day. These findings suggest that many chronic schizophrenic patients who are on high doses of maintenance medication may improve clinically with dose reduction, especially in terms of positive symptoms, and maintain that improvement over time.

NR561 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Quality of Life in Schizophrenic Outpatients

Julio Bobes, M.D., Psiquiatria, Oviedo University, Julia Claveria 6, Oviedo 33006, Spain; Maria P. Gonzalez, Ph.D., Manuel Bousono-Garcia, M.D., Laura A. Munoz, Micaela G-Quiros, M.D., David Wallace

Summary:

Objective: This study is being done to assess quality of life in chronic schizophrenic outpatients and the relationships between global satisfaction with life and psychopathology, disability, and satisfaction in each life domain.

Method: Subjects were a group of chronic schizophrenic outpatients (ICD-10 criteria) from Asturias, Spain currently undergoing neuroleptic maintenance treatment. All patients are being assessed for clinical factors using PANSS, disability using DAS (Disability Assessment Scale, WHO), and quality of life using Lehman's Interview. Spearman correlation coefficient, multiple linear regression, and multidimensional scaling are being employed for statistical analysis.

Results: The results obtained up to now ($n = 59$) show that the level of global satisfaction is lower than the level of satisfaction in each life domain. Daily living activities (.73, p .001) and health (.66, p.001) appear to correlate the highest with global satisfaction, and psychopathology (PANSS + −.39, p .01; PANSS- −.42, p .001) and legal aspects (.32, p .01) the lowest.

Conclusions: Global satisfaction appears to be a more complex construct than the sum satisfaction obtained when we add single life domains together. The impact of psychopathology on global satisfaction is low in our study. Daily living activities and health are the major domains for global satisfaction, whereas work is of little influence.

NR562 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Length of Psychiatric Hospitalization in Veterans With or Without Service Connected Pensions

Benedict J. Connolly, M.A., Psychiatry, FD Roosevelt VA Hospital, PO Box 100, Montrose NY 10548; Cecile E. Sison, Ph.D., Robert G. Stern, M.D., Edward R. Allan, M.D., Miklos F. Losonczy, M.D., Deborah A. Widmer, M.A.

Summary:

Objectives: This study examined the relationship between length of stay (LOS) of hospitalized veterans with major psychiatric disorders (excluding primary substance abuse or dependence) and their service connected (SC) disability percentage awarded by the Veteran Administration.

Methods: Data on 6921 admissions to a VA hospital between 1985–1995 were analyzed. Admissions were grouped into four categories, nonservice-connected ($n = 1781$),0% ($n = 601$), 10–90% ($n = 754$) and 100% ($n = 3783$) service-connected. Mean LOS was compared between the groups.

Results: Preliminary results indicate that higher SC disability percentages were associated with significantly shorter periods of hospitalization (nonservice-connected: 228 days; 0 SC: mean = 219 days, 10–90 SC: 90 days; 100 SC 157 days; $F = 11.74$, $p = .000$). The difference between the NSC and all other-SC groups was significant ($t = 3.66$; $p = .000$). Data will also be analyzed by diagnostic group.

Conclusions: Services and benefits provided to veterans with 10%–100% service-connected disabilities appear to significantly reduce the LOS. It is conceivable that providing similar services and benefits to all patients with major psychiatric disorders might reduce length of hospitalizations and overall cost of care.

NR563 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Cigarette Smoking and Psychiatric Illness: A VA Outpatient Survey

Gregory W. Dalack, M.D., Mntl Hlth Clinic, Ann Arbor VAMC, 2215 Fuller Rd, Ann Arbor MI 48105; Lisa M. Becks, B.A., Elisabeth Abrams, Michael Castine, Cynthia Pomerleau, Ph.D., James H. Meador-Woodruff, M.D.

Summary:

Objective: To understand the relationship among cigarette smoking, psychiatric illness, and drug use among VA mental health clinic outpatients.

Methods: We have developed a smoking questionnaire to administer in a psychiatric outpatient setting. This instrument collects information about individual smoking history, family history of smoking, current smoking behavior, and attempts to quit, as well as data about caffeine use and other drug use. We are in the process of linking these data to diagnostic data obtained from SCID interview of these patients.

Results: Preliminary data collected from a convenience sample of 36 schizophrenic patients (mean age ± SD: 38 ± 6.5 years) in outpatient treatment at the mental health clinic of the Ann Arbor VAMC indicate an elevated prevalence of smoking (92%). Currrent smokers smoke about 1.5 packs per day (30.4 ± 14.8 cpd) and have a high level of addiction (Fagerstrom Test for Nicotine Dependence [FTND] score of 6.6 ± 1.9). A number of these patients have never tried to quit. "Ex-smokers" (6% of total sample) differed from current smokers in important ways. They retrospectively reported that they began smoking later, smoked fewer cigarettes per day, and were less addicted (FTND 1.5 ± 0.7). Data from a smaller sample of patients with bipolar disorder indicate a lower prevalence of current smoking (40%) with lower level of addiction (FTND 5.8 ± 3.4) and later age of starting smoking compared with current smokers with schizophrenia.

Conclusions: These data suggest that smoking history and smoking behavior differ between current and former smokers with schizophrenia and between smokers with schizophrenia and smokers with other chronic psychiatric conditions. This information will be extended to describe the relationship among smoking and other drug use in these patients and may guide plans to provide smoking cessation treatment tailored to a dual diagnosis population.

Supported by Department of Veterans Affairs Research Advisory Group Award

NR564 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Nicotine Withdrawal and Psychiatric Symptoms in Smokers with Schizophrenia

Gregory W. Dalack, M.D., Mntl Hlth Clinic, Ann Arbor VAMC, 2215 Fuller Rd, Ann Arbor MI 48105; Lisa M. Becks, B.A., Elizabeth M. Hill, Ph.D., Ovide Pomerleau, Ph.D., James H. Meador-Woodruff, M.D.

Summary:

Objective: To better understand the nature of the relationship between cigarette smoking and schizophrenia, we are testing the hypothesis that acute nicotine withdrawal exacerbates psychiatric symptoms and treatment-related side effects in smokers with schizophrenia.

Methods: We are measuring withdrawal symptoms, psychiatric symptoms, nicotine blood levels, and medication side effects in well-characterized, psychiatrically stable, nicotine-addicted VA outpatients with chronic schizophrenia under the following closely monitored inpatient conditions: *ad libitum* smoking over one day (no blind) followed by (in a randomized, cross-over design) acute smoking abstinence (over three days) while wearing placebo 24-hour transdermal nicotine patch (double-blind), or acute smoking abstinence (over three days) wearing 21 mg/day, 24-hour transdermal nicotine patch (double-blind) with a return to four days of *ad libitum* smoking between the two patch conditions.

Results: Among the first 11 subjects, preliminary results indicate that in both patch conditions, subjects are acutely abstaining (per daily nicotine blood levels and CO measurements). In the placebo condition, clinically significant decreases in heart rate suggest that they are experiencing withdrawal. Further analysis will assess the relationships among withdrawal symptoms, psychiatric symptoms (BPRS, SANS, HAM-D), and treatment-related side effects (Parkinson-like, and tardive dyskinesia) by patch condition and day of withdrawal.

Conclusions: Understanding whether nicotine withdrawal modulates symptoms in schizophrenia is important in defining the shared neurobiology of the two conditions and in enhancing efforts to help smokers with schizophrenia quit smoking.

Supported by Department of Veterans Affairs Research Advisory Group Award

NR565 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Rapid Dose Escalating Safety, Tolerability and Pharmacokinetic Study of Sertindole

Jerome F. Costa, M.D., Irials Medical, California Clinical, 8500 Wilshire Blvd. 7th Floor, Beverly Hills CA 90211; Neal R. Cutler, M.D., Randall J. Mack, B.S., John J. Sramek, Pharm. D., Terri B. Sebree, B.S., Janet M. O'Neil, B.S.

Summary:

The novel antipsychotic sertindole, discovered and patented by H. Lundbeck (Copenhagen) and under development by Abbott Laboratories in the United States and Canada, has demonstrated efficacy in psychosis without extrapyramidal syndrome. This has been attributed to its 100-fold greater selectivity for limbic D_2 receptors compared to nigrostriatal D_2 receptors. Sertindole also demonstrates nanomolar affinities for $5HT_2$ and α_1 adrenergic receptors.

Objective: Prior trials have involved titration of sertindole with the dose increases of 4 mg every third day. This study evaluated the safety, tolerability, and pharmacokinetics of two untested rapid-dose escalations.

Method: Sixteen schizophrenic patients entered a four-day, single-blind, placebo wash-out period in two consecutive groups. All patients then received open-label sertindole in 4 mg dose increments either every other day for Group 1 (n = 8), up to a maximum of 24 mg, maintained for five days. Adverse events, ECGs, routine laboratory tests, and plasma sertindole analyses were recorded.

Results: The most frequent adverse events were tachycardia upon orthostatic challenge and nasal congestion. The incidence of these was greater in Group II. No clinically significant laboratory abnormalities were detected in either group.

Conclusion: Titration of sertindole in 4 mg increments every other day was well tolerated, allowing for a reduced overall titration period.

NR566 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Reduction of Hospital Days in Sertindole-Treated Patients: One-Year Findings

Azmi A. Nabulsi, M.D., 42J AP6C, Abbott Laboratories, 110 Abbott Park Road, Abbott Park IL 60085; Randall J. Mack, B.S., Terri B. Sebree, B.S., Laura F. Copeland, M.S., Kathryn L. Holgate, B.S.C., Bruce A. Wallin, M.D.

Summary:

Sertindole, discovered and patented by H. Lundbeck (Copenhagen) and under development in the United States and Canada by Abbott Laboratories, is a novel antipsychotic for the treatment of the manifestations of psychosis.

Objective: Any new therapy for schizophrenia must demonstrate cost-effectiveness by a reduction in the number and length of hospital readmissions. This retrospective analysis assessed the impact of sertindole on the number of hospital days during a one-year period.

Method: Data were derived from a Phase II, open-label, multicenter, long-term safety study of sertindole; supplemented by review of medical charts. Analysis included 35 sertindole-treated patients (sertindole group) and 40 "usual care" patients (comparison group). Hospital days for each group were calculated during the 12 months prior to the patients initiation into the double-blind period (period 1) and the 12 months following the transition from the double-blind period to open-label (period 2).

Results: The two groups were similar for demographics, clinical characteristics, and period 1 hospital days. Both groups had fewer hospital days during period 2 than period 1. However, the number of hospital days in period 2, excluding the initial brief study-required dosing schedule, was significantly lower in the sertindole group (4.3) than in the comparison group (18.4).

Conclusion: Sertindole is cost-effective in the treatment of schizophrenia as demonstrated by a reduction in the number of hospital days during one year of treatment compared with the previous year and with a similar group of patients receiving usual care.

NR567 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Co-Occurrence of Vulnerability Markers in Relatives of Schizophrenic Patients

Rosemary Toomey, Ph.D., Psychiatry 116A, Harvard Medical School, Brockton VAMC 940 Belmont St, Brockton MA 02401; Stephen V. Faraone, Ph.D., Larry J. Seidman, Ph.D., William

S. Kremen, Ph.D., Michael J. Lyons, Ph.D., Ming T. Tsuang, M.D.

Summary:

Objective: Previously, we identified three neuropsychological functions as risk indicators of the schizophrenia genotype in a sample in progress. Currently, we report on the co-occurrence of these indicators in the complete sample.

Method: The sample includes 54 first-degree relatives of schizophrenic patients identified through the Brockton/West Roxbury Veteran's Affairs Medical Center and 72 normal controls. The groups do not differ significantly on age, parental education, sex, handedness, and ethnicity. The controls have significantly more education than the relatives, but both groups display comparable reading ability. All subjects were administered tests measuring the neuropsychological functions of abstraction, verbal memory, and auditory attention.

Results: The relatives display significantly lower mean scores than controls on tasks within each function and display significantly greater variance in abstraction and auditory attention. Within the relative group, there are significant intercorrelations among these three functions. The significant correlations among relatives between attention and verbal memory and between attention and abstraction differed significantly from these correlations among controls.

Conclusions: The greater level of co-occurrence between these neuropsychological risk indicators within the relative group provides further support for their status as risk indicators. The use of multiple risk of indicators may enable improved identification of vulnerable relatives.

NR568 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neuropsychological Measures of Prefrontal Dysfunction in Schizophrenia

Larry J. Seidman, Ph.D., Psychiatry, MA Mental Health Center, 74 Fenwood Road, Boston MA 02115; Marlene Oscar-Berman, Ph.D., Anthony G. Kalinowski, Ph.D., Olu Ajilore, B.S., William S. Kremen, Ph.D., Stephen V. Faraone, Ph.D., Ming T. Tsuang, M.D.

Summary:

Objective: Abnormalities of prefrontal brain systems in schizophrenia were evaluated using experimental and clinical measures sensitive to prefrontal damage.

Method: Eighteen schizophrenics and 14 controls were given "comparative neuropsychological" tests, which have been linked primarily to either ventral (orbitofrontal) or dorsolateral prefrontal dysfunctions in neurological patients and in animals with discrete frontal lesions.

Results: Schizophrenics were significantly impaired on object alternation (OA) and delayed alternation (DA) tasks, but not on classical delayed response (DR). The prominence of OA impairments supports the hypothesis that orbitofrontal dysfunction exists in some schizophrenic patients. However, strong convergent validation for this hypothesis was not obtained from another measure of orbitofrontal dysfunction in patients, olfactory identification ($r = .26$). Although the schizophrenics performed well on the classical DR task (which is sensitive to dorsolateral damage in monkeys), their DR performance correlated significantly with sustained attention, especially at longer delays.

Conclusions: Together, these corroborate findings linking neuropsychological dysfunction to frontal system damage in schizophrenia. Future research is needed to interpret the contributions of attention, interference, and memory load to neuropsychological performance in schizophrenia and to determine whether the frontal deficits reflect diffuse brain damage, circumscribed prefrontal damage, or damage in other brain regions having prefrontal connections.

NR569 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Symptom Instability and Fluphenazine Decanoate

Anthony G. Kalinowski, Ph.D., Psychiatry, Harvard Medical School, 74 Fenwood, Boston MA 02115; Mohammed Y. Alam, M.D., Jayendra K. Patel, M.D., Joseph J. Schildkraut, M.D., Alan I. Green, M.D.

Summary:

Introduction: Anecdotal reports suggest that some psychotic patiens maintained on fluphenazine decanoate have increasing symptoms shortly before each injection. In this study, we evaluated this phenomenon and assessed the clinical and biochemical factors associated with such symptom changes.

Method: 21 patients with schizophrenia or schizoaffective disorder were rated with the Brief Psychiatric Rating Scale (BPRS) longitudinally over three injection cycles. On the last day of two subsequent injection cycles, patients were given a challenge test of the growth hormone (GH) response to 0.75 mg apomorphine (SC) or the prolactin (PRL) response to 2 mg of haloperidol (IM).

Results: Focusing on shifts in total BPRS that exceeded measurement error, 12 of the 21 subjects ("unstable") showed symptom instability that did not conform to the predicted symptom increase before each injection, but instead indicated long-term instability relatively unaffected by the timing of injections. The other nine subjects had stable symptoms over the observation period. Unstable patients had a higher mean BPRS ($p = 0.04$), more frequent hospitalizations ($p = 0.03$), and tended to receive more medication ($p = 0.08$). The GH response to apomorphine was significantly greater ($p = 0.03$), and the PRL response to haloperidol showed a trend toward significant increase ($p = 0.1$) in the stable group.

Conclusions: The data show that patients with a stable course on prolixin decanoate also have lower scores on BPRS, require less neuroleptic, and have fewer hospitalizations than patients whose symptoms are unstable. Challenge data suggest that the stable patients are more responsive to both apomorphine and haloperidol than are unstable patients. The implications of the data will be discussed.

NR570 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Orienting Response and Instrumental Functioning in Schizophrenia and Mania

David B. Schnur, M.D., Psychiatry, Elmhurst Hospital, 79-01 Broadway, Elmhurst NY 11373; Jamie L. Weinstein, M.S.W., Scott P. Smith, M.A., Faisal Siddiqui, M.D., Phone M. Win, M.D., Adam Smith, Ph.D.

Summary:

Objective: This study examines the relationship between orienting response (OR) frequency and instrumental functioning in schizophrenic and manic patients. The OR is manifested by autonomic activity that is dependent on limited capacity information processing.

Method: Subjects underwent psychophysiological assessments while inpatients. Reactivity of the skin conductance response (SCR) and the finger pulse amplitude response (FPAR) OR components to neutral tones and to an attentional task comprising targeted and nontargeted tones was assessed. We have shown previously that OR reactivity under these conditions is similar in schizophrenic and manic patients. Instrumental functioning was evaluated after discharge to the community using the Level of Functioning scale (LOF).

Results: Preliminary analyses in 13 schizophrenic and even manic patients indicate the following significant negative relations between autonomic reactivity and LOF items (Spearman Rho ℓ −.5; $p \leq .05$): SCR to neutral tones and Overall Level of Functioning; SCR to targeted tones and Quality of Social Relations, and Fullness of Life; and SCR to nontargeted tones and Fullness of Life.

Conclusions: Heightened autonomic activity during acute schizophrenic and manic episodes may be associated with poorer functioning after discharge. These findings will be discussed in the context of the OR as a vulnerability indicator in psychotic disorders.

NR571 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Associated Psychiatric Syndromes in Schizophrenia

Paul C. Bermanzohn, M.D., Psychiatry, Hillside Hospital, 87-80 Merrick Blvd, Jamaica NY 11432; Samuel G. Siris, M.D., Linda Porto, M.S.N.

Summary:

Symptoms of a variety of psychiatric conditions have been described in the course of schizophrenia, but diagnostic conventions have generally steered attention away from these clinical features. However, since the classical diagnostic subcategories of schizophrenia have typically been of negligible value for treatment selection and contributed little to prognosis, the authors directed specific attention to selected associated syndromal manifestations in a lifetime diagnostic assessment of a cohort of chronic schizophrenic and schizoaffective patients in day treatment to ascertain their prevalence and significance.

Data were analyzed for 37 patients with a diagnosis of schizophrenia or schizoaffective disorder, by DSM-IV criteria, interviewed with a Structured Clinical Interview for Diagnosis (SCID) instrument for DSM-IV, which was modified not to have "skip outs" for other syndromes. Fifty-one percent (N = 19) of these patients were found to have significant obsessive-compulsive (O/C) symptoms, 49% (N = 18) had depressive syndromes, 32% (N = 12) had panic attacks, and 22% (N = 18) met criteria for full panic disorder. Rates of treatment refractiveness for patients with major depression, panic disorder, and OCD were 50%, 62%, and 63%, respectively. Patterns of intertwining of APS with psychosis were noted, including psychotic elaborations of O/C and panic symptoms.

Thus, the occurrence of APS in this population of chronic patients was found to be substantial, warranting continued exploration of its potential relevance to treatment outcomes, functional impairments, and chronicity, as well as comparisons of its pathophysiology with the noted primary psychiatric syndromes.

NR572 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

A Profile of Obsessive-Compulsive Symptoms in Schizophrenia

Linda Porto, M.S.N., Research QDC, Hillside Hospital, PO Box 38, Glen Oaks NY 11004; Paul C. Bermanzohn, M.D., Samuel G. Siris, M.D.

Summary:

Objective: Obsessive-compulsive (OC) symptoms and the schizophrenias often present as intertwined phenomena whose relationship remains poorly understood. The purpose of this research is to provide a detailed phenomenological description of OC symptoms in schizophrenia.

Method: Fifty chronic schizophrenia patients from a comprehensive New York outpatient treatment program were interviewed to make lifetime diagnoses of schizophrenia or schizoaffective disorder and for obsessive-compulsive disorder (OCD) using the Structured Clinical Interview for DSM-IV and the Yale-Brown Obsessive-Compulsive Scale symptom checklist.

Results: Forty-six percent (n = 23) evidenced clinically significant OC symptoms and 26% (n = 13) met criteria for OCD. Three distinct groups emerged: (1) patients whose OCD was unrelated to their psychotic symptoms; (2) patients whose OCD was related to, but not restricted to, psychotic symptoms; and (3) patients whose OCD existed on a continuum with their psychosis. The last group tended to incorporate their OC symptoms into delusional beliefs during the active phase of illness and shift to OCD during full or partial remissions.

Conclusions: These findings support previous clinical constructs that OCD and schizophrenia are not always dichotomous disorders, but may be interconnected. Illustrative cases will be presented.

NR573 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Sex Differences in Neuropsychological Function in Nonpsychotic Relatives of Schizophrenic Probands

William S. Kremen, Ph.D., Psychiatry, NAPA State Hospital, 2100 NAPA-Vallejo Hwy, Napa CA 94558; Jill Goldstein, Ph.D., Larry J. Seidman, Ph.D., Rosemary Toomey, Ph.D., Michael J. Lyons, Ph.D., Ming T. Tsuang, M.D., Stephen V. Faraone, Ph.D.

Summary:

Objective: Male schizophrenia patients may have more neuropsychological deficits than females. This study addressed the issue of sex differences in biological relatives of schizophrenia patients.

Method: Neuropsychological functioning of 54 nonpsychotic relatives of schizophrenia patients and 73 demographically similar normal volunteers was evaluated with a comprehensive neuropsychological battery. Tests were grouped into composite neuropsychological functions, which were tested with multivariate analysis of variance. Atypical sex differences were defined by the presence of Group × Sex interactions.

Results: There were significant Group × Sex interactions for verbal memory and motor function, and trends toward significant interactions for auditory attention and mental control/encoding. With the exception of motor function, female relatives were impaired, whereas male relatives showed little difference from male controls. Findings were not accounted for by psychopathology in the relatives or diagnostic subtype of the proband.

Conclusion: The authors previously identified verbal memory and auditory attention as neuropsychological vulnerability indicators for schizophrenia. The findings suggest that among nonpsychotic relatives, women may primarily account for deficits in these functions. Although speculative, genetically at-risk women might have a higher threshold than men for developing schizophrenia. That is, they may be able to sustain greater impairment than men before developing psychotic symptoms.

NR574 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Hypofrontality in Schizophrenia: Assessment During Metabolic and Cognitive Challenge

Igor Elman, M.D., ETB DIRP, NIMH, Bldg. 10, Rm 4N212, MSC 1380, Bethesda MD 20892; Neil I. Weissenfeld, B.S., Caleb M. Adler, M.D., Christopher Bir, B.S., Kayleen Hadd, M.S.N., David Pickar, M.D., Alan F. Breier, M.D.

Summary:

Objective: One of the more consistent functional brain imaging findings in schizophrenia is hypofrontality, i.e. failure to activate prefrontal regions during cognitive challenges. The interpretation of this phenomenon is, however, problematic because it is unclear

if decreased cerebral perfusion results from a primary cortical lesion or is secondary to unrelated factors as motivational and attentional deficits. To resolve this issue we examine cortical perfusion during two different challenges, one metabolic, which is free of performance confound, and one cognitive.

Method: We examined regional cerebral blood flow (CBF) using 0-15/PET in schizophrenics and age- and gender-matched healthy volunteers. The metabolic stressor was IV administration of 2-deoxyglucose (2-DG), a compound inducing a mild hypoglycemic-like state. The cognitive challenge was a verbal fluency task, which tests higher order information processing and executive function. Absolute and normalized PET data were analyzed by region of interest and pixel by pixel analysis.

Results: In 17 healthy volunteers there was significant prefrontal activation. Preliminary results from two schizophrenics suggest decrements in cortical CBF. A complete analysis including a comparable sample size of schizophrenics will be presented.

Conclusion: These data indicate that the differential cortical challenge paradigm may resolve the controversy regarding hypofrontality in schizophrenia.

NR575 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Expression of Serotonin Transporter in Schizophrenia

Boris P. Sokolov, Psychiatry, Mt. Sinai Med School, One Gustave Levy Place, New York NY 10029; Ivan A. Hernandez, M.S., Varham Haroutunian, Ph.D., Kenneth L. Davis, M.D.

Summary:

Objective: The aim of this study is to determine whether schizophrenia involves an abnormal expression of the serotonin transporter (SERT) mRNA. Significant evidence indicates that dysfunction in the serotonergic system and, in particular, abnormalities in SERT, may be involved in the pathophysiology of schizophrenia. SERT terminates the synaptic action of 5-HT and recycles it into the neurotransmitter pool. It is a site of action for several drugs with CNS effects, including both therapeutic agents and drugs of abuse. Abnormalities in SERT protein density have been observed in schizophrenia.

Method: We developed a highly sensitive RT-PCR assay and analyzed expression of SERT mRNA in left superior temporal gyrus, left middle temporal gyrus and left superior frontal gyrus (Brodmann's areas 22, 21 and 9 respectively) of brains from schizophrenics and controls.

Results: Preliminary analysis of tissue samples from 15 schizophrenics and five controls indicated a decrease of SERT mRNA in schizophrenia.

Conclusions: These results are supported by our earlier finding of decreased levels of 5-hydroxyindoleacetic acid and decreased citalopram binding efficiency (increased Kd) to the 5-HT reuptake site in cognitively impaired schizophrenics. Currently, we are completing analysis of SERT mRNA in brain specimens derived from 22 schizophrenics and eight controls.

NR576 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Serial Changes of P300 and Plasma Catecholamine Metabolites in the Course of 8 Weeks Pharmacological Treatment of Schizophrenia

Shin-Ichi Niwa, M.D., Neurology, Fukushima Medical College, 1 Hikarigaoka, Fukushima City 960-12, Japan; Satoshi Takeuchi, M.D.

Summary:

Serial changes in P300, p-HVA and p-MHPG were observed in the course of eight weeks of pharmacological treatment of 16 DSM-III-R schizophrenic subjects. The following results were obtained; 1) Clinical state, as measured by PANSS, was significantly improved after eight weeks treatment. 2) P300 amplitudes in the eight weeks did not show a consistent change across subjects and remained smaller compared with healthy controls. 3) Augmentation of P300 at one week after treatment predicted better clinical improvement after eight weeks. 4) Changes in P300 amplitudes significantly correlated with percent changes in p-MHPG, but not with p-HVA. 5) P300 amplitudes after eight weeks of treatment showed a significant negative correlation with p-HVA after eight weeks. Based upon these results, the followings are suggested: 1) Both noradrenergic and dopaminergic transmission correlate with P300 reduction, but in a different way, in schizophrenia. 2) Modifiable component of P300 reduction seems to be regulated by noradrenergic transmission. 3) Dopaminergic dysfunction in combination with factors other than catecholaminergic dysfunction may be involved in stubborn component of P300 reduction.

NR577 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Mini Mental State Examination Score Fluctuation in Chronic Psychiatric Inpatients

Cheryl K. Cantrell, M.D., Psychiatry, Delaware State Hospital, 1901 N. Dupont Highway, New Castle DE 19720; Eric S. Cole, Ph.D.

Summary:

Objective: While the Folstein Mini Mental State Examination (MMSE) is widely used to screen patients for cognitive impairment, longitudinal research assessing score variability over time in psychiatric populations is lacking. This investigation examines longitudinal MMSE score fluctuation among subgroups of chronic psychiatric inpatients.

Method: The MMSE was administered 15 times over 41 months to 41 chronic inpatients (average length of stay 15 years). Mean MMSE scores, ranges, and standard deviations were computed and statistically compared across diagnostic categories, using the two sample t-test assuming unequal variances.

Results: Patients with Axis I psychoses (+/– complicating dementia or mental retardation), (N = 31), when compared with patients without Axis I psychoses (N = 10), showed significantly higher ranges (mean 11.8 vs. mean 7.9, $p = 0.019$) and standard deviations (mean 3.37 vs. mean 2.32, $p = 0.017$) of MMSE scores over time. The mean MMSE scores for the two groups were not significantly different (22.8/30 vs. 20.3/30, $p = 0.28$).

Conclusion: Longitudinal MMSE administration shows considerable score fluctuation, with significantly more pronounced fluctuation in patients with Axis I psychoses. We hypothesize that the state of the psychotic illness has a considerable influence on MMSE score.

NR578 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Informed Consent: Assessment of Comprehension

Donna Ames, M.D., West LA VAMC B151H Bldg 210, Los Angeles CA 90073; William C. Wirshing, M.D., Stephen R. Marder, M.D., Alix B. Strough, B.S., Doreen Ross, Danielle Goldstein, B.A., Robert E. Benveniste, Joanna Pashdag, Sun S. Hwang, M.S., Peggy J. Bowman

Summary:

Objective: To design and evaluate a stereotyped and rigorous informed consent procedure that maximizes the comprehension and learning of critical aspects of experimental treatment protocols involving subjects with schizophrenia.

Methods: 49 schizophrenia patients were screened for participation in several ongoing clinical research trials. The protocols' consent forms were read and explained. Subjects were then asked

a series of standardized questions relating to critical aspects (i.e., procedures, risks, benefits, and alternatives to participation) of each protocol. Incorrect responses resulted in targeted re-education. This question, response, and education procedure was reiterated until the patient answered 100% of the questions correctly. Subjects were tested again seven days later.

Results: Patients' median scores on the first trial were 80% correct; 53% of patients required a second trial to be 100% correct, and 37% of patients required three or more trials. Scores improved between the first trial and day 7 ($X^2 = 9.8$ $p = 0.02$). A total of 96% felt that they were adequately informed; 66% claimed they were participating for personal benefits or altruistic reasons, whereas 34% claimed they were participating in the study at the suggestion of others.

Conclusions: Schizophrenia research subjects appear to be able to understand and retain the critical components of informed consent.

NR579 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Efficacy and Safety of Two Fixed Doses of Ziprasidone in Schizophrenia

Karen R. Reeves, M.D., Clinical Research, Pfizer Central, Eastern Point Road, Groton CT 06340

Summary:

Ziprasidone's high affinity for $5HT_{2A}$ receptors and moderate affinity for D_2 receptors suggest significant antipsychotic efficacy with low extrapyramidal side-effect liability. This 6-week, double-blind, placebo-controlled multicenter study was designed to compare the safety, toleration and efficacy of two fixed-dose regimens of ziprasidone in subjects with an acute exacerbation of schizophrenia or schizo-affective disorder. After a 3 to 7-day placebo washout, patients were randomized to receive either ziprasidone 40 mg bid on days 1 to 41 (106 patients); ziprasidone 40 mg bid on days 1 to 2, followed by 80 mg bid on days 3 to 41 (104 patients); or placebo (92 patients). On day 42, subjects received a single morning dose. Both the 80 mg and 160 mg dose groups demonstrated statistically significant changes from baseline in BPRSd total, BPRSd core items, CGI severity and PANSS total scores. All differences were statistically significant. Measurement of negative symptoms by the PANSS negative subscale also showed statistically significant differences between both ziprasidone groups and placebo. Side-effects were limited in both the 80 mg and 160 mg groups. This indicates that ziprasidone at doses of 80 mg and 160 mg daily is an effective and well-tolerated antipsychotic.

Last visit change in Primary Efficacy Scores (All Subjects, Last Observation Carried Forward)

Ziprasidone 40 mg bid	Ziprasidone 80 mg bid		Placebo	
BPRSd-total	-7.7*	-10.3**	-3.4	*$p<0.05$
BPRSd-core	-3.4*	-4.4**	-2.0	**$p<0.001$
CGI-severity	-0.5*	-0.8**	-0.2	
PANSS-total	-12.4*	-17.1**	-5.4	
PANSS-negative subsc	-3.2*	-3.9**	-0.9	

The author thanks the Ziprasidone Study Group for participation in this study.

NR580 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Psychosocial Rehabilitation Affects Positive and Negative Symptoms of Chronic Schizophrenics

Mario Guazzelli, M.D., Psychiatry, University of Pisa, Via Rome 67, Pisa 56100, Italy; Antonio Ciapparelli, M.D., Alessio Dani, M.D., Loretta Giuntoli, Ph.D., Stefano Marchetti, M.D., Laura Palagini, M.D., Alberto Parrini, M.D., Pietro Pietrini, M.D., Simonetta Starnini, M.D.

Summary:

Objective: To investigate the relationship between response to rehabilitation and clinical course of positive and negative symptoms in schizophrenia during the first three years of a psychosocial rehabilitation program in a residential community.

Methods: Fourteen schizophrenics (DSM-IV criteria; age 29 ± 5, and illness duration 12 ± 5 yrs) under continuous neuroleptic treatment were studied at admission [T0], six months [T1], one [T2], two [T3], and three yrs [T4] by using SAPS, SANS, and COTES (Comprehensive Occupational Therapy Evaluation Scale). Patients with COTES total score reduction at T4 vs. T0 > 40% were considered responders. Mann-Whitney U and Friedmann tests were used for analysis.

Results: At T0 responders (seven patients) and no-responders (seven patients) did not differ on demographic and clinical variables or on neuroleptic treatment dosage. Responders showed significant decrease from baseline on COTES since T1 ($p < .01$), on SAPS item Bizarre Behavior at T3 and T4 ($p < .05$) and on SANS items Avolition since T2 ($p < .05$) and Anhedonia at T4 ($p < .05$). In no-responders COTES significantly decreased at T3 and at T4 ($p < .05$), whereas no significant changes were found on SAPS and SANS during the entire study. As compared with no-responders, responders showed significant lower values on COTES since T2; on SAPS items Bizarre Behavior (2.9 ± .7 vs. 4.1 ± 1.1, $p < .05$) and Formal Thought Disorders (2.6 ± .5 vs. 4.3 ± 1, $p < .01$) at T4 and on SANS item Avolition at T3 (3.6 ± .8, $p < .05$) and T4 (3 ± .6 vs. 4.3 ± 1, $p < .05$).

Conclusions: To date, response to rehabilitation was seen in half of the patients and preceded improvement on positive and negative symptoms. Follow-up evaluations will clarify if no-responders require longer periods of time to benefit from this rehabilitation program.

NR581 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Symptoms in Chronic Schizophrenic: The Oldest Old

Cynthia Blum, M.A., B-23 CNC, Pilgrim Psych Ctr, Box A, West Brentwood NY 11717; Philip D. Harvey, Ph.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

Research addressing aging and symptomatology in chronic psychiatric disorders has compared schizophrenia in late life and the symptomatology of degenerative dementia. Schizophrenic patients can be discriminated from patients with cortical dementia on the basis of reduced rate of cognitive decline and reduced memory impairments. These studies of patients with average age 70 leave open the issue of continued decline and more profound deterioration in even later life. This study compared 18 schizophrenic and eight affective patients with 20 demented patients over age 90 (range = 91–104, mean = 93.5) on measures of cognitive functioning (the CERAD Dementia Battery), psychiatric symptoms, and individual difference variables. Affective patients had a later age of onset than schizophrenics ($t [24] = 3.50$, $p < .001$). MMSE scores of demented patients were lower than the schizophrenics (3.4 vs 10.5, $t(36 = 2.78$, $p < .01$) as were scores on naming, praxis, verbal learning, and delayed recall (all $t > 2.01$, all $p < .05$). Median CDR score of the two samples was 2.0, similar to that previously reported on patients 20 years younger. Profound cognitive impairment in chronic psychiatric patients may stop declining at some point, in contrast to cortical dementia, where all cognitive functions decline continuously to the 0 point, unless death intervenes.

NR582 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Family Burden of Chronic Psychotic Patients: An Italian Multicenter Study

Gabriella Belelli, University of Bologna, Institute of Psychiatry, Viale Pepolis, Bologna 60100, Italy; Mirella Ruggeri, M.D., Diana De Ronchi, M.D., Prof. Vittoris Volterra

Summary:

Objective: To evaluate practical and emotional family burden relating to chronic psychotic patients in some Italian community-based psychiatric services (CPSs), which put into practice the principles of the Psychiatric Reform Law.

Method: The study has been conducted at four CPSs in Northern Italy on all patients of the catchment areas who: a) fulfilled the DSM-III-R criteria for a diagnosis of schizophrenia, delusional, or schizoaffective disorder; b) had been treated for at least 10 years by these services; c) had not been institutionalized for most of the time during the preceding three years; d) had a key relative in touch with both patient and service. Patients were assessed by the *Brief Psychiatric Rating Scale* and the *Global Assessment of Functioning Scale* and key-relatives by the *Social Behavior Assessment Scale.*

Results: Seventy-nine pairs have been assessed. Patients' impairment was higher in social functioning than in psychopathology. Relatives experienced a considerable amount of distress as a consequence of some patients' behaviors (specifically offensive behavior, heavy drinking, misery, self-neglect) and disabilities (specifically in sexual relationship, support, affection, decision making, everyday conversation, spare-time activities). They had many problems in the areas of leisure time, social life, physical and emotional health; such problems were frequently judged a consequence of the patient's presence in the family and caused high levels of distress. The relatives judged their link with the CPSs close and a source of great psychological relief, but not so efficient in terms of practical help.

Conclusions: These data obtained in four Italian CPSs indicate that chronic psychotic patients may not have high levels of psychopathology; nevertheless, their behavior and disability may cause high practical and emotional burden in their families. The CPSs included in this study provide considerable psychological relief to relatives and continuity of care; still, these data indicate that strategies aimed at relieving practical family burden should be sharpened.

NR583 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Tardive Dyskinesia in Older Outpatients

Lawrence A. Labbate, M.D., Psychiatry, Walter Reed Army, Bldg 6, Washington DC 20307; R. Gregory Lande, D.O., Franklin D. Jones, M.D.

Summary:

Objective: To determine the incidence and severity of tardive dyskinesia (TD) in older outpatients treated with antipsychotics (AP) after age 35.

Method: The records of 43 current patients (31 women; 25 schizophrenia, 12 bipolar, six major depression; mean age 67 ± 10, current age > 45) who began continuous neuroleptics after age 35 were examined. Annual AIMS evaluations were available for the last eight years. Clinical diagnoses of TD (AIMS ℓ 1) and TD (Kane) proposed by Schooler and Kane (AIMS score = 2 in two body areas) were examined. TD (Kane) was compared with diagnosis, age, AP years, sex, and anticholinergic and lithium use.

Results: Patients began AP at age 46 ± 10 (range 35–80) and were taking them 18 ± 10 years (range 2–35). All patients were retired military or dependents. All were married or widowed. Current MMSE average was 28.6 (range 11–30). Mean chlorpromazine equivalent dose was 380 mg/d ± 316. Seven (16%) had history of alcohol dependence. Five (11%) had current diagnosis of dementia. Twenty-eight (65%) were given the clinical diagnosis of TD and 18 (42%) met TD (Kane) criteria. Three cases were of moderate severity (AIMS > 10, no subscore > 3) and the rest were mild (AIMS < 10, no subscore > 2). TD (Kane) was associated with age ($t = 2.3$, $p = .03$) and years on AP ($t = 2.3$, $p = .009$). Diagnosis was not associated with TD (Kane) ($X^2 = 2.97$, DF = 2, $p = .23$). TD (Kane) was not associated with exposure to lithium for more than one year, use of anticholinergic agents, sex, AP dose, or dose X years (p = NS).

Conclusion: In a relatively high functioning older patient sample with late-onset psychosis, patients were treated with low dose neuroleptics. Even though TD was common and associated with age and years on AP, TD was mild and usually did not progress.

NR584 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Schizophrenia and Date of Birth in New York

Nigel M. Bark, M.D., Bronx Psychiatric Ctr, 1500 Waters Drive, Bronx NY 10461; Ilya Kerelevich, B.A.

Summary:

Objective: To look for environmental effects during pregnancy that might increase the rate of schizophrenia in the offspring: specifically influenza, season of the year, and heatwaves.

Method: Dates of birth of all English-speaking patients (66,389) born between 1950 and 1984 in the New York State Office of Mental Health System within 50 miles of New York City were analyzed by chi-square and comparing schizophrenia to other diagnoses, in relation to the 1957 influenza epidemic, month of the year, and rigidly defined heatwaves.

Results: The only significant effect of influenza was a decrease of schizophrenia if flu occurred in the fifth month of pregnancy. More patients with schizophrenia were born in late summer and December. Heatwaves appeared to increase schizophrenia significantly, especially if they occurred in the third and fourth months of pregnancy, but more severe heatwaves did not show the same results.

Conclusions: Further examination of the data is required to determine if these results are due to some confounding factors or are true for this population in New York.

NR585 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Efficacy and Safety of 28-Day Treatment with Ziprasidone in Schizophrenia

Edmund P. Harrigan, M.D., Clinical Research, Pfizer Central Research, Eastern Point Road, Groton CT 06340

Summary:

Objective: This was a double-blind, randomized study comparing the safety and efficacy of treatment with ziprasidone (an antipsychotic with combined antagonism at $5HT_{2A}$ and D_2 receptors) and placebo in patients with an acute exacerbation of schizophrenia or schizoaffective disorder.

Method: After a 4- to 7-day placebo washout period, patients were given 20 mg or 60 mg ziprasidone or placebo twice daily for 28 days.

Results: A total of 131 patients were included in the intention-to-treat efficacy analysis and 76 patients completed the trial. There was a statistically significant improvement in psychotic symptoms vs. placebo in the 120 mg ziprasidone group, as measured by the total BPRS and CGI scores. Evaluations for parkinsonian symptoms, akathisia, abnormal movements, and sedation did not reveal any notable treatment effects. There were no notable treatment differences in the incidence or severity of adverse events, laboratory test abnormalities, or serious adverse events.

Conclusions: This study, therefore, showed that 60 mg ziprasidone twice daily was an effective dose in this group of patients.

NR586 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neuropsychophysiological Study of Severely Disturbed Children

Robert L. Hendren, D.O., Child & Adolescent Psych, UMDNJ-RWJ Med School, 675 Hoes Lane, Piscatawav NJ 08854; Janet Hodde-Vargas, Ph.D., Ronald Yeo, Ph.D., Luis Vargas, Ph.D., William Brooks, Ph.D., Corey Ford, M.D.

Summary:

Objective: The long-term objective of this study is to demonstrate whether children and adolescents who develop schizophrenia show specific neuropsychological, anatomic, and physiologic marker abnormalities prior to or coincident with the onset of schizophrenia.

Method: This project has studied 20 children between the ages of 8 and 12 classified with K-SADS assessment as having a schizophrenia spectrum disorder and 20 matched controls without a psychiatric disorder. Both groups underwent neuropsychological testing 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.

Results: Analysis of the data from all 20 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.

Conclusions: The findings lend support for a neurodevelopmental theory of schizophrenia.

NR587 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Sustained Serotonin Receptor Occupancy of Ziprasidone Using PET Ligand 18F Setoperone in Healthy Volunteers

Grant N. Ko, M.D., Clinical Research, Pfizer Central Res, Eastern Point Avenue, Groton CT 06340; Stephen A. Williams, Alan J. Fischman, Celena E. Drury, Pierre G. Etienne, Robert T. Rubin, M.D.

Summary:

Ziprasidone is a novel antipsychotic in late clinical development. The time course of its D_2 receptor occupancy has been previously demonstrated in healthy volunteers and ziprasidone is associated with a low incidence of extrapyramidal side effects (EPS).

Objective: This study aimed to determine $5HT_{2A}$ receptor occupancy and whether high occupancy may account for the low incidence of EPS.

Method: Eight healthy volunteers were each scanned on two separate occasions approximately one week apart Nanomolar doses of ^{18}F-setoperone (7mCi) were used as the $5HT_{2A}$ receptor ligand. The first scan provided baseline binding for each individual. At predetermined time points prior to the second scan, after at least four hours fasting, they received 40 mg ziprasidone orally, so that two volunteers were scanned at each time point post dose. Three-compartment modelling of setoperone pharmacokinetics was performed.

Results: The mean $5HT_{2A}$ receptor occupancy by ziprasidone is shown below:

Ziprasidone receptor occupancy at various time points (hr)

	4	8	12	18
$5HT_{2A}$(%)	95.4	92.0	78.4	46.7
D_2(%)	79.4	68.2	52.8	32.2

Means of two individuals are shown, but differences between subjects were very small. Data on D_2 occupancy obtained following the same dose of ziprasidone in a separate study are listed for comparison. Plasma levels of ziprasidone are being determined to confirm that exposure was similar in the two studies.

Conclusions: $5HT_{2A}$ receptor occupancy in this study substantially exceeds the known D_2 occupancy at all time points. This may explain the low incidence of EPS with ziprasidone.

NR588 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Cognitive Impairment and Negative Symptoms in Schizophrenia: Evidence for Diverse Patient Group

Paul Hartel, M.A., Psychiatry 116A, Mt. Sinai Hospital, 130 West Kingsbridge Road, Bronx NY 10468; Serge M. Sevy, M.D., Seamus Oflaithbheartaigh, M.D., Philip D. Harvey, Ph.D., Peter Powchik, M.D., Michael Davidson, M.D.

Summary:

Objective: To elucidate the relationship between cognitive impairment and negative symptoms in schizophrenic patients.

Methods: One-hundred-sixty chronic, institutionalized schizophrenics (aged 27–91) were assessed with Boston Naming, Praxis, Word List Learning and Recall, and the Clinical Dementia Rating Scale (CDR). Negative symptoms were measured using PANSS negative symptom-subscale. Patients comprised two groups: no/mild cognitive impairment (CDR < 2; aged 27–91) and moderate-severe cognitive impairment (CDR > or = 2; aged 38–93). Independent t tests compared the groups on negative symptoms and composite Z-transformed cognitive test scores. Pearson-Product-Moment correlations were performed within each group on negative symptom scores and composite Z-transformed cognitive test scores.

Results: Patients with moderate-severe cognitive impairment had more severe negative symptoms ($t = -8.46$, $p < .001$) and lower cognitive test composite scores ($t = 11.91$, $p < .001$). A significant correlation between negative symptoms and composite cognitive test scores was found for patients with moderate-severe cognitive impairment ($r = -.35$, $p < .05$). Despite adequate range in both sets of scores, no significant correlation was found in cognitively intact/mildly impaired patients ($r = -.17$, $p = .09$).

Conclusion: These findings support previous studies which suggest cognitive impairment and negative symptoms distinguish subgroups of patients. Some patients exhibit negative symptoms and lifelong absence of severe cognitive impairment, while others experience severe cognitive impairment in conjunction with more severe negative symptoms.

NR589 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Quetiapine Does Not Differ From Placebo in the Incidence of Extrapyramidal Syndrome or Effect on Plasma Prolactin

Walter W. Hong, M.D., CMA, Zeneca Pharm, 1800 Concord Pike, Wilmington DE 19850; Lisa A. Arvanitis, M.D., Barbara G. Miller, M.S.

Summary:

The atypical antipsychotic, clozapine, has minimal extrapyramidal symptom (EPS) liability and does not cause sustained hyperprolactinemia. These features of atypical antipsychotics are expected to improve compliance, reduce hospitalizations, and enhance the quality of lives of patients with schizophrenia. 'Seroquel' (quetiapine, ICI 204,636) is a promising new antipsychotic

with an atypical profile. In Phase II clinical trials there were no differences between quetiapine and placebo groups in EPS as assessed by the Simpson Scale total score, use of concomitant anticholinergic medications, and the incidence of motor system adverse events. Acute dystonic reactions were not reported. Further, there were no differences between the quetiapine and placebo groups in change from baseline in prolactin levels (PRL) after six weeks of treatment. EPS and PRL were also assessed in a six-week, multicenter, placebo-controlled, double-blind, randomized, Phase III clinical trial. This trial evaluated the efficacy, tolerability, and optimal dose range of quetiapine in the treatment of patients with acute exacerbation of schizophrenia (n = 361) with five fixed doses of quetiapine (75, 150, 300, 600, 750 mg daily), one fixed dose of haloperidol (12 mg daily), and placebo. EPS was assessed weekly using the Simpson Scale, and PRL was assessed at baseline (following a one-week placebo phase) and after four weeks of treatment. Blood samples for PRL were drawn prior to the morning dose of study medication. Mean Simpson Scale total scores decreased in all quetiapine groups (–1.0 to –1.8) and the placebo group (–0.6), with the largest decreases in the 600 and 750 mg quetiapine groups, whereas the mean Simpson Scale total score in the haloperidol group increased (+ 1.1). There were no significant differences between any quetiapine group and the placebo group in Simpson Scale total score grouped responses at end point. There were no significant differences between any quetiapine group and the placebo group in mean change from baseline in PRL levels at the final observation, whereas the difference between the haloperidol and placebo groups in respect of PRL was significant ($p < 0.009$). The mean change from baseline in the haloperidol group was in the positive (increasing) direction. These results confirm Phase II data that quetiapine has an atypical profile and that it does not cause a dose dependent increase in EPS or PRL. Quetiapine does not differ from placebo in its induction of EPS or effect on PRL.

NR590 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Immigration in the Use of Schizophrenia Research: A Study in Israel

Haim Y. Knobler, M.D., Jerusalem, Eitanim Psych Center, 16B Hazait Street, Rehovot NY 76349, Israel; Wladislaw Fainstein, M.D., Yehuda Kuniavsky, M.D., Bella Hanin, Shmuel Maizel, M.D., Yaacov Lerner, M.D.

Summary:

The recent immigration of over half a million Jews from the former USSR to Israel provides unique psychiatric research settings.

Objective: The aims of the present study were: to compare the rate of schizophrenia, demographic data, age of onset, presenting symptoms, and past treatment, between immigrant and non-immigrant psychiatric inpatients; and to compare the symptoms' profile between immigrant and non-immigrant schizophrenic patients.

Method: 58 immigrant inpatients, who were admitted to a psychiatric hospital in Jerusalem, were matched and compared with the 58 successively admitted non-immigrant inpatients. Thirty immigrant schizophrenic patients were then compared with 30 non-immigrant schizophrenics using the Positive and Negative Syndrome Scale (PANSS).

Results: No differences were found in the rate of schizophrenia, gender distribution, age of onset, the present age of the patients, or past treatment. However, immigrant inpatients had prominent suicidal ideation, and suicidal attempts were a common reason for their admission.

Immigrant schizophrenics did not have different rates of PANSS symptoms, including positive, negative, and depressive symptoms. Most immigrant schizophrenics had first-rank Schneiderian symptoms, while most non-immigrants did not.

Conclusions: The interpretation of the results may suggest differences between genetic and environmental factors in the course and the outcome of schizophrenia.

NR591 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Clozapine Versus Risperidone in Treatment Refractory State Psychiatric Inpatients

Jean-Pierre Lindenmayer, M.D., Psychiatry, NY Univ Med Ctr/Manhattan Psyc, Med Ctr Res Ctr/Ward's Island, New York NY 10035; Mohan Park, M.D., Adel Iskander, M.D., Nigel M. Bark, M.D., Robert M. Smith, M.D., Thomas B. Cooper, M.A.,

Summary:

The number of treatment refractory schizophrenic state psychiatric patients is significant. Clozapine is the only compound available with proven efficacy for these refractory patients, but its use is limited due to its risk of agranulocytosis. Risperidone is a new atypical antipsychotic which has been shown to be effective in acute schizophrenics with past history of neuroleptic response. Its efficacy in refractory patients has not yet been established. Our study investigates the comparative efficacy of these two compounds in a prospective 12-week, open-label study in treatment refractory state psychiatric patients (mean length of present hospitalization 47.5 months). Thirty DSM-IV schizophrenic patients (mean age 38.4 years) with a documented history of prior nonresponse were treated with either clozapine or risperidone at clinically optimal dosages. Response was assessed biweekly by independent raters with the PANSS, neurological rating scales including neurological soft signs, neurocognitive tests, and plasma levels. *Results* showed an overall significant trend for superior efficacy of clozapine as compared to risperidone on PANSS total, PANSS positive, negative, excitement, and cognitive factors. Only for the anxiety/depression factor did risperidone show a similar improvement trend. Extrapyramidal side effects were minimal for clozapine, while some were present for risperidone. Results will be discussed with the aim of defining a psychopathological and neurocognitive response profile for each drug.

NR592 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Prefrontal Cortical Structure-Function Correlations in Schizophrenia

Todd Lencz, Ph.D., Research, Hillside Hospital, 75–59 263rd Street, Glen Oaks NY 11004; Robert M. Bilder, Ph.D., Manzar Ashtari, Ph.D., Houwei Wu, M.D., Jose Alvir, D.P.H., Jeffrey A. Lieberman, M.D.,

Summary:

Objective: To examine the relationship between magnetic resonance imaging (MRI) measures of prefrontal volume and measures of neuropsychological (NP) performance in patients with schizophrenia.

Method: Subjects were 52 patients (21 female) in the first episode of schizophrenia. MR images were acquired on a 1.0 Tesla magnet using a 3D "FLASH" sequence yielding 3.1 mm contiguous coronal slices (Bilder et al. 1994). Prefrontal volume included all gray and white matter anterior to the genu of the corpus callosum. Total cotrical gray and white matter volume, excluding subcortical and ventricular spaces, was also measured. Regression analysis was used to obtain a standardized residual measure of prefrontal volume controlling for total cortical volume. An extensive NP battery was administered after clinical stabilization; composite scales were constructed for the following NP domains: language, memory, attention, executive, motor, and visuospatial functioning (Bilder et al. 1995).

Results: The prefrontal residual measure was significantly correlated with the memory ($r = .45$, $p < .01$) and the attention (r =

.27, p = .05) indices; correlations with other NP indices were nonsignificant. The correlation between the prefrontal measure and the memory index remained significant after partialling attention (r = .36, p < .01).

Conclusions: Patients with schizophrenia demonstrate a linear relationship between size of the prefrontal cortex and neuropsychological performance on tests of attention and memory.

NR593 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Cognitive Correlates of Spatial Working Memory in Schizophrenia

James J. Levitt, M.D., Psychiatry Brockton VAMC, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Paul G. Nestor, Ph.D., Jay E. Allard, B.A., Maria E. Karapelou, Ed.M., 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 code directionality of the intended movement during the delay phase.

Method: In this study, 21 chronic right-handed male SZ veterans and 20 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 (1.4 vs. 1.0 cm; t(39) = -3.42, p < .001); the delay mean error distance for SZs was also significantly longer than for NCLs (3.6 vs. 1.8 cm; t(39) = -4.20, p < .001). Moreover, an ANOVA revealed a significant group by task interaction with SZs' performance deteriorating more than NCLs with the delay condition (F = 11.52, df = 1, 39, p = .002). In addition, the delay mean error distance and the mean error distance difference (delay minus non-delay) both correlated significantly with the Trails B (r = .60, p < .02; r = .54, p < .03), the WMS Visual Memory Span Forward task (r = -.79, p = .02; r = -.82, p = .01), and the WMS Visual Memory Span Backwards task (r = -.92, p = .001, r = -.89, p = .003), the WMS Digit Span Forward task (r = –.48, p = .08; r = –.54, p < .05), and the WMS Digit Span Backwards task (r = -.61, p = .02; r = -.58, p < .03).

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 and to working memory operations.

NR594 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Odor Discrimination Performance and Deficit Schizophrenia

Delores Malaspina, M.D., Psychiatry, Columbia University, 722 West 168th Street, New York NY 10032; Fabien Tremeau, M.D., Scott Yale, M.S.W., Marleen Van Kammen, M.P.H., Xavier F. Amador, Ph.D., Jack M. Gorman, M.D.,

Summary:

Sensory processing deficits are well described in schizophrenia, but olfaction has been relatively unstudied. The neurobiology of odor discrimination shares remarkable overlap with schizophrenia brain abnormalities. Also, central processing of the odor environment with respect to past experiences is arguably the most phylogenetically ancient cognitive capability; the limbic cortex evolved initially to process odor information.

Methods: We examined associations among odor discrimination (by UPSIT), to SPEM, neuropsych measures, and consensus rated deficit symptoms in 30 schizophrenia patients.

Data: Spearman r's of UPSIT to deficit measures (absolute value): restricted affect .62 (p = .01); emotional range .69 (.006); poverty of speech .57 (.03); curbed interests .52 (.05); sense of purpose .64 (.01); social drive .72 (.003); to smooth pursuit eye tracking -.75 (.002); FS IQ .82 (.01); P IQ .69 (.06); V IQ .87 (.002); Trails A .50 (.017), Trails B .52 (.014); FAS .54 (.007)

Results: UPSIT odor identification scores were uniquely correlated with all measures.

Conclusion: Neocortical-limbic networks for odor discrimination may also be central to deficit symptoms and cognitive impairments in schizophrenia.

NR595 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Gender Differences in Schizophrenia

Ashok K. Malla, M.D., Psychiatry, University of Western Ontario, 375 South Street/Victoria Hosp, London ON, Canada N6A 4G5; Ross M. Norman, Ph.D., Sandra Morrison-Stewart, Ph.D., Edward Helmes, Ph.D., Peter J. Williamson, M.D., Leonardo Cortese, M.D.,

Summary:

Gender differences in schizophrenia have been receiving increasing attention in recent years (Wahl & Hunter, 1992; Castle & Murray, 1995). Most past studies in this area have examined differences in level of symptomatology or associated variables. Given evidence of possible differences in the organization of brain function between males and females, it is important to examine whether there are differences between male and female patients with schizophrenia in the *relationships* between brain functioning and symptoms. The data to be reported in this paper examine gender differences between men and women in the relationship of three different dimensions of symptoms (psychomotor poverty, disorganization, and reality distortion) with 1) neuropsychological test performance; and 2) EEG coherence. The data regarding neuropsychological test performance are derived from a total sample of 87 DSM-III-R schizophrenia patients and includes neuropsychological measures of frontal and temporal lobe functioning. The data regarding EEG coherence are based on a sample size of 73 patients and include measures of connectivity between frontal, temporal, parietal, and occipital areas. There were no significant gender differences in the level of symptoms or cognitive deficits. Significant differences were found between males and females in the correlations of their symptoms with neuropsychological and EEG coherence measures. The implications of these findings for schizophrenic research are discussed.

NR596 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Intact Affective Preference for Familiar Stimuli Despite Impaired Recognition Memory in Schizophrenics

Ariane Marie, B.A., Psychiatry, Stanford University, 3801 Miranda Avenue MC:116A3, Palo Alto CA 94304; John D.E. Gabriel, Ph.D., Richard Shaw, M.D., Bonny R. Brown, M.A., Kaaren Hanson, M.A., Felicia Pratto, Ph.D., R.B. Zajonc, Ph.D.,

Summary:

Schizophrenia patients are known to have deficits in affect expression and affect recognition. However, it is not known whether schizophrenics develop a liking for novel material due to frequent exposure to that material, which is referred to as affective preference. This study examined whether schizophrenics have normal

affective preference. The subjects were clinically stable, medicated schizophrenics (N = 8) diagnosed by SCID interviews according to DSM-III-R criteria, and normal controls (N = 7) matched in age, sex, and childhood socio-economic status. In the study phase, subjects were exposed visually to verbal (meaningless words) and nonverbal (male faces with neutral expressions) stimuli. In the test phase, subjects performed a two-alternative forced-choice preference test for half the study-phase stimuli, and a two-alternative forced-choice preference test for the other stimuli. Schizophrenics had impaired recognition for the study-phase items ($p < .01$). Subjects demonstrated a significant preference for materials seen in the study phase ($p < .01$), and the magnitude of the preference did not differ between schizophrenic and control groups ($p > .7$). These preliminary findings suggest that schizophrenia patients have a normal gain in affective preference from mere exposure to materials despite impaired recognition for those materials.

NR597 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Effect of Ziprasidone on Steady-State Pharmacokinetics of a Combined Oral Contraceptive

Gray J. Muirhead, Pfizer Central Res, Ramsgate Road, Sandwich Kent, United Kingdom; Philip R. Holt, Stuart Oliver, Jane Harness, Richard J. Anziano,

Summary:

Ziprasidone is a novel antipsychotic agent with combined antagonism at $5HT_{2A}$ and D_2 receptors. A double-blind, placebo-controlled, two-way crossover study was conducted to assess ziprasidone's effect on the pharmacokinetics of a combined oral contraceptive. The study was divided into two 21-day treatment periods with a seven-day contraceptive-free interval. A total of 19 healthy female volunteers received 0.15 mg levonorgestrel (LNG) and 0.03 mg ethinyloestradiol (EE) daily on days 1 to 21. On days 8 to 15, the subjects also received either 20 mg ziprasidone or placebo, twice daily (once daily on day 15). Plasma samples were collected up to 24 hours post-dose on day 15 for analysis of LNG and EE. Plasma prolactin concentrations were determined pre-dose and four hours post-dose on day 15. The pharmacokinetic data showed no statistically significant differences in mean C_{max}, T_{max} and AUC_{24} for EE in plasma when multiple doses of ziprasidone were administered, compared with placebo. There were also no significant differences in mean C_{max} and AUC_{24} for LNG, although there was a statistically significant (but not clinically relevant) difference in mean T_{max}.

Mean pharmacokinetic parameters (*geometric mean)

		EE		LNG		
C_{max}* (pg/ml)	T_{max}. AUC_{24}* (hr)	C_{max}* (pg•hr/ml)	T_{max} (ng/ml)	AUC_{24}* (hr)	(ng•hr/ml)	
Ziprasidone	72	2.9	954	6	2.3	86
Placebo	77	2.3	960	6	1.7	88

Conclusions: After dosing with ziprasidone, plasma prolactin concentrations pre-dose and four hours post-dose were higher than after dosing with placebo. One subject discontinued due to nausea, tiredness, dizziness, and vomiting after the first dose of ziprasidone, but no serious adverse events occurred during the study.

NR598 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

A Role of Working Memory in Language Dysfunction in Schizophrenia

Margaret Niznikiewicz, Ph.D., Psychiatry Brockton VAMC, Harvard Medical School, 940 Belmont Street 116A, Brockton MA 02401; Paul G. Nestor, Ph.D., Brian F. O'Donnell, Ph.D., Jay E. Allard, B.A., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D.,

Summary:

Language difficulties in schizophrenia such as loose associations, tangentiality, and insensitivity to context have been recently attributed to problems in lexical memory. Our recent ERP study of language dysfunction in schizophrenia found a more negative N400 amplitude in schizophrenic patients (Sz) relative to normal controls (Nc). This result may be related to abnormal processes within lexical networks, compromised working memory, or both. In the present study, we examined the effect of memory load on processing language using an event-related potential paradigm. We used two-sentence paragraphs. The first sentence was either short (low memory load) or long (high memory load). In half of the paragraphs, a second sentence did not make sense (incongruent sentence condition); in the other half, the second sentence made sense but contradicted the information included in the first sentence (incongruent paragraph condition). So far, we have tested four chronic Sz and three (Nc) subjects. The preliminary results indicate that a high memory load affected language processing in schizophrenic patients more than it did in normal controls. In patients, the N400 was more negative in the incongruent paragraph, high memory load condition (Pz: .2 microvolts) than in low memory condition (Pz: 1.6). In Nc, the N400 amplitude in the high and low memory conditions was similar (at Pz: 1.6 vs 1.8 microvolts). These results suggest that working memory processes contribute to language difficulties in schizophrenia.

NR599 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neuropsychological Correlates in Schizophrenia

Ross M. Norman, Ph.D., Psychiatry, Victoria Hospital, 375 South Hospital, London Ontario N6A 4G5, Canada; Ashok K. Malla, M.D., Sandra Morrison-Stewart, Ph.D., Edward Helmes, Ph.D., Peter J. Williamson, M.D., Jill Thomas, B.Sc., Leonardo Cortese, M.D.,

Summary:

Recently, there has been increased evidence for the existence of at least three dimensions underlying symptoms of schizophrenia: psychomotor poverty (negative symptoms), disorganization (thought disorder), and reality distortion (hallucinations and delusions). Liddle (1987) and others have suggested that there may be different neurocognitive deficits associated with each of these profiles. The three hypotheses being tested in this study were derived from Liddle's original statement of his three syndrome models of schizophrenia. The hypotheses were that 1) symptoms of psychomotor poverty would be particularly correlated with impaired performance on neuropsychological tests likely to reflect functioning of the left dorsolateral prefrontal cortex; 2) disorganization would be particularly correlated with impaired performance on tests sensitive to medio-basal prefrontal functioning; and 3) reality distortion would be particularly correlated with measures sensitive to temporal lobe functioning. These hypotheses were tests on 87 subjects, with a SCID confirmed diagnosis of schizophrenia, whose symptoms were scored for each of the three syndromes and who completed the Wisconsin Card Sort Test; the Wechsler Memory Scale - Logical Memory Subtest; the Benton Visual Retention Test, Rey-Osterrieth Complex Figures Test; Chicago Word Fluency Test, and the Design Fluency Test. The results confirmed a specific relationship between reality distortion and measures related to left temporal lobe functioning.

These findings do not appear to be a result of confounding with other variables such as age, length of illness, or medication. Although the results did not directly support the first two hypotheses, they are consistent with there being different cortical-subcorti-

cal circuits associated with each of psychomotor poverty and disorganization.

NR600 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Amantadine Disrupts Prepulse Inhibition in Rats

Michael S. Rappaport, M.D., Psychiatry, University of Nebraska Med Ctr, 600 S. 42nd Street, Omaha NE 68198; David P. Yells, Ph.D., Stephen R. Paige, Ph.D., Shelton Hendricks, Ph.D.,

Summary:

Objectives: The efficacy of amantadine (AMA) to inhibit prepulse inhibition (PPI) in rats was assessed relative to the classic DA receptor agonist apomorphine (APO) and the NMDA-type glutamate receptor (NMDAR) antagonist MK-801, respectively.

Methods: Disruption of PPI was measured 15 min after AMA doses of 0 to 30 mg/kg (ip) to ascertain a minimal effective dose. In a subsequent study, rats received haloperidol (HAL; 0.1 mg/kg, sc) or 0.9% NaCl prior to receiving injections of AMA (20 mg/kg, ip), APO (0.5 mg/kg, sc), MK-801 (0.25 mg/kg, sc) or 0.9% NaCl followed by PPI testing 15 min later.

Results: At doses of 20 mg/kg or higher, AMA disrupted PPI. HAL effectively prevented this disruption, and that caused by APO but not MK-801.

Conclusions: Although both indirect DA agonist and NMDAR antagonist properties have been ascribed to AMA, HAL prevention of AMA-disruption of PPI suggests that the indirect DA-agonist rather than NMDAR-antagonist properties of AMA mediate its disruption of PPI. Thus when used with a potent DA antagonist antipsychotic, potential psychotogenic effects of AMA are likely to be effectively antagonized.

NR601 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Cognitive Subtypes of Schizophrenia According to Verbal Fluency Performance

Philippe H. Robert, M.D., Psychiatry, Memory Ctr PAV J, Hospital Pasteur 30 Av Voie, Romaine Nice 06002, France; Sandrine Thauby, M.D., Isabelle Chaix, Ph.D., Valerie Migneco, M. Benoit, M.D., Guy Darcourt, M.D.,

Summary:

Schizophrenia is a heterogeneous disorder often characterised by neuropsychological dysfunctioning. In the first part, this study attempted to characterize relationships between verbal fluency and other frontal tests to determine if self directed search attention, and working memory are involved in the fluency performances. Verbal fluency, Trail Making, Stroop, and Brown Peterson paradigm were administered to 45 patients with schizophrenia and 45 healthy subjects matched for sex, age, and education. Significant correlations were found between verbal fluency and all neuropsychological tests for schizophrenics but not for control subjects. In the second part performance on verbal fluency was used to subtype the schizophrenic population. A two cluster solution was considered optimal. Cluster S1 (n = 21) comprised patients with the lowest performances and cluster S2 (n = 24) patients with the highest performances. The subtypes differed significantly for all neuropsychological tests, negative symptoms, and social functioning. Comparison with matched controls indicated that in cluster S1 patients had poorer results in all tests. In cluster S2 patients differed from their controls only for verbal fluency, Trail A, and one subtest of the Brown Peterson paradigm.

NR602 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Age-Related Changes in Formal Thought Disorder in Chronic Schizophrenic Patients

Janel Lombardi, M.D., CNC, Pilgrim Psych Ctr, Box A, Bldg. 23–5, West Brentwood NY 11717; Philip D. Harvey, Ph.D., Martin Leibman, Ph.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Peter Powchick, Ph.D.,

Summary:

Formal thought disorder, one of the most common symptoms of schizophrenia, is present across the life course of the illness, including periods of relative remission. Few studies have examined age-related changes in thought disorder across the life span of the disorder. We report a cross-sectional study of the prevalence and severity of 18 different signs of thought disorder in schizophrenic patients ranging in age from 19 to 96 (n = 392). All patients were examined with the Scale for Assessment of Thought Language and Communication. Geriatric patients (age > 64) were also examined for cognitive functioning using the MMSE.

Poverty of speech was more common and more severe in geriatric patients, and four different signs of disconnected speech were less common and less severe in geriatric patients. When patients with poverty of speech were eliminated from both samples, all differences in the prevalence of disconnection-type thought disorders were eliminated. Among the geriatric patients, MMSE scores were ten points lower in those with poverty of speech than in patients without this sign. The major change in thought disorder accompanying aging in schizophrenia was poverty of speech, with all other changes accounted for by alterations in the prevalence and severity of this aspect of communication disorder. An increase in poverty of speech was associated with the presence of cognitive impairment in the geriatric patients, suggesting that poverty of speech may be intrinsically related to cognitive impairment in schizophrenia.

NR603 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Haloperidol: Results of a Large Multi-Center International Trial

Winston G. Satterlee, M.D., CNS/GI/GU/Medical, Eli Lilly & Company, Lilly Corp Ctr Drop Code 0538, Indianapolis IN 46268; Charles M. Beasley, Jr., M.D., Pierre V. Tran, M.D., Roy N. Tamura, Ph.D., John A. Krueger, M.B.A., Gary D. Tollefson, M.D.,

Summary:

This double-blind, six-week, parallel trial compared the efficacy and safety of a dose range of olanzapine, 5–20 mg/day, to a dose range of haloperidol, 5–20 mg/day, in 1,996 patients with a DSM-III-R diagnosis of schizophrenia (83.1%), schizophreniform disorder (1.9%), or schizoaffective disorder (15.0%). Patients were assigned by random allocation to double-blind therapy.

A statistically significantly ($p < .001$) greater proportion of 1,336 olanzapine patients (66.4%) than the 660 haloperidol patients (46.8%) completed the acute phase. The proportions of patients discontinuing for lack of efficacy (LOE) and adverse events (ADE) were also statistically significantly smaller with olanzapine.

On the primary analysis of overall efficacy, the difference in baseline to endpoint (LOCF) mean change on the BPRS, olanzapine was statistically superior to haloperidol (-10.89, -7.93, $p = .015$). Mean change on CGI-S and response rate (> 40% improvement on BPRS with three or more weeks treatment) significantly favored olanzapine as did improvement on BPRS-negative and PANSS-negative. Positive symptom improvement was comparable.

There was statistically significantly less treatment emergent dystonia, parkinsonism, and akathisia with olanzapine than with haloperidol. Scores on Simpson Angus, Barnes, and AIMS de-

creased for olanzapine treated patients and were statistically significantly superior to haloperidol.

The efficacy and safety data will be reviewed in greater detail.

NR604 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Comparison of Extrapyramidal Syndromes Between Olanzapine and Placebo in Schizophrenia

Jamie S. Street, M.D., MC 0541, Eli Lilly and Co, Lilly Corporate Center, Indianapolis IN 46285; Mary Anne Dellva, M.S., Roy N. Tamura, Ph.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.,

Summary:

Olanzapine exhibits a polyvalent receptor profile inclusive of 5-HT, mACh, DA, and alpha-1 binding sites. The combination of high 5-HT and mACh affinity, coupled with DA selectivity (eg, D4/D3) is strongly suggestive of a low EPS potential. To date, in vitro electrophysiology, imaging, and animal behavioral pharmacology have been confirmatory. Data were integrated from the acute phase (six weeks) of two double-blind, placebo-controlled studies in patients meeting DSM-III-R criteria for schizophrenia and schizophreniform and schizoaffective disorders treated with olanzapine (N = 248; 2.5 to 17.5 mg/day, mean modal maintenance dose of 11.0 mg/day) and placebo (N = 118). Evaluation of EPS was based on the analysis of treatment-emergent extrapyramidal events (TEEPE) and data obtained from the Simpson-Angus Scale (SAS), Barnes Akathisia Scale (BAS), and the Abnormal Involuntary Movement Scale (AIMS). TEEPE were grouped into one of five event categories: dystonic, parkinsonian, akathisia, dyskinetic, residual, and an overall category of any extrapyramidal event. There were no statistically significant differences between olanzapine and placebo for any of the five categories or for the overall category. Data from the assessment scales reflecting change from baseline to endpoint and change from baseline to maximum for both the SAS and AIMS demonstrated no statistically significant difference between the two treatment groups. BAS data assessing change from baseline to maximum were also not statistically significantly different; however, change from baseline to endpoint revealed a statistically significant decrease in the BAS endpoint score for the olanzapine treatment group compared with the placebo treatment group. These outcomes, utilizing treatment-emergent events and analyses of validated scales for drug-induced Parkinsonism, akathisia, and dyskinesia, corroborated preclinical predictions that olanzapine would have a very favorable EPS profile. EPS incidence did not statistically differ significantly from placebo and the significant reduction in baseline akathisia relative to placebo suggests that olanzapine holds promise as a better tolerated agent for the treatment of psychosis.

NR605 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Long-Term Treatment-Emergent Dyskinetic Symptoms in Patients Treated with Olanzapine and Haloperidol

Jaime S. Street, M.D., MC 0541, Eli Lilly and Co, Lilly Corporate Center, Indianapolis IN 46285; Roy N. Tamura, Ph.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.,

Summary:

Olanzapine is a novel, atypical antipsychotic agent with acitivity and high muscarinic affinity binding at serotonin 5-HT2A/C, 5-HT3, 5-HT6, dopamine D4, D3, D2, muscarinic 1–5, and adrenergic α-1 receptors. With an activity profile showing 5-HT and muscarinic predominance over D2, olanzapine would be predicted to have a reduced incidence of drug-induced extrapyramidal symptoms including tardive dyskinesia. Data were integrated from three active-controlled long-term studies in patients meeting DSM-III-R criteria for schizophrenia, schizophreniform disorder, and schizoaffective disorder treated with olanzapine (N = 894, up to 20 mg/day, 237 median days of exposure) and haloperidol (N = 261, up to 20 mg/day, 203 median days exposure). Both olanzapine and haloperidol treatment populations regarding disease duration were principally chronic (mean > 10 years) with no between-group differences for age on admission, age of first episode, or previous therapy. Research diagnostic criteria for tardive dyskinesia suggested by Schooler and Kane (1982) and the Abnormal Involuntary Movement Scale (AIMS) were used to define long-term treatment-emergent dyskinetic symptoms (LTTEDS). The incidence of olanzapine-treated patients with LTTEDS at any post-baseline visit, endpoint (final AIMS assessment), and the final two AIMS assessments was statistically significantly less compared with haloperidol-treated patients at all three time points ($p < .001$, $p < .001$, $p = .003$, respectively). The incidence of LTTEDS in a subset of patients (olanzapine = 707; haloperidol = 197) without a history of dyskinesia or tardive dyskinesia at baseline and treated with olanzapine was also statistically significantly lower at all three points compared with patients treated with haloperidol ($p < .001$, $p = .001$, $p = .003$, respectively). These findings support the unique activity profile of olanzapine and its significant clinical contribution of decreasing the incidence of LTTEDS.

NR606 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Comparison of Weight Gain During Risperidone and Clozapine Treatment in Chronic Schizophrenia

Tung-Ping Su, M.D., ETB Bldg 10 4N214, NIMH, 9000 Rockville Pike, Bethesda MD 20892; Igor Elman, M.D., Anil K. Malhotra, M.D., Caleb M. Adler, M.D., David Pickar, M.D., Alan F. Breier, M.D.,

Summary:

Objective: This is a preliminary report to compare the effect of risperidone and clozapine on body weight and to determine the relationship between treatment response and weight gain in patients with chronic schizophrenia.

Method: Twenty chronic schizophrenics (Age 30.5 ± 9.2 years, male 16, female 4) underwent a short-term (5–6 weeks) parallel design study either with risperidone (4–8 mg/day, n = 10) or clozapine (400–450 mg/day, n = 10) following fluphenazine treatment. Antipsychotic response was defined as reduction of BPRS score > 20% from fluphenazine or BPRS total score < 36 or Bunney-Hamburg Psychosis rating < = 6 by week 6.

Results: By the end of the study, significant weight gain, compared with fluphenazine, was observed in both clozapine responders (n = 7) and nonresponders (n = 3) (5.6 ± 6 Kg [7.9 ± 8.5%] and 5.6 ± 1.9 Kg [7.8 ± 2.9%], respectively) as well as in risperidone responders (n = 5) (6.8 ± 4.8Kg[7.2 ± 5.2%]) ($p < 0.05$). In contrast, risperidone nonresponders (n = 5) had a mean 2.1% (1.9Kg) weight loss. A comparison of the changes in weight between risperidone nonresponders and the former three groups were significant ($t = 2.4–3.9$, $p < 0.05$). No significant difference in weight change was found between risperidone and clozapine responders (p = NS). Plasma cholesterol (24%), triglyceride (46%), and glucose (18%) levels significantly increased during clozapine treatment (compared to baseline fluphenazine) ($p < 0.05$). However, risperidone did not significantly alter these biochemical indices. Clozapine's effects were also significant when compared to these indices (cholesterol and glucose) during risperidone treatment ($p < 0.05$).

Conclusions: These data suggest that the effect of risperidone and clozapine on body weight are not different during short-duration treatment trials. Lack of weight gain during risperidone treatment may be associated with risperidone nonresponse.

NR607 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Clinical Experience with Long-Term Continuation Treatment with Olanzapine

Pierre V. Tran, M.D., MC 541, Eli Lilly Company, Lilly Corporate Center DC 0538, Indianapolis IN 46285; Mary Anne Dellva, M.S., Charles M. Beasley, Jr., M.D., Winston G. Satterlee, M.D., Lynne M. Cousins, B.A., Gary D. Tollefson, M.D.,

Summary:

Olanzapine is a promising new "atypical" antipsychotic agent. We report the efficacy results in maintenance treatment of three fixed-dose ranges of olanzapine (Olz-L, 5.0 ± 2.5 mg; Olz-M, 10.0 ± 2.5 mg; Olz-H, 15.0 ± 2.5 mg) compared to placebo (study HGAD) and one fixed-dose range of haloperidol (Hal, 10.0 ± 5 mg) (meta-analysis from two trials of similar design, studies HGAD and E003). Statistically significantly more patients completed one year of therapy in the Olz-H treatment group than in the placebo or Hal treatment group. Survival analysis of time to relapse indicated that statistically significantly fewer patients in the Olz-H treatment group experienced relapse at any given point in time than patients in the placebo treatment group. Relapse was defined as re-hospitalization for psychotic symptoms.

In another study (study HGAJ) where olanzapine (5–20 mg) was compared to haloperidol (5–20 mg), the survival analysis of time to relapse indicated that statistically significantly fewer patients in the olanzapine treatment group experienced relapse at any given point in time than patients in the haloperidol treatment group. These results demonstrated that olanzapine offered superior effectiveness over the conventional neuroleptic haloperidol in maintaining treatment response in continuation therapy.

NR608 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Relationship of Specific Areas of Prefrontal Cortex to Temporal Lobe Abnormalities and Symptomatology in Schizophrenia

Cynthia G. Wible, Ph.D., Surgical Planning, Harvard Medical School, 75 Francis Street/Brigham Hosp, Boston MA 02115; Martha E. Shenton, Ph.D., Robert W. McCarley, M.D., Ronald Kikinis, M.D., Ferenc Jolesz, M.D.,

Summary:

The volume of prefrontal regions was measured in schizophrenic and control subjects using magnetic resonance imaging (MRI). The prefrontal cortex was subdivided into orbital, inferior, middle, superior, cingulate, and frontal pole regions. Subjects were also assessed using the SANS, SAPS, and the Thought Disorder Index (TDI). 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. There were no overall significant differences in volume for the prefrontal subdivisions; however, these subjects were previously shown to have left-lateralized volume reductions in several temporal lobe areas. High correlations were found between volumes of specific temporal and prefrontal areas, most notably with the orbital cortex. Orbital volume was also associated with asociality scores (r = -.61 for left, and r = -.68 for right), and with apathy scores only on the left (r = -.56). Anterior cingulate volume was associated with attention (r = -.60 for left, r = -.55 for right), and with auditory hallucinations only on the left (r = -.55). Right middle frontal gyrus volume was also associated with attention (r = -.55) and with total SAPS scores (r = -.62). These data suggest that specific areas of the prefrontal cortex of schizophrenic subjects participate in the production of symptoms, both positive and negative, and that there may be pathological changes in schizophrenic prefrontal cortex that are too subtle to detect with MRI.

NR609 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Anxiolytic Effects of Ziprasidone Compared with Diazepan and Placebo Prior to Dental Surgery

Keith D. Wilner, Ph.D., Clinical Research, Pfizier Central Res, Eastern Point Road, Groton CT 06340; Richard J. Anziano, Arlene C. Johnson, Jeffrey J. Miceli, Ph.D., James R. Fricke, D.D.S., Cynthia K. Titus, R.N.,

Summary:

Ziprasidone is a combined $5HT_{2A}$/D2 antagonist undergoing evaluation as a new treatment for schizophrenia. In addition to its $5HT_{2A}$ antagonist activity, ziprasidone has high affinity for $5HT_{1A}$ receptors.

Objective: Since anxiolytic activity is reputed to result from $5HT_{1A}$ stimulation, ziprasidone was evaluated in a double-blind, placebo-controlled study in subjects about to undergo minor dental surgery. Diazepam was included as a positive control.

Method: A total of 90 subjects were equally divided to receive a single oral dose, three hours prior to surgery, of one of the following treatments: 20 mg ziprasidone, 10 mg diazepam, or placebo. Scales evaluating the degree of anxiety and sedation were completed by the investigator and subjects at various time points up to three hours post dose.

Results: The data indicated that ziprasidone and diazepam were associated with similar anxiolytic activity, with approximately 55% decrease from baseline (prior to dosing) in the subject self-evaluation of anxiety. Similar results were observed with the investigator rating. Less sedation was observed in the ziprasidone group than in the diazepam group (63% vs. 90% increase from baseline).

Conclusions: These results show that ziprasidone given prior to dental surgery has anxiolytic effects comparable with diazepam, but with less potential for sedation.

NR610 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Effects of Ziprasidone on Steady-State Lithium Levels and Renal Clearance of Lithium

Keith D. Wilner, Ph.D., Clinical Research, Pfizer Central Res, Eastern Point Road, Groton CT 06340; Richard J. Anziano, Thomas G. Tensfeldt, M.S., Shawn N. Pelletier, B.S., Glen Apseloff, M.D., Nicholas Gerber, M.B.,

Summary:

Ziprasidone is a novel antipsychotic agent with combined antagonism at $5HT_{2A}$ and D_2 receptors.

Objective: An open-label, randomized, placebo-controlled study was conducted to assess ziprasidone's potential to alter the renal clearance and steady-state levels of lithium.

Method: A total of 25 healthy male volunteers received oral lithium carbonate (450 mg) twice daily on days 1 to 14, and once in the morning on day 15. Subjects received either ziprasidone 20 mg twice-daily on days 9 to 11 followed by 40 mg twice-daily on days 12 to 15 (n = 12), or placebo twice-daily (n = 13). Ziprasidone and placebo were administered two hours prior to lithium dosing.

Results: Concomitant ziprasidone administration for seven days was associated with a 0.066 mEq/L (14%) increase in steady-state lithium levels compared with an increase of 0.057 mEq/L (11%) in the placebo group. Renal clearance of lithium decreased by 0.089 L/h (5%) in the ziprasidone group and decreased by 0.151 L/h (10.5%) in the placebo group.

Conclusions: These differences between the two groups were neither statistically nor clinically significant. There were no serious or untoward adverse events observed in this study.

NR611 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Single and Multiple Dose Pharmacokinetics of Ziprasidone in Healthy Males

Keith D. Wilner, Ph.D., Clinical Research, Pfizer Central Res, Eastern Point Road, Groton CT 06340; Robert A. Hansen, M.S., Arlene C. Johnson, Jeffrey J. Miceli, Ph.D., Glen Apseloff, M.D., Nicholas Gerber, M.B.,

Summary:

Objective: The pharmacokinetics of ziprasidone, an antipsychotic agent with combined antagonism at $5HT_{2A}$ and D_2 receptors, were investigated in 30 healthy male subjects using a randomized, placebo-controlled study design.

Method: Once-daily (days 1 and 18) and twice-daily doses (days 4 to 17) of placebo, and 5, 20, 40, and 60 mg ziprasidone were administered in the fed state to five groups of six subjects. The 40 and 60 mg ziprasidone groups received 20 mg on day 1 and were titrated to the final dose by day 10.

Results: Mean pharmacokinetic parameters (day 1/day 18) were:

Dose (mg)	AUC (0-12) (ng·hr/ml)	C_{max} (ng/ml)	T_{max} (hr)	$T_{1/2}$ (hr)
5	74/110	12/15	5.0/5.2	3.2/4.0
20	176/259	27/45	4.8/3.8	4.8/4.8
20→40	315/658	60/119	3.8/3.7	4.0/8.8
20→60	215/1028	34/139	4.0/4.7	4.3/10.0

Steady-state conditions were attained after one day of dosing. Mean C_{max} and AUC (0–12) increased with increasing dose and mean accumulation ratios for the 5 and 20 mg dose levels were 1.49 and 1.48 respectively. Accumulation ratios were not calculated for the higher doses because of the titration.

Conclusions: Longer steady-state half-lives at the higher doses were associated with increased body load of drug leading to the appearance of an additional dispositional phase. The steady-state peak to trough concentration ratios generally ranged from 2 to 5.

NR612 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Multiple-Dose Pharmacokinetics of Quetiapine in Elderly Schizophrenic Patients

James Y.W. Wong, Ph.D., CMA, Zeneca Pharm, 1800 Concord Pike, Wilmington DE 19850; Barbara J. Ewing, Ph.D., George E. Jaskiw, M.D., Per T. Thyrum, M.D., Chiao Yeh, Ph.D.,

Summary:

Seroquel (quetiapine, ICI 204,636) is a dibenzothiazepine derivative currently in Phase III clinical development as an antipsychotic agent. The primary objectives of this study were to investigate the multiple-dose pharmacokinetics and safety of quetiapine in elderly psychotic patients. Twelve patients aged 63 to 85 years meeting the DSM-III-R criteria for chronic schizophrenia and bipolar disorder entered this trial. After a two-day washout period, patients were given quetiapine every eight hours with stepwise increases in dose from 25 to 250 mg per dose. Serial plasma samples were collected following the morning dose after achieving steady state at 100 and 250 mg per dose to evaluate the pharmacokinetics of quetiapine. Nine patients completed this trial. Three patients withdrew because of postural hypertension, dizziness, or tachycardia. There were no deaths. Steady-state pharmacokinetic parameters were calculated by noncompartmental methods. The mean (± SEM) parameters are summarized below:

Dose (mg)	T_{max} (h)	C_{max}(SS) (ng/ml)	C_{min}(SS) (ng/ml)	AUC_{0-8h}(SS) (ng.h/ml)	$t_{1/2}$ (h)	CL/f (L/h)	V_z/f (L)
100	1.2±0.28	507±43.1	146±30.1	2130±243	6.2±0.38	51.5±5.92	471±72.9
250	1.8±0.26	1080±122	355±45.3	4940±504	6.8±0.56	54.7±5.23	513±25.8

No significant differences among doses were found for T_{max}, $t_{1/2}$, oral clearance (CL/f), and volume of distribution (V_z/f), and for dose-normalized C_{max}(SS), C_{min} (SS) and AUC_{0-8h}(ss) values. This indicated that the pharmacokinetics of quetiapine was independent of dose within the dose range studied. Compared to younger patients, the oral clearance (CL/f) in elderly patients was up to 50% lower. This suggests that the clinical effective dose for elderly patients may be 50% lower than that for younger patients.

NR613 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Intensive Group Treatment for Low-Motivated Patients

Douglas M. Ziedonis, M.D., Psychiatry, CMHS, 34 Park Street, New Haven CT 06519; Leslie A. Harmon, B.S., Edna Arlin, M.S.W., Larry Davidson, Ph.D., Bryce Kasuba, B.A., Karen D'Avanzo, Ph.D.,

Summary:

The treatment of individuals with a chronic psychiatric illness and low motivation to address their substance abuse is difficult. This report evaluates a six-month outpatient program for this population. This intensive program focused on motivational enhancement therapy and integrated case management, psychoeducation, relapse analysis, role playing, social skills training, and monitoring of both psychiatric and substance abuse symptoms.

Thirty patients were treated and evaluated for six months. They all had low motivation at entry into the program (35% were in precontemplation and 65% in contemplation). Baseline evaluations included standard psychiatric and substance abuse research assessments, including motivational level assessments. Data were collected weekly and at termination. About 50% of the precontemplators continued in the treatment program and were now "contemplators" who had overall reduced their amount of substance usage, but had not stopped using. One-fourth of the contemplators moved into preparation level of motivation and 20% moved to the action level (these were the only patients who became completely abstinent from substance usage). Seventy-seven percent of the patients completed the treatment program, and these patients had reduced rates of unemployment, hospitalizations, legal problems, psychiatric problems, and substance abuse problems. New strategies must be further developed to address the low motivated clients.

NR614 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Medications for Cocaine Abusing Schizophrenics

Douglas M. Ziedonis, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06525; Jennifer M. Camerato, B.A., Patricia A. Harris, A.S., Kimberlee J. Trudeau, B.A., Surita Rao, M.D., Thomas R. Kosten, M.D.,

Summary:

Cocaine abuse is common among individuals with schizophrenia and impairs psychosocial and treatment outcomes. There are few reports on medication studies in this population.

This outpatient 12week, open-label study compared 13 schizophrenic cocaine abusers treated with adjunctive selegiline and antipsychotics (SEL, 5 to 10mg) to 12 treated with desipramine and antipsychotics (DMI, 100mg to 150mg) and to 15 treated with only antipsychotic agents (NOMED). Selegiline is a "selective" MAO-type B inhibitor which indirectly elevates dopamine levels and may decrease cocaine cravings and negative symptoms of schizophrenia. All 40 patients were in our Dual Diagnosis Relapse Prevention Therapy (substance abuse relapse prevention and social skills training). The average patient was a 30-year-old, single, unemployed, black (60%) male (60%). Subjects receiving DMI had significantly better outcomes than the SEL or NOMED groups (83% of the DMI group completed the study compared to 53% of NOMED and 46% of SEL). Subjects receiving SEL who did better

were those with previous substance abuse treatment and engagement with our clinical program. The sample was too small to determine if patients with higher negative symptoms or other specific subtypes might still benefit with SEL.

Supported by NIDA grant P50-DA04060 & K02-DA0112 (TRK) and K20-DA0193 (DMZ)

NR615 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Pharmacology of Quetiapine: An Atypical Clozapine-Like Antipsychotic

Jeffrey Goldstein, Ph.D., Pharmacology, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850

Summary:

Seroquel (quetiapine, ICI 204,636) is a new antipsychotic drug that resembles clozapine in a broad range of pharmacologic tests predictive of antipsychotic activity and extrapyramidal side effects (EPS) or tardive dyskinesia (TD). In receptor binding, quetiapine interacts with multiple neurotransmitter receptors including dopamine (DA) D_1 and D_2 (IC_{50} = 1243 and 329 nM, respectively), serotonin 5-HT_{1A} and 5-HT_{2A} (IC_{50} = 720 and 148 nM, respectively), adrenergic α_1 and α_2 (IC_{50} = 90 and 270 nM, respectively), and histamine H_1 receptors (IC_{50} = 30 nM). Quetiapine has no appreciable affinity for muscarinic and benzodiazepine receptors (each IC_{50} > 5000 nM). In behavioral tests, quetiapine blocks conditioned avoidance in primates with potency greater than clozapine, and reverses the behavioral effects induced by DA agonists in mice, rats, cats, and monkeys. Like clozapine, it produces only weak catalepsy at doses that antagonize other DA agonist-induced behaviors. In electrophysiologic tests, quetiapine reverses the inhibitory effects of amphetamine on midbrain DA cell firing with limbic selectivity. Neurochemical indices of D_2 receptor blockade, eg, increase in DA metabolites in brain, could also be demonstrated. Quetiapine also meets other pharmacologic criteria that indicate clozapinelike properties. These include low affinity for the D_2 site and greater 5-HT_2/5-HT_6 relative to D_2 ratios, limbic selectivity as evidenced by depolarization blockade of A10 but not A9 DA-containing cells after 28 days' administration, a tendency to produce nonsustained elevations in plasma prolactin levels, minimal dystonic liability in haloperidol-sensitized and drug-naive monkeys, full substitution for clozapine in drug discrimination tests in squirrel monkeys, selective limbic expression of the early gene products c-Fos and FosB, reversal of apomorphine and PCP-induced disruption of prepulse inhibition, reversal of social isolation induced by amphetamine in monkeys, and clozapine-like actions in the Paw Test. The pharmacologic profile of quetiapine predicts that this agent should have atypical antipsychotic actions including enhanced efficacy, compared with standard agents, and minimal EPS and TD liability.

NR616 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Electrophysiological Effects of Olanzapine, a Novel Atypical Antipsychotic, on A9 and A10 Dopamine Receptors

Kurt Rasmussen, Ph.D., CNS Research, Eli Lilly and Co, Lilly Corporate Ctr, Indianapolis IN 46285; Marsha E. Stockton, B.S.,

Summary:

The atypical antipsychotic clozapine is known to have different effects on midbrain dopamine neurons than classical antipsychotics (e.g., haloperidol). In this study, we examined the effects of the novel atypical antipsychotic olanzapine (Zyprex™) on the electrophysiological properties of dopamine neurons in the substantia nigra (A9) and ventral tegmental area (A10).

Methods: Single-unit, extracellular recordings were made from A9 and A10 dopamine neurons in male rats anesthetized with chloral hydrate. The number of spontaneously active dopamine cells was examined following both acute (10, 20 mg/kg, ip) and chronic (10, 20 mg/kg/day for 21 days, ip) administration of olanzapine. In addition, the ability of olanzapine (iv) to reverse the inhibition of A9 and A10 dopamine cells caused by the administration of d-amphetamine (0.5–1.0 mg/kg, iv) was examined.

Results: Similar to clozapine, acute administration of olanzapine caused an increase in the number of spontaneously active A10, but not A9, dopamine cells and chronic administration of olanzapine caused a decrease in the number of spontaneously active A10, but not A9, dopamine cells. In addition, olanzapine, again similar to clozapine, was more potent at reversing the inhibitory effects of d-amphetamine on A10 (ED100 = 0.18 mg/kg) versus A9 (ED100 = 1.0 mg/kg) dopamine cells.

Implications: Olanzapine has electrophysiological effects on dopamine cells that are very similar to clozapine. These electrophysiological properties may play an important role in the atypical antipsychotic profile of olanzapine observed clinically.

NR617 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Effect of Smoking and Gender on Population Pharmacokinetics of Olanzapine

Bela Patel, Ph.D., Pharmacokinetics, Eli Lilly and Co, 1001 West 10th Street, Indianapolis IN 46202; Darcie L. Kurtz, M.S., J. Thomas Callaghan, M.D., Charles M. Beasley, Jr., M.D., Richard F. Bergstrom, Ph.D.,

Summary:

Population pharmacokinetics (pop pk) of olanzapine (OL), a new atypical antischizophrenic agent, were characterized in a multiple-dose, dose-ranging Phase III study. OL plasma concentrations (Cp) from 910 patients (606 men and 304 women, age 18–86 years) obtained during six weeks of double-blind treatment were included in the analyses. Patients received 5 to 20 mg of OL once daily. Plasma samples were collected using a sparse sampling paradigm and analyzed by HPLC/EC. The pop pk analyses were conducted using NONMEM. The pharmacostatistical model was comprised of a one-compartment model, parameterized in terms of the absorption rate constant, clearance (Cl/F), and volume of distribution, and a proportional error model for the inter-individual and residual variability. OL Cp were directly proportional to the dose administered with larger between patient versus within patient variability in Cp. Smoking status and gender were the most influential factors affecting OL Cl/F. Male or female nonsmokers had 37% or 48% lower Cl/F than smokers, respectively. Women had lower Cl/F than men (19% and 33% in smokers and nonsmokers). CYP1A2 metabolic enzyme activity, prominent in OL metabolism, is likely responsible for these differences. Although there was a propensity among nonsmoking females to receive lower doses, participants from each smoking/gender group tolerated the full spectrum of doses.

NR618 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

An Event-Related Potential Study of Visual Spatial and Object Selection in Students and Schizophrenic Patients

Geoffrey F. Potts, Ph.D., Psychiatry, Harvard Med School, 940 Belmont Street, Brockton MA 02401; Brian F. O'Donnell, Ph.D., Jay E. Allard, B.A., Robert W. McCarley, M.D.,

Summary:

Patients with schizophrenia show disruptions in visuo-spatial attention, attributed to parietal lobe deficits. Attention deficits in schizophrenia have also been attributed to frontal lobe dysfunc-

tion. If the dysfunction is frontal, then the attention deficit might be general; if the dysfunction is parietal, then the deficit might be larger in the spatial domain. This study used 64 channel event-related potentials to address this question. Twenty-four students and four DSM-III-R schizophrenic patients viewed four objects appearing at four different locations, one per trial, and pressed a key to targets. In the location task the target was defined by stimulus location; in the object task the target was defined by stimulus shape. P300 amplitude, providing an index of task relevance, was the dependent measure. In the college students, the P300 was equivalent across tasks (P = .19); the patients showed a trend for the P300 to be larger in the object task (p = .07). While not significant with this small N, a visual inspection of the waveforms suggested that processing disruption in the spatial task began before the P300, perhaps by the N1. Thus, spatial attention appears to be differently affected in schizophrenia.

NR619 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Short-Term Visual Memory Deficits in Schizophrenia: Medication and Electrophysiological Correlates

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., Gerard E. Bruder, Ph.D., Craig Tenke, 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 spatial judgements of the same dot patterns, indicated deficits in the short-term visual memory (STVM) of schizophrenia patients. The present study had two goals: a) determine medication (haloperidol, clozapine, or medication withdrawn) effects and, b) examine ERP correlates of DEPOT performance.

Method: A new sample (N = 73: 28 schizophrenic patients, 9 schizoaffective patients, 36 nonpsychiatric controls) was administered DEPOT. A subsample (18 schizophrenic, 3 schizoaffective) was tested on and off haloperidol; eight schizophrenia patients were also compared on clozapine. Patients were recruited from the Schizophrenia Research Unit at NYSPI, and DSM-III-R consensus diagnosed.

Results: There was no medication main nor interaction (by group or tasks) effect. Delayed recall (which measures STVM) interacted with diagnosis and medication ($p < .05$). These findings are consistent with other working memory deficit paradigms. Schizophrenia patients showed marked N1–N2, but not P3, amplitude reductions compared to controls. DEPOT performance correlated with the negative brain potential reduction.

Conclusions: Visual processing in schizophrenia is unaffected by medication, apparently reflecting enduring cognitive deficits. The medication data on the schizoaffective patients are suggestive, but must be interpreted cautiously due to the small sample size. However, if borne out, they may provide important diagnostic and clinical cues. The clozapine results are paradoxical. Larger samples or longer stabilization may be required. These results indicate that medicated schizophrenic patients can be used in future studies of deficit specification.

NR620 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Differential Frontal Deficits in Schizophrenia

Godehard Oepen, M.D., Psychiatry, Boston University, 200 Springs Road, Bedford MA 01730; Edward Federman, Ph.D., Jeff Zareff, Charles Drebbing, Ph.D.,

Summary:

Neuropsycholigical (attention, set shifting, working memory), structural (brain imaging, postmortem) and developmental data support hypofrontality as a main factor in acute and chronic schizophrenia. Negative symptoms (NS) have been better studied in that respect than positive symptoms (PS) generally seen as "functional" and treatment responsive. But PS might conceivably be related to frontal disinhibition (seen as pathological "release" phenomena [H. Jackson]), especially if they are chronically unremitting. In our study, persisting positive and negative symptoms in 22 payed male chronic (5–30 years) schizophrenic inpatients of the Bedford VAMC were documented with the PANSS. Performance in (partially computerized) frontal lobe (FL) tests (CPT, Trails-B, FAS, Working Memory "dot test") was then correlated with the PANSS scores, using t-test and regression analysis. NS correlated strongly with *all* (sign.intercorrelated) FL tests (r = -.5439), but PS did not (r = .1200). This is supported by scatter plots (no outliers). NS correlated significantly with number [P = .02] and speed [p = .05] of false positives (CPT). Thus, hypofrontality is part of NS only, not a general factor in schizophrenic psychopathology, lending support to a dichotomy even of "persisting PS" and NS. In NS, frontal deficits appear pervasive, thus supporting Crow's "bad brain" model of NS.

NR621 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Selegiline for Negative Symptoms and Tardive Dyskinesia

Alan I. Stearns, M.D., NPB, NIMH, 2700 Martin L. King, Jr. Ave, Washington DC 20032; Angelo Sambunaris, M.D., Ahmed M. Elkashef, M.D., Fuad Issa, M.D., Michael F. Egan, M.D., Richard Jed Wyatt, M.D.,

Summary:

Selegiline is a selective and irreversible inhibitor of MAO-B. MAO-B blockade decreases dopamine catabolism and free radical production. Since dopamine agonists have been postulated to help the negative symptoms of schizophrenia, and free radical scavengers have been reported to be helpful in treating tardive dyskinesia, we looked at selegiline's efficacy in the treatment of negative symptoms and tardive dyskinesia. Fourteen patients, 11 males and three females, 11 with tardive dyskinesia, elected to enroll in a double-blind, crossover trial of selegiline. Each subject was randomized to receive selegiline for either the first or last eight weeks of the 16-week protocol. The SANS and AIMS were rated at the end of each leg. A repeated measures Hotelling's T^2 examining for changes in SANS and AIMS was significant (Wilks' lambda = 0.72; F = 4.93; df = 1, 13; < 0.05). Negative symptoms as measured by the SANS improved significantly while patients were on active selegiline (mean decrease in SANS 6.1 $\pm$ 9.9, t = 2.3, p < 0.04). AIMS scores were not affected by selegiline.

NR622 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Reduced Subcortical Brain Volumes in Nonpsychotic Siblings of Schizophrenic Patients

Ming T. Tsuang, M.D., Psychiatry, Mass Mental Hlth Center, 74 Fenwood Road, Boston MA 02115; Larry J. Seidman, Ph.D., Stephen V. Faraone, Ph.D., Jill Goldstein, Ph.D., Julie Goodman, Ph.D., Genichi Matsuda, M.D., William S. Kremen, Ph.D., David Kennedy, Ph.D., Nikos Makris, M.D., Verne S. Caviness, M.D.,

Summary:

Objective: Genetic predisposition to schizophrenia is expressed in nonpsychotic manifestations including abnormalities in eye movements, evoked potentials, and neuropsychological functions

(reasoning, memory, and attention). Because schizophrenics demonstrate severe neuropsychological impairments and also have brain abnormalities, we hypothesized that adult first-degree relatives of schizophrenics might also have brain abnormalities.

Method: Six sisters of schizophrenics and 11 matched female controls participated. These relatives were representative of our larger relatives sample and demonstrated mild neuropsychological deficits such as more WCST perseverations. T-1 weighted 3D images of the entire brain were acquired (slice thickness = 3 mm). Cortical and subcortical gray and white matter were segmented using a semi-automated intensity contour mapping algorithm. Volumes were adjusted for total brain volume.

Results: Gray matter volumes were consistently smaller and ventricular volumes were larger in relatives. In relatives, significant reductions were found in the left thalamus, the right amygdala, pallidum, putamen, and the brain stem.

Conclusions: These preliminary results suggest that some non-psychotic adult siblings of schizophrenic patients have anomalies of subcortical brain structures. If replicated in a larger sample, these results indicate that the schizophrenia genotype is expressed in structural as well as cognitive dysfunctions.

NR623 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Lack of Clinically Significant Abnormalities in MRIs of Older Patients with Schizophrenia and Related Psychoses

Laura L. Symonds, Ph.D., Psychiatry, VA Medical Ctr UCSD, 3350 La Jolla Village Drive, San Diego CA 92161; John M. Olichney, Terry Jernigan, Ph.D., Jody Corey-Bloom, M.D., Dilip V. Jeste, M.D.,

Summary:

Background and Objective: There is a controversy regarding the nature and causation of late-onset schizophrenia. Some investigators have suggested that late-onset schizophrenia and related psychoses often result from various brain lesions such as strokes, and may be different in etiology from early-onset psychoses. We asked the question: Are late-onset psychoses (especially schizophrenia) associated with more frequent clinically-detectable brain abnormalities on MRI than early-onset psychoses?

Method: We employed a qualitative rating scheme to review blindly neuroradiologists' written reports of MRI brain studies of 69 psychosis patients (30 early-onset schizophrenia; 24 late-onset schizophrenia; 15 other late life psychosis, six with early onset, nine with late onset) and 41 normal comparison subjects, all over the age of 45 years. We determined type and severity of clinically-significant abnormalities, including volume loss, infarcts, and white matter hyperintensities.

Results: We found no significant differences between patients and normal comparisons subjects, nor between early-onset and late-onset schizophrenia patients in frequency, type or severity of abnormalities.

Conclusions: The results indicate that late-life psychosis, including late-onset schizophrenia, can exist without clinically-detectable structural brain abnormalities, and in this respect is similar to early-onset schizophrenia.

NR624 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

The Predictors of Schizophrenia

Matti K. Isohanni, M.D., Psychiatry, University of Oulu, Kajaanintie 43, Oulu SF 90220, Finland; Paula Rantakallio, M.D., Peter Jones, M.C.R., Juha Moring, M.D., Jari Tiihonen, Ph.D., Antero Myhrman, Ph.D.,

Summary:

The Northern Finland 1966 Birth Cohort Study is based upon 12,068 pregnant women with an expected delivery date during 1966. Their 12,058 live-born children represent 96% of all births in the region. Data concerning biological, socio-economic and health conditions, living habits, and family characteristics of cohort members have been collected prospectively from pregnancy up to the age of 27. The current investigation of psychiatric morbidity arising in adult life concerned only the 11,017 individuals alive and living in Finland at the age of 16 years. We investigated all their entries to National Finnish Hospital Discharge Register. Until the end of 1993 (age 27 years), a total of 515 subjects had a register diagnosis indicating a psychiatric illness. When operational criteria (DSM-III-R) were applied to clinical information in the original hospital records, 76 fulfilled criteria for schizophrenia. In the preliminary analysis, the following predictive and associating factors are found: pregnancy and obstetric complications were associated with future schizophrenia. Confirmed central nervous system viral infections during childhood carried an increased risk of adult onset schizophrenia and other psychoses. Unwantedness of pregnancy, as asked of mothers at the sixth or seventh month of pregnancy, was associated with future schizophrenia. The risk of criminal behaviour was higher among subjects with schizophrenia, other psychotic disorders, personality disorders, and substance abuse. In the near future, we want to utilize this unique longitudinal data to analyze other predictors and determinants of adult onset mental disorders, especially schizophrenia.

NR625 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Landmark Neuroanatomy of 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. Brookstein, 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 midsagittal MRI scans, utilizing landmark-based shape analysis and image averaging that allow the identification of averaged anatomy via joint registration on multiple landmarks simultaneously. We have previously analyzed MRI scans obtained in the midsagittal plane for 14 patients with schizophrenia and compared them with 14 neurologic controls. The relationship between averaged landmark configuration in the two groups was visualized as a deformation. The data suggest that the neuroanatomic abnormality in the midsagittal plane in schizophrenia is circumscribed (focal), involving primarily the region of the posterior corpus callosum, upper brainstem, and superior cerebellum. 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; however, several limitations of the study impact on generalizability: The imaging parameters for acquiring MRI scans were not identical in patient and control groups, control subjects had not been systematically evaluated prior to inclusion ("neurologic controls"), and the sample size was small. The present study is an attempt to replicate and expand our previous findings while addressing the methodologic shortcomings present in our initial investigation. Subjects included 35 DSM-III-R schizophrenia patients and 26 normal controls. MRI scans were obtained in the coronal plane using identical (3D SPGR) acquisition parameters in both groups. The images used in the analysis were produced by resampling the coronal series in the sagittal plane——this allowed the operator to select the best mid-sagittal slice. Landmark-based shape analysis employing thin-plate splines and image averaging were employed to

identify regional and/or global neuroanatomic differences between groups. The landmarks utilized included frontal, parietal and occipital cortex, genu, mid-point and splenium of corpus callosum, upper and lower pons, tip of fourth ventricle, and superior cerebellum. There were no differences in landmark shape identified between groups; the averaged MRI images for each group corroborate this finding. Important methodologic factors include MRI image acquisition parameters, slice and landmark selection, plane of section, stage of illness when patients are scanned, and treatment history. Three-dimensional curve-based shape analysis may be required to clearly delineate structural neuroanatomic abnormalities and their spatial relationships in schizophrenia.

NR626 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Quality of Life and the Chronically Mentally Ill: A Critical Examination of the Self-Report Methodology

Mark J. Atkinson, Ph.D., Psychiatry, Foothills Hospital, 1403 29th Street, NW, Calgary Alberta, Canada; Henry T. Chuang, M.D.,

Summary:

Objective: The purpose of the study were to evaluate the validity of a self-report methodology among three chronic mentally ill patient groups using several objective indicators of life quality.

Method: The sample consisted of chronic mentally ill patients with a diagnosis of schizophrenia (n = 69), bipolar disorder (n = 37), or major depression (n = 35). Subjects were administered the Quality of Life Index (QLI) and asked about their current financial, living, relational, and health circumstances using a semi-structured interview procedure. The groups were compared on both objective and self-report life quality indices in order to evaluate the validity of a self-report methodology as well as describe differences among groups.

Results: Both mood disordered groups reported significantly lower quality of life on all QLI scales than schizophrenics. When groups were compared with respect to objective life quality indicators in the areas of finances, health, education, and social involvement the opposite relationship was observed. Schizophrenics experienced more objectively aversive life circumstances than either of the affectively disturbed groups.

Conclusion: The validity of self-report methodologies for use with mental health patients is dubious. Scores are likely influenced by reporting bias, poor awareness, and differences in inter- and intrapersonal comparisons.

NR627 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Does Reprovision Benefit Elderly Psychiatric Patients?

Noam Trieman, M.D., TAPS Research Unit, Royal Free Hospital, 69 Fleet Road, London NW3 2QU, United Kingdom; Julian Leff, M.D., Walter Wills,

Summary:

A survey of all inpatients aged 70 years or more was conducted in one of London's mental hospitals (Anderson & Trieman). Baseline measures of cognitive and behavioral disabilities were established for each of the 130 functionally-ill long-stay patients. Three years later 71 patients were still alive, being equally distributed between hospital and community facilities. The study examines the outcomes of patients who had left hospital in comparison with a similar group who remained there. The results indicate that behavior of patients who were settled in the community was stable and even improved slightly over time, as opposed to those who remained in hospital, who became more disabled. Direct examinations demonstrate that while those remained in hospital markedly deteriorated in their cognitive ability, patients who left hospital had also declined, but to a much lesser extent.

We conclude that new forms of milieu, which have shown to be more stimulating and interactive than EMI wards (Wills et al., 1995), seem to sustain a potential of slowing down the declining course of cognitive functioning among elderly schizophrenics and preserving their existing communicative and self-care skills.

NR628 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Outcomes of Homeless Persons with Mental Illness and Substance Use Disorders

Lisa B. Dixon, M.D., Psychiatry, University of Maryland, 645 West Redwood Street, Baltimore MD 21201; Bruce Deforge, Ph.D., Eimer Kernan, M.S.W., Anthony F. Lehman, M.D.,

Summary:

Objective: This study assessed the impact of co-morbid substance use on outcomes in homeless persons with severe mental illness (HPSMI) who participated in a 12-month, prospective, randomized trial comparing assertive community treatment to standard services.

Methods: 123 HPSMI had complete baseline, 2-, 6-, and 12-month data for service use, quality of life (QOL), residential, and clinical status. We compared persons with a current SCID substance use disorder (SUD) (N = 59), a past SUD (N = 33), and no SUD (N = 31) at baseline on these outcomes.

Results: Over the year, current SUD patients spent more nights on the streets ($p < .02$) and in jail ($p < .02$), and more nights in community housing ($p = .055$). All groups had fewer inpatient days, but patients with no SUD had greater reductions than those with current SUD ($p < .05$). QOL improved for all groups. Group by time effects on satisfaction with social relations and safety favored persons with no SUD. Psychiatric symptoms were greater in the current than the no SUD group ($p < .05$).

Conclusions: A baseline current substance use disorder had an adverse impact on housing outcomes and on the reduction of inpatient hospitalization in this study. However, even individuals with a substance use disorder evidenced significant benefits of the program. These data provide more evidence for the importance of addressing substance use in homeless persons with severe mental illness.

NR629 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

An Ounce of Prevention: What Our Patients Don't Know?

Sharon G. Dott, M.D., Psychiatry, University of Texas, 301 University Blvd., D28, Galveston TX 77555; David P. Walling, Ph.D.,

Summary:

Primary prevention of diseases in the chronic mentally ill has become increasingly relevant with the growing presence of this population residing in community settings, epidemic proportions of individuals with communicable diseases, and the effects of new medications in relationship to teratogenicity. The development of novel pharmacotherapy for the severe mentally ill has also increased the attention focused on psychosocial aspects of treatment.

Objectives: 1.) Given the known cognitive deficits of schizophrenia, what is the level of understanding and knowledge of communicable disease in this population? 2.) Is there a relationship between knowledge and behavior in this population?

Methodology: Subjects (n = 88) with the diagnosis of schizophrenia were recruited from a community mental health center population. Three questionnaires were administered: 1.) A general infor-

mation/demographics questionnaire; 2.) Sexual behavior questionnaire; 3.) Infectious disease knowledge questionnaire.

Results: Pilot data reveal that the chronic mentally ill have an impoverished understanding of communicable disease risk factors and prevention techniques. Attempts at general education may encounter subsequent difficulties in implementing preventive measures.

Conclusions: The chronic mentally ill may be at increased risk for transmittable diseases due to limited understanding and knowledge of disease processes and prevention techniques. Cognitive deficits may also contribute to the inability to personalize educational information.

NR630 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Evaluating Models of Condom Use and Risky Sexual Behavior in Young Heterosexual Men

Michael C. Seto, M.A., Forensic, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Vernon L. Quinsey, Ph.D.,

Summary:

Objective: evaluate models of condom use and risky sexual behavior informed by the Fishbein-Ajzen theory of reasoned action, using the technique of structural equation modeling.

Method: questionnaire survey of 221 heterosexual male university students recruited from campus and 58 heterosexual men recruited from the community, all between 18 and 35 years of age. Scales measured attitudes, subjective norms, and intentions regarding condom use and risky sexual behavior (e.g., number of sexual partners, types of activities), and actual condom use and sexual behavior; scales measuring self-efficacy, perceived risk, and a seemingly relevant personality trait, sensation seeking, were also administered.

Results: Models were specified using the student sample and then cross-validated on the community sample. Models based on the Fishbein-Ajzen theory provided good fits to the observed covariances in students for both condom use, GFI = .992, AGFI = .979, and risky sexual behavior, GFI = .958, AGFI = .937. The addition of self-efficacy, perceived risk, and sensation seeking did not improve goodness-of-fit. These models did not generalize to the community sample.

Conclusions: The Fishbein-Ajzen theory of reasoned action has utility in predicting behaviors associated with risk for sexually transmitted diseases, including AIDS, in young heterosexual male university students, and could therefore be useful in guiding public campaigns targeting AIDS risk reduction.

NR631 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Gender Differences in Patients with Chronic Temporomandibular Disorder

Donald S. Ciccone, Ph.D., Psychiatry, NJ Medical School, 185 S. Orange Avenue, Newark NJ 07103; Nancy Just, Ph.D., Erin B. Bandilla, M.A., Richard A. Pertes, D.D.S.

Summary:

Research shows that women with chronic temporomandibular disorders (TMD) outnumber men by at least 3:1. Despite the prevalence of TMD among women, few studies have examined gender differences in this population. At issue in the present study is the extent to which females with chronic TMD differ from their male counterparts in mood, illness behavior, and in the incidence of masticatory muscle and TM joint pathology. The study sample consisted of 98 female and 24 male consecutive referrals to a TMD center (4.1:1 ratio). Females did not differ from males on the basis of age, marital status, education, race, symptom duration, depression, or anxiety. However, on the Sleep and Rest scale of the Sickness Impact Profile, females reported a lower level of activity than males, $t(103) = 2.3$, $p < .03$. They also reported an average of 38.4 disability days during the preceding six months compared to only .74 days for males, $t(97) = 2.5$, $p < .001$. Females rated their pain symptoms as more intense, $t\ (106) = 3.0$, $p < .003$, and indicated higher levels of discomfort on the Hopkins Somatization Scale, $t(103) = 2.1$, $p < .04$. Females were diagnosed with concurrent joint and masticatory muscle disorders more often than males. While 76% of females received a diagnosis of both muscle and joint pathology, only 40% of males received this dual diagnosis, $x^2\ (3) = 10.40$, $p < .02$. The higher incidence of organic pathology among female patients may account for some or all of the observed differences in psychosocial functioning.

NR632 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Neuropsychological Functioning Before and After Methylphenidate Treatment in Adults with ADD

Henry J. Riordan, Ph.D., Psychiatry, Dartmouth Medical, One Medical Center Drive, Lebanon NH 03756; Kevin E. Carroll, Ph.D., Laura A. Flashman, Ph.D., Andrew J. Saykin, Psy.D., Leighton Y. Huey, M.D.

Summary:

Objective: To characterize the neuropsychological (NP) test performance of adult patients with ADD and evaluate any changes in cognitive and personality functioning following a brief trial of methylphenidate.

Method: 40 consecutive adult outpatients who presented to the neuropsychiatry clinic at DHMC for evaluation of possible residual ADD underwent a standardized clinical interview (based on DSM-IV criteria for ADD) and a comprehensive NP test battery. Of these patients, 21 met formal criteria for ADD.

Results: Univariate analyses suggested no difference between ADD and non-ADD in terms of age, education, or intelligence. However, the ADD group performed significantly worse on the distractibility condition of a visual continuous performance test ($t = 4.76$, $p < .01$), and all conditions of the Stroop color-word interference test ($t = 2.4$, $p < .02$; $t = 2.3$, $p < .02$; $t = 3.26$, $p < .002$). There was also a trend for the ADD patients to perform worse on measures of verbal fluency, cognitive flexibility, and verbal memory. Additionally, ADD patients endorsed fewer symptoms of depression and anxiety on the BDI ($t = 2.6$, $p < .01$) and the STAI ($t = 1.98$, $p < .05$; $t = 3.39$, $p < .002$). Both patient groups were then compared to 130 normal controls on z-transformed NP summary scores. While both patient groups performed somewhat lower than normal controls in general, the ADD patients demonstrated specific deficits in distractibility ($Z = -1.32$) and verbal memory ($Z = -1.28$). Nineteen ADD patients were retested after an average of 30 days on methylphenidate (0.5 mg/kg). Repeated measures analyses suggested improved NP test performance on measures of complex visual attention ($F = 26$, $p < .0001$), auditory distractibility ($F = 17$, $p < .0007$), fine motor and psychomotor speed ($F = 7.6$, $p < .0001$; $F = 38.8$, $p < .0001$). ADD patients also reported significant fewer symptoms of depression ($F = 13.9$, $p < .001$) and state and trait anxiety ($F = 18.23$, $p < .0006$; $F = 25.63$, $p < .0001$) following treatment.

Conclusions: A significant proportion of individuals who are self-referred or referred by another caregiver for evaluation of possible residual adult ADD do not meet criteria for this disorder. These results support the importance of utilizing psychometric testing in the diagnosis of adult ADD and its role in evaluating the effectiveness of pharmacologic intervention.

NR633 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Criteria for Separating Normality and Psychopathology

Massimo Biondi, M.D., Clinical Psychiatry, Viale Universita 30, Rome 00158, Italy; Maria Caredda, M.D., Angelo Ricciardi, M.D.

Summary:

Background: DSM-IV and ICD-10 suggest psychosocial functioning and symptom distress to discriminate between mental disorders and normality. The present study examines nine different criteria (c.): 1) uncommon and bizarre behaviors (statistical c.) 2.) somatic or CNS alterations (biological c.), 3) socially divergent behavior (conformity c.), 4) formal and content thought disorders (thought alterations c.), 5) behavior diverging from original cultural-background (cultural anthropological c.), 6) psychosocial and job functioning, 7) subjective suffering and reduction of freedom, 8) emotional development (psychodynamic c.), 9) alterations of basic "human ethology" behaviors (ethological c.).

Aim: To explore if these nine criteria are applicable in a clinical population.

Methodology: Eighty consecutive psychiatric outpatients (eight groups, each of 10 subjects with eight DSM III-R diagnosis) and 20 normal controls (15–65 yrs) were included. A visual analogue scale rated each subject on a 0–10 score according to each criterion.

Results and discussion: Different DSM-III-R groups show different profiles of alteration of normality according to the nine criteria. Number of altered criteria increases with severity of psychopathology. Each criterion shows different descriptive power in different disorders and within diagnostic groups. DSM-IV and ICD-10 criteria were confirmed as useful (although rough) indicators of the normality/psychopathological boundary. The proposed nine criteria could be of interest from a theoretical point of view for a better definition of mental disorder. They could also be of practical interest in cases of clinical uncertainty.

NR634 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Artificial Neural Network Improves Psychiatric Diagnosis

Yizhuang Zou, M.D., Washington Institute, 9601 Steilacoom Blvd, SW, Tacoma WA 98498; Yu-Cun Shen, M.D., Liang Shu, M.D., Feng Feng, M.D., Yixin Zhong, Ph.D., Ying Qu, M.D.

Summary:

Artificial Neural Network (ANN), as a potential powerful classifier, was used to assist psychiatric diagnosis of the Composite International Diagnostic Interview (CIDI). Both Back-Propagation (BP) and Kohonen networks were developed to fit psychiatric diagnosis and trained (using 60 cases) to classify neurosis, schizophrenia, and normal people. The structure, initial weights, learning rate, training coefficient, training model, and fuzzy weights of the networks were selected, tested, and modified repeatedly. The trained networks were cross-tested using another 222 cases. Compared to the diagnosis of senior psychiatrists, the overall Kappa of BP network was 0.94 and that of Kohonen was 0.88. In classifying patients who were difficult to diagnose, the Kappa of BP network was 0.69. ANN assisted CIDI was compared with expert system assisted CIDI (Kappa = 0.72 – 0.76). The result showed that ANN was more powerful than the traditional expert system, and BP network was better than Kohonen. This suggests that ANN might be used to improve psychiatric diagnosis, though further research is necessary.

NR635 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Negative Symptoms in a Major Depressive Disorder

Igor I. Galynker, M.D., Psychiatry 6K, Beth Israel Med Ctr, First Avenue at 16th Street, New York NY 10003; Jun Cai, M.D.

Summary:

Objective: We have recently shown that negative symptoms (NS) as measured by the Scale for the Assessment of Negative Symptoms (SANS) and Positive and Negative Symptom Scale negative subscale (PANSS-N) are prevalent in patients with dementia of Alzheimer's type (DAT) and patients with basal ganglia strokes. The purpose of this study was to examine the interrelationship of negative symptoms, depressive symptoms, and cognitive deficits in patient with major depressive disorder (MDD).

Methods: Hamilton Rating Scale for Depression (HRSD), Positive and Negative Symptom Scale (PANSS), SANS, the Mini-Mental Status Examination (MMSE), and the Trail Making Test A (TMA) were administered to 23 patients with MDD and 10 normal control subjects.

Results: The mean scores of HRSD, PANSS, SANS, and TMA were significantly higher than in control subjects (Mann-Whitney U-statistic > 190.0 $p < .001$). Within the MDD group, there was a significant correlation between HRSD scores and PANSS general subscale (PANSS-G) scores (Spearman $r = .60$ $p < .005$) and between SANS scores and PANSS-N ($r = .77$ $p < .001$) and PANSS-G ($r = .45$, $p < .05$) scores. The HRSD scores did not correlate significantly with SANS, PANSS-N, MMSE, or TMA scores. There was no significant correlation between SANS or PANSS-N, and MMSE or TMA score. There was no significant correlation between PANSS-P scores and any of the other measures.

Conclusion: These results indicate that NS are prevalent in patients with MDD, but are distinct from symptoms of depression and positive psychotic symptoms. Specifically, in MDD the NS severity does not correlate with the severity of depressive symptoms.

NR636 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Negative Symptoms Associated with Hypofrontality in Stroke Patients

Igor I. Galynker, M.D., 46 Valley Ln, Chappaqua NY 10514; Naomi Vilkas, B.A., Dragos Serseni, M.D., Eamon Dutta, M.D., Marias Focseneanu, M.D., Richard N. Rosenthal, M.D., Fukiat Ongseng, M.D., D. Howard Finestone, M.D.

Summary:

Objective: The purpose of the current study was to establish if correlation exists between regional cerebral blood flow (rCBF) in stroke patients and psychiatric symptom severity in these patients.

Method: Eleven patients with the diagnosis of cerebrovascular accident (CVA), were administered the Hamilton Rating Scale for Depression (HRSD), Scale for the Assessment of Negative Symptoms (SANS), the Positive and Negative Symptom Scale (PANSS), and the Mini-Mental Status Examination (MMSE). Each patient underwent a SPECT scan using Tc-99m HMPAO and an ADAC 1 head SPECT camera. Images were analyzed by two raters who were blind to the patients' identities, diagnoses, and the purpose of the study. Transaxial images were displayed on a computer terminal. Cortical and subcortical regions of interest (ROIs) were symmetrically defined in each hemisphere. Cerebellar ROIs were selected in the middle portion of each cerebellar hemisphere. Cortical-to-cerebellar perfusion ratios were established quantitatively and correlation analyses performed using SYSTAT 5.2 software package.

Results: There was a significant negative correlation between the SANS and PANSS negative subscale scores and rCBF in the orbitofrontal cortex bilaterally (SANS: left Pearson $r = .59$ $p < .05$,

right r = .58, p = .05; PANSS: left r = –.53, p = .07, right r = –.55, p = .06). In patients with CVA there was no significant correlation between HRSD, PANSS positive and general subscale scores, and MMSE scores and rCBF. None of the subjects in this study had CVA directly involving orbitofrontal cortex.

Conclusion: These results are consistent with the previous report of decreased perfusion in the antero-medial frontal cortex in CVA patients with NS and with the frontal cortex involvement in the etiology of negative symptoms.

NR637 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Suicide by Self-Immolation and Ethnicity: An Epidemiological Study

Manohar K. Shetty, M.D., Psychiatry, St. Frencis Medical Ctr., 410-B Glen Malcolm Drive, Glenshaw PA 15116; Thyagaraja Kumaran, M.D., David J. Lynn, M.D., Radha K. Kambanpati, M.D.

Summary:

Introduction: We retrospectively studied suicidal self-immolation in a multi-cultural and multi-ethnic population of Trinidad. South Asians comprise 38% of the population and have been present for three generations. Other studies have found self-immolation at a high frequency in South Asia.

Method: The Burns unit treats all the burns in the country. Among 1,208 burn cases for the period 1985 to 1992, there were seven cases of self-immolation. We compared the findings with other violent methods of suicide in Trinidad and compared the data with international studies.

Results: Six of the seven cases were fatal. Five of the six fit the following profile: Females aged 25 to 35, South Asians, married with children in intact families, no prior psychiatric history, abusive marital relationship, and lived in rural settings. Other violent methods were concentrated in other ethnic groups. None of the six descriptors above predicted a high risk for completed suicides of Western population.

Conclusions: Self-immolation has traditional meanings for South Asians and has been socially accepted. Cultural factors persisting for three or more generations account for the high rate of self-immolation. Demographic risk factors for completed suicide generated from Western population data are not valid far ethnically non-Western population. Clinicians should be aware of this while assessing suicide risk.

NR638 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Ethnic Consonance As a Determinant of Treatment Adherence

Leon L. Bernhardt, M.D., Psychiatry, Metropolitan Hospital, 1901 First Avenue, New York NY 10029; Joanne Caring, M.D.

Summary:

At an inner-city hospital that provides care for the seriously and persistently mentally ill, the highest risk inpatient groups were targeted to search for methods to improve compliance with treatment plans. The two highest risk groups, the homeless and those who had not previously been followed-up in our OPD, both presented with a 30% rate of outpatient follow-up after discharge from inpatient hospitalization. The patients were randomized to intervention or control groups. The intervention design was based on principles summarized by Meichenbaum & Turk in the book *Facilitating Treatment Adherence.*

The results showed that there were two statistically significant factors that resulted in a decrease in patients' adherence: substance abuse and ethnicity. The link between ethnicity and substance abuse was not strong enough to achieve statistical significance.

It is postulated that ethnicity plays an unappreciated role in outcome, and that ethnic groups that feel accepted in a given institution will utilize that institution. In order to maximize treatment outcome for under-represented ethnic groups in a specific population, there is a possible interactive role for consumer advocates or staff of the same ethnic group as the patients.

NR639 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Course of Acute Affective Disorders in India

Alan S. Brown, M.D., Psychiatry, New York State Psych Inst, 722 West 168th Street Unit 2, New York NY 10032; Vijoy K. Varma, M.D., Savita Malhotra, Sarah A. Conover, M.P.H., Ezra S. Susser, M.D.

Summary:

Objective: Despite a substantive literature on course of affective disorders in industrialized countries, little is known about the course of affective illness of an acute onset, and this question has rarely been addressed in a developing country.

Method: The Chandigarh Acute Psychosis Study (CAPS) in India included 41 cases of acute onset affective disorder (17 depressive and 24 manic subjects), who were assessed at intake and evaluated at selected intervals up to one year. The rates of recovery and relapse and the total duration of the index episode were determined for both the depressive and manic groups, and the relationship between possible predictors of outcome to the duration of the index episode was examined.

Results: All subjects experienced full recovery within a one-year period and 83% of the sample recovered within four months. At one-year follow-up, 71% of depressive patients and 75% of manic patients demonstrated no symptoms or social impairment. For depression, the mean episode duration of depression was only 14.2 weeks, and for mania, our subjects had a lower rate of relapse than in developed countries. These outcomes are considerably more favorable than those of affective disorders in developed settings.

Conclusion: Our findings suggest that acuteness of onset may be a major prognostic factor in predicting the course of affective disorders. These results clearly indicate the need for future studies in order to separate the influences of mode of onset and sociocultural setting to these favorable outcomes.

NR640 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Ethnicity and Imipramine Responses

Dora C. Anderson, B.S.N., Psychiatry, Rei Harbor-UCLA, 1124 West Carbon Street, Torrance CA 90502; Michael W. Smith, M.D., Yan-Ping Zheng, M.D., Keh-Ming Lin, M.D., Russell Poland, Ph.D., Inocencia Nuccio, M.S.N.

Summary:

Objective: This study examines the pharmacokinetics of imipramine, a tricyclic antidepressant (TCA), and its relationship to CYP2D6 activity (debrisoquine hydroxylase) in four ethnic groups.

Methods: A total of 119 healthy volunteers (28 African-Americans, 33 Asians, 28 Caucasians, and 30 Hispanics) were included in this placebo-controlled, double-blind, single-dose study of the pharmacokinetics of imipramine. On three separate testing sessions, each subject was given imipramine (50 mg PO), imipramine (25 mg IM), or placebo. Baseline and 14 post-treatment blood samples were obtained sequentially for up to 48 hours during each of the sessions. Plasma imipramine and desipramine concentrations were determined by a specific radioimmunoassay. CYP2D6 activity also was measured in 100 of the 119 subjects (25 African-Americans, 24 Asians, 25 Caucasians, and 25 Hispanics) by assessing the metabolic ratio between dextromethorphan

and dextrophan (DMMR) in the urine after the administration of 35 mg of dextromethorphan.

Results: No significant differences among the four ethnic groups were found in all pharmacokinetic parameters for imipramine. There were also no significant differences in the concentration of desipramine among the Asian, Caucasian, and Hispanic groups. However, African-Americans had significantly higher desipramine AUC and C^{max}. This difference remained statistically significant after controlling for body surface area, age, gender, smoking, coffee, tea, and alcohol consumption. CYP2D6 activity correlated significantly with both imipramine and desipramine concentrations. Three subjects (two Caucasians and one Hispanic) were classified as poor metabolizers (PM). They had significantly higher PO imipramine and desipramine concentrations compared to the other subjects, who were classified as extensive metabolizers (EM).

NR641 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Psychiatric Emergency Room Visits of Asian-Indians

Chitra M. Shenoy, M.D., Psychiatry, Nassau County Med Ctr, 3303 Shore Road, Oceanside NY 11572-2822

Summary:

Objective: The purpose of this study was to examine the emergency help-seeking behavior of Asian Indians.

Methods: Emergency psychiatric visit charts of Asian Indians from 1990–95 were reviewed. The demographic data examined included age, gender, marital status, employment history, mode of arrival, prior psychiatric contacts, reason for the visit, diagnosis, disposition, and number of revisits.

Results: Of a total of 26,952 emergency room (ER) visits, 33 were Asian Indians. Of the 33, 24 (73%) were immigrants and nine (27%) born and raised in the United States.
Age: mean 30 years (range 13–56) *Gender:* male 14 (42%); female 19 (58%) *Marital status:* married 14 (42%); single 19 (58%)
Employed and students: 24 (73%); others 9 (27% unemployed 2, housewife 3, unknown 4)
Mode of arrival: Brought by police 24 (73%); others 9 (27% self 3, family 3, other 3) *Prior psychiatric contacts:* 10 (30%)
Reasons for visit: suicidal attempt/ideation 16 (49%); homicidal ideation 2 (6%); behavioral aggression 11 (33%); other 4 (12%)
Diagnoses: Adjustment disorder 11 (33%); Depressive disorder nos 4 (13%); Major depression, bipolar disorder, psychotic disorder nos 3 (9% each); substance (alcohol, cannabis, cocaine) abuse 3 (9% comorbid 3); delusional disorder, anorexia/bulimia nervosa, conduct disorder, oppositional defiant disorder, mental retardation 1 (3% each); marital problems 1 (3% comorbid marital 3, other relationship problems 14)
Disposition: Hospitalized 16; outpatient treatment 14, referral to forensic services 2; no referral 1. *ER revisits:* 2

Conclusions: The Asian Indians formed 0.12% of the patients visiting the psychiatric ER during the past six years. They were usually young, more likely to be single females. The majority were employed or students. Police contact was frequent (73% of cases). Affective disorders were predominant. Marital and other relationship problems were prominent (50%). Schizophrenia was strikingly absent. Successful crisis intervention probably accounts for rare revisits to the ER.

NR642 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Differential Behavioral and Physiological Responses to Cholinergic Agonist Challenge Before and After Chronic Scopolamine Alzheimer's Disease

Ruth A. Dukoff, M.D., LCS 10-3D41, NIMH, 10 Center Drive MSC 1264, Bethesda MD 20705; Marcel Bahro, M.D., Judy Friz, M.A., Karen Putnam, B.A., Anne Conway, M.A., Susan E. Molchan, M.D., Trey Sunderland, M.D.

Summary:

Introduction: We have recently demonstrated that Alzheimer's patients (AD) and elderly normal controls (NC) have significantly different brain imaging responses (^{123}I-QNB and ^{99}TcHMPAO SPECT) to chronic blockade with low-dose scopolamine (Sunderland 1995). Our current study further tested that finding with acute cholinergic challenges of physostigmine before and after chronic high-dose scopolamine treatment. Our hypothesis was that chronic blockade would result in differential behavioral and physiologic responses across groups of AD and NC subjects.

Method: Nine NC (mean age 65.5 ± 5.1 years) and eight AD (mean age 70.3 ± 6.4 years) received two infusions of physostigmine (0.5 mg iv push over 5 minutes), separated by 21 days of 1.2 mg of nightly scopolamine. No scopolamine was given the night prior to a physostigmine infusion. Vital signs and behavioral rating scales (BPRS, physical symptom check list, and self rating scale) were administered at baseline and 30 minutes after the physostigmine infusion.

Results: After chronic scopolamine, AD patients showed a statistically significant change in systolic blood pressure (baseline to + 30 minutes) during the physostigmine infusion ($p < 0.01$), but this did not occur with the NCs. The AD group also showed a significant increase in the BPRS-24 ($p < 0.05$) after receiving physostigmine ($p < 0.05$), whereas the NCs were essentially unchanged. On self-report, AD patients complained of a significant increase in irritability and weakness compared to controls when given physostigmine after chronic treatment ($p < .01$).

Conclusion: Contrasting behavioral and physiologic responses between the AD and NC groups were observed on a physostigmine challenge test after treatment with chronic scopolamine. Consistent with our previous finding of different responses in brain imaging following a lower dose of scopolamine, AD patients appeared more sensitive to cholinergic stimulation after chronic cholinergic blockade. These data lead to speculation about differential cholinergic upregulation in AD and NC, suggesting that underlying cholinergic integrity may influence neuronal plasticity responses to chronic treatments.

NR643 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

A Review of Psychiatric Consultations for Mental Capacity in an Urban Teaching Hospital

Cheryl A. Kennedy, M.D., Psychiatry, UMDNJ-NJ Med School, 185 South Orange Avenue, Newark NJ 07103; James M. Hill, Ph.D.

Summary:

Objective: To monitor patient care and service interface, we explored factors which might predict follow-up for medical inpatients who receive psychiatric consultation for determination of mental capacity for informed consent or for participation in discharge planning.

Method: Sequential psychiatric consultation records for 15 months were reviewed. Demographic data, time from admission to consult request, substance use history, HIV status, capacity status, and recommendations for follow-up were collected. Multivariate analysis was used to predict follow-up.

Results: Of 480 consultations, 67 (14%) were for mental capacity. Of those, 63% were male, 76% were African-American, 12% white, 7% Latino, and 4% other races. The average age was 52 (range 20–87). The average time, in days, from admission to consultation request was 10 days (range 0–62). Sixty-seven percent received follow-up. Capacity status was not predictive of follow-up. Nearly 20% of those with HIV and lacking capacity, did not receive follow-up. Only race (not being black, $p = 0.02$) and

more days before consult request (p = 0.03) were positively associated with follow-up.

Conclusions: Follow-up was not dependent on evaluation outcome. Capacity can be dynamic; these results suggest that psychiatrists must be alert for particular follow-up needs in these patients and potential bias in determining follow-up.

NR644 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Stimulants for SSRIs-Induced Sexual Dysfunction

Barbara D. Bartlik, M.D., Psychiatry, NY Hospital Cornell Med., 1625 Third Avenue, New York NY 10128; Peter M. Kaplan, M.D., James H. Kocsis, M.D., Carol A. Roeloffs, M.D., Richard A. Friedman, M.D., Alan J. Cohen, M.D.

Summary:

In her 1974 book, *The New Sex Therapy*, Helen Singer Kaplan, M.D., Ph.D. stated that stimulants enhance libido and sexual functioning when used acutely, but are inhibitory when used chronically, in high dosages. We too have observed that the intermittent use of low dose psychostimulants enhances sexual responsivity, and we are using them in patients with a variety of sexual disorders, medication induced and otherwise. For patients on selective serotonin re-uptake inhibitors (SSRIs), stimulants are particularly helpful in reversing the well known inhibitory effects of these medications upon sexuality.

This poster will present an open study in which the psychostimulants dextroamphetamine and methylphenidate were 80% effective in reversing SSRI-induced sexual dysfunction in twenty-five patients. All treatment failures were unable to tolerate side effects, and did not experience a lack of sexual responsivity in itself. The positive effects of stimulants across all phases of the sexual response cycle——desire, excitement (erection), orgasm and resolution——will also be described.

In addition, anecdotal information will be presented on other prescribed and over-the-counter medications with stimulatory or cerebral enhancing effects that are also thought to augment sexual functioning. These are: pemoline, ginseng, ginkgo biloba, pseudoephedrine and caffeine.

NR645 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

GAD: Influence of Comorbid Bipolar Illness on the Age of Onset

Gary S. Sachs, M.D., Psychiatry, Mass General Hospital, 815 WACC 15 Parkman Street, Boston MA 02114; Claudia F. Baldassano, M.D., Christine J. Truman, B.A., Beny Lafer, M.D., Una Jain, B.A.

Summary:

Objective: Comorbidity of generalized anxiety disorder (GAD) and bipolar mood disorder is common. To determine if such comorbidity represents the course of one illness or independent psychopathology, the age of GAD onset in patients with comorbid bipolar illness (GB) was compared to the age of GAD onset in patients without bipolar illness (GO).

Method: GO subjects (n = 17) were participants in a GAD treatment trial which excluded bipolar patients. These subjects were age- and sex-matched with a sample GB patients drawn from a naturalistic bipolar illness study. Paired t-test was used to compare age of GAD onset recorded at study entry by interviewers using the Structured Clinical Interview for DSM III-R.

Results: GAD onset was significantly earlier in the GB group (13.41 ± 7.70 vs. 22.12 ± 14.82, p = .03). In the GB group mean age at first affective episode was 16.31 (± 9.32) years.

Conclusions: The early onset of GAD when comorbid with bipolar disorder suggests that childhood anxiety disorders might be an antecedent to bipolar illness. Prepubertal GAD may be a risk factor identifying children vulnerable to early onset of bipolar mood disorder.

NR646 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Comorbidity of ADHD with Early- and Late-Onset Bipolar Disorder

Gary S. Sachs, M.D., Psychiatry, Mass General Hospital, 815 WACC 15 Parkman Street, Boston MA 02114; Claudia F. Baldassano, M.D., Christine J. Truman, B.A., S. Nassir Ghaemi, M.D.

Summary:

Objective: To examine the relationship between attention deficit hyperactivity disorder (ADHD) and bipolar mood disorder.

Methods: Fifty-four adult bipolar subjects participating in an ongoing naturalistic study were interviewed using the Structured Clinical Interview for DSM III-R, Schedule for Affective Disorders and Schizophrenia, Epidemiologic Version (Kiddie-SADS-E), and Diagnostic Interview for Children and Adolescents-Revised (DICA-R). Subjects were classified as early onset bipolar (EOB) (≤ age 18) or late onset bipolar (LOB) (ℓ age 19). Bipolar subjects also meeting criteria for ADHD (B/A) and were age- and sex-matched with eight probands without a history of ADHD (B/O).

Results: B/A subjects had a significantly earlier age of onset of the first affective episode than B/O subjects (12.1 ± 4.64 vs. 20 ± 11.3 years, p < .01, paired t test). The prevalence of ADHD among the EOB subjects (61.5%) was significantly higher than LOB subjects (0%) (chi square, p < .05). All observed cases of ADHD were found in those with early onset bipolar illness.

Conclusions: These findings suggest that early onset of non-affective illnesses, such as ADHD, might be useful markers identifying children at risk for early development of bipolar disorder.

NR647 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Low Energy Radio Waves for the Treatment of Anxiety: A Double-Blind Study

Gary S. Sachs, M.D., WACC 815/Psychiatry, Mass General Hospital, 15 Parkman Street, Boston MA 02114; Boris Pasche, M.D., Beny Lafer, M.D., Alexandre Barbault, B.A., Claudia F. Baldassano, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: For the most part, the interaction between living cells and background radio frequency electromagnetic waves appears to have little physiological consequence. Low energy emission therapy (LEET), a program of AM frequencies selected for treatment of anxiety, appeared beneficial in a preliminary open trial. This double-blind, placebo-controlled trial evaluated the efficacy of LEET for the treatment of patients meeting DSM III-R criteria for generalized anxiety disorder.

Methods: Patients were randomly assigned to treatment with an active or placebo transmitter device. Investigators blind to the treatment assignment rated anxiety symptoms using the Hamilton Anxiety Scale (Ham-A) at follow-up visits. Because there was a significantly higher drop-out rate in the placebo treated group, completer and endpoint analyses were carried out based on the a priori criteria for response (Ham A ≤ 9).

Results: The completer analysis revealed no significant differences. Endpoint analysis, however, demonstrated a higher response rate in the active treatment group (71.4%) than the placebo group (37.5%) that reached marginal levels of significance (Chi Square = 3.45, 2 tailed, p = 0.063).

Conclusion: This study suggests that selected AM electromagnetic waves have anxiolytic efficacy. LEET is a novel treatment modality and may have broad medical and psychiatric applications.

NR648 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Prevalence of Depression During Hospitalization for Bone Marrow Transplantation: Effects of Diagnostic Criteria

Jesus Prieto, Psiquiatria, Hosp. de Sant Jaume, Mulleres N15, Olot 17800, Spain; Jordi Blanch, Jorge Atala, Cristobal Gasto, Esteve Cirera

Summary:

Objective: This study used different approaches to case identification to examine prevalence rates for major (MD) and minor depression (md) in a group of patients with hematological malignancies.

Method: A consecutive series of 103 patients hospitalized for bone marrow transplantation at the Hospital Clinic in Barcelona were evaluated on admission and weekly until discharge.

Results: Diagnosis according to DSM-IV (exclude somatic symptoms related to a physical condition), DSM-III (include all somatic symptoms), and Endicott's revised criteria (replace somatic symptoms with non-somatic ones) are shown in the following table:

	DSM-IV		DSM-III		Endicott Criteria	
Diagnosis	N	%	N	%	N	%
MD	3	3	26	25	10	10
md	31	30	16	15	25	24

Taking into account the existing literature, a low rate of major depression was obtained when using DSM-IV criteria. The higher rate obtained with DSM-III can be related to the prevalence of somatic symptoms. After receiving intensive treatment and during the following four weeks, 95% to 81% of patients reported an energy loss ℓ 30%, with 98% to 78% reporting a moderate decrease in appetite.

Conclusions: When somatic symptoms are prevalent, an approach that relies more on psychological features can increase the diagnostic accuracy for mood disorders.

NR649 Wednesday, May 8, 3:00 p.m.-5:00 p.m.

Psychiatric Morbidity in the Bone Marrow Transplantation Setting

Jesus Prieto, Psiquiatria, Hosp. de Sant Jaume, Mulleres N15, Olot 17800, Spain; Jordi Blanch, Jorge Atala, Esteve Cirera, Cristobal Gasto

Summary:

Objective: This prospective inpatient study was conducted to determine the nature, extent, and timing of psychiatric morbidity in a group of patients hospitalized for bone marrow transplantation.

Method: A consecutive series of 103 patients admitted at the Hospital Clinic in Barcelona were evaluated on admission and weekly until discharge. We used DSM-IV criteria for diagnosis as well as the Hospital Anxiety Depression Scale to monitor affective symptomatology. Endicott's revised criteria (substitution of somatic symptoms by non-somatic alternatives) were used to diagnose major depression.

Results: Forty-nine (48%) patients received at least one DSM-IV diagnosis. We found the following prevalence rates: adjustment disorders 29%, major depression 10%, other anxiety and mood disorders 3%, medication-induced disorders 16%, delirium 6%, and personality disorders 3%. When only considering anxiety and mood disorders, we diagnosed 28 (27%) patients on admission and 15 (15%) during hospitalization; 28% of these affective disorders persisted until discharge, whereas 37% were considered to last $\leq$ than two weeks. Psychotropic medication was prescribed in a high percentage of patients: antihistamines 69%, benzodiazepines 64%, methadone 46%, neuroleptics 25%, and antidepressants 12%.

Conclusion: High prevalence of psychiatric disturbances (mainly affective disorders) is observed in this population. Consultation-liaison psychiatry plays an important role in the management of these patients.

NR650 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Mood Disorders in 3,372 Male Twin Pairs

Michael J. Lyons, Ph.D., Psychiatry, Harvard University, 940 Belmont Street, Brockton MA 02401; Nong Lin, Ph.D., Seth Eisen, M.D., William True, Ph.D., Rosemary Toomey, Ph.D., Joanne Meyer, Ph.D., Stephen V. Faraone, Ph.D., Ming T. Tsuang, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the influence of genetic and environmental factors on mood disorders in men.

Summary:

Objective: This study addresses the question of the extent to which genetic and environmental factors influence the risk of mood disorders in men.

Method: Data were collected from 3,372 pairs of male veteran twins from the Vietnam Era Twin Registry. Subjects were administered the Diagnostic Interview Schedule by telephone. *DSM-III-R* diagnoses of major depression, bipolar disorder, cyclothymia, and dysthymia were derived from the interview data.

Results: The prevalence of major depression was 10%, which is consistent with male prevalence rates in other large epidemiological samples. A significantly higher concordance rate for monozygotic versus dizygotic twins indicated a significant genetic influence on the risk of major depression. The results of biometrical modeling indicated that additive genetic factors and the unique environment explain significant variance in major depression.

Conclusion: Familial resemblance for major depression in males is due to genetic factors and is not influenced by the environment shared by the twins (i.e., the family environment). However, aspects of the environment that are not shared by twins (i.e., the unique environment) are an important influence on the risk for major depression in males. Bipolar disorder, cyclothymia, and dysthymia were also examined using identical methods.

References:

1. Kendler, K.S., Neale, M.C., Kessler, R.C., Health, A.C., Eaves, L.J. Familial influences on the clinical characteristics of major depression: a twin study. *Acta Psychiatrica Scandinavica*, 86(5), 1992, 371–378.

2. Kendler, K.S., Kessler, R.C., Walters, E.E., MacLean, C., Neale, M.C., Heath, A.C., Eaves, L.J. Stressful life events, genetic liability, and onset of an episode of major depression in women. *Am J Psych*, 152(6), 1995, 833–842.

NR651 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Clinical Features of Bipolar Disorder Linked to Chromosome 18

Francis J. McMahon, M.D., Psychiatry, Johns Hopkins, 600 N Wolfe St. Meyer 3–181, Baltimore MD 21287–7381; Jianfeng Xu, M.D., Colin Stine, Ph.D., Sylvia G. Simpson, M.D., J. Raymond DePaulo, Jr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the clinical features characteristic of bipolar disorder that is linked to chromosome 18; and understand methods of genotype/phenotype correlation.

Summary:

Objective: Previously we reported significant excess sharing of alleles at several chromosome 18 marker loci by sib-pairs with bipolar disorder. The greatest excess sharing was observed for paternally transmitted alleles at D18S41. We have now investigated whether affected sib-pairs sharing paternally-transmitted alleles at D18S41 also share clinical features.

Method: Within 28 families genotyped for markers on chromosome 18, all sib pairs affected with bipolar I (BPI), bipolar II (BPII), or recurrent unipolar disorder were scored for unambiguous sharing of paternally-transmitted alleles at D18S41. Phenotype data were obtained from SADS-L interviews performed by psychiatrists. Clinical subtype was based on best-estimate diagnoses. The sample comprised 113 affected sib-pairs: 51 pairs shared alleles, 21 pairs did not share, and 41 pairs were uninformative.

Results: Significant differences in allele sharing were observed between sib pairs based on clinical subtype ($p < .05$): 47% of BPI/BPI sib pairs shared alleles, compared to 86% of BPI/BPII sib pairs, and 100% of BPII/BPII sib pairs. Sharing pairs were significantly correlated for age at first mania or major depression ($p < 0.01$), while non-sharing pairs were not. No significant correlations were observed in either group for number of episodes of mania or major depression.

Conclusions: We conclude that paternally-transmitted alleles at D18S41 are significantly associated with clinical subtype, particularly BPII, and that sharing pairs have more similar ages at onset than non-sharing pairs. Some cases of BPII may differ genetically from BPI disorder.

References:

1. OC Stine, JF Xu, R Koskella, et al.: Evidence for linkage of bipolar disorder to chromosome 18 with a parent-of-origin effect. *Am J Hum Genet* 57:1384–1394, 1995.

2. FJ McMahon, OC Stine, DA Meyers, et al.: Patterns of maternal transmission in bipolar affective disorder. *Am J Hum Genet* 56:1277–1286, 1995.

NR652 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Treatment of Pregnancy-Related Mood Disorders

Susanne I. Steinberg, M.D., Psychiatry, St. Marys Hospital, 3830 Lacombe Ave, Montreal PQ H3T 1M5, Canada; Francois Bellavance, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize a more comprehensive list of risk factors that place women at risk for antenatal and postpartum mood disorders; and to recognize different patterns of response of depressive symptoms, marital difficulties and personality features to an eclectic form of treatment. (e.g., demonstrate, recognize, diagnose, treat...)

Summary:

This investigation involves a population of 151 women, 105 diagnosed by DSM-IV criteria as having a mood disorder during pregnancy or with a postpartum onset and 46 healthy women, followed prospectively during pregnancy and the puerperium, who served as a reference group. An eclectic *non* time-limited form of treatment, including individual therapy, using strategies from both cognitive and interpersonal psychotherapy, pharmacotherapy, and marital interventions were offered to each index case. Both groups completed the same battery of questionnaires, scoring mood, (Hamilton Depression Rating Scale) marital adjustment, (Spanier Dyadic Adjustment Scale) and personality scales (Eysenck Personality Inventory and Interpersonal Sensitivity Measure) over a six-month period. The results suggest some novel factors that place women at risk for mood disorders associated with pregnancy: immigrant status, intermarriage, failed attempts at breast feeding, deceased fathers, concurrent bereavement, and adult child of alcoholic. Furthermore, patterns of response to treatment of depressive symptoms varied significantly ($p < 0.001$) over time between the two index groups: adjustment disorders vs. major depression. This was also true for marital adjustment as measured by the total score of the DAS, ($p < 0.017$), and the subscales of cohesion ($p = 0.076$) and satisfaction ($p = 0.005$). No such changes were noted for the personality traits. In conclusion, mood disorders associated with pregnancy required the full six months of treatment for a sufficient response, which calls into question the benefit of the cost efficient short-term interventions currently in style.

References:

1. Stewart S., O'Hara M.W. Interpersonal psychotherapy for postpartum depression: A Treatment Program. J *Psychotherapy Practice and Research* 4:18–29, 1995.

2. Wisner K.L., Wheeler S.B. Prevention of recurrent postpartum major depression. H & CP 45:1191–1196, 1994.

NR653 Thursday, May 9, 9:00 a.m.-10:30 a.m.

PMS: Do Ovarian Steroids Modulate Mood?

Dianne E. Schechter, Ph.D., Psychiatry, Columbia University, 722 West 168th Street, New York NY 10032; Tracey J. Strasser, B.A., Jean Endicott, Ph.D., Eva Petkova, Ph.D., John Nee, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize a menstrual cycle pattern of symptom expression. The participant also will have a greater understanding of how ovarian steroids may modulate mood and such knowledge may influence the evaluation and treatment of women with mood disorders.

Summary:

Objective: The aim of this pilot study was to test whether premenstrual mood varies as a function of ovarian steroid levels among women with "pure" PMS.

Method: Eleven women monitored mood and collected a urine sample daily for three cycles. Specimens were assayed for metabolites of estradiol (E) and progesterone (P). We postulated that each individual has a "trait" level of premenstrual mood and hormone, expressed as an average of several cycles, as well as a "state" level of mood and hormone, expressed as a deviation from the individual's mean.

Results: Longitudinal random regression was used to model the intensity of premenstrual mood as a function of mean luteal hormone level for each individual (between-subjects) and deviation of the observed hormone level from an individual's own mean (within-subject). Severity of premenstrual negative mood was positively related to luteal phase P (regr coeff = 1.89, df = 21, T = 3.20, $p < .005$), but was not related to luteal phase E. Positive mood was negatively related to P (regr coeff = −1.76, df = 21, T = −2.14, $p < .05$) and positively related to E (regr coeff = 1.90, df = 21, T = 2.82, $p < .02$), with the E/P ratio being the best predictor (regr coeff = 1.87, df = 21, T = 3.46, $p < .003$). The within-subject (across multiple cycles) and between-subjects relationship between ovarian hormones and premenstrual mood did not differ.

Conclusion: Ovarian steroids may play a role in modulating premenstrual mood in women who show sensitivity to the menstrual cycle.

References:

1. Halbreich U, Bancroft J, Dennerstein L, Endicott J, Faccinetti F, Genazzani A, Morse C, Parry B, Rubinow D, Reid R, Schiff I,

Smith S, Bäckström T: Menstrually related disorders: Points of consensus, debate, and disagreement. *Neuropsychopharmacology* 9:13–15, 1993.

2. Schechter D, Bachmann GA, Vaitukaitis JL, Philips D, Saperstein D: Perimenstrual symptoms: Time course of symptom intensity in relation to endocrinologically defined segments of the menstrual cycle. *Psychosom Med* 51:173–194, 1989.

NR654 Thursday, May 9, 9:00 a.m.-10:30 a.m.

HPT and HPA Axis Dysfunction in Depression: Dopaminergic, Noradrenergic and Serotoninergic Correlates

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 end of this presentation, the participant should be able to understand the interrelationships of the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-adrenal (HPA) axes with the dopaminergic, noradrenergic, and serotoninergic systems in depression.

Summary:

Objective: The aim of this study was to examine the interrelationship of the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-adrenal (HPA) axes with the dopaminergic (DA), noradrenergic (NA), and sero-toninergic (5HT) systems in depression.

Method: We studied hormonal responses to 8AM and 11PM protirelin (TRH) tests, dexamethasone suppression test (DST), apomorphine (APO) test, clonidine (CLO) test, and d-fenfluramine (FEN) test in 52 medication-free inpatients with DSM-IV major depressive disorder.

Results: We found significant associations between post-DST cortisol (COR) nonsuppression (DST positive) and blunted TRH-induced TSH release (ΔTSH), both at 8AM and 11PM (both: $p < 0.02$). However, abnormally low difference between 11PM-ΔTSH and 8AM-ΔTSH (ΔΔTSH) was independent of DST nonsuppression. A factorial correspondence analysis characterized four groups defined by TRH tests and DST status. Group 1 (blunted ΔΔTSH alone (33%)) was characterized by blunted growth hormone (GH) response to CLO, blunted prolactin and COR responses to FEN, and normal COR response to APO. Group 2 (blunted 11PM-ΔTSH and ΔΔTSH without DST abnormality (22%)) was characterized by blunted COR response to APO. Group 3 (DST positive associated with at least one TRH abnormality (24%)) was characterized by blunted GH response to CLO. Group 4 (no abnormality (21%)) was characterized by normal GH response to CLO.

Conclusions: These results suggest that HPA hyperactivity may be related to α2-adrenoreceptor dysfunction. However, α2-adrenoreceptor dysfunction in conjunction with defective central 5HT response may be involved in chronobiological dysregulation of the HPT axis (blunted ΔΔTSH). Blunted 11PM-ΔTSH may be related to functional alteration of the DA receptors.

References:

1. Holsboer F. Neuroendocrinology of mood disorders. In: Bloom; F.E.; Kupfer, D.J. *Psychopharmacology: the fourth generation of progress.* New York: Raven Press, pp. 957–969, 1995.

2. Duval F, Macher JP, Mokrani MC. Difference between evening and morning thyrotropin response to protirelin in major depressive episode. *Arch Gen Psychiatry* 47:443–448, 1990.

NR655 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Focal Neuroanatomic Correlates of Minor Depression

Anand Kumar, M.D., Psychiatry, University of Pennsylvania, 3615 Chestnut Street, Philadelphia PA 19104; David S. Miller, M.D., Edward E. Schweizer, M.D., Jin Zhisong, M.S., Warren Bilker, Ph.D., Susan Romberg, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that focal neuroanatomical abnormalities contribute to Minor Depression occurring in Late Life. (e.g., demonstrate, recognize, diagnose, treat...):

Summary:

While magnetic resonance imaging (MRI) studies have provided us with information on the neuroanatomical basis of late life major depression, the structural correlates of minor depression in late life remain unexplored. The purpose of our study was to examine the structural correlates of late life minor depression using MRI-determined focal and global volumetric measures of brain and CSF and to compare them to similar measures obtained in age-matched non-depressed controls. Our study groups were comprised of 32 subjects with minor depression using DSM-IV criteria (15 M, 17 W, Mean age = 70 SE–7.2) and 31 controls (7 M, 24 W, Mean age = 70.5 SD = 6.4). Subjects with minor depression had Hamilton Depression Rating Scale Scores between 8 and 16 inclusive without any evidence of dementia or other CNS disease. Axial spin echo images were obtained using a 1.5 tesla GE signa scanner with head coil. Five mm thick contiguous slices were obtained using a repetition time of 3000 msec (TR) and echo time (TE) of 30 and 80 msec in planes parallel to the canthomeatal line. Anatomical boundaries and landmarks used in the analysis have been previously described. (Cowell et al. J. *Neurosci* 1994). Focal and global measures of brain and CSF, Normalized to total brain and intracranial volumes, were used for comparison between groups. Normalized frontal lobe volume was significantly smaller ($p < 0.01$) in the minor depression group when compared to controls. Normalized temporal lobe volume and global measures of CSF were not significantly different between the two groups. These data demonstrate that frontal lobe atrophy, determined using quantitive MRI, may underlie minor depression occurring in late life.

References:

1. Coffey CE, Figiel GS, Djang WT, et al. *Biol. Psychiatry* 24:143–161, 1988.

2. Krishnan KRR, Annual Rev Med 42:261–266, 1991

NR656 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Treatment of Major Depression After Acute Myocardial Infarction with Sertraline: A Preliminary Study

Peter A. Shapiro, M.D., Psychiatry, Columbia University, 622 West 168 Street, New York NY 10032; Alexander H. Glassman, M.D., Francois Lesperance, M.D., Christopher M. O'Conner, M.D., Brian Baker, M.B., Lidia Lidagoster, M.D., Wei Jiang, M.D., Paul Dorian, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to treat patients with depression following acute myocardial infarction with an understanding of the effects of sertraline treatment.

Summary:

Background: Depressive disorder and depressive symptoms following acute myocardial infarction are associated with in-

creased mortality. Recent research suggests increased risks with tricyclic antidepressant treatment in this population, but there are no comparable data for serotonin reuptake inhibitors.

Methods: A multi-center, open-label pilot study of sertraline treatment (50–200 mg/day) was conducted with consecutive patients hospitalized for acute myocardial infarction and screened for major depressive disorder within 5 to 30 days. Outcome measures included efficacy, adverse events, and effects on cardiovascular and hemostatic function.

Results: Twenty-six patients enrolled in the study. The mean Hamilton Depression Rating declined from 20.2 to 9.7. Mean resting heart rate increased from 62.8 to 67.8 beats/minute. Bleeding time increased in 12 patients, decreased in four patients, and was unchanged in two patients. There were no significant effects on left ventricular ejection fraction, ventricular premature depolarizations, ventricular arrhythmias, or prothrombin time, and no adverse events requiring study withdrawal.

Conclusion: Sertraline treatment was associated with clinical improvement and no major adverse effects in this open-label treatment of post-myocardial infarction patients with major depression. Controlled trials are indicated to further establish the effects of treatment for this high-risk population.

References:

1. Frasure-Smith N, et al. Depression Following Myocardial Infarction. Impact on 6-Month Survival. *JAMA* 270:1819–1825, 1993.

2. Glassman AH, et al. The Safety of Tricyclic Antidepressants in Cardiac Patients. Risk-Benefit Reconsidered. *JAMA* 269:2673–2675, 1993.

NR657 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Effects of Acute and Chronic Paroxetine on Regional Brain Metabolism in Depression

Sidney Kennedy, M.D., Psychiatry, Clarke Institute of Psych, 250 College Street Room 1125, Toronto ON 00054, Canada; Franco J. Vaccarino, Ph.D., Sylvain Houle, M.D., Gregory M. Brown, M.D., Kenneth R. Evans, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to distinguish immediate (acute) from delayed (chronic) pharmacological effects of paroxetine on regional cerebral metabolism; and to identify the overlap between these regions and areas associated with major depression (e.g., demonstrate, recognize, diagnose, treat...):

Summary:

The efficacy of selective serotonin reuptake inhibitors (SSRIs) has been established after chronic but not acute administration. However, little is known about neuroanatomical sites of action for these agents, or about differences in affected brain regions following chronic and acute administration. In an effort to explore these issues, PET and FDG were used to measure regional cerebral glucose metabolism following acute and chronic paroxetine treatment of unipolar depressed patients.

Drug-free male subjects who met DSM-IV criteria for major depression (with HAM-D > 17) received PET scans (FDG) before and during paroxetine treatment. All subjects were scanned immediately prior to paroxetine treatment; the acute group received a second scan five hours after the initial dose of paroxetine, while the chronic group received a second scan following six weeks of continuous paroxetine treatment. Brain regions which showed increased or decreased activity following acute or chronic treatment were delineated using the SPM method.

Findings indicate that chronic paroxetine treatment produced increases in the right cuneus and parietal regions while decreases were found in the anterior cingulate, right caudate, and right prefrontal cortex. None of these changes were observed following acute treatment, nor were there any sites which were selectively activated by acute treatment. These results suggest that the brain regions implicated in the effects of chronic treatment with paroxetine are distinguishable from the regions implicated in acute effects and may reflect sites of antidepressant action. In addition, the present results are consistent with previous reports implicating prefrontal cortex, caudate, and cingulate regions in the pathophysiology of depression.

References:

1. Bench CJ, Frackowiak RSJ, Dolan RJ. Changes in regional cerebral blood flow on recovery from depression. *Psycho Med* 1995; 25:247–251.

2. Martinot JL, Hardy P, Feline A, et al. Left prefrontal glucose hypometabolism in the depressed state: a confirmation. *Am J Psychiatry* 1990; 147:1313–1317.

NR658 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Identification and Treatment of Depression in Primary Care

M. Philip Luber, M.D., HT4, NY Hospital-Cornell, 525 East 68th St, New York NY 10021; George S. Alexopoulos, M.D., James Hollenberg, M.D., Mark Callahan, M.D., Mary E. Charlson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify primary care physicians' level of recognition of depressive illness in their patients and their choices of pharmacological treatment when recognized. Further to understand the correlation of depression in primary care with increased medical comorbidity and increased utilization of resources.

Summary:

The purpose of this study was to examine the recognition, treatment, comorbidity, and resource utilization of depressed patients in a general internal medicine practice.

Methods: Clinical and demographic information were obtained from the computerized practice database for all 15,126 patients seen at a university-based general internal medicine practice from over a period of one year.

Results: 4.7% (N = 707) patients received an ICD-9 diagnosis of depression. Middle-aged and elderly patients were diagnosed as depressed more frequently than younger patients, with no significant differences between middle-aged and elderly. A total of 39.5% (N = 279) of these patients were treated with an antidepressant; of these, 22.9% with a selective serotonin reuptake inhibitor and 13.4% with a tricyclic (most common: amitriptyline). Depressed patients suffered from more comorbid medical illnesses (mean Charlson Comorbidity Index score of 1.89 versus 1.19), and used more health care resources as measured by number of outpatient visits (mean of 5.3 versus 2.9), number of medications (mean of 12.1 versus 6.3), and length of stay when hospitalized (mean of 8.4 excess days versus 4.3 over calculated expected length of stay). ($P < .0001$ for all.)

Conclusion: Given the higher frequency of depression reported by the ECA study, it appears that depression was under-recognized and under-treated in this general medical practice. The selection of antidepressant medication was generally within accepted clinical algorithms except for the frequent choice of amitriptyline for medically ill and elderly patients. Depression was significantly correlated with increased medical comorbidity and with high utilization of health care resources across all age groups.

References:

1. Wells KB, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients; results from the Medical Outcomes Study. *JAMA* 262:914–919; 1989.

2. Regier DA, Narrow WE, Rae DS, et al. The de facto US mental and addictive disorders service system; epidemiologic catchment area prospective 1-year prevalence rates of disorders and service. *Arch Gen Psychiatry.* 50:85–94; 1993.

NR659 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Prevalence of Subclinical Hypothyroidism in Depressed Patients with Normal Baseline TSH

Robert P. Kraus, M.D., Psychiatry, Victoria Hospital, 375 South Street, London ON N6A 4G5, Canada; Elizabeth Phoenix, B.Sc.N., Merrill W. Edmonds, M.D., Ian R. Nicholson, Ph.D., Praful C. Chandarana, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that up to 35% of depressed patients with screening TSH 3.00–5.50 mIU/L may have subclinical hypothyroidism contributing to their depression; and demonstrate evidence of subclinical hypothyroidism in such patients by performing the TRH Stimulation Test and noting exaggerated (ℓ25 mIU/L) TSH responses to TRH. (e.g., demonstrate, recognize, diagnose, treat...):

Summary:

Objective: Subclinical hypothyroidism can produce depression and is confirmed by an exaggerated TSH response to TRH on the TRH stimulation test (TRH-ST). The "normal" TSH range is 0.35–5.5 mIU/L. We performed the TRH-ST in depressives with "high normal" TSH to determine the prevalence of subclinical hypothyroidism.

Method: Fifty-one depressed patients with TSH 3.00–5.50 mIU/L underwent an early morning TRH-ST. TRH 400 μg was injected intravenously, and post-TRH TSH determined at +20 mins., +30 mins, and +40 mins. A TSH rise ℓ25 mIU/L after TRH defined an exaggerated ("positive") response.

Results: Eighteen patients (35%) had a positive TRH-ST, suggesting subclinical hypothyroidism. This prevalence is significantly ($\chi^2_{(1)} = 59.65$, $p < 0.001$) greater than the 6% prevalence of positive TRH-ST reported in the euthyroid general population. Unexpected observations were a lack of correlation in TSH levels week to week ($r = 0.17$, ns), and a lack of correlation between screening TSH value and subsequent TRH-ST results ($r = 0.28$, ns).

Conclusions: Thirty-five percent of depressed patients with TSH in the "high normal" range revealed evidence of subclinical hypothyroidism on the TRH-ST. Subclinical hypothyroidism may be contributing to depression in these patients. Assumptions that a TSH less than 5.50 mIU/L "excludes hypothyridism" in depressed patients may be invalid.

References:

1. Haggerty JJ, Stern RA, Mason GA, Beckwith J, Morey CE, Prange AJ. Subclinical hypothyroidism: a modifiable risk factor for depression? *Am J Psychiatry* 150:508–10; 1993.

2. Klee GG, Hay ID. Assessment of sensitive thyrotropine assays for an expanded role in thyroid function test: proposed criteria for analytic performance and clinical utility. *J Clin Endocrine & Metabolism* 64:461; 1987.

NR660 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Low-Dose Amisulpride Versus Fluoxetine in 281 Dysthymic Patients: A Randomized Medium-Term (3 months), Double-Blind Study

Franco Biondi, M.D., Medical Department, Synthelabo SPA, Via Rivoltana 35, Limito Milan 20090, Italy; Gianluigi Casadet

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the therapeutical role of drugs increasing dopaminergic activity (specially at limbic level) in dysthymia.

Summary:

Introduction: Amisulpride is a substituted benzamide with high affinity for presynaptic D_2/D_3 dopamine autoreceptors and virtually no affinity for D_1 receptors; it also shows a preferential affinity for limbic rather than striatum structures; at low doses (50 mg/day) it has important activating and prohedonic properties justifying its use in conditions involving lack of motivation and inability of getting pleasure from usual activities, typical of dysthymia.

Objective: to compare efficacy and safety of Amisulpride (A) 50 mg/day vs Fluoxetine (F) 20 mg/day in patients meeting DSM III-R criteria for dysthymia.

Method: study design: one week of single-blind placebo run in to exclude placebo responders (>20% reduction of Montgomery-Asberg depression rating score or score ≤ 14), and three months of double-blind, per parallel groups, active treatment. *Clinical setting*: 19 University and/or Hospital centers of Psychiatry. *Evaluation criteria*: efficacy primary outcome: ℓ 50% reduction of baseline MADRS total score; secondary outcomes: MADRS, Hamilton-anxiety (HAM-A), Retardation Scale, Sheehan Disability Scale, CGI (items 1–2). Safety: Somatic inventory (CHESS), Columbia University Rating Scale, CGI (item 3), adverse events (AE) and routine laboratory controls.

Results: 281 patients entered the study; 268 patients (139 A, 129 F) with at least one follow-up evaluation were considered for intention-to-treat analysis of efficacy and 278 for safety (three patients lost to follow-up immediately after baseline). Withdrawals were 72 (A 32, F 40) with no between-group difference for lack of efficacy and AE. *Efficacy*: responders (primary outcome of efficacy) were 74.1% (103) in A group and 67.4% (87) in F group ($p = 0.230$, n.s.). For all but one (HAM-A) efficacy scales no between-group statistically significant difference was found; for HAM-A a statistically significant difference in favour of A was found (before/final HAM-A mean total scores were 21.4/7.7 for A and 21.6/10.1 for F; $p = 0.0293$). *Safety*: clinical tolerability was similar in the two groups: no difference was found in number of patients experiencing ℓ1 AE (A 67/141, F 56/137; $p = 0.324$, n.s.); no clinically relevant change of laboratory parameters was found.

Conclusions: Amisulpride 50 mg/day was at least as effective as Fluoxetine 20 mg/day in the medium-term treatment (three months) of dysthymic patients; both drugs showed satisfactory clinical and biological tolerability.

References:

1. Maubrey MC: Profil Pharmacologique et Biochimique de L'Ami-Sulpride. *Ann Psychiatr.* 3:284–297, 1988, Book.

2. Borenstein P. et al: *Amisulpride* Paris, Expansion Scientifique Francaise, 1989

NR661 Thursday, May 9, 9:00 a.m.-10:30 a.m.

Two-Year Outcome of Anxious Depression in Late-Life

Alastair J. Flint, M.B., Psychiatry, Toronto Hospital, 200 Elizabeth St, 8 Eaton N., Toronto ON M5G2C4, Canada; Sandra L. Rifat, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that symptomatic anxiety at index assessment does not appear to have an impact on the longterm outcome of geriatric depression, once the episode of depression has remitted and patients are maintained on full-dose antidepressant treatment.

Summary:

Objective: To determine whether there was a difference in the long-term outcome between elderly patients with anxious depression and those with nonanxious depression.

Method: Eighty-four patients with nonbipolar, nonpsychotic major depression who had responded to treatment of the index episode were maintained on full-dose antidepressant medication and followed on a monthly basis over a period of two years. Based on their score on the hospital anxiety and depression scale at index assessment, subjects were divided into anxious and nonanxious groups and were then compared on the frequency of relapse and recurrence, and the cumulative probability of survival over two years.

Results: There were no statistically significant differences between groups on rates of relapse or recurrence. Anxiety status was not a significant predictor of survival. Of the patients who suffered a recurrence, anxious and nonanxious groups did not differ in the total duration of the recurrence or the time to respond to treatment of this new episode.

Conclusions: In contrast to studies of mixed-age patients, we did not find that elderly patients with anxious depression had a significantly worse long-term outcome compared with nonanxious patients. The fact that all patients entering this study had responded to treatment of the index episode and were then maintained on full dose antidepressant treatment throughout the follow-up period may have accounted for the better prognosis of this anxious depressed group.

References:

1. Flint AJ. Epidemiology and comorbidity of anxiety disorders in the elderly. *Am J Psychiatry* 151:640–649, 1994.

2. Lydiard RB. Coexisting depression and anxiety: special diagnostic and treatment issues. J *Clin Psychiatry* 52(6)suppl:48–54, 1991.

NR662 Thursday, May 9, 12 noon-2:00 p.m.

The Efficacy of Once-a-Week Fluoxetine Dosing in the Treatment of Panic Disorder

Naresh P. Emmanuel, M.D., Dept of Psych, MUSC, 171 Ashley Avenue, Charleston SC 29425–0002; Carolyn Cosby, R.N., Michael R. Ware, M.D., R. Bruce Lydiard, M.D.

Summary:

The cost of psychotropic medications influences the management of patients. High cost of medications can lead to noncompliance or taking medication in less than optimal doses. Panic disorder is a chronic condition that consumes significant medical resources. The SSRI's are useful in the treatment of panic disorder. Fluoxetine is an SSRI with an extensive half life. The aim of this investigation was to determine if patients can be maintained panic free on a single weekly dose of fluoxetine. To date, 12 patients who met DSM-IV criteria for panic disorder with or without agoraphobia were prescribed fluoxetine once daily (10–30 mg) till the patient reported no panic attacks. The patient was then switched to once a week dosing (10–40 mg), giving the subject the previously effective daily dose once weekly.

Of the 12 patients enrolled so far, 10 were switched to once a week dosing, after two to six weeks of daily medication. To date, these 10 patients remain panic free utilizing once a week fluoxetine dosing. Safety and efficacy data will be presented on maintenance once weekly fluoxetine therapy for panic disorder in an larger sample.

NR663 Thursday, May 9, 12 noon-2:00 p.m.

The Benefit of Client-Centered Treatment on Panic and Agoraphobia Symptoms

Ludwig Teusch, D.R., Psychiatry, Uni Essen, Virchowstr 174, Essen 45147, Germany; Hildegard Boehme, Prof. Dr. Markus Gastpar

Summary:

Objective: Shear et al. (Am. J. Psychiat. 150:6, 1993) say that psychodynamic treatment is of little benefit in amelioration of panic and agoraphobia symptoms. This is subject of the present controlled study.

Methods: 40 patients with severe panic and agoraphobia (DSM-III-R No. 300.21) were admitted to an inpatient anxiety treatment program at the psychiatry department of Essen University Hospital. The patients were randomly assigned to pure client-centered therapy or to additional behavioral exposure treatment. Client-centered (Teusch & Finke) and behavioral (Mathews et al.) agoraphobia manuals were used. The patients were examined at admission, at discharge, and at three, six, and 12 months follow-up with regard to panic (SCID) and anxiety (HAMA), agoraphobia (SCID, FSS), and depressive (HAMD) symptoms.

Results: Both client-centered treatment and a combination with exposure treatment reduced panic, avoidance, and depressive symptoms significantly. The combined treatment reduces agoraphobia symptoms faster. At one-year follow up both treatment conditions do not differ concerning anxiety and depressive symptoms.

Comment: Although psychodynamic methods will be at a disadvantage by exclusively considering reduction of symptoms, they prove to be highly effective. The results are discussed with regard to recent process- and disorder-related approaches of client-centered therapy and to its combination with exposure treatment.

NR664 Thursday, May 9, 12 noon-2:00 p.m.

Gender-Mediated Clinical Features of OCD and Obsessive-Compulsive Syndrome: New Data From a Large French Clinical Sample

Elie G. Hantouche, M.D., SHU, Hospital Sainte Anne, 29 Avenue Georges Bernanos, Paris 75005, France; Marc L. Bourgeois, M.D., Myriam Bouhassira, M.D., Sylvie Lancrenon, Ph.D.

Summary:

A French survey "Screening-Understanding-Treating OCD" was conducted with 240 psychiatrists. Phase 1 (screening OCD and OCS) was conducted in 4,364 patients. Phase 2 (clinical phase) included a cohort of 646 OCD or OCS patients (screened from phase 1, DSM-III-R criteria) and explored the clinical aspects of the OC illness: typology and symptomatic categories (YBOCS check list), clinical intensity (NIHM-OC, CPRS-OC 2 items), OCD spectrum (Hollander and Rapoport definitions), comorbidity, and psychiatric, family, and treatment history.

The results concerning the gender-mediated clinical manifestations of OCD/OCS are as follows: Male patients suffered more from aggressive, sexual, or religious obsessive thoughts (36% vs. 28%, p = 0, 06) and from symetric-order obessions (40% vs. 26%, p = 0,0003). They showed higher rate of OCD than OCS (65% vs. 54%, p = 0,03), higher scores on NIMH-OC (7, 3±2, 3 vs. 6, 8±2, 5, p = 0,005), CPRS-OC 2 (6, 8±2, 4 vs. 6, 4±2, 4, p = 0, 04), more avoidance behavior (25% vs 16%, p = 0, 02) and severe slowness (23% vs. 16%, p = 0, 05), higher comorbidity rate with hypochondriasis (45% vs. 34%, p = 0, 03) and compulsive para-

philia (5% vs. 2%, p = 0, 01). Female patients presented higher comorbidity with eating disorders (31% vs. 12%, p < 0, 0001) and compulsive buying (22% vs. 15%, p = 0, 02). The results are relevant in practice and explain some aspects of gender-mediated clinical expression in obsessions and compulsions. More investigations are needed to detail the severity augmentation of OCD and OCS in male patients (clinical subtypes, comorbidity, associated features).

NR665 Thursday, May 9, 12 noon-2:00 p.m.

Death Anxiety and Death Attitudes in Panic Disorder and GAD

Vladan Starcevic, M.D., Psychiatry, Institute of Mental Health, Palmoticeva 37, 11000 Belgrade, Yugoslavia; Stephanie K. Fallon, M.D., Eberhard H. Uhlenhuth, M.D.

Summary:

Objective: To assess levels of death anxiety and determine death attitudes in patients with panic disorder (PD) and generalized anxiety disorder (GAD), compared with control group (CG) subjects.

Method: The Death Anxiety Scale (DAS) and Attitudes Toward Death Questionnaire were administered to 54 PD patients, 49 GAD patients, and 35 CG subjects. The SCID was used to diagnose PD and GAD as principal conditions, with PD patients and GAD patients having similar patterns of Axis I and Axis II comorbidity.

Results: PD patients had a significantly higher DAS score (9.50 on the scale from 0 to 15) than both GAD patients (6.59) and CG subjects (5.80), and they endorsed more death attitudes per patient (the mean of 6.0 for PD vs. 4.16 for GAD vs. 3.57 for CG). PD patients endorsed six out of 20 death attitudes with significantly higher frequency than CG subjects, and four death attitudes with significantly higher frequency than GAD patients. GAD patients differed very little from CG subjects in terms of frequency with which they endorsed death attitudes.

Conclusions: PD patients are more afraid of death and more pre-occupied with death than both GAD patients and controls. Since death anxiety is negatively correlated with suicidal ideation (Minton and Brush, 1980–1981), PD patients may be less likely to exhibit suicidal ideation as long as their death anxiety remains high.

NR666 Thursday, May 9, 12 noon-2:00 p.m.

Personality Change After Treatment of Panic

Vladan Starcevic, M.D., Institute of Mental Health, Palmoticeva 37, 11000 Belgrade, Yugoslavia; Stephanie K. Fallon, M.D., Eberhard H. Uhlenhuth, M.D.

Summary:

Objective: To determine personality changes after effective short-term treatment of panic disorder (PAD).

Method: Fourty-two PAD patients were administered SCID-II before and after a 12-week effective treatment with alprazolam. The interviewer conducting the second SCID-II was blind to the results of the baseline SCID-II. Each DSM-III-R personality disorder (PD) trait was scored on a 3-point scale (1 = absent; 2 = subthreshold; 3 = present), and comparisons were made for each trait score between the baseline and 12-week assessments.

Results: Three traits of the avoidant PD (unwillingness to get involved in the absence of certainty of being liked, reticence in social situations, and fear of embarrassment), indecisiveness, and excessive social anxiety showed the greatest decrease in scores. Two traits of the passive-aggressive PD (complaints of being asked to do too much and negative reaction in response to being asked to do what one does not want to do) and anger-laden sensitivity characteristic of paranoid PD showed the greatest increase in scores. Traits of schizoid, schizotypal, and histrionic PD appeared most stable, as their scores changed minimally.

Conclusions: Traits of avoidant PD in PAD patients may be more likely to represent a consequence of PAD since they do not endure even over the course of its short-term treatment. Personality traits that appear more prominent after treatment of PAD may reflect greater assertiveness or perhaps some of the disinhibition phenomena associated with the alprazolam treatment.

NR667 Thursday, May 9, 12 noon-2:00 p.m.

Evaluating Suffocation False Alarm Hypothesis of Panic Disorder

Hisanobu Kaiya, M.D., Psychiatry, Nagoya Mental Clinic, 1–16 Tsubaki-Ch Recru Bld 3Flr, Nagoya Wakamura Ku 453, Japan; Matui Akira, M.D.

Summary:

From the evidence that carbon dioxide hypersensitivity elicits panic attacks, Klein's group hypothesized that physiologic misinterpretation by a suffocation monitor misfires an evolved suffocation alarm system. This produces sudden respiratory distress followed swiftly by a brief hyperventilation, panic, and the urge to flee. They proposed a distinction between panic disorder with and without respiratory symptoms.

The present study was conducted to evaluate their hypothesis in 351 patients with DSM-III-R panic disorder (F/M = 42/58, mean age = 34.7 ± 9.5 years).

Results: Klein's proposal that patients with respiratory symptoms as a main sign (PRS) have fewer nonsituational attacks, more attacks during sleep, more early separation, and fewer attacks during pregnancy than patients with nonrespiratory symptoms as a main sign of panic attacks (PNRS) could not be confirmed. But PRS is possibly a clinical subentity, because PRS showed less agoraphobia, better drug response, and fewer alcoholics in first-degree relatives than PNRS.

NR668 Thursday, May 9, 12 noon-2:00 p.m.

Parental Representations Predict Social Avoidance in Patients with Panic Disorder

Richard J. Maddock, M.D., Psychiatryych, University of Calif Davis, 4430 V Street, Sacramento CA 95817; Mark H. Townsend, M.D., James G. Barbee IV, M.D., Cameron S. Carter, M.D.

Summary:

Agoraphobia is considered part of the core syndrome of panic disorder (PD) and responds well to standard treatments with medications and/or behavioral therapy. Social avoidance also occurs in PD. It is less frequent than agoraphobia, is not considered a core component of the disorder, and less is known about how it responds to usual treatments for PD. We have observed clinically that many panic patients who appear to benefit from psychodynamic psychotherapy have significant social anxiety. Treatment of these patients often includes working through distortions related to suboptimal parenting. Parental styles characterized as "affectionless control" are more frequently reported by adult patients with anxiety disorders than control subjects. We hypothesized that PD patients with more severe social phobic symptoms would have evidence of more negative internal representations of their parents.

Seventy-two medication-free PD patients were administered the agoraphobic and social phobic subscales of the Fear Questionnaire, and the EMBU (a cross-culturally validated measure of parental representations that yields three factors: emotional warmth [EW], overprotection [OP], and rejection [R]). Multiple re-

gression analysis revealed a significant association between the three maternal EMBU factors scores and the social phobia rating ($R = .40$, $p = .007$). High ratings of social phobia were associated with low EW ($p = .006$) and high OP ($p = .004$). There was a trend for the three paternal factors to be associated with social phobia ratings ($R = .31$, $p = 10$), with low EW and high OP accounting for the trend. No relationships were seen between EMBU factors and agoraphobia ratings.

These results support the idea that internal representations of the mother influence the extent of social phobic but not agoraphobic symptoms in patients with PD. Further studies should assess the role of adjunctive short-term dynamic therapy in the treatment of panic patients with significant social avoidance.

NR669 Thursday, May 9, 12 noon-2:00 p.m.

Screening for PTSD in Primary Care Samples: Prevalence and Patterns of Health Care Utilization, Psychosocial Functioning and Life Satisfaction

Sharon Younkin, Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence RI 02903; Mark Zimmerman, M.D., Bruce Horowitz, M.D., Anne Moulton, M.D., Jill I. Mattia, M.A.

Summary:

Objective: To determine the prevalence of posttraumatic stress disorder (PTSD) in a primary care setting, and to determine the impact that PTSD has on functioning, quality of life, and health care utilization.

Methods: 544 medical outpatients in two general medical practices were given the SCREENER, a previously validated, self-report, multidimensional instrument that includes a six-item subscale for PTSD. Screening positive was defined as having experienced or witnessed a traumatic event (such as combat, rape, assault, sexual abuse, or someone dying in an accident) followed by recurrent memories, dreams, distress, or avoidance of activities or attempting to block out feelings that relate to the event. A second instrument evaluated current level of functioning, overall perception of quality of life, mental and physical health, and utilization of primary care services and the emergency department (ER). Significance tests are two-tailed at a level of 0.05.

Results: The prevalence of screen-positive PTSD was 7.5%. When compared with those screening negative for PTSD, patients who screened positive were: significantly younger (40 vs. 47 years); significantly more impaired in their work outside and inside the home, school work, relationships with significant others and family members' and social, sexual and overall functioning. The PTSD positive patients rated their quality of life and physical and mental health significantly lower, and made twice as many doctor visits in the past three months (2.7 vs. 1.5 times) and the past year (7.0 vs. 3.8). There were no differences in the following variables: gender; ER utilization in the past three months or the past year; and lifetime rates of having seen a mental health professional.

Conclusions: In this, the first study to estimate the prevalence and effects of PTSD in a primary care population, PTSD was prevalent and was associated with substantial morbidity, interference with all aspects of function, and higher rates of primary care service use, though not with an increased rate of ever having seen a mental health care professional.

NR670 Thursday, May 9, 12 noon-2:00 p.m.

OCD: Gender Differences

Marijo B. Tamburrino, M.D., Psychiatry, Medical College Ohio, PO Box 10008, Toledo OH 43699; Kathleen N. Franco, M.D., Nancy B. Campbell, M.D., Cynthia L. Evans, M.D., Rachel E. Kaufman, M.D.

Summary:

Some researchers have proposed that it is important to study disorders by gender to better understand cultural and societal influences on symptoms. This study examined gender differences in patients with obsessive-compulsive disorder (OCD). Subjects with OCD were recruited through letters sent to area psychiatrists. The study consisted of 40 patients: 28 females and 12 males. Participants completed a demographic survey and the Yale Brown Obsessive Compulsive Scale. There were 46.2% ($N = 30$) of the women's obsessions that concerned contamination, while 25% ($N = 4$) of the men's obsessions focused on contamination ($x^2 = 5.3$, $df = 1$, $p < .03$). Similarly, women were significantly more likely than males to have cleaning/washing compulsions: 30.4% ($N = 21$) of female compulsions vs. 17.6% ($N = 6$) of male compulsions consisted of cleaning/washing ($x^2 = 4.09$, $df = 1$, $p < .04$). On comorbidity, 50% ($N = 14$) of the women and 8% ($N = 1$) of the men had a history of an eating disorder ($x^2 = 6.7$, $df = 1$, $p < .01$). There were no significant gender differences in other demographics such as age, marital status, and education. Although this study is limited in size, the findings do suggest some gender shaping of symptoms. The authors discuss cultural influences and societal roles that contribute to the presentation and comorbidity of OCD in women.

NR671 Thursday, May 9, 12 noon-2:00 p.m.

SSRIs Normalizes Noradrenergic Function in Panic

Jeremy D. Coplan, M.D., BSU, NYS Psychiatric Institute, 722 West 168th Street Unit 24, New York NY 10032; Laszlo A. Papp, M.D., Daniel S. Pine, M.D., Donald F. Klein, M.D., Jack M. Gorman, M.D.

Summary:

The antipanic efficacy of the selective serotonin reuptake inhibitors (SSRI's) raises the question of whether modifications of the serotonin system may be associated with normalization of a postulated dysregulated noradrenergic (NA) system in panic disorder. We report the noradrenergic function in 17 panic disorder subjects and 16 healthy volunteers who underwent measurement of the plasma noradrenergic metabolite, 3-methoxy-4-hydroxyphenylglycol (MHPG) prior to and at four hourly time points following oral clonidine administration. Patients with panic disorder were rechallenged using the same clonidine paradigm after 12 weeks of open SSRI treatment with fluoxetine. Healthy volunteers underwent repeat clonidine challenges at 12 weeks without treatment between challenges.

Greater decreases of preclonidine MHPG from pre- to post fluoxetine-treatment predicted a greater degree of clinical global improvement. Results of the study also indicate that panic disorder patients in comparison to healthy volunteers show a markedly elevated amount of intrasubject volatility of plasma MHPG. Fluoxetine antipanic responses were associated with a significant between-visit decline in volatility of the noradrenergic system relative to unchanged MHPG volatility levels in controls. Measures of patients' noradrenergic volatility post-fluoxetine were indistinguishable from either the controls' first or second clonidine challenge. Evidence is provided for the hypothesis of noradrenergic dysregulation in panic disorder as reflected by increased intrasubject volatility of plasma MHPG during clonidine challenge. Effective SSRI-antipanic treatment in this clinical sample was paralleled by normalization of noradrenergic function.

NR672 Thursday, May 9, 12 noon-2:00 p.m.

Respiratory Challenges in Panic Disorder

Laszlo A. Papp, M.D., BSU, NYS Psychiatric Institute, 722 West 168th Street, New York NY 10032; Jose Martinez, M.A.,

Jeremy D. Coplan, M.D., Randolph Cole, M.D., Donald F. Klein, M.D., Jack M. Gorman, M.D.

Summary:

Background: Respiratory abnormalities may play a central role in the pathophysiology of panic disorder (PD). The current study was undertaken to examine the respiratory response in the largest series of subjects to date during a series of respiratory challenges utilizing improved methodology.

Methods: Fifty-nine patients with DSM-III-R PD and 39 normal volunteers were challenged with 5% and 7% carbon dioxide (CO2) inhalation and room air hyperventilation (HV) separated by room air breathing with continuous spirometry.

Results: PD patients were more sensitive to the anxiogenic effects of CO2 than normals, and CO2 was a more potent stimulus to panic than HV. Self-rating of panic differentiated the two groups better than blind rating. Patients increased their respiratory rate more quickly during CO2 inhalation than controls and this increase preceded the panic attacks. Patients who panicked to 5% CO2 demonstrated continued rise in end-tidal CO2 (ETCO2), while the ETCO2 of the comparison groups stabilized. Low ETCO2 and high variance in minute ventilation at baseline predicted panic attacks during CO2 inhalation. Following CO2 or HV challenges respiratory rate dropped sharply, while tidal volume remained elevated longer in patients than controls.

Conclusions: The findings confirm the increased behavioral and physiological sensitivity of panic patients to CO2 inhalation and identify a series of respiratory abnormalities. Panic attacks in PD may be explained by inefficient compensatory mechanisms primarily of respiratory rate.

NR673 Thursday, May 9, 12 noon-2:00 p.m.

24-Hour Growth Hormone Pattern in Panic Disorder

George C. Curtis, M.D., Psychiatry, U of MI Med Inn 437/0840, 1500 E Medical Center Dr, Ann Arbor MI 48109–0840; James L. Abelson, M.D., Thomas W. Uhde, M.D.

Summary:

Blunted growth hormone (GH) responses to the alpha-2 noradrenergic receptor agonist clonidine, and perhaps to growth-hormone-releasing hormone, are found in both nondepressed panic disorder patients and in major depression. Increased spontaneous GH secretion during waking hours has also been reported in depression. The present study characterizes the 24-hour profile of GH in panic disorder. Twenty nondepressed patients with DSM-III-R defined panic disorder, with or without agoraphobia, and 12 control subjects had blood sampled for GH assay through an indwelling intravenous catheter every 15 minutes or 24 hours. Analyses of variance conducted on mean GH values for each of the 12 two-hour time blocks revealed a highly significant effect of time, but no significant diagnosis effect or time-by-diagnosis interaction. The time effect was due to a major peak between midnight and 2 a.m. corresponding, as expected with the clinically estimated onset of sleep, EEG data being unfortunately unavailable. Visual inspection of individual profiles and a variety of other statistical comparisons failed to detect any differences between patients and controls. These preliminary analyses suggest that the GH profile in panic patients is normal. Additional analyses and discussion of implications will be presented.

NR674 Thursday, May 9, 12 noon-2:00 p.m.

Respiratory Irregularity in Panic Disorder

George C. Curtis, M.D., Psychiatry, U of MI Med Inn 437/0840, 1500 E Medical Center Dr, Ann Arbor MI 48109–0840; James L. Abelson, M.D., John G. Weg, M.D., Randolph M. Nesse, M.D.

Summary:

We have shown that the respiratory stimulant doxapram triggers panic attacks and excessive ventilatory responses in panic disorder patients, and that the excessive responses were only partially corrected by a cognitive intervention designed to reduce catastrophic misinterpretation of symptoms and to increase perceived controllability. Increased irregularity of tidal volume (Vt) during sleep in panic disorder has also been reported. To further explore respiratory dysregulation in our doxapram model, we obtained breath-by-breath records of Vt on our previously studied subjects and used von Neumann's statistic (sum of squared differences between successive points) to quantify Vt irregularity. Sixteen patients and 16 matched controls were studied. Half of each group received a standard orientation to the experiment and half received the cognitive intervention. Vt irregularity was calculated over five-minute blocks during an accommodation phase, a placebo injection phase, and a doxapram injection phase. Patients had robust elevations ($p < .003$) in Vt irregularity in all three phases, which were not significantly affected by the cognitive intervention, the doxapram-induced hyperventilation, or the combination of the two. The results suggest intrinsically irregular breathing patterns in panic disorder, perhaps due to brainstem/autonomic nervous system hyperactivity and instability.

NR675 Thursday, May 9, 12 noon-2:00 p.m.

Embarrassment About the First Panic Attack Predicts Agoraphobia in Panic Disorder Patients

Michaela Amering, M.D., Psychiatry, University Vienna, Waehringer Guertel 18–20, Vienna 1090, Austria; Heinz Katschnig, M.D., Peter Berger, M.D., Johann Windhaber, M.D., Wolfgang Baischer, M.D., Karl Dantendorfer, M.D.

Summary:

Objective: To test the hypothesis that the context and the reaction to the first panic attack contribute to the development of agoraphobia in panic disorder patients.

Method: 60 panic disorder patients with and 30 without agoraphobia reported on their first panic attack. Comparisons between groups and a logistic regression model were calculated.

Results: The feeling of embarrassment as a reaction to the initial panic attack and the fact that the first panic attack had occured in public were significantly associated with the development of agoraphobia.

Conclusions: Embarrassment as a reaction to the first panic attack is an early predictor of agoraphobia in panic disorder patients and could help to identify patients at risk and maximize therapeutic efforts.

NR676 Thursday, May 9, 12 noon-2:00 p.m.

Self-Reported Sexual Dysfunctions in Anxiety Disorder Patients

Michael R. Ware, M.D., Psychiatry, Medical University of SC, 171 Ashley Ave, Charleston SC 29425; Naresh P. Emmanuel, M.D., Michael R. Johnson, M.D., Olga Brawman-Mintzer, M.D., Rebecca Kapp, R.N., R. Bruce Lydiard, M.D.

Summary:

Objective: A consistent data base on the effects of Axis I psychopathology on sexual functioning in psychiatric patients is lacking. Essentially no investigation into the sexual functioning of patients with anxiety disorders has been conducted. We speculate that social phobics (SP) and panic disorder (PD) patients will show diminished sexual desire and functioning as a group compared with normal controls.

Methods: The Sexual Function Questionnaire (SFQ)[2] is a self-report instrument designed to measure treatment-emergent changes in psychosexual dysfunctions including inhibited sexual desire, inhibited sexual excitement, and inhibited orgasm. To date, 153 unmedicated patients (61 male, 92 female) diagnosed with DSM-III-R social phobia (N = 58) panic disorder (N = 45), and generalized anxiety disorder (N = 50) using a structured clinical interview have entered psychopharmacology trials and have completed the SFQ at baseline. A comparison group of 37 normal controls (13 male, 24 female) has also been collected.

Results: Preliminary data analysis utilizing Fisher's Exact Test (2 tailed) reveals the following significant findings: Patients with GAD, PD, and SP are all more likely as a group to report a current sexual dysfunction versus normal controls. Second, PD patients rate sex in the life as less important to them than the control group. Third, SP patients are much less likely to enjoy a good to excellent nonsexual relationship with their partner and do not usually to often enjoy sex with their partner compared with controls. (all $p \leq 0.01$).

Conclusions: Unmedicated patients with anxiety disorders are at significant risk for experiencing sexual dysfunctions. SP and PD patients report greater difficulty than subjects with GAD. Further data analysis will be presented at the meeting.

NR677 Thursday, May 9, 12 noon-2:00 p.m.

Symptom Profiles of Adult Versus Childhood OCD

Daniel J. Fischer, M.S.W., Psychiatry, University of Michigan, 1500 Medical Center Drive, Ann Arbor MI 48109; Joseph A. Himle, Ph.D., Gregory L. Hanna, M.D.

Summary:

Sixty nonmedicated adults and children presenting for treatment of obsessive-compulsive disorder were given either the adult or child version of the Yale-Brown Obsessive-Compulsive Scale. Using the symptom checklist portion of the rating scales, symptom profiles were compared between the two age groups. In keeping with our study hypotheses, children were found to experience significantly fewer checking compulsions, aggressive obsessions, mental rituals, obsessions about losing things, and obsessions about saying certain things or not saying just the right things in social settings. Contrary to our predictions, children did not endorse touching, tapping, and rubbing compulsions or obsessions related to symmetry significantly more often than their adult counterparts. In keeping with our expectations, on nearly all items related to contamination obsessions and washing/cleaning rituals, children and adults did not differ significantly. Overall, adults endorsed a significantly greater number of obsessive-compulsive symptoms.

NR678 Thursday, May 9, 12 noon-2:00 p.m.

Episodic Dyspnea As a Marker for Panic Disorder and Asthma in Young Adults: Results of Pulmonary and Psychiatric Evaluations

Norman B. Schmidt, Ph.D., Medical/Clinical Psych., Uniformed Serv University, 4301 Jones Bridge Road, Bethesda MD 20814; Jeffrey P. Staab, M.D., John E. Brown, Jr., David A. Holden, M.D., Margaret A. Koselka, B.A.

Summary:

Objective: Episodic dyspnea has a broad differential diagnosis, including asthma, obstructive pulmonary disease, other medical illnesses, panic disorder, and possibly a hyperventilation syndrome (HVS). This study sought to refine this differential diagnosis for young adults, an age group at highest risk for panic disorder, but less likely to have pulmonary diseases, other than asthma.

Method: Twenty-four of 26 adults, aged 19–43, referred to a tertiary care pulmonary clinic with episodic dyspnea agreed to participate in extensive evaluations including pulmonary function tests, bicycle ergometry, measurement of end-tidal CO_2 during hyperventilation, and the Structured Clinical Interview for DSM-IV.

Results: Seventeen (70.8%) subjects received medical diagnoses [13 (54.1%) asthma, two (8.3%) HVS, one mild restrictive disease, one recurrent vaso-vagal syncope]. Fourteen (58.3%) subjects received at least one current psychiatric diagnosis [all 14 (58.3%) had panic disorder, two social phobia, three specific phobia, two alcohol abuse]. Ten (41.7%) subjects had comorbid medical and psychiatric conditions, most commonly (9/10) asthma and panic disorder. Three (12.5%) subjects received no diagnosis.

Conclusions: Episodic dyspnea may be an important marker for panic disorder in young adults. Among pulmonary patients under age 45, panic disorder was as common as asthma. The two diagnoses often were comorbid. HVS occurred infrequently.

NR679 Thursday, May 9, 12 noon-2:00 p.m.

Panic Disorder: Heat As a Significance Stressor

Gregory M. Asnis, M.D., Psychiatry, Monterfiore Med Ctr, 111 E 210th Street, Bronx NY 10467; Iulia Dogaru, M.D., Galina Bass, M.D., Margaret L. Kaplan, Ph.D., Lata K. McGinn, Ph.D., Paresh Pandya, M.D.

Summary:

Panic disorder (PD) is known to be sensitive to a number of stimuli: caffeine, lactate, carbon dioxide, etc. We have been particularly interested in what appears to be the influence of heat (hot weather) on panic disorder. A subgroup of patients have their panic attacks triggered or exacerbated by heat leading to marked avoidance of going out during hot days.

A self-rating questionnaire assessing a number of potential stressors such as anger, caffeine, humidity, cold and heat, rated on a continuum from never, sometimes, most of the time, and always was given to PD patients. The preliminary findings on the first 23 patients (mean age 33, SD 10 years, 18 females, 5 males) diagnosed by DSM-IV are presented here. The following are prevalence rates of those patients endorsing the presence of a stressor at least most of the time or always: heat (26%), cold (4%), humidity (22%), anger (26%), exercise (9%), caffeine (17%), premenstrual period (22% of women). In addition, 39% of PD patients acknowledge a seasonal pattern to their illness; 66% of those patients who were sensitive to heat had a seasonal pattern.

It is clear that heat is a significant variable for a sizeable subgroup of PD. In addition, seasonality appears to be highly prevalent. Whether heat sensitivity relates to seasonality, other stressors, or to a potential thyroid dysfunction will be discussed.

NR680 Thursday, May 9, 12 noon-2:00 p.m.

Serum Cholesterol Levels in Patients with Anxiety Disorders: A Comparison with Normal Controls

Helmut Peter, M.D., Hospital, Psychiatric University, Martinistr 52, Hamburg 20246, Germany; Susanne Muller, Philipp Goebel, Iver E. Hand, M.D.

Summary:

Panic disorder and agoraphobia are reported to be associated with elevated cholesterol levels. The studies so far show methodological shortcomings (lack of control for dietary and physical exercise habits).

Method: Serum cholesterol, LDL, and the ratio cholesterol/HDL of 28 patients with different anxiety disorders and 28 normal controls were compared with each other. Subjects were matched according to gender, age, and body mass index. Patients met DSM-III-R criteria for an anxiety disorder (300.0, 300.2, 309.89).

Controls had no current or past psychiatric illness. Dietary and physical exercise habits were measured by self-rating questionnaires.

Results: 1.) Patients with anxiety disorders have significantly elevated cholesterol, LDL, and cholesterol/HDL ratio. 2.) These effects could partly be explained by differences in dietary and physical exercise habits between the groups. 3.) After statistical control of these intervening variables, anxiety patients still had significantly elevated cholesterol levels.

Discussion: Data support the assumption that anxiety-specific elevation of serum cholesterol might lead to an increased risk for cardiovascular disorders. The underlying mechanism could be related to a noradrenergic hyperarousal. Further investigation is needed to clarify whether this lipid alteration is a state or trait factor.

NR681 Thursday, May 9, 12 noon-2:00 p.m.

The Role of the Beta-Noradrenergic System in CCK-4-Induced Panic Symptoms

Jean-Michel Le Melledo, M.D., Clarke Institute of Psych, 250 College Street, Toronto Ontario M5T 1R8, Canada; Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., Jean-Phillipe Boulenger, M.D., Roger J. Cadieux, M.D., Francois Bellavance, Ph.D.

Summary:

The involvement of the noradrenergic (NE) system, particularly the beta NE system, in panic disorder has been suggested for some time. However, attempts at blocking pharmacologically induced panic attacks with propranolol (a central and peripheral beta-1 and beta-2 NE blocker) have yielded inconsistent results. These inconsistencies might be explained by a failure to verify the effectiveness of beta blockade. Our study objectives were to assess the effects of controlled beta-blockade on CCK-4-induced panic symptoms and associated biological changes in healthy volunteers. The study was double-blind and placebo-controlled. The beta-blocking effects of 0.2 mg/kg i.v. of propranolol were controlled for every subject, using the Cleaveland method. This method consists of verifying that the injection of a predetermined CD25 dose of isoproterenol has no effect on heart rate following the administration of a beta blocker (CD25 is the dose of isoproterenol which increases the heart rate of a subject by 25 beats per minute). Subjects exhibiting beta blockade were included in the study. Two days later, the same dose of propranolol or placebo was administered to these subjects followed by an i.v. injection of CCK-4 (50 ug).

Preliminary results based on 19 subjects (10 received propranol, nine received placebo) showed that pretreatment with propranolol, compared with placebo, decreased sum intensity of panic symptoms ($p < 0.01$) and reduced CCK-4-induced increases in heart rate ($p < 0.05$). In conclusion, our preliminary results suggest that the beta NE system mediates at least part of the CCK-4-induced effects. The final results based on 40 subjects and the results of the effects of propranolol on CCK-4-induced arginine vasopressin, oxytocin, and NPY release will be presented. *This study was funded, in part, by the Medical Research Council of Canada.*

NR682 Thursday, May 9, 12 noon-2:00 p.m.

Open Trial of Fluvoxamine for Combat PTSD

Charles R. Marmar, M.D., Psychiatry, UCSF Langley Porter, 401 Parnassus Avenue, San Francisco CA 94143; Frank B. Schoenfeld, M.D., Daniel S. Weiss, Ph.D.

Summary:

The present study was undertaken to assess the efficacy of fluvoxamine in a 10-week, open-label trial for 10 male Vietnam combat veterans with chronic PTSD. Subjects were excluded if they met full current criteria for panic disorder or agoraphobia, and lifetime or current criteria for schizophrenia, schizoaffective disorder, bipolar disorder, or organic mental syndrome. Repeated measures analyses of variance with post-hoc Tukey's tests were performed to determine the significance of changes with treatment period.

Fluvoxamine was well tolerated by this population of male Vietnam combat veterans. Side effects were observed primarily early in treatment, with headache, insomnia, sedation, and gastrointestinal distress being the most frequent complaints. Fluvoxamine was effective for treating the core re-experiencing, avoidance and numbing, and hyperarousal symptoms of post-traumatic stress disorder. Large effects were seen in diminution of both self-reported and clinician-rated PTSD symptomatology. Maximal treatment effects were seen by four to six weeks, and maintained at 10 weeks. The magnitude of change was larger than has been previously reported for tricyclic antidepressants or monoamine oxidase inhibitors, and substantially better than the results reported by van der Kolk and colleagues for fluoxetine in the treatment of male Vietnam combat veterans with PTSD.

NR683 Thursday, May 9, 12 noon-2:00 p.m.

Peritraumatic Dissociation in Rescue Workers

Charles R. Marmar, M.D., Psychiatry, UCSF Langley Porter, 401 Parnassus Avenue, San Francisco CA 94143; Daniel S. Weiss, Ph.D., Thomas J. Metzler, Ph.D.

Summary:

The aim of this study was to identify characteristics of emergency services personnel related to acute dissociative responses at the time of critical incident exposure (peritraumatic dissociation). One hundred fifty-seven rescue workers who responded to the Nimitz Freeway Collapse during the 1989 Bay Area earthquake and 201 controls were studied. In univariate tests the group with clinically meaningful levels of peritraumatic dissociation was younger, reported greater critical incident exposure, greater perceived threat, lower scores on the Adjustment, Identity, Ambition, and Prudence scales of the HPI, higher scores on escape-avoidance, self-control, and active problem-solving, coping, and greater externality in locus of control. Linear modelling using multiple logistic regression analyses indicated that increases in perceived threat, escape avoidance coping, and self-control coping were associated with increases in the likelihood of being in the peritraumatic dissociation group, above and beyond age and exposure. Rescue workers who are shy, inhibited, uncertain about their identity, reluctant to take leadership roles, have global cognitive styles, believe their fate is determined by factors beyond their control, and cope with critical incident trauma by emotional suppression and wishful thinking are at higher risk for acute dissociative responses to trauma and subsequent PTSD.

NR684 Thursday, May 9, 12 noon-2:00 p.m.

Paroxetine Normalizes Heart Rate Variability in Panic Disorder

Phebe M. Tucker, M.D., Psychiatry 5SP520, University of Oklahoma, PO Box 26901, Oklahoma City OK 73190; Philip Adamson, M.D., Samuel E. Payne III, M.D., Alfretia Scarborough, M.P.H., Audrey Chang, M.S., Monica Bottoms, B.A., Lawrence A. Labbate, M.D., Brian Conley, Ph.D., Heather McLean, M.S.

Summary:

Objective: This study uses power spectral analysis to compare autonomic components of heart rate variability in panic patients before and after treatment with paroxetine. Decreased heart rate

variability, from increased sympathetic or decreased parasympathetic activity, is present in panic and those at risk for sudden cardiac death. Other studies have found imipramine to further decrease heart rate variability in panic.

Methods: Fifteen panic patients by SCID-1 were recruited by advertisements. All were medically healthy and off medications for over one week. Relative sympathetic activity (low to high frequency ratio) and parasympathetic activity (high frequency percent) were calculated for 15 minutes in supine and standing positions before and after four weeks of paroxetine at 20 mg. per day. Two-way ANOVA's showed significant position effect for both sympathetic (P = 0.005) and parasympathetic (P = .0001) components. Post-hoc paired T-tests compared autonomic and positional differences.

Results: Panic patients had nonsignificantly higher sympathetic activity before drug than after in both positions, but similar parasympathetic activity. Upon orthostatic challenge, pre-drug panic patients failed to show the expected rise in sympathetic activity (P = 0.08, N.S.). However, pre-drug parasympathetic decrease on standing was intact (P = 0.001). After medication, patients had expected orthostatic parasympathetic decrease (P = 0.02) and sympathetic increase (P = 0.01) found in normal controls in other studies by this group and others. Eight patients had over 50% reduction of attacks.

Conclusions: SSRI's, often effective in improving subjective panic, may provide additional benefits over tricyclics in normalizing heart rate variability. In the presence of heart disease, this may potentially lower panic patients' reported greater risk for sudden cardiac death.

NR685 Thursday, May 9, 12 noon-2:00 p.m.

Caffeine Anxiety and Depression in Outpatients

R. Gregory Lande, D.O., Psychiatry, Walter Reed AMC, Borden Pavilion, Washington DC 20307

Summary:

Objective: To determine the correlations between reported use of caffeine, measured plasma concentrations, and psychometric instruments for anxiety and depression.

Method: Three hundred fifty-eight outpatients (180 men, mean age 40 ± 16) participated in the study. A detailed questionnaire gathered reported caffeine consumption, demographics, medication use, and related physical symptoms expected with caffeine use. Patients completed the Beck Depression Inventory (BDI) and the Spielberger State Anxiety Index (STAI). A total of 107 patients had plasma caffeine concentrations measured by gas chromatography and a mass selective detector.

Results: Patients reported daily consumption of 231 mg (SD = 243; range 0–2300) caffeine. Forty-three patients reported no caffeine use. Mean BDI was 14 (SD = 11), and mean STAI was 45 (SD = 16). Although the BDI score did correlate with the STAI score (R = .75, p < 0.00001), there was no significant correlation between reported caffeine use and the BDI or the STAI. Men reported higher use than women (263 mg vs 201 mg; p < 0.02). Age was not correlated with reported caffeine use. Plasma concentration was obtained on 107 patients. Patients giving blood were no different than patients not giving blood by demographics, reported caffeine use, BDI or STAI scores. Mean plasma concentration was 1.23 ± 0.36 μg/ml (SEM). Fifty-two patients had plasma concentrations below 0.5 μg/ml, the limit of detection of our assay. Plasma caffeine concentration was not correlated with reported caffeine use (R = 0.1, F = 1.1, p = 0.29). Plasma concentration or reported caffeine use were not correlated with the BDI or STAI. When BDI scores was stratified to high (ℓ 30; N = 32) and low (≤ 5; N = 97) scores, we found that patients with higher scores reported higher caffeine use than patients with lower scores (297 mg vs 192 mg, p < 0.05), and similarly, plasma concentrations were also higher (1.5 ± 0.36 μg/ml vs 0.5 ± 0.2 μg/ml (SEM); p < 0.02). When STAI was stratified into high (> 60, N = 57) versus low scores (< 30, N = 78), we found that anxious patients reported no different caffeine use, but they did have lower plasma concentrations (0.36 ± 0.17 vs 1.2 ± 0.36, p < 0.05).

Conclusion: Caffeine use was common at low to moderate levels. While plasma concentration and reported use were not correlated with the BDI or STAI, when symptoms were stratified into high and low groups, reported caffeine use and plasma concentration directly correlated with BDI scores, and plasma concentration inversely correlated with STAI scores.

NR686 Thursday, May 9, 12 noon-2:00 p.m.

The Effect of Aging on Cholecystokinin-Induced Panic

Alastair J. Flint, M.B., Psychiatry, Toronto Hospital, 200 Elizabeth St, 8 Eaton N., Toronto ON M5G 2C4, Canada; Jacques Bradwejn, M.D., Franco J. Vaccarino, Ph.D., Diana Koszycki, Ph.D.

Summary:

Objective: Epidemiological studies have reported that panic disorder is rare in late life. Age-related changes in brain neurochemistry may contribute to this decreased frequency. To further test this hypothesis, we examined whether younger and older individuals differed in their symptomatic response to CCK-4, a potent panicogenic agent.

Method: The sample consisted of 20 men and 20 women aged 18–35 and a similar number of subjects aged 65–85. All were physically healthy volunteers who did not have a current or past history of panic attacks or other psychiatric disorder. Using a double-blind, placebo-controlled design, subjects were randomly assigned to receive an IV bolus of either 50 ug of CCK-4 or normal saline.

Results: Older and younger groups did not differ in their response to placebo. However, in response to CCK-4, the older group had fewer symptoms of panic (5.0 ± 2.8 vs. 11.2 ± 3.5, p < 0.001), lower sum intensity of symptoms (10.4 ± 7.8 vs. 25.2 ± 13.3, p < 0.001) and shorter symptom duration (123.6 ± 55.6 vs. 193.4 ± 93.5 seconds, p = 0.001) compared with younger subjects. For those individuals experiencing DSM-III-R-defined panic attacks (6/20 older vs. 9/20 younger subjects), the elderly had fewer symptoms (8.0 ± 2.2 vs. 13.0 ± 2.7, p < 0.001) and lower sum intensity of symptoms (18.2 ± 9.5 vs. 34.2 ± 13.3, p < 0.001).

Conclusions: These results support the hypothesis that age-related changes in brain biochemistry may contribute to older persons' reduced vulnerability to panic attacks. Further studies to delineate the nature of these changes are warranted.

NR687 Thursday, May 9, 12 noon-2:00 p.m.

The Relationship Between Acute Stress Disorder and Subsequent PTSD in Three Disaster Populations

Jeffrey P. Staab, M.D., Psychiatry, Uniformed Serv University, 4301 Jones Bridge Road, Bethesda MD 20814; Thomas A. Grieger, M.D., James E. McCarroll, Ph.D., George T. Brandt, M.D., Carol S. Fullerton, Ph.D., Robert J. Ursano, M.D.

Summary:

Objective: The hypothesis that acute stress disorder (ASD) may predict posttraumatic stress disorder (PTSD) is untested. This study examined acute stress symptoms and subsequent PTSD following three disasters (a series of typhoons, N = 320; an earthquake, N = 93; and body recovery after an airline crash, N = 45).

Methods: Eight months after each disaster, validated measures of ASD, PTSD, and depression were administered to exposed

individuals. Based on symptoms reported for the week after exposure, subjects were divided into three acute groups, [1] ASD (+), [2] ASD (–) with many symptoms (instrusion + avoidance + arousal, but no dissociation) and [3] ASD (–) with few symptoms. The eight-month point prevalence of PTSD was examined in each group. The earthquake struck part of the typhoon population, so earthquake subjects were surveyed twice. Seven earthquake subjects with typhoon-related PTSD were examined separately.

Results: In each population, the point prevalence of PTSD was higher among ASD (+) (30–100%) than all ASD (–) (0–4.0%) subjects (Fisher's exact tests, all $p < 0.05$). Rates of PTSD were similar for ASD (–) subjects with many (0–4.2%) or few (0–4.3%) acute symptoms. All subjects with typhoon-related PTSD reported PTSD and/or depression after the earthquake.

Conclusions: ASD was associated with an increased risk of PTSD. A small group of subjects with known PTSD remained ill when retraumatized.

NR688 Thursday, May 9, 12 noon-2:00 p.m.

Autonomic Reactivity of Panic Patients During Carbon Dioxide Inhalation Procedures

Alexander Bystritsky, M.D., Medicine, 300 UCLA Medical Plaza, 300 Medical Plaza Ste 2340, Los Angeles CA 90024; Michelle G. Craske, Ph.D., Emanuel Maidenberg, Ph.D., Tanya Vapnik, R.N., David Shapiro, R.N.

Summary:

The psychophysiological basis of panic attacks is yet to be fully understood. It remains unclear, for example, whether panic patients differ from the normal population in psychophysiological responsiveness. We applied continuous psychophysiological monitoring of panic patients (N = 33) and normal controls (N = 25) during 20 minutes of breathing room air (baseline) followed by 30 minutes of 5.5% CO_2 inhalation and 20 minutes of room air (recovery). Subjective reports of distress using potentiometer and "panic button" and physiological measures of skin conductance, heart rate, respiration configuration, tidal carbon dioxide values, systolic and diastolic blood pressure, and electrocardiogram were recorded continuously.

Minute-by-minute analysis of data showed statistically significant differences between groups at baseline and during CO_2 inhalation. However, when using baseline as covariate, differences between the two groups became nonsignificant. Within the panic patient group, those who had panic attack during the experiment and indicated so by pressing the "panic button" (N = 8) were significantly different on physiological measures compared with controls and other panic patients at baseline.

Our data suggest that level of anticipatory anxiety may play a central role in panic disorder; these data agree with Roth et al.'s (1992) data using different methodology.

NR689 Thursday, May 9, 12 noon-2:00 p.m.

Within Class Safety and Efficacy Comparison of Imipramine Versus Desipramine in Early PTSD Treatment

Neal A. Kline, M.D., Psychiatry 0603, Univ Calif San Diego, 9500 Gilman Drive, La Jolla CA 92093

Summary:

Objective: Though across-class comparisons may be made regarding the efficacy and safety of tricyclics vs. SSRIs vs. MAOIs for PTSD, might there also be significant distinctions within-class for instance, between the tricyclic imipramine and its demethylated derivative desipramine.

Method: Twelve combat veterans with PTSD and depression seen at our Department of Veterans Affairs outpatient PTSD clinic were to be prospectively assigned to two cells, with six subjects in each cell: six subjects on imipramine, and six on desipramine. Prior exposure to either medication excluded membership in this open-label pilot study. Other exclusion criteria 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 for improvement with the Clinical Global Impression scale (CGI). Scores for the imipramine group were: 2, 2, 3, 4, 6, 6. Data collection for the desipramine group was terminated after the initial three subjects' CGI scores were 6, 6, and 7, all reporting marked hyperarousal. GCP dictated discontinuing our comparison, as safety issues became paramount.

Conclusion: With PTSD's neurobiology characterized by noradrenergic instability, and desipramine's antidepressant effect medicated primarily by enhanced norepinephrine availability, treating PTSD with desipramine may be contraindicated, as it may further agitate an already hyperaroused population. Imipramine may be less problematic as its modes of action may include serotonergic modulation of noradrenergic influences.

NR690 Thursday, May 9, 12 noon-2:00 p.m.

Lesopitron: A Bridging Study in Patients with GAD

Jerome F. Costa, M.D., California Clinical Trials, 8500 Wilshire Blvd. 7th Floor, Beverly Hills CA 90211; John J. Sramek, Pharm.D., Neal R. Cutler, M.D., Gaston Marion-Landais, M.D., Christof M. Jensen, M.S., Neil M. Kurtz, M.D., Ann T. Carrington, Ph.D.

Summary:

Objective: To assess the safety, tolerability, and PK of the potential anxiolytic lesopitron, a 5-HT_{1A} agonist in the azapirone class.

Method: Fixed doses of 20, 25, 30, 40, 45, 50, and 60 mg bid lesopitron were administered to seven consecutive panels of six GAD patients each (four lesopitron/two placebo) over a 6 1/2-day inpatient period in this double-blind bridging study.

Results: One patient withdrew voluntarily due to increased anxiety (25 mg bid lesopitron). Another experienced severe orthostatic hypotension at 60 mg bid lesopitron on the third day of dosing; symptoms resolved within one hour and the patient completed the study. Moderate to severe dizziness, lightheadedness, nausea, and/or headache occurred in two other patients at 60 mg bid; 50 mg bid was defined as the maximum tolerated dose (MTD). The most commonly reported adverse events overall were lightheadedness, dizziness, headache, and nausea. Lesopitron absorption and elimination were rapid (T_{max}: 0.5 to 1 hr; $T_{1/2}$: 1.1–5.6 hours). Lesopitron plasma concentrations were highly variable among individuals and dose-independent. C_{max} ranged from 1.3 to 194.2 ng/ml. C_{max} of the metabolite 5-hydroxylesopitron ranged from 6.0 to 507.6 ng/ml and was, on average, dose-dependent.

Conclusions: The MTD of lesopitron in GAD patients was 50 mg bid, 100% greater than the highest dose tested in healthy volunteers. Identifying the MTD in a bridging study such as this one permits use of a tolerable, safe, and potentially efficacious dose range in Phase II.

NR691 Thursday, May 9, 12 noon-2:00 p.m.

A Comparison of CCK-4 Panickers and Non-Panickers

Diana Koszycki, Ph.D., Clarke Institute of Psychiatry, 250 College Street, Toronto Ontario M5T 1R8, Canada; Robert M. Zacharko, Ph.D., Jean-Michel Le Melledo, M.D., Jacques Bradwejn, M.D.

Summary:

Systemic injection of CCK-4 has a profound panicogenic influence in humans, provoking significant somatic, affective, and cognitive symptoms. Although vulnerability to CCK-4 is increased in panic disorder patients, high doses of CCK-4 can provoke panic attacks in a substantial number of healthy subjects.

Objectives: Scant information is available describing the behavioral and biologic consequences of CCK-4 induced panic in healthy subjects. Accordingly, we compared the behavioral, cardiovascular, and hormonal profile of CCK-4 panickers (n = 24) and nonpanickers (n = 16).

Method: Forty males with no personal or family history of panic participated in the study. A subject was classified as a "panicker" if he reported at least four DSM-IV panic symptoms plus a subjective experience of anxiety, fear, or apprehension of at least moderate intensity.

Results: The propensity to panic was unrelated to baseline arousal. Panickers were demonstrably more sensitive than nonpanickers to the behavioral effects of CCK-4; they reported a significantly greater number of symptoms, more intense symptoms, and symptoms of a longer duration. Panickers also showed a greater elevation in diastolic blood pressure during the period associated with peak panic symptoms, but there was no differential heart rate or systolic blood pressure response. Perhaps the most interesting difference that emerged was the exaggerated ACTH, prolactin, and growth hormone response to CCK-4 in panickers. Cortisol response was also greater in panickers but not significantly so.

Conclusion: These data indicate that CCK-4 panickers can be reliably distinguished from nonpanickers on both behavioral and hormonal measures.

NR692 Thursday, May 9, 12 noon-2:00 p.m.

Twelve-Year Follow-Up of Treated Specific Phobia

Joshua Lipsitz, Ph.D., Psychiatry, New York State PI/Columbia, 722 West 168th Street, Unit 13, New York NY 10032; Salvatore Mannuzza, Ph.D., Donald F. Klein, M.D., Donald C. Ross, M.D., Cindy Aaronson, C.S.W., Abby J. Fyer, M.D.

Summary:

Patients (N = 29) initially treated for specific phobia as part of a comparative treatment study, were followed up 10 to 16 years (X = 12 years) later. A comprehensive, in-person, semistructured, diagnostic interview was utilized, which also assessed comorbid disorders. Of 21 subjects who had been rated as responders (much improved or very much improved) at treatment termination, 13 (62%) had significant avoidance or endurance with dread subsequent to treatment. Among a subgroup of these responders (n = 11) who had been considered completely recovered (improved and asymptomatic), five (45%) had significant avoidance or endurance with dread at follow-up. The eight subjects who had been rated as nonresponders at treatment termination all had clinically significant avoidance and/or endurance with dread in response to the same phobic stimulus subsequent to treatment.

Phobia subtype, age of onset, baseline severity, lifetime comorbidity, and type of treatment were not related to long-term outcome in this sample. Results support prior findings that specific phobia without the benefit of successful treatment tends to run a chronic course. However, findings challenge the notion that recovery from specific phobia following treatment is generally complete and enduring.

NR693 Thursday, May 9, 12 noon-2:00 p.m.

Childhood ADHD in Adults with Anxiety Disorders

Catherine L. Mancini, M.D., Psychiatry, Chedoke McMaster Hospital, 1200 Main Street West, Hamilton ON L8N 3Z5, Canada; Michael A. Van Ameringen, M.D., Steve Collins, M.D., Carol Wilson, M.Sc.

Summary:

Objective: One-third to one-half of children diagnosed as having attention deficit/hyperactivity disorder (ADHD) exhibit symptoms into adulthood. High rates of comorbidity are also found in adult ADHD, particularly, major depression, anxiety disorders, antisocial personality disorder, and substance use disorders. This investigation attempts to study patients in an anxiety disorder clinic who have a childhood history of ADHD.

Method: One hundred and forty-nine patients admitted to an anxiety disorders clinic were assessed using the SCID and psychometric measures of anxiety, depression, and disability. The Wender Utah Rating Scale was administered to obtain a retrospective diagnosis of childhood ADHD.

Results: Thirty-six patients (24%) qualified for a childhood diagnosis of ADHD. These patients tended to be male, have an increased prevalence of a lifetime history of alcohol abuse/dependence and dysthymia, and an increased mean number of comorbid diagnoses. They also demonstrated significantly higher scores on the Beck Depression Inventory, State-Trait Anxiety Inventory, and Social Adjustment Scale-Self Report.

Conclusion: Prevalence estimates of the disorder suggest that ADHD is found in 5% of all school-aged children. Therefore, the rate of 24% in an anxiety disorder clinic population is higher than that found in the general population. This finding suggests that ADHD may be a precursor to anxiety disorders in adults.

NR694 Thursday, May 9, 12 noon-2:00 p.m.

Clonazepam Efficacy in the Treatment of Panic Disorder: Results of a Multicenter Placebo-Controlled Trial

Georges Moroz, M.D., Clinical, Hoffmann-Laroche, 340 Kingsland Street, Nutley NJ 07110

Summary:

Objective: To conduct a placebo-controlled trial aimed at confirming the efficacy of clonazepam in panic disorder and characterizing its therapeutic effect on the main clinical components of the condition.

Methods: A multicenter (20 investigators), placebo-controlled, flexible-dose study involving 438 patients (222 on clonazepam and 216 on placebo) with a primary diagnosis of panic disorder. Patients were treated for six weeks with individually titrated doses of clonazepam ranging from 0.5 mg/day to 4 mg/day. Outcome measures included the number of panic attacks, CGI-severity for panic disorder, intensity of anticipatory anxiety, fear and avoidance associated with the main phobia, CGI-change for panic disorder, and ratings of work and social disability. The completion rates were 82% for patients on clonazepam and 75% for patients on placebo.

Results: At endpoint, clonazepam showed statistically significant and clinically relevant superiority over placebo in the global measures assessing the severity (CGI-S) and the change from baseline (CGI-C), as well as in the results concerning the components of panic disorder (number of panic attacks, intensity of anticipatory anxiety, severity of fear and avoidance associated with the main phobia), and in the ratings of work and social disability.

Conclusion: Those results confirm and expand the data from the literature on the therapeutic relevance and comprehensive effect of clonazepam in panic disorder.

NR695 Thursday, May 9, 12 noon-2:00 p.m.

Functional Impairment in Anxiety Disorders

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:

Objective: This study reports on the use of two new rating scales, the Disability Profile (DP) (clinician rated), and the Liebowitz Self-Rated Disability Scale (LSRDS), that have been designed to describe the functional impairment in social phobia. These scales were administered in four DSM-IV primary anxiety disorders: social phobia, panic disorder (PD), agoraphobia, and obsessive-compulsive disorder (OCD), in order to compare their functional impairment.

Method: Two hundred fifty-two consecutive patients seen in our anxiety disorders clinic were administered the DP and the LSRDS, as well as the Sheehan Disability Scale, the Social Adjustment Scale-Self Report, and the Medical Outcome Study (MOS) SF36.

Results: Using the DP and the LSRDS, social phobic patients were found to be significantly more impaired due to their illness in the areas of friendships, marital relationships, and education compared with PD and OCD patients, and had significantly less impairment in activities of daily living than OCD. Current and lifetime scores of the DP and LSRDS significantly correlated with scores on the SAS-SR, GAF, and Sheehan Disability Scale as well as with measures of symptom severity.

Conclusion: The DF and LSRDS appear to be useful tools in the measurement of social impairment in a variety of anxiety disorders.

NR696 Thursday, May 9, 12 noon-2:00 p.m.

Haloperidol in the Treatment of Trichotillomania

Michael A. Van Ameringen, M.D., Psychiatry, McMaster University Med Ctr, 1200 Main Street, Hamilton ON L8N 3Z5, Canada; Catherine L. Mancini, M.D.

Summary:

Objective: Trichotillomania has been described as belonging to the obsessive-compulsive disorder (OCD) spectrum. Trichotillomania differs from OCD by the lack of obsessions and other compulsions, the different sex distribution of the two disorders, and the different pattern of cerebral blood glucose metabolism. Trichotillomania may be related to Tourette's syndrome, since both hair pulling and tics are repetitive, involuntary behaviors that reduce tension and discomfort. Neuroleptics have successfully been used to treat Tourette's syndrome. They have also been used in combination with SRI's in treatment-refractory OCD. This study reports on the treatment of trichotillomania using low-dose haloperidol.

Method: Seven patients meeting DSM-IV criteria for trichotillomania were treated with haloperidol in doses from 0.5–2.5 mg daily. Eighty-five percent (6/7) had adequate trials with an SRI, which were unsuccessful. In these six patients, haloperidol was added to the SRI.

Results: Seventy-one percent (5/7) demonstrated marked improvement in the trichotillomania symptoms with almost complete hair regrowth. Two patients dropped out due to side effects. Sedation was the most common side effect.

Conclusion: Haloperidol may be an effective treatment for trichotillomania. This study provides some preliminary evidence to support the hypothesis that trichotillomania is a tic disorder. Controlled trials are required to investigate this finding further.

NR697 Thursday, May 9, 12 noon-2:00 p.m.

Parental Bonding in OCD and Body Dysmorphic Disorder

Katharine A. Phillips, M.D., Butler Hospital, 345 Blackstone Blvd, Providence RI 02906; Gail Steketee, Ph.D., Leslie Shapiro, M.S.W.

Summary:

Background: The relationship between OCD and body dysmorphic disorder (BDD) is controversial. It has been hypothesized that BDD may be a form of, or related to, OCD. In this study, we examined similarities and differences between BDD and OCD using the Parental Bonding Instrument (PBI), a validated and widely used measure of parental care and overprotection up to age 16. Some data suggest that patients with anxiety disorders report poor parenting (in particular, low parental care and high overprotection), but data are limited for OCD and absent for BDD.

Methods: 43 subjects with OCD, 40 with BDD, and 18 with both disorders completed the PBI. Symptom severity and global functioning were assessed with the Y-BOCS and GAF. The groups were similar in age, sex, symptom severity, and global functioning.

Results: BDD and OCD parental care scores did not differ significantly (21.0 ± 9.7 vs. 23.7 ± 9.6 on maternal care, and 19.1 ± 8.3 vs. 21.1 ± 9.4 on paternal care) but were lower than normative means. However, the comorbid group scored significantly lower than the OCD group on care (17.5 ± 8.0 vs. 23.7 ± 9.6 on maternal care [$p < .05$], and 15.0 ± 9.4 vs. 21.1 ± 9.4 on paternal care [$p < .05$]). The groups did not differ in terms of overprotection and were similar to or somewhat higher than normative means. The OCD and comorbid groups also differed significantly on paternal parenting patterns (based on a combination of care and overprotection), with less "optimal" parenting and more "absent or weak bonding" in the comorbid group. Bonding scores did not correlate significantly with illness severity or global functioning.

Conclusion: These preliminary findings suggest that BDD and OCD are similar in terms of parental bonding, but are lower than normative means for care; however, the comorbid group reported significantly poorer parenting than the OCD group.

NR698 Thursday, May 9, 12 noon-2:00 p.m.

Reliability and Validity of the Body Dysmorphic Disorder: Yale-Brown Obsessive-Compulsive Scale

Katharine A. Phillips, M.D., Butler Hospital, 345 Blackstone Blvd, Providence RI 02906; Bonnie R. Aronowitz, Ph.D., Concetta De Caria, Ph.D., Eric Hollander, M.D., Steven A. Rasmussen, M.D.

Summary:

Background: Body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, is a distressing, impairing, and relatively common disorder that is receiving increasing clinical and research attention. Since a scale to assess the severity of this disorder is not available, we developed such an instrument.

Methods: Because BDD shares phenomenologic similarities with OCD (prominent obsessional preoccupation with the perceived defect and ritualistic behaviors), we developed a slightly modified version of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) to assess BDD severity. The BDD-YBOCS is a 10-item, semistructured, clinician-rated instrument with two additional experimental items. The scale was administered to 125 DSM-IV-diagnosed subjects with BDD, and interviews with 15 subjects were audiotaped and independently rated by three additional raters. The Global Assessment of Functioning scale (GAF; n = 54), Clinical Global Impressions scale (CGI; n = 20), and Beck Depression Inventory (BDI; n = 52) were completed to assess convergent

and discriminant validity. Sensitivity to change was assessed in an open-label study of fluvoxamine (n = 21).

Results: Interitem and total score interrater reliability were excellent (intraclass r for total score = .99). Internal consistency was also high (Cronbach's alpha = .77). Each item was frequently endorsed across a range of severity. Total BDD-YBOCS score was significantly negatively correlated with GAF score ($r = -.44$, $p = .001$) and positively correlated with CGI score ($r = .56$, $p < .01$); it was modestly positively correlated with BDI score ($r = .38$, $p < .01$). The scale was also sensitive to medication-induced changes in BDD severity.

Conclusions: The BDD-YBOCS appears to be a reliable and valid measure of BDD severity and is a suitable outcome measure in medication trials of BDD.

NR699 Thursday, May 9, 12 noon-2:00 p.m.

Fluvoxamine in Body Dysmorphic Disorder

Katharine A. Phillips, M.D., Butler Hospital, 345 Blackstone Blvd, Providence RI 02906; Susan L. McElroy, M.D.

Summary:

Background: Body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, has been noted in case reports, clinical series, and a retrospective study to respond to SRIs, perhaps preferentially. Furthermore, available data, although limited, suggest that BDD's delusional variant (delusional disorder, somatic type) may respond to SRIs rather than neuroleptics. However, further data are needed. This is the first open-label treatment trial of BDD; we report a preliminary analysis of the first 20 subjects with DSM-IV BDD (or its delusional disorder variant) treated with fluvoxamine.

Methods: Patients were evaluated at baseline and at regular intervals with the BDD Y-BOCS, the Brown Assessment of Beliefs Scale (BABS), the Clinical Global Impressions Scale (CGI), and other scales. Response was defined as 30% or greater improvement on the BDD Y-BOCS and much or very much improved on the CGI.

Results: 14 (70%) of 20 subjects were responders; on the CGI, 7 (50%) were much improved and 7 (50%) were very much improved. BDD Y-BOCS scores decreased from 27.2 ± 3.9 at baseline to 11.9 ± 9.9 at termination ($p < .001$). Delusional subjects were as likely to respond as nondelusional subjects, and insight significantly improved (BABS score of 16.2 ± 5.5 [poor insight] at baseline to 9.8 ± 5.2 [good insight] at study endpoint [$p < .001$]. 5 of 6 responders who were delusional at baseline were no longer delusional at study endpoint. The mean dose of fluvoxamine was 240 ± 81 mg/day, and mean time to response was 5.2 ± 2.7 weeks (range 2–12 weeks).

Conclusions: These preliminary findings support previous suggestions that fluvoxamine is effective for BDD, including its delusional disorder variant, and that insight may improve with SRI treatment. Controlled treatment studies are in progress.

NR700 Thursday, May 9, 12 noon-2:00 p.m.

Autonomic Dysfunction in Comorbid Panic Disorder and Depression

Mark H. Townsend, M.D., Psychiatry, LSU, 1542 Tulane Ave, New Orleans LA 70112; Nancy B. Bologna, Ph.D., James G. Barbee IV, M.D.

Summary:

Secondary major depression is common in patients with panic disorder and has been reported to complicate treatment. Little is known about the effect of comorbid depression on the autonomic and cognitive symptoms associated with panic disorder. Panic disorder patients have been shown to have a higher resting blood pressure and heart rate than normals and to score higher on the Anxiety Sensitivity Index (ASI), a measure of fear of autonomic arousal.

In this study, the heart rate and blood pressure of 44 patients with panic disorder, 20 patients with major depression, and 12 patients with both panic disorder and depression were measured during postural change. The ASI was also administered. All patients were diagnosed using the SCID. Patients with comorbid panic disorder and depression were found to have higher resting diastolic and systolic pressures than patients in either group and to have a higher cardiac load factor ($p < 0.05$). They also showed higher diastolic pressures at one, two, and three minutes after assuming an upright posture ($p < 0.05$). ASI scores were equivalent among the three groups, although higher among pure panic patients. The results suggest that the development of secondary depression among panic disorder patients is concurrent with an increase in autonomic dysfunction.

NR701 Thursday, May 9, 12 noon-2:00 p.m.

PTSD and Existential Life Attitudes in Bone Marrow Transplantation Survivors

Suzanne M.J. Vickberg, B.A., Psychiatry, Memorial Sloan-Kettering, 1275 York Avenue, New York NY 10021; William H. Redd, Ph.D., Meridith Smith, Ph.D., Katherine N. DuHamel, Ph.D., Esperanza Papadopoulous, M.D., Lisa N. Rosen, M.A.

Summary:

This study examined the relationship between post-traumatic stress disorder (PTSD) and existential life attitudes in survivors of bone marrow transplantation (BMT) for the treatment of cancer and related diseases. We administered the PTSD Check List-Civilian (PCL-C) and the Life Attitude Profile-Revised (LAP-R) to 96 BMT recipients (one to nine years post-BMT). Fourteen of the 96 survivors (14.6%) met the full criteria for PTSD. A MANOVA comparing PTSD and non-PTSD groups on the six subscales of the LAP-R was significant: Wilks criterion = .74484, $F(6, 82) = 4.682$; $p < .001$. The groups differed on five of the life attitude subscales: Purpose $F(1, 87) = 9.058$; $p < .01$; Life Control $F(1, 87) = 6.326$; $p < .01$; Existential Vacuum $F(1, 87) = 28.839$; $p < .001$; Goal Seeking $F(1, 87) = 6.361$; $p < .01$; and Coherence $F(1, 87) = 3.852$; $p = .05$. The PTSD group scored lower than the non-PTSD group on the Purpose, Life Control, and Coherence subscales and higher on the Goal Seeking and Existential Vacuum subscales. The Death Acceptance subscale was not significant. Results suggest that Bone Marrow Transplantation is associated with PTSD, and that PTSD is significantly related to pessimistic existential life attitudes.

NR702 Thursday, May 9, 12 noon-2:00 p.m.

A Twin Study of Gene Environment Interaction in GAD

Francis A. O'Neill, M.D., Psychiatry, Mater Hospital, Crumlin Road, Belfast BT14 6AB, Northern Ireland; Kenneth S. Kendler, M.D.

Summary:

Genetic liability and stressful life events (SLEs) are both recognized risk factors for the onset of generalized anxiety disorder (GAD); however, we know little about how they interact. We applied discrete time survival analysis to a population-based sample of female-female twins (590 monozygotic and 440 dizygotic pairs) evaluated on two occasions by interviews that assessed for SLEs and the onset of GAD in the preceding year. Four of the "personal" SLEs and two of the aggregate "network" SLEs predicted the onset of GAD (four week definition) in the month of occurrence, with odds ratios (OR) ranging from 2.3 to 4.6. The impact of genetic

liability on the risk for GAD was also significant. The best-fitting model for the joint effect of SLEs and the genetic liability on onset of GAD suggested genetic control of the sensitivity to the anxiogenic effects of the SLEs. A linear regression analysis indicated significant genotype x environment interaction in the prediction of episode onset of GAD by severe SLEs. There were, however, differences in the pattern of the type of SLEs that were predictive of GAD and major depression in the same sample, loss events in particular being more depressogenic than anxiogenic.

NR703 Thursday, May 9, 12 noon-2:00 p.m.

Cytokine Production in OCD

Ronit Weizman, M.D., Mental Health Center, 9 Hatzvi Street, Ramat Hatayassim 67197, Israel; Nathaniel Laor, M.D., Yerachmiel Barber, M.D., Haggai Hermesh, M.D., Meir Djaldetti, M.D., Hanna Bessler, Ph.D.

Summary:

OCD is an anxiety disorder associated with distress and frequently also with major depression. Cytokine production was previously demonstrated to be reduced in untreated major affective disorder patients. Moreover, recovery from the depressive episode following clomipramine (CMI) treatment was accompanied by the restoration of interleukin-1β (IL-1β) and interleukin-3-like-activity (IL-3-LA) to normal range. In the present study we examined the capacity of peripheral blood mononuclear cells to produce IL-1β, IL-2, and IL-3-LA activity in nondepressed OCD patients compared with healthy individuals and to assess the impact of CMI treatment on cytokine production.

CMI treatment induced a significant improvement in OCD symptoms. No alteration was observed in cytokine production in untreated OCD patients compared with controls. In addition, eight weeks of drug treatment had no effect on cytokine production. Thus, OCD is not associated with changes in IL-1β, IL-2, and IL-3-LA production, and CMI treatment seems not to interfere with the production of these cytokines.

NR704 Thursday, May 9, 12 noon-2:00 p.m.

Dream Content in OCD: A Semantic and Emotional Analysis in Comparison with Controls

Dr. Alain Sauteraud, Centre Hospitalo, Universitaire de Bordeaux, 121 Rue de la Bechade, Bordeaux 33076, France; Jean-Claude Menny, M.D., Pierre Philip, M.D., Franck Peyre, M.D., Jean-Marie Bonnin, M.D., Marc L. Bourgeois, M.D.

Summary:

Objectives: We sought to investigate the content of the dreams of obsessive-compulsive outpatients to assess whether dreams play a role in processing of information and storage of events of the day and if so whether the dreams recollections of OCD patients present evidence of diurnal obsessive or ritual themes. If dreaming contributes to the control of stressful situations, dreams should reveal emotional disturbances present in obsessive-compulsive disorder.

Method: Each morning immediately after awakening, 14 nondepressed OCD outpatients and 11 controls recorded their recollections of the night's dreams on an audiotape. After randomization of dreams, two judges were asked to carry out a blind evaluation of the emotional characteristics perceptible in these dreams and of the presence of obsessive or ritual themes.

Results: 68 dreams were collected in the OCD group and 55 in the control group. No differences were found between the two groups regarding anxiety, sadness, the theme of failure, or the presence of obsessive or ritual themes. In both groups, 50% of subjects had anxious dreams, 20% sad dreams, and 50% failure dreams. Surprisingly, 36% of subjects had obsessive or ritual themes in their dreams.

Conclusions: These data support the hypothesis that there is no direct relation between diurnal and nocturnal mental activity. The links between dreams and psychopathology remain unclear. Sleep mentation is not a peaceful or pleasant process.

NR705 Thursday, May 9, 12 noon-2:00 p.m.

PMS: Does Ongoing Stress Modulate Its Severity?

Tracey J. Strasser, B.A., Psychiatry, Columbia University, 722 West 168th Street, Unit 123, New York NY 10032; Dianne E. Schechter, Ph.D., Jean Endicott, Ph.D.

Summary:

Objective: The aim of this study was to assess the relationship between stress level and the pattern of dysphoric mood in women who meet criteria for "pure" PMS ranging in severity from mild to severe.

Method: For study inclusion, subjects had to demonstrate a clear association between mood and menstrual cycle phase, but impairment was not required. Thirty-one women completed daily ratings of mood and perceived stress on a 0–4 scale for four to six menstrual cycles. "Trait" levels of stress (mean of 120–180 days) and premenstrual dysphoric mood (mean of last four days of each cycle across cycles) were defined for each individual. The sample was divided into lower (n = 21) and higher (n = 10) stress groups on the basis of trait stress level (means 0.97 ± .23 vs. 1.73 ± .33).

Results: As expected, there was a significant group difference in trait stress ($t = 7.48$, $p < .001$), which reflected a higher stress level during the midfollicular phase (means .94 ± .37 vs. 1.54 ± .27, $p < .0001$) as well as during the premenstrual phase (means 1.26 ± .42 vs. 2.13 ± .47, $p < .0001$). A 2 x 2 ANOVA (stress group x phase) examining the effects of stress level and cycle phase on negative mood yielded a significant group x phase interaction ($p < .025$). Both groups showed a phase change in mood, but the higher stress group reported more severe premenstrual negative mood than the lower stress group (lsmean = 1.15 vs. 0.80, $p < .0001$). The groups did not differ during the midfollicular phase (lsmean = 0.38 vs. 0.42), indicating that higher average stress was not associated with higher baseline negative mood.

Conclusions: These findings suggest that ongoing stress level may play a role in modulating the severity of premenstrual negative mood in women who are sensitive to their menstrual cycle.

NR706 Thursday, May 9, 12 noon-2:00 p.m.

Association Between Appetite and Mood in PMS

Tara M. Singer, B.A., Psychiatry, Columbia University, 722 West 168th Street, Unit 123, New York NY 10032; Dianne E. Schechter, Ph.D., Jean Endicott, Ph.D.

Summary:

Two studies assessed premenstrual increases in appetite and negative mood. Fifty-one women completed daily ratings for two menstrual cycles. "Trait" levels of mid-follicular (mean of days 5–8 of each cycle) and premenstrual (mean of last four days of each cycle) mood and appetite were defined. Study #1 evaluated the between-subjects relationship between trait changes in appetite and negative mood (mid-follicular to premenstrual level expressed as a percent of 0–4 scale). Three groups, divided on trait change in mood, differed in severity of mood change (group #1 = 0.2%, group #2 = 7.2%, group #3 = 19.8%, $p < .0001$), but not in the intensity of increased appetite (group #1 = 12.5%, group #2 = 23.2%, group #3 = 17.4%). The lack of association between trait changes in appetite and mood also was demonstrated in a correlational analysis ($n = 51$, $r = -0.04$). Within group t-tests found

significant premenstrual increase in appetite in all groups (p values < .01), but only groups 2 and 3 showed significant mood changes (p values < .01). Study #2 evaluated the within-subject association between premenstrual increases in appetite and negative mood in a subgroup of the sample (n = 13) who met criteria for "pure" PMS. Subjects completed 3–5 additional cycles of daily ratings. A most and least symptomatic cycle was selected for each subject based on premenstrual increase in negative mood. Comparison cycles differed in severity of mood change (3% vs. 28%, p < .002), but not in intensity of increased appetite (14% vs. 16%). The within cycle change in appetite was significant in both cycles (p values < .03), but the within cycle change in mood was significant only in the subjects' more symptomatic cycle (p < .0001). These findings suggest premenstrual increases in negative mood and appetite may have somewhat different mechanisms.

NR707 Thursday, May 9, 12 noon-2:00 p.m.

Diagnostic Status of Women Presenting to a PMS Clinic

Carol S. Birnbaum, M.D., Psychiatry, Mass General Hospital, 15 Parkman ST. WACC 815, Boston MA 02114; Lee S. Cohen, M.D., Jennie W. Bailey, B.A.

Summary:

Introduction: Many women suffer symptoms of premenstrual reactivity of mood and anxiety and present for evaluation and treatment of "PMS" to a spectrum of clinicians including primary care providers, gynecologists, and psychiatrists. The purpose of this study is to formally evaluate a cohort of women responding to an announcement outlining a study of potential treatment for PMS or mood disturbance with premenstrual worsening.

Methods: In response to a number of local advertisements outlining a treatment study for women suffering from premenstrual symptoms or mood disorder with premenstrual worsening, 168 women were screened by phone in a primary effort to assess diagnostic status. A screening instrument keyed to the Structured Clinical Interview for Diagnosis (SCID-P) was employed and was administered to patients responding to the advertisement. Patients who met the criteria for major depression, dysthymia, or premenstrual dysphoric disorder were then sent daily rating forms (Endicott and Harrison) to document significant change in severity of symptoms between follicular and luteal phase of the cycle.

Results: Of those subjects screened by phone, 66% met criteria for dysthymia or major depression with premenstrual worsening or premenstrual dysphoric disorder. However, following review of daily rating forms, symptoms ascribed to the luteal phase appeared to be much more scattered through the menstrual cycle than indicated by patient report.

Conclusion: Many patients with primary complaints of "PMS" may suffer from underlying mood disorders such as dysthymia or major depression. While several investigators suggest that premenstrual exacerbation of symptoms is common in this population, prospective daily rating forms obtained in this cohort of women suggested that while some patients suffer from premenstrual worsening of mood, others appear to have affective instability manifesting across the menstrual cycle. Implications for screening and treatment of patients presenting with the primary complaint of premenstrual syndrome are discussed.

NR708 Thursday, May 9, 12 noon-2:00 p.m.

The Relationship Between the Menstrual Distress Questionnaire and Aggressive Responding

Donald M. Dougherty, Ph.D., Psychiatry, University of Texas, 1300 Moursund Street, Houston TX 77030; Patrick Bordnick, Ph.D.

Summary:

Objective: This study investigated the relationship between the severity of self-reported menstrual cycle symptoms and a laboratory measure of aggression.

Method: Two groups of women were recruited, one group reporting low and one group reporting moderate to high perimenstrual symptoms. Scores of the negative affect subscale of the Menstrual Distress Questionnaire (MDQ) were used to define groups. Each of 40 subjects participated in three testing sessions of the Point Subtraction Aggression Paradigm. This paradigm gives subjects the opportunity to earn points by responding on one button, and/or to subtract points (aggression) from a partner by responding on another button. Subjects were periodically provoked by subtracting a point from the subject's counter and attributing these subtractions to the responding of the partner.

Results: There were two significant findings: (a) the high symptom group emitted higher rates of aggressive responding than the low symptom group; and (b) rates of aggressive responding were significantly correlated with the negative affect and behavior change scales.

Conclusions: These findings indicate that MDQ scores are related to an individual's tendency to respond aggressively when provoked, and are consistent with previous studies demonstrating that the severity of MDQ scores are correlated with a diversity of self-report and performance measures.

NR709 Thursday, May 9, 12 noon-2:00 p.m.

Dissociation and Somatization in Psychiatrically Disturbed Adolescents with Traumatic Life Experiences

Romuald M. Brunner, M.D., Child Psychiatry, University Heidelberg, Blumenstrasse 8, Heidelberg 69115, Germany; Prof. Franz Resch, Peter Parzer, DiplPsyc., Eginhard Koch, M.D.

Summary:

Objective: The purpose of this study was to examine the phenomenology of dissociation and somatization in a clinical group of adolescents. The relationship between the degree of dissociation, somatization, and the degree of different types of childhood trauma was analyzed.

Method: 112 consecutive admissions to the inpatient psychiatric treatment at the department of child and adolescent psychiatry, University of Heidelberg, were investigated. Patients, 12–18 years old, completed our German version of the Dissociative Experiences Scale (DES) and the Giessen Subjective Complaints List for Children and Adolescents (GSCL-C). Also the Frankfurt Self-concept Scales (FSKN) were used. The psychiatric diagnoses were assessed by ICD-10. The different types of reported childhood trauma were differentiated and categorized.

Results: The phenomenology of the interrelationship among dissociation, somatization, and childhood trauma are described. In accordance with findings in North American Studies, adolescents with a sexual abuse history showed Significant higher scores on the dissociative experiences scale compared to adolescents without such a history. Also we saw that somatization is mainly related to physical abuse and strongly connected to a negative self-concept in our adolescent patients.

Conclusions: The degree of dissociation and somatization are connected with specific type of childhood trauma. We saw that dissociation is mainly related to sexual abuse and to a lower degree to physical abuse, while somatization depends on physical abuse only.

NR710 Thursday, May 9, 12 noon-2:00 p.m.

Serum Pemoline Levels in Adult ADD

Faruk S. Abuzzahab, Sr., M.D., Psychiatry, U of Minnesota Hosp & Clinic, Box 393 Mayo Bldg, Minneapolis MN 55455–0100; J.M. Gillund, R.L. Zimmermann, Ph.D.

Summary:

Introduction: Twenty outpatients meeting the DSM-IV criteria for adult attention deficit disorder and comorbid major depression ranging in age from 22 to 68 with an average age of 44.8 ± 10.4 years were treated with pemoline (Cylert). Eight patients were male and 12 were female. Dosages ranged from 150 mg per day to 450 mg per day with the average dose being 254.7 ± 89.1 mg per day. All patients exceeded the maximum recommended daily dose in the 1996 Physician's Desk Reference which is 112.5 mg. Serum through pemoline levels ranged from < 0.1 to 6 μg/ml with the average being 1.85 ± 1.52 μg/ml. All levels were determine through high performance liquid chromatography. Normal values for the lab used are 1.5–7.0 μg/ml.

Results: Twelve out of the 24 levels (some patients had more than one level drawn) were below 1.5 μg/ml and 22 were below the midway point of 4.25 μg/ml. Twenty-four pairings of prescribed dosages and blood levels were available for analysis from 20 patients. Dosages were converted to mg per square meter of body surface area per day, ranging from about 1.5 to 6.8 m^2, with a mean of 2.9 m^2. In this form there was sufficient variation to compute meaningful correlations. The correlation of dose per unit surface area with blood level across the 20 subjects was 0.48, which for a sample of 20 is significantly greater than zero at the 5 per cent level, using a one-tailed test. The same correlation of dose per unit surface with blood level based on the 24 assays instead of 20 patients was 0.33, which falls just at the 0.05 level. While the mean blood level was 2.9 μg/ml, 12 of the 24 blood levels were below the recommended minimum blood level of 1.5. Even though all patients required dosage of pemoline above the manufacturer's recommended daily dosage to reach therapeutic benefit, half of them fall below the lowest values of therapeutic blood level of 1.5 μg/ml. Furthermore, none of the patients achieved blood levels above 7.0 μg/ml although three received 450 mg/d.

Conclusions: In this limited number of adult attention deficit disorder with comorbid major depression, all 20 subjects required dosages of pemoline above the recommended daily dose of 112.5 mg/d.

NR711 Thursday, May 9, 12 noon-2:00 p.m.

Depersonalization Measured by a Questionnaire

Dr. Nannet Buitelaar, De Wellen, Deventerstraat 459, Apeldoorn, Holland; Dr. Robert Ferdinand

Summary:

Objective: Depersonalization is a very important symptom in various psychiatric disorders. Research on depersonalization would be facilitated by a questionnaire to assess depersonalization. However, such questionnaires are not available. Therefore, we developed the 14-item Depersonalization Symptom Check List (DSCL). The objective was to assess its reliability and its validity against DSM-IV criteria for depersonalization disorder assessed via the SCIDD (Structured Clinical Interview for DSM-IV Dissociative Disorders).

Methods: Subjects were 43 psychiatric patients and 40 normal subjects.

Results: Indices for reliability were very high (internal consistency for all items: *alpha* = .87; 1 week test-retest: *r* = .95). Furthermore, DSCL scores almost flawlessly predicted DSM-IV depersonalization assessed by interview (sensitivity = 92%, specificity = 100%).

Conclusion: The DSCL, which can be applied within 15 minutes, appeared to be a very reliable and valid instrument for assessing depersonalization. The DSCL will probably enhance further research on depersonalization on a large scale. However, further research on its properties in larger samples is needed.

NR712 Thursday, May 9, 12 noon-2:00 p.m.

The Effects of Methylenedioxymethamphetamine ("Ecstasy") on Human Sexual Function

Zvi Zemishlany, M.D., GEHA Hospital, PO Box 102, Petah Tikva 49100, Israel; Dov Aizenberg, M.D., Abraham Weizman, M.D.

Summary:

Objective: 3, 4-methylenedioxymethamphetamine (MDMA, "Ecstasy"), a popular recreational drug of abuse, is structurally related to the stimulant, amphetamine, and the hallucinogen, mescaline. Its effect appears to be mediated by release and reuptake inhibition of brain monoamines, particularly serotonin and dopamine. These biogenic amines have been implicated in the modulation of sexual desire, arousal, and orgasm as facilitatory (dopamine) and inhibitory (serotonin) mediators. The aim of this study was to determine the short-term effects of MDMA on human sexual function.

Method: Sexual function following MDMA consumption was evaluated in a series of healthy recreational users (20 males and 15 females, aged 21–48 years) with regard to four major domains of sexual activity: desire, erection (lubrication in females), orgasm, and satisfaction. Each item was rated in comparison to baseline function on a scale of –3 to +3 (0 = unchanged, –1, +1 = slight, –2, +2 = moderate, –3, +3 = profound decrease or increase, respectively).

Results: Desire and satisfaction were moderately to profoundly increased by MDMA. Orgasm was more intense and delayed. Erection was affected negatively in several cases. Interestingly, 60% of the subjects reported on concomitant use of marijuana, a cannabinoid with dopamine releasing activity, for further enhancement of desire.

Conclusion: Results support the hypothesis that central dopaminergic transmission facilitates sexual desire and satisfaction while central serotonergic activity is inhibitory to erection and orgasm attainment.

NR713 Thursday, May 9, 12 noon-2:00 p.m.

Imipramine Treatment for Retrograde Ejaculation Induced by Thioridazine

Dov Aizenberg, M.D., GEHA Hospital, PO Box 102, Petah Tikua 49100, Israel; Roni Shiloh, M.D., Zvi Zemishlany, M.D., Abraham Weizman, M.D.

Summary:

Objective: Chronic treatment with neuroleptic agents is necessary for most schizophrenic patients. However, it is often associated with a variety of sexual side effects which may lead to patients' noncompliance. Retrograde ejaculation is frequently encountered among patients treated with thioridazine. This side effect interferes with the quality of orgasm and general sexual satisfaction.

Method: In this preliminary study, eight schizophrenic patients who complained of retrograde ejaculation during thioridazine treatment were given concomitant low-dose imipramine (25–50 mg at bedtime).

Results: Four out of the eight patients reported complete resumption of their previous ejaculatory function. In another patient, there was also a substantial improvement; three noted no change.

Conclusion: Imipramine may be beneficial for some patients with thioridazine-induced retrograde ejaculation.

NR714 Thursday, May 9, 12 noon-2:00 p.m.

Retrospective Review of Psychotropic-Induced Sexual Dysfunction in Women

Angela P. Aldrich, Ph.D., Pharmacy, Boise VA Med Ctr, 500 West Fort Street, Boise ID 83702; Marcus D. Cook, Ph.D., Leslie Pedersen, M.D.

Summary:

The purpose of this retrospective review was to estimate the incidence of selective serotonin reuptake inhibitor (SSRI) induced sexual dysfunction in female psychiatric patients.

Four hundred forty-four outpatient charts were reviewed for inclusion. Ninety-five subjects with birth years between 1945 and 1977, with a record of SSRI pharmacotherapy while under psychiatric care, and with records documenting drug utilization and ongoing sexual dysfunction were identified. Data collected included gender, age, medications, primary diagnosis, sexual dysfunction at initial visit (if any), and ongoing incidence of dysfunction after initiation of SSRI therapy. The primary outcome measure was a symptom assessment sheet (SAS), which was completed by each outpatient at every clinic visit to survey symptoms from which the patient might be suffering.

Results included a population ranging in birth year from 1946 to 1977 (1959 ± 8.3). Medications surveyed included paroxetine, fluoxetine, sertraline, and fluvoxamine. Forty of 95 subjects had no initial dysfunction present. Eighteen of these 40 (45%) experienced sexual dysfunction after less than one year of therapy with a SSRI. These data suggest that SSRI induced sexual dysfunction occurs frequently in women, and can assist the clinician in providing quality care to female patients in order to improve outcomes management.

NR715 Thursday, May 9, 12 noon-2:00 p.m.

Treatment of Antidepressant-Induced Sexual Dysfunction with Ginkgo Biloba Extract

Alan J. Cohen, M.D., Psychiatry, University of CA at SF, 37 Quail Court #200, Walnut Creek CA 94596

Summary:

Antidepressant-induced sexual dysfunction (ASD) is a common complaint among patients. A pilot study using formulations of the extract of Ginkgo biloba (EGb) to reverse ASD proved successful. All 37 patients had attempted to control sexual dysfunction through other means which included pharmacological interventions (cyproheptadine, yohimbine, buspirone, amantadine), dosage adjustment, drug holidays, and alternative antidepressants. All patients met DSM IV criteria for a depressive disorder and reported ASD. Patients were prescribed a formulation of EGb (24:1), two 60 mg. capsules, B.I.D., four times daily. After four weeks they were reevaluated for symptoms of ASD. Thirty-two of the 37 patients reported significant response and marked improvement in their sexual function, an 86% response rate. No significant adverse effects were reported with the exception of one patient who reported a worsening of urinary difficulties related to prostatic hypertrophy. The mechanism of action for EGb appears to be the improvement of circulation by way of active ginkgoloides. Reversal of ASD is due to enhanced vascular flow to the genitalia via inhibition of platelet activating factor, serotonin-receptor changes, and increases in prostaglandin levels. Further study is warranted to pursue this option in refractory sexual dysfunction.

NR716 Thursday, May 9, 12 noon-2:00 p.m.

A Double-Blind Placebo-Controlled Trial of Yohimbine for Treatment of SRI-Induced Sexual Dysfunction

Frederick M. Jacobsen, M.D., Transcultural Mental Institute, 1301 20th St NW Suite 711, Washington DC 20036–6023; Lillian Comas-Diaz, Ph.D.

Summary:

Objectives: 1) To determine response to yohimbine (YOH) *vs* placebo (PBO) compared with baseline (BSL) ratings of sexual dysfunction induced by SRIs in affective and anxiety patients; 2) to determine side effects of YOH *vs* PBO.

Method: Two sequential random-ordered three-week trials of YOH 5.4 mg T.I.D. and PBO T.I.D. Four-point scales rating libido, orgasm, erection (males), mood, anxiety, sleep disturbance, GI distress, and flushing were completed by patients at study entry and weekly on each condition. Five-point positive and negative expectation scales were rated prior to each condition.

Results: In 33 patients (22 women, 11 men; 22 fluoxetine, 11 sertraline), there were no ordering effects in expectations of benefit. Improvement in libido and orgasm occurred on both YOH and PBO conditions ($p \leq 0.001$ for both *vs* BSL). There were trends for improved erections ($p = 0.083$) but more anxiety ($p = 0.058$) on YOH but not PBO, and for men to have greater improvement in orgasms than women ($p = 0.092$). No significant differences were found in ratings of depression, sleep disturbance, flushing, or GI distress between YOH and PBO.

Conclusions: 1) yohimbine can improve SRI-induced sexual dysfunction in some patients; 2) yohimbine's effects on erections may be more significant than its effects on libido, and may be more pronounced in men than in women.

NR717 Thursday, May 9, 12 noon-2:00 p.m.

Sexual Dysfunction with SSRIs: A Comparitive Analysis

Angel L. Montejo, M.D., Psychiatry, Hospital Universitario, Paseo De San Vicente 58–182, Salamanca 37007, Spain; Gines Llorca, M.D., Juan A. Izquierdo, M.D., Work Group of Spain to Study Sexual Dysfunction

Summary:

The authors analyze the incidence of sexual dysfunction (SD) with different SSRIs (fluoxetine, fluvoxamine, paroxetine, and sertraline) and hence the qualitative and quantitative changes in SD throughout time. For the study 215 outpatients (120 women, 95 men; mean ± SD age = 41 ± 7) under treatment with SSRIs were interviewed with an SD questionnaire designed for this purpose by the authors. It included questions about the following items: decreased libido, delayed orgasm or anorgasmia, delayed ejaculation, inability to ejaculation, impotence, and general sexual satisfaction. Patients with the following criteria were included: normal sexual function before SSRIs intake, exclusive treatment with SSRIs or associated with benzodiazepines, previous heterosexual or self-erotic current sexual practices. We excluded patients with previous sexual dysfunction, association of SSRIs with neuroleptics, hormone intake, and significant medical illnesses.

Results: There is a significant increase in the incidence of SD when the physicians ask the patients direct questions (55%) versus spontaneous SD reported (2% to 7%). There are some significant differences among different SSRIs: paroxetine provoked more anorgasmia than fluvoxamine (ANOVA $p < 0.05$) and more impotence than fluoxetine and sertaline ($p < 0.05$). A total of 25% of the patients had a bad tolerance about their dysfunction. SD has positive correlation with the dose. The patients experienced substantial improvement in sexual function when the dose was diminished or the drug was withdrawn. Six of eight patients (75%)

experienced total improvement when the treatment was changed to Moclobemide (450 mg/day).

NR718 Thursday, May 9, 12 noon-2:00 p.m.

The Effects of Short and Long Naps Among Narcoleptic, Sleep Deprived and Alert Subjects

Leon D. Rosenthal, M.D., Sleep Disorders Ctr, Henry Ford Hospital, 2921 W Grand Blvd NCP-5, Detroit MI 48202–2691; Todd Helmus, B.A., Thomas Roth, Ph.D.

Summary:

Short naps are recommended in the management of narcolepsy because of their alerting effects. We studied the effects of naps (15 vs 120 min long) among narcoleptic (NC), healthy sleep deprived (SD), and non-deprived (ND) subjects. NCs and controls (age and gender matched) were screened to determine their eligibility. Subjects spent two sessions in the laboratory. NC and ND subjects spent eight hrs Time in Bed (TIB: 2300–0700 hrs) while SD subjects were kept awake. Subjects were counterbalanced to each nap condition. Naps were terminated at noon. At 1215 hrs a modified multiple sleep latency test (MSLT) was administered (times: 1215, 1240, 1305, 1330, and 1355). Naps were terminated after any indication of sleep or 20 minutes of wake. Sessions concluded with a one hour nap (1500–1600 Hr). On the screening MSLT, NC subjects (2.1 ± 1.4) had a shorter mean latency when compared to controls (SD = 13.8 ± 4.0, ND = 13.3 ± 2.3). On the modified MSLT, NC and SD subjects had shorter latencies (3.8 ± 2.6 and 4.2 ± 3.1, respectively) than ND subjects (13.7 ± 4.2). The 120 min. nap was more beneficial (9.0 ± 6.8) than the 15 min. nap (5.5 ± 5.2). There was no group by nap interaction. On the one hour nap, a group by nap interaction was demonstrated ($p < 0.05$). While SD subjects had a longer latency following the 120 min. nap (11.9 ± 11.7 vs. 3.3 ± 4.2 on the 15 min. nap), NC (2.5 ± 2.3 vs. 2.4 ± 2.1), and ND subjects (18 ± 18.1 vs. 17.2 ± 10.1) did not differ. A long nap resulted in greater immediate improvement. The improvement was not differential to the groups. However, differential benefits were documented three hrs later. SD subjects experienced long-term benefits from the 120 min nap, while narcoleptics failed to show sustained improvement.

NR719 Thursday, May 9, 12 noon-2:00 p.m.

Epidemiology of Frequent Nightmares in Adults

Thomas C. Neylan, M.D., Psychiatry Service 116N, UCSF-VAMC, 4150 Clement Street, San Francisco CA 94121; Charles R. Marmar, M.D., Thomas J. Metzler, Ph.D., Roger M.Y. Wu, M.D., Douglas F. Zatzick, M.D., Daniel S. Weiss, Ph.D.

Summary:

The National Vietnam Veterans Readjustment Study (NVVRS) was a population-based study, sampled to represent the 3.1 million men and women who served in Vietnam. The study described the prevalence of post-traumatic stress disorder (PTSD) and other psychiatric disorders in Vietnam veterans and civilian Vietnam era controls. This study analyzes the questionnaire items that address complaints about sleep.

Results: Frequent nightmares occur in less than 5% of the Vietnam theater sample and less than 1.5% of civilian controls. Frequent nightmares are found exclusively in subjects with PTSD who comprise 15.2% of the combat veteran sample and 1.2% of the civilian controls. Combat exposure is strongly correlated with frequency of nightmares ($r = 0.63$, $p < 0.0001$), moderately correlated with sleep onset insomnia ($r = 0.45$, $p < 0.0001$), and weakly correlated with disrupted sleep maintenance ($r = 0.14$, $p < 0.0001$). An hierarchical multiple regression model developed to explain nightmares in Vietnam veterans shows that war zone exposure accounts for 40% of the variance. Adding to the model, history of alcohol abuse, chronic medical illnesses, panic disorder, major depression, and mania as a set collectively explains an additional 5% of the variance.

Conclusion: Complaints of frequent nightmares are virtually specific for PTSD in adults.

NR720 Thursday, May 9, 12 noon-2:00 p.m.

Circadian Rest-Activity Rhythms in Demented/ Nondemented Elders and Their Caregivers

Charles P. Pollak, M.D., Sleep Medicine, Ohio State University, 105 Upham Hall/473 W. 12th Ave, Columbus OH 43210; Peter E. Stokes, M.D., Patricia R. Mourilhe, M.D.

Summary:

Disruptive nocturnal behaviors of elderly people often threaten the caregiving arrangements on which their community tenure depends. Dementing disorders are especially prone to result in disrupted sleep and agitated behaviors ("sundowning"). Circadian rest-activity cycles were therefore compared in community residents consisting of demented elders and their caregivers as well as nondemented elders and their caregivers. Activity was measured and stored with wrist-worm micro processor recorders. A novel method was devised to detect periods when the recorders had not been worn. Such non-compliance artifact was surprisingly common. If not removed, it would have biased the activity level data toward small values normally associated with sleep. Mean hourly activity patterns showed that demented and nondemented elders were more active at night than their caregivers and presumably slept less soundly. However, demented subjects were contrastingly less active in the daytime than their nondemented peers as well as their caregivers. The consequent flatter rest-activity rhythms of the demented elders are not entirely explained by age, nor by decreased output of a circadian pacemaker. According to fitted cosine models, the phase of the circadian rest-activity cycle recorded peaked between 2 p.m. and 3 p.m. in all elder and caregiver groups and did not significantly differ among them. The increased activity of elders at night is probably explained by sleep disorders which remain to be identified.

NR721 Thursday, May 9, 12 noon-2:00 p.m.

Predictive Value of Alexithymia: A Prospective Study in Somatizing Patients

Michael Bach, M.D., Psychiatry, University of Vienna, Waehringer Guertel 18–20, A-1090 Vienna, Austria; Doris Bach, Ph.D.

Summary:

In the present study, the potential role of alexithymia in predicting the long-term treatment outcome was investigated prospectively in 30 patients with DSM-III-R somatoform disorders and anxiety disorders (11 patients with a somatoform disorder, 19 patients with panic disorder, and 13 patients with both somatoform and panic disorder). Using SCID interviews, diagnoses were assessed before inpatient treatment and two years after discharge. Patients who met criteria for DSM-III-R undifferentiated somatoform disorder at follow-up exhibited significantly ($p < 0.02$) higher pre-treatment alexithymia scores (as measured by the Toronto Alexithymia Scale = TAS) as compared with patients who showed remission of their somatoform disorder (TAS scores: 76.7 vs. 69.3, $p = 0.02$). In contrast, comparable pre-treatment TAS scores were found in patients with persistent as compared to those with remitted anxiety disorders ($p = 0.42$). As a result of stepwise logistic regression analyses, high alexithymia scores emerged as a significant predictor of persistent somatoform disorders, independent from other measures of psychopathology, sociodemographic vari-

ables, and measures of illness severity (improvement of regression model: chi-square = 4.51, p = 0.03). These results underline the potential role of alexithymia in predicting an unfavorable long-term outcome in somatizing patients.

NR722 Thursday, May 9, 12 noon-2:00 p.m.

Trichotillomania: Etiology, Phenomenology, Comorbidity and Treatment Recommendations

Iver E. Hand, M.D., Psychiatry, University Hospital, Martinistrasse 52, Hamburg D 20246, Germany; Annette Neudecker, Ph.D., Nicole Monchau, Ph.D.

Summary:

Method: 106 subjects (105 female) with trichotillomania participated in a questionnaire study investigating phenomenological and cognitive-behavioral aspects of trichotillomania, as well as comorbidity and personality traits. Symptomatic and personality assessments were conducted with: Structured Clinical Interview for DSM-III-R (SCID), Symptom-Check-List (SCL-90-R), Beck Depression Inventory (BDI), Freiburg Personality Inventory (FPI-R), HOCI (Hamburg Obsessive Compulsive Inventory).

Results: The data support earlier American studies: Hair pulling mainly occurs on the head; onset is mainly around puberty, mostly in a state of juvenile depression. The main reason subjects continue hairpulling into adulthood is the calming and distracting effect in any state of negative affect (generalization from the initial trigger depression).

Comorbidity results: Depression 40% (BDI)-65% (SCID); anxiety disorders 60% (SCID); substance abuse 20% (SCID); OCD 50% (HOCI), 51% (SCL), and 23% (SCID). The lower SCID rating seems due to a hiding of OC-symptomatology, in contrast to the anonymous self-rating; anxious-avoidant personality traits % (FPI). The OCD results are clearly above published comorbidity (around 15%).

Discussion: Results will be discussed with reference to "OCD-spectrum" disorders, "affective spectrum" disorders and "substance Independent addictions" (particularly the first author's model of pathological gambling). Recommendations for treatment (taking into account published studies) will be proposed.

NR723 Thursday, May 9, 12 noon-2:00 p.m.

Olanzapine: Impact of An Atypical Antipsychotic Candidate on Prolactin Release

Ann Marie Crawford, Ph.D., D.C. 0538, Eli Lilly and Company, Lilly Corp Ctr, Indianapolis IN 46285; Charles M. Beasley, Jr., M.D., Gary D. Tollefson, M.D.

Summary:

One defining clinical characteristic of an atypical profile for an antipsychotic is minimal sustained elevation of prolactin. In a large placebo- and haloperidol-controlled study of olanzapine (Olz), its impact on prolactin was evaluated.

Methods: 335 schizophrenic patients were randomized to double-blind therapy with one of five treatments. Of these 335 patients, 139 patients completed the six weeks of acute therapy. Ninety-five patients completed acute therapy and continued into long-term therapy. During acute therapy, prolactin was measured at baseline, Weeks 2, 4, and 6, and at any discontinuation visit. Concentrations were measured at Weeks 12, 24, 36, 52, and/or the discontinuation visit during long-term therapy.

Results: Of 330 patients with measurements at baseline, 9% had prolactin above the upper limit of normal. Of the 91% with baseline concentrations at or below the upper limit, 39% of the Olz-H (15 ± 2.5 mg/day) treatment group, 24% of the Olz-M treatment group, and 8% of the Olz-L treatment group had elevated prolactin after two weeks of treatment. After six weeks of treatment, 22% of the Olz-H treatment group, 16% of the Olz-M treatment group, and 4% of the Olz-L treatment group had elevated prolactin. Eighty-seven patients continued into long-term treatment and had prolactin at or below the upper limit at baseline. At Week 12 of treatment, only 14% of the Olz-H treatment group, 7% of the Olz-M treatment group, and 2% of the Olz-L treatment group had elevated prolactin. The magnitudes of these elevations were minimal. These rates are approximately one-half to one-third the rates observed with haloperidol (15 ± 5 mg/day). These results will be compared in detail with those for haloperidol and placebo. Mean concentration data will be presented as well.

Conclusions: Olanzapine, even at the highest doses used clinically, has only a mild and transient tendency to increase prolactin concentration. The finding supports the designation of olanzapine as an atypical antipsychotic.

NR724 Thursday, May 9, 12 noon-2:00 p.m.

Self-Report of Psychiatric Symptoms in Rotterdam

F.M. Baker, M.D., Department of Psychiatry, University of Maryland, 645 West Redwood Street, TSM04, Baltimore MD 21201–1549; Lenore J. Launer, Ph.D., Marie M.B. Breteler, Ph.D., Albert Hofman, M.D.

Summary:

Ommoord District residents of Rotterdam, the Netherlands, age 55 and older, completed a two-phase interview to assess the risk factors for chronic disease (cardiovascular disease, hypertension, diabetes, osteoporosis, myocardial infarction, stroke) and disability. Some 7,983 persons completed the Phase I home interview where demographic data and medical history were obtained. During the Phase II physician interview, the resident was asked about a history of psychiatric disorders and the interviewing physician probed for the lifetime prevalence of psychiatric disorders. Psychiatric disorders self-reported included unipolar and bipolar depression combined (5.1%), psychotic disorders (0.27%), alcoholism (0.07%), drug addiction (0.04%), and other diagnoses (3.71%). In contrast to other studies no association was found between a self-report of depression and the presence of single or multiple chronic medical problems. The reported lifetime prevalence of affective disorders was similar to the rates of depression found in the Stirling County Study (Canada) and the Epidemiologic Catchment Area Survey (United States). Rates for the other psychiatric disorders were lower than the prevalence rates reported by these studies and may reflect either under-reporting, an age cohort effect, or a sampling bias reflecting the difference between the study participants and residents with missing data for the key question.

NR725 Thursday, May 9, 12 noon-2:00 p.m.

Rehabilitation: The Black Chronically Mentally Ill

F.M. Baker, M.D., Department of Psychiatry, University of Maryland, 645 West Redwood Street, TSM04, Baltimore MD 21201–1549; Judie Stokes, M.S.W., Orlando R. Davis, M.D.

Summary:

The level of function was determined for the 76 patients participating in an intensive, seven-day per week psychosocial rehabilitation program in Baltimore, Maryland. Sixty-two percent (N = 47) of the original 76 patients were available for a six-month and 24-month re-evaluation. Ninety-six percent of the sample (N = 45) were African American. These patients were male (68%), between the ages of 25 and 44 (72%), single (85%), with a high school education or beyond (53%), and had worked in non-skilled employment (67%) as a janitor, maid, or common laborer. When men and women were compared on these demographic parameters, there was no statistically significant difference between the gen-

ders. Fifty-three percent of the sample had a DSM-III diagnosis of schizophrenia. The level of psychosocial function was determined by an updated version of the 14-item scale of predictors of the outcome of schizophrenia that evolved from the International Pilot Study of Schizophrenia data, first described by Strauss and Carpenter in 1974. Eighty-three percent of participating patients had made significant improvements in their level of function during the 24-month follow-up, and 40% of the sample had no deficits in level of function at 24 months. Among the 96% of the sample that were improved, 47% (22 of 47 patients) reported current symptoms, but stated that their medications made the symptoms less distracting to them. Six percent of the sample, three males, had become employed. Our data provide evidence for the efficacy of a rehabilitation program in the 1990's for urban, black patients with chronic, psychiatric illness including those with dual diagnoses.

NR726 Thursday, May 9, 12 noon-2:00 p.m.

Screening for Psychiatric Disorders in Primary Care

Jill I. Mattia, M.A., Psychiatry, Rhode Island Hospital, 593 Eddy Street POB-4, Providence 02 02903; Mark Zimmerman, M.D., Bruce Horowitz, M.D.

Summary:

There is a growing consensus that depression is a major public health problem in primary care settings. Studies of general population and psychiatric patient samples, however, indicate that depression is frequently comorbid with other disorders, and non-depressive disorders constitute a psychosocial functioning and impairment hazard in their own right.

Seven hundred and sixty-seven medical outpatients were administered a newly developed self-report, multidimensional questionnaire (the SCREENER) that screens for 15 DSM-IV disorders. Fifty-one percent of the sample screened positive for at least one disorder, and one quarter of the sample screened positive for depression. Overall, 74% of those who screened positive for depression screened positive for at least one other disorder. Depressive disordered, non-depressive disordered, both depressive and non-depressive disordered, and no disordered individuals were significantly different in reports of dissatisfaction with quality of life, mental and physical health, as well as global rating of psychosocial impairment. These results suggest that screening for psychiatric disorders in general medical outpatients should not be limited to depression and must include a broader compliment of other Axis I disorders. Implications of these findings for increased health care costs and need for psychiatric treatment are discussed.

NR727 Thursday, May 9, 12 noon-2:00 p.m.

Prevalence of Hepatitis-C Antibody Positivity in Vietnam Veterans with PTSD

M. Michele Murburg, M.D., Psychiatry, University of Washington, 4260 Shoreclub Drive, Mercer Island WA 98040; Shirley Shultz, M.S.N., Susan A. Ballagh, M.D.

Summary:

Hypothesis: Vietnam veterans are at high risk for hepatitis C infection.

Method: To determine the prevalence of hepatitis C antibody positivity in Vietnam veterans hospitalized for PTSD, we tested 118 consecutively admitted Vietnam Veteran inpatients (112 males and 6 females) at the National Center for PTSD for hepatitis C antibody using the second generation ELISA assay.

Results: Of those tested, 42 males and 0 females (40.7%) were positive. In comparison, only one of the 118 tested positive for hepatitis BsAg. Serum transaminases were elevated on admission in 20 of the 42 HCV positive patients, and were significantly higher in the hepatitis C positive than negative group.

Conclusions: In our sample of Vietnam veteran inpatients with PTSD, over 40% had evidence of HCV infection. While no patients experienced symptoms of hepatitis during hospitalization, nearly half of the HCV positive patients had elevated transaminases on admission, and these transaminases normalized during hospitalization in only 25% of cases. Thus, nearly 20% of admissions had significant, although clinically silent, liver disease at the time of admission. This unexpected finding has important implications for pharmacological treatment of PTSD and of comorbid physical and psychiatric problems in this population.

NR728 Thursday, May 9, 12 noon-2:00 p.m.

Chile: What Determines Primary Care Physicians Detection of Psychiatric Morbidity?

Ricardo Araya, M.D., Psychiatry, University of Chile, AVDA La Paz 1003, Santiago, Chile; Graciela Rojas, M.D., Julia Acuna, M.D.

Summary:

Objectives: To examine primary care physicians' (PCPs) detection rates of psychiatric morbidity and patients' and doctors' variables which influence these rates.

Method: Psychiatric morbidity was assessed using General Health Questionnaire (GHQ-12) and Clinical Interview Schedule-Revised (CIS-R). PCPs assessed patients' mental health blindly with rating scales. Patients' and doctors' variables influencing the detection of psychiatric morbidity (DPM) were examined using univariate and multivariate methods.

Results: 4,079 randomly chosen patients (95% response) and 67 PCPs (93% response) from 23 PHC clinics participated. 53% of patients presented a psychiatric disturbance and approximately half were detected by PCPs. According to PCPs, 42% of their patients showed a psychiatric disturbance. Variables related to patients, particularly reason for consultation, showed the closest association with the DPM. Undetected "cases" consulted more frequently and took more tranquilizers than detected "cases".

Conclusions: This is the largest study ever done on this subject in South America. Our results confirm previous findings. Chile shows the highest prevalence rate of psychiatric morbidity in PHC in the world. Almost one of every two patients suffering from a psychiatric disturbance goes undetected by the PCP. Detection rates are more influenced by variables related to the patient than those related to doctors.

NR729 Thursday, May 9, 12 noon-2:00 p.m.

Chile: World's Highest Psychiatric Morbidity Prevalence Rates in Primary Health Care

Ricardo Araya, M.D., Psychiatry, University of Chile, AVDA La Paz 1003, Santiago, Chile; Graciela Rojas, M.D., Julia Acuna, M.D.

Summary:

Objectives: To estimate the prevalence rate of psychiatric morbidity among Primary health care (PHC) patients and its association with sociodemographic factors and frequency of consultations.

Method: A cross-sectional survey of psychiatric morbidity was made of randomly chosen attenders to PHC clinics. A structured interview which contained the General Health Questionnaire (GHQ-12), Clinical Interview Schedule-Revised, and other questions was used. Reported frequency of consultations over last six months was confirmed with medical records. Variables were examined using univariate and multivariate (logistic regression) methods.

Results: 4,079 randomly chosen patients (95% response) from 23 PHC clinics participated in this study. The prevalence rate of psychiatric morbidity was 53%. Five percent of the sample gave a psychological reason for consultation. Anxiety was the most prevalent symptom. All individual symptoms were more prevalent among women. Previously married women with poor income and education were at higher risk. Attenders with psychiatric morbidity consulted more often even after controlling for physical illness.

Conclusions: This is the largest study ever done on this subject in South America. Our results confirm previous findings. Chile shows the highest prevalence rate of psychiatric morbidity in PHC in the world. Our findings contradict the assumption that people from "developing countries" report more somatic than psychological symptoms.

NR730 Thursday, May 9, 12 noon-2:00 p.m.

Prevalence of Affective and Anxiety Disorders in Hungary

Erika Szadoczky, Psychiatry, Hiete University, Nyeki Ut 10, Budapest 1021, Hungary; Janos Furedi, M.D., Ilona Fazekas

Summary:

Several epidemiological studies have called attention to the high prevalence of affective and anxiety disorders in the general population all over the world. At present, however, no reliable data from Hungary or other East-European countries are available. An attempt is made in this study to fill this gap. A total of 1,559 randomly selected subjects between 18 and 60 years were assessed by DIS questionnaire in four areas of Hungary (further investigations are in progress).

The most common disorder was found to be major depression with a lifetime prevalence of 19.1%. This rate is somewhat higher than most recent international findings (Zürich 1992, USA 1994). Concerning anxiety disorders (panic disorder 5.9%, GAD 5.6%, agoraphobia 17.5%, social phobia 8.1%, simple phobia 7.8%) or dysthymia (4.9%) our results do not differ significantly from the above mentioned studies.

Lifetime and current comorbidity are discussed in detail.

NR731 WITHDRAWN

NR732 Thursday, May 9, 12 noon-2:00 p.m.

Medication Refusal: The Vermont Experience

Sandra Steingard, M.D., Howard Ctr for Human Services, 300 Flynn Avenue, Burlington VT 05401; John Pandiani, Ph.D., Andrew Zovistoski

Summary:

Objective: In 1985, Vermont established a formal judicial procedure for determining whether committed psychiatric patients who refuse medications could be treated involuntarily. We reviewed the state's entire experience with this process.

Method: We reviewed all petitions filed between 2/6/85 and 8/20/93 for patients who were refusing prescribed medications. We established the outcome for each petition. We compared refusers with all other patients admitted during that period for sex, age, length of stay, and diagnosis. These data were compared to reports from other studies.

Results: 164 petitions were filed, representing 4.7% of all admissions. A total of 152 petitions were unduplicated. Of those 97 were granted, 20 denied, 30 withdrawn, and 5 dismissed. Sixty-four percent of refusers were female, compared to 36% of all other admissions, and 57% had a diagnosis of schizophrenia, compared to 39% of others. These findings were significant. There were no significant differences between groups in age or length of stay.

Conclusion: Despite a rigorous, judicial procedure, only a minority of patients who refuse medications in Vermont have their refusal upheld in court. The Vermont outcome is consistent with that of other studies despite the variety of methods used to make the decision.

NR733 Thursday, May 9, 12 noon-2:00 p.m.

Criminal Recidivism in the Mentally Ill

Victoria L. Harris, M.D., University of Washington, Box 355300 3747 15th Ave. NE, Seattle WA 98105; Thomas Koepsell, M.D.

Summary:

The importance of criminal recidivism among mentally ill offenders lies in resource allocation and community services for the mentally ill. It has been suggested that jails are used, in part, to simply house the mentally ill.

Objective: To determine whether mentally ill criminal offenders have higher rates of recidivism than non-mentally ill offenders.

Methods: The study group (n = 127), was drawn by a random number generator applied to all admissions to the psychiatric unit at the King County Jail, in Seattle, Washington, in 1990. The frequency matching method was used to draw a comparison sample (n = 127) of non-mentally ill offenders who were housed in the general population during 1990. The comparison group was matched for age, gender, and crime at index arrest. Both groups were followed for up to four years until the next arrest.

Results: After 12 months, 54.3% of the mentally ill group and 51.2% of the non-mentally ill group were re-arrested ($0.84 < RR < 1.34$). Using Kaplein-Meier survival analysis, no statistical difference in the relative risk of re-arrest occurred for the mentally ill group (log-rank 0.04; df 1; rr 0.84). The presence of substance abuse or psychosis at arrest did not aid in the development of a risk assessment model for re-arrest of mentally ill offenders. Noncompliance with community psychiatric care was found to be a significant factor for the re-arrest of the mentally ill offenders ($p < 0.01$; df 1).

Conclusions: While mentally ill offenders may not be at increased risk for re-arrest, there may be specific high-risk subgroups that can benefit from early intervention.

NR734 Thursday, May 9, 12 noon-2:00 p.m.

Homicides and Psychiatric Disorders

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:

Objective: To estimate the risk increase associated with specific mental disorders among homicide offenders.

Method: Due to the fact that Finnish police have been able to solve about 95% of homicides during the last decades, and because most of the homicide offenders are subjected to an intensive psychiatric evaluation, it was possible to examine data on 693 of 994 homicide offenders during an eight-year period. The prevalences of mental disorders of the homicide offenders are used to calculate odds ratios for the statistical risk increase associated with specific mental disorders.

Results: The results indicate that schizophrenia increases the odds ratio of homicidal violence by about 8-fold in males and 6.5-fold in females. Antisocial personality disorder increases the odds ratios over 10-fold in males and over 50-fold in females. Affective disorders, anxiety disorders, dysthymia, and mental retardation

did not elevate the odds ratio to any significant extent (odds ratio < 5.0).

Conclusion: Homicidal behavior in a country with a relatively low crime rate appears to have a statistical association with some specific mental disorders classified according to DSM-III-R classification.

NR735 Thursday, May 9, 12 noon-2:00 p.m.

Risperidone for Treating Violence and Aggression in Forensic Hospital Patients

John W. Thompson, Jr., M.D., Psychiatry, Tulane University, 1430 Tulane Avenue, New Orleans LA 70112

Summary:

Objective: To evaluate the effectiveness of risperidone in treating patients with chronic psychiatric disorders who were incarcerated at the Feliciana Forensic Facility.

Method: Data were collected retrospectively from 36 patients who had been treated with psychotropic medications for various psychiatric disorders. Most patients had been diagnosed with chronic schizophrenia or schizoaffective disorders of many years' duration and had a history of multiple psychiatric hospitalizations. Subjectively rated reports of hallucinations, delusions, aggressive and hostile behavior, and depression before and after treatment with risperidone were extracted from patients' records.

Results: Most patients (30/36) had been switched to risperidone because of lack of response to or intolerance of conventional neuroleptics. Risperidone was administered initially at 2 mg/day. The dose was increased by 2 mg/day over a one-week titration period to a maintenance dose of 6–8 mg/day for three to 13 months. Clinically significant improvements were observed in the severity of hallucinations, delusions, impaired thought processes, violence/hostility, agitation/volatility, and depression in patients treated with risperidone.

Conclusions: Risperidone is effective in treatment-refractory forensic hospital patients with chronic schizophrenia or schizoaffective disorders. The results are consistent with previous reports that risperidone can reduce hostility and aggression in schizophrenic patients.

NR736 Thursday, May 9, 12 noon-2:00 p.m.

Survey of How Education Decreased Sexual Harassment Among Medical Students

Rebeka Moscarello, M.D., Psychiatry, Womens College Hosp, 76 Grenville Street, Toronto ON M5S 1B2, Canada; Katalin J. Margittai, M.D., Miriam Rossi, M.D.

Summary:

Objective: Assess the effect of faculty education about sexual harassment on the incidence of sexual harassment experiences among medical students.

Design: Voluntary, anonymous cross-sectional survey.

Participants: 168 fourth-year medical students in 1991, and 159 fourth-year medical students in 1994.

Outcome Measures: Comparison of contact and non-contact sexual harassment of years 1991 and 1994, before and during medical training; the relation between sexual harassment prior to and during medical training; the psychological impact of sexual harassment; the most common sources of such abuses; and gender differences of above.

Results: A significant decrease in sexual harassment between 1991 and 1994, from 22% (37/168) in 1991 to 12% (20/159) in 1994 ($P < 0.025$). However, the number of students who experienced contact sexual harassment remained the same, 14 and 13, respectively. Those who experienced sexual harassment prior to entering medical school were more likely to repeat their experience during their training than those who denied such experiences ($P < 0.025$). Females experienced more sexual harassment than males prior to and during medical training. Clinicians were a significant source ($P < 0.025$) and the surgical rotation was most common site.

Conclusion: Sexual harassment continues as a major problem, among women more than men, with a small group of faculty whose behavior remains unchanged.

NR737 Thursday, May 9, 12 noon-2:00 p.m.

Resident Research Seminar: Program Description

Anita L.H. Clayton, M.D., Psychiatry, University of VA, Drawer C. BRH UVA HSC, Charlottesville VA 22901; Adrienne E.R. Keller, Ph.D.

Summary:

Objective: To describe and evaluate a model for incorporating a research experience into a psychiatric residency.

Method: All general psychiatry residents and combined internal medicine-psychiatry residents participate in a weekly research seminar during their assignment to outpatient psychiatric services. The course goal is to provide experience to residents in all aspects of a clinical research project from idea to manuscript. Supplemental goals of the seminar are to develop abilities to critically evaluate clinical and research data, participate in the design and conduct of a specific clinical research project, stimulate creative research ideas, develop skills in accurate data collection, presentation of results, and provide the experience of "ownership" of a research project. The weekly seminars are led by two experienced faculty members: a clinical researcher and a behavioral epidemiologist. Process and outcome evaluation standards are used to evaluate the impact and effectiveness of the model.

Results: During the past two years, the process of the course has been refined and standardized and is now well-described in a time-dependent flow chart. The outcome of the course include the design, approval, and funding of a number of clinical drug trials by the participating residents.

Conclusion: The incorporation of research training into a clinical residency program is essential and can be accomplished interactively with a group of residents through a combination of didactic presentations, learner-centered seminars, and hands-on experience. This successful model has been well-received by the residents, well-documented, and is amenable to replication in a variety of settings.

NR738 Thursday, May 9, 12 noon-2:00 p.m.

Hormones and Premenstrual Dysphoric Disorder

Anita L.H. Clayton, M.D., Psychiatry, University of VA, Drawer C, BRH UVA HSC, Charlottesville VA 22901; Adrienne E.R. Keller, Ph.D., Catherine A. Leslie, M.D., William Evans, M.D.

Summary:

Objective: To investigate whether abnormalities in the pattern of serotonin cycling are associated with premenstrual dysphoric disorder (PDD).

Method: Twenty healthy menstruating women age 18 to 45 years were recruited: 10 with premenstrual dysphoric disorder and 10 controls. Subjects kept a daily symptom rating scale and basal body temperature through at least two cycles. Baseline SCID and Menstrual Distress Questionnaire (MDQ) were performed. Transvaginal ultrasounds determined time of ovulation. Sex hormone levels were monitored at five points: at baseline, one week prior to menses, and during two admissions (one two days prior to the onset of menses, and one two days following menstrual onset). During each admission, plasma 5-HIAA samples were

obtained every 90 minutes over 24 hours, and the MDQ was repeated.

Results: Mean daily symptom ratings were significantly higher in the PDD subjects. Premenstrual 5-HIAA levels were similar in both groups, with controls showing a decrease in 5-HIAA during the menstrual period while PDD subjects demonstrated a rise. Diurnal variation was much greater in control subjects with little change across the 24-hour period in PDD subjects. Significant differences in FSH, progesterone, and prolactin were also noted between the two groups.

Conclusion: There appear to be differences in hypothalamic-pituitary axis hormones and the serotonin metabolite, 5-HIAA, in comparisons of women with PDD versus normal controls. These may suggest the etiology of menstrually-related mood disorders.

NR739 Thursday, May 9, 12 noon-2:00 p.m.

Tobacco Smoking Assessments and Treatment Outcomes Within a Community Mental Health Center

Douglas M. Ziedonis, M.D., Psychiatry, Yale University, 34 Park Street, New Haven CT 06525; Patricia A. Harris, A.S., Brandt Patricza, Thomas R. Kosten, M.D., Surita Rao, M.D., Amal Tanagho, M.D.

Summary:

Tobacco smoking is common among psychiatric patients, and few reports have described smoking rates, motivational levels to quit smoking, and response to treatment. From two surveys of 1,400 psychiatric patients, we found that about 70% of psychiatric outpatients smoke and most have low motivation to quit (85% were in the precontemplation or contemplation stage). However, we have found the more motivated patients are interested in smoking cessation treatment when offered: 82% of patients who inquired about treatment entered treatment. We developed a smoking cessation program in which patients receive individual and group psychotherapy and nicotine replacement medication (gum and/or patch). Patients presenting to our program had an average Fagerstrom Tolerance Questionnaire scores was 7. The average carbon monoxide exhalation levels were 27 ppm. Patients presented in the following motivational levels: 22% action, 18% contemplation, and 60% preparation. The average number of cigarettes smoked per day was 31. The patients in this program have done better with the combination of intensive psychotherapy (individual and group-once or twice per week-for more than ten weeks of treatment) and nicotine replacement medication (patch and/or gum). Attendance for the higher motivated patients was excellent (about 90%). Patients with lower motivation attended about 40% of their sessions. Assessment and treatment of tobacco smoking is important for psychiatric patients and treatment services should be provided.

NR740 Thursday, May 9, 12 noon-2:00 p.m.

Immunologic Measurements in PTSD

Scott N. Wilson, M.D., Freedom Trail Clinic, 25 Staniford Street, Boston MA 02114

Summary:

Whereas immunologic studies in psychiatric illnesses have often yielded conflicting results, there is reproducible evidence that stress in man is associated with changes in immunological activities. Traumatized patients recurrently experience stress responses related to stimuli evocative of their traumas. Immunologic studies of psychiatric illnesses have yielded inconsistent results, and none have examined patients with a diagnosis of post traumatic stress disorder (PTSD). In the present study, the peripheral blood was examined for changes in immune phenotype and lymphokine production in patients with a history of childhood trauma and a diagnosis of post-traumatic stress disorder and age-and sex-matched controls. The percentage of lymphocyte subsets was comparable between groups; however the ratio of CD45RA-positive to CD45RO-positive lymphocytes as measured by flow cytometry was significantly lower ($p = 0.046$) in traumatized patients, suggesting an increased level of immune activation in vivo. No significant differences were observed in the secretion of interleukins 2, 4, or gamma interferon. This finding is consistent with existing evidence for down regulation of the hypothalamic-pituitary-adrenal axis in PTSD.

NR741 Thursday, May 9, 12 noon-2:00 p.m.

Serum Concentration and HPA Axis in Major Depressed Patients

So-Hyun Choi, M.D., Yong-In Mental Hospital, 4, Sangha-Ri, Kusung-Myun, Yongin-Kun, Kyunggi 449-910, Yong-Gu Kim, M.D., Kwang-Yoon Suh, M.D.

Summary:

The present study was carried out in order to investigate the relationship between immune function and the hypothalamic-pituitary-adrenal (HPA) axis in major depression. The subjects were 16 female major depressives and 16 female healthy controls. We measured mitogen-induced production of IL-1β, IL-2, IL-6 and serum level of IL-1β, IL-2, IL-6 and 8 a.m. basal plasma cortisol levels in 16 major depressives and 16 healthy controls. And we measured post-DST cortisol level in 16 major depressives. The results were as follows: basal cortisol level was significantly higher in the patients with major depression than in the healthy controls (respectively 14.4 ± 4.6 μg/dl, 10.1 ± 5.2 μg/dl, $p < 0.05$). IL-2 production was significantly lower in the patients with major depression than in the healthy controls (respectively 1747.3 ± 387.9 pg/ml 2520.2 ± 884.1 pg/ml, $p < 0.05$). There were no significant differences in IL-1β, IL-6 production between the patients with major depression and the healthy controls. There was no significant difference in serum level of IL-2 between two groups. There was significant negative correlation between IL-2 production and post-DST cortisol level ($r = -0.89$) in the 16 patients with major depression. There was significant negative correlation between serum level of IL-2 and post-DST cortisol level ($r = -0.97$) in the 12 patients with major depression. There was significant negative correlation between serum level of IL-2 and basal cortisol level ($r = -0.65$) in the 12 patients with major depression. But there was no significant correlation between IL-2 production and basal cortisol level in the 16 patients with major depression. These findings suggest that immune function is decreased in major depression and hyperactivity of the HPA axis is highly related to the decreased immune function.

Serum level of IL-2 was detectable in 12 of 16 patients with major depression and in 10 of 16 healthy controls. Serum level of IL-1β was detectable in 3 of 16 patients with major depression and of 16 healthy controls respectively. We could not detect serum level of IL-6 in both groups.

NR742 Thursday, May 9, 12 noon-2:00 p.m.

Phenotypic and Functional Changes of Immune Reactivity in Schizophrenia and Depression

Prof. M.T. Abou-Saleh, Ph.D., Psychiatry, UAE Univ. EMHS, P.O. Box 17666, Alain, U. Arab Emirates; M. Shahin Allen, B.S., Yousreya Amin, M.D., M.L. Lukic, M.D.

Summary:

There is growing evidence that psychoneuroimmunological interactions contribute to the pathogenesis of depression and schizophrenia. We have initiated a comprehensive study of phenotypic and functional determinants of immune reactivity in 60 pa-

tients with these conditions and 30 normal control subjects. The study involved screening of the subpopulation of immunocompetent ($CD3^+T$, $CD15^+B$, $CD4^+$ and CDB^+T) cell subsets, NK cells and monocytes. Further, we determined the level of proinflammatory cytokines (IL-1, TNF-α, IL-6), and a marker of T-cell activation (soluble IL-2 receptor) in the serum, and analyzed the production of immunoregulatory cytokines (IL-2, IL-4, TGF-β) in unstimulated and in vitro Con A stimulated lymphoid cells. Initial evaluation revealed significantly increased monocyte counts and serum levels of soluble IL-2 receptor in the patient group ($p < 0.01$). These findings support the notion of enhanced monocyte and T cell reactivity indicating the role of altered cell-mediated immune reactions in schizophrenia and depression. More detailed analyses of the relationships between well defined clinical types of these disorders and measured immunological parameters are undertaken and the results will be presented (supported by FMHS, UAE University grant).

NR743 Thursday, May 9, 12 noon-2:00 p.m.

AIDS Patients' Attitudes Toward Assisted Suicide and Euthanasia

Ramaswamy Viswanathan, M.D., Psychiatry, SUNY Health Sci Ctr, 450 Clarkson Avenue, Brooklyn NY 11203-2012; Shanthi Thangam, M.D., Anwarul Ahad, M.D., Jonathan Moreno, Ph.D., Martin Kramer, M.D.

Summary:

Objective: To study the attitudes of patients with advanced acquired immune deficiency syndrome (AIDS) regarding physician-assisted suicide and euthanasia.

Method: All cognitively able patients admitted to an AIDS medical inpatient unit July-December 1995, were interviewed by a psychiatrist.

Results: Of 58 admissions, 47 patients were approached, and 40 agreed to participate; their median CD4 lymphocyte count was 12/cu mm. Seventy-five percent of the subjects said that a person who had AIDS and was suffering terribly with no hope of improvement should be allowed to end his or her own life if he or she so wished (Yates-corrected $x^2 = 9.03$, df = 1, $p < .01$); 63% said that the law should allow assisted suicide; 50% were in favor of physician-assisted suicide; 33% would like physician-assisted suicide if they were in such a situation; 58% said that the law should allow active euthanasia by the physician (by injection of a lethal drug); all 20% of the subjects who acknowledged history of intravenous substance abuse were in favor of physician-assisted suicide ($x^2 = 7.66$, df = 1, $p < .01$) and euthanasia ($x^2 = 5.38$, $p = .02$). The preferences were not related to depression (measured by Center for Epidemiologic Studies Depressed Mood Scale).

Conclusions: This population is split in its opinion on physician-assisted suicide, but the majority would allow suicide.

NR744 Thursday, May 9, 12 noon-2:00 p.m.

Stress and Depressive Symptoms Predict Immune Change in HIV

Jane Leserman, Ph.D., Psychiatry, University of NC, CB #7160, Chapel Hill NC 27599; John M. Petitto, M.D., Diana O. Perkins, M.D., James D. Folds, Ph.D., Robert N. Golden, M.D., Dwight L. Evans, M.D.

Summary:

Objective: This study examines how stress and depressive symptoms are related to changes in measures of immunity over a two-year period in a sample of gay men with HIV infection. These longitudinal analyses follow-up our initial cross-sectional observations that severe stress correlates with lower levels of natural killer (NK) cells and CD8+ T-cytotoxic lymphocytes (*Am J. Psychiatry*, 152:543–50, 1995).

Method: Data are from the Coping in Health and Illness Project (CHIP). Every six-months for two years, we assessed 66 HIV-infected gay men, who were asymptomatic at baseline. Stressful events and difficulties were given a severity rating based on an interview to assess the context of each event; stress scores were calculated by summing the severe stresses during the second study year, excluding those caused by HIV progression. Depressive symptoms were measured with the Hamilton Depression Rating Scale (HDRS) (deleting symptoms possibly related to HIV).

Results: Based on partial rank correlations, stress and depressive symptoms during the previous year were related to declines in CD8+ T-cytotoxic/suppressor cells, and CD56+ and CD16+ NK cell subsets from entry to two-year follow-up. Those most likely to have decreases in immune status were subjects who scored above the median on both stress and depressive symptoms.

	CD8+		CD4+		CD16+NK		CD56+NK		CD57+NK	
	r_s	p	r_s	p	r_s	p	r_s	p	r_s	p
Stress	-.31	.02	-.16	.21	-.35	.007	-.26	.05	-.17	.19
HDRS	-.26	.04	-.09	.47	-.29	.02	-.34	.009	-.12	.35
Stress/HDRS scale*	-.37	.004	-.13	.33	-.48	.0001	-.41	.001	-.23	.08

*1=below median on both stress and HDRS, 2=above median on either stress or HDRS, 3=above median on both stress and HDRS.

Conclusions: Our findings are among the first prospective data showing that stress and depressive symptoms, particularly in combination, are associated with decreased number of NK and T-cytotoxic/suppressor lymphocytes; these immune cells may play a protective role in HIV infection.

NR745 Thursday, May 9, 12 noon-2:00 p.m.

Retrospective Study of Risperidone in Illinois Department of Mental Health Developmental Disabilities

Daniel J. Luchins, M.D., Psychiatry, Univ of Chicago, 5841 S. Maryland Ave, Chicago IL 60637-2602; Patricia Hanrahan, Ph.D., Randy Malan, R.Ph., John Harris

Summary:

Risperidone is a promising new antipsychotic that may provide advantages over conventional antipsychotics. However, its widespread use could have major financial implications, especially in public psychiatric settings where the severely mentally ill are served. Only one cost-effectiveness study of risperidone has been completed to date, by Addington and colleagues (1993). They found a mean reduction in hospital stays of 21 days in the year after risperidone treatment. The relevance of these findings to public settings in the United States is debatable. Although clozapine has been shown to be cost effective in such settings, the drug is not widely used. The present study was designed to test the feasibility of using existing state databases to describe the utilization and effects of antipsychotic medications, including risperidone (N = 834), clozapine (N = 108), and conventional agents (N = 3,645) for all patients with schizophrenia treated in Illinois State Operated Facilities during 2/20/94 to 2/20/95. Patients discharged on risperidone were matched to those on conventional medication on length of current hospitalization, number of previous hospitalizations, substance abuse, age, and discharge dates. Once matched, patients were compared on re-hospitalization and length of stay in the community. Fewer risperidone patients were re-hospitalized ($p < .01$), and their community tenure was greater than those on conventional neuroleptics ($p < .04$).

NR746 Thursday, May 9, 12 noon-2:00 p.m.

Satisfaction with Treatment Pilot Study

Adrienne E.R. Sheldon-Keller, Ph.D., Psychiatry, University of Virginia, Box 16 Blue Ridge Hospital, Charlottesville VA 22901; Randolph J. Canterbury, M.D., Kimberly Largay, B.A.

Summary:

Objectives: To investigate factors putatively related to patient satisfaction with psychiatric care in an inpatient setting and to compare patient and physician ratings of satisfaction.

Method: Inpatients treated between January and July 1995 with diagnoses of major depressive disorder or adjustment disorder. Individuals with these diagnoses make up 46% of inpatient admissions in this setting. Twenty-nine patients were interviewed by phone, using the Center for Epidemiological Studies Depressed Mood Scale (CES-D) and the Client Satisfaction Questionnaire (CSQ). The attending and resident physicians for each patient were interviewed in person, using an adaptation of the CSQ.

Results: The sample included 14 patients with major depression and 13 patients with adjustment disorder; 20 females and 7 males. The mean length of stay was 15.77 days for depression and 4.8 days for adjustment disorder ($F(1,25) = 12.06$, $p = .0019$). The mean patient satisfaction score was 26.0 (s.d. = 11.7) (maximum possible = 32). Patient satisfaction was not significantly related to sex, diagnosis, length of stay, CES-D score, attending or resident physician. Only the residents' estimation of patient satisfaction correlated significantly with self-reported patient satisfaction ($r = .61$, $p = .02$).

Conclusion: Patient satisfaction with treatment was independent of demographic, illness, and physician variables. Attending physicians are not reliable judges of patient satisfaction.

NR747 Thursday, May 9, 12 noon-2:00 p.m.

Primary Care in Santiago, Chile: Mental Health and Psychosocial Problems

Maria G. Rojas, M.D., Psychiatry, University of Chile, AVDA La Paz 1003, Santiago, Chile; Rosemarie Fritsch, M.D., Isabel Gonzalez, M.D., Berta Diaz, S.A., Fernando Lolas, M.D.

Summary:

Objective: To study the prevalence of psychiatric disorders in primary care users and their association with sociodemographic variables, social problems, life events, and social support.

Method: 815 consecutive patients from 15 to 50 years were interviewed. A structured interview was applied that included: sociodemographic data, the Clinical Interview Schedule-Revised (CIS-R), a social problem questionnaire, a life event list based on Holmes and Rahe, and social support questions.

Results: The prevalence of psychiatric disorders was 49.4%. Higher scores in CIS-R were associated significantly with being women ($t = 5.38$; p 0.01); being part of a couple ($F = 5.2378$; p 0.01); being less educated ($t = 4.38$; p 0.01); having lower income ($F = 3.2281$; p 0.05); having more social problems ($F = 51.056$; p 0.01); no affiliation to community organizations ($t = 2.6$; $p = 0.010$); having problems with their couple ($t = 6.73$; p 0.01); couple separation ($t = 3.01$; p 0.01); suffering an accident or an illness themselves ($t = 2.85$; p 0.01) or a relative or friend ($t = 2.84$; p 0.01); suffering the death of a relative or friend ($t = 2.63$; p 0.01) or of the spouse ($t = 13.44$; p 0.01); having retired or being fired ($t = 2.28$; p 0.05) and having an important income decrease ($t = 8.54$; p 0.01). Finally there was a significant correlation between CIS-R and age, and number of close persons living in the house ($r = .1288$; p 0.001).

Conclusions: This study contributes important information to the planning of actions that could improve mental health at the primary care level.

NR748 Thursday, May 9, 12 noon-2:00 p.m.

Acute Stress Disorder in Newly Diagnosed Cancer Patients

Elizabeth L. McGarvey, Ed.D., Psychiatry, University of Virginia, BRH Box 16, Charlottesville VA 22901; Randolph J. Canterbury, M.D., Cheryl Koopman, Ph.D., Gail J. Clavet, Ph.D.

Summary:

Acute stress disorder (ASD) may occur after being diagnosed with a life threatening illness (DSM-IV). The goals of this study are 1) to investigate the extent to which patients experience clinically significant psychological trauma upon learning that they have been diagnosed with cancer; and 2) to determine the relationship between patient-reported satisfaction with the manner in which the physician communicated the diagnosis of cancer and the development of subsequent ASD.

Method: A consecutive sample of 49 cancer patients have been mailed information about the study. Follow-up telephone contact is in progress. To date, of those contacted, 12 have completed a set of four questionnaires: Stanford Acute Stress Reaction Questionnaire, Communication of Diagnosis Questionnaire, Social Network & Support Assessment, Behavioral Change Questionnaire.

Results: **Prevalence of ASD.** 56% of patients meet criteria for ASD following hearing their diagnoses. **Alcohol use.** Of the total, 82% (9 of 11) reported weekly drinking. 27% (3 of 11) reported **increased** alcohol use after learning that they had cancer, and 9% (1 of 11) reported drinking less. Those who reported increased drinking met the criteria for acute stress disorder. **Satisfaction with diagnosis.** Scale scores ranged from "1 = not satisfied" to "4 = very satisfied." Mean score for satisfaction with diagnosis for participants with ASD was 3.28, compared to 4.0 for those without ASD.

NR749 Thursday, May 9, 12 noon-2:00 p.m.

PTSD After a Building Collapse Accident in Korea

S. Peter Kim, M.D., Psychiatry, Samsung Med Center, 50, Ilwon Dong, Kangnam-KU, 135-230 Seoul 00172, Korea

Summary:

Objective: This is a prospective clinical study on PTSD in subjects involved in the collapse of a major department store in Seoul in June 1995.

Method: 27 subjects were interviewed with a modified Korean version of "PTSD interview" (DSM-III-R). The degree of anxiety and depression was measured with Hamilton Anxiety and Depression Scales, one month and three months after the accident.

Results: The incidence rates of PTSD in our subjects during that period were 41% by full criteria and 80% by partial criteria, respectively. During the same period, the overall severity of PTSD symptoms for all subjects remained unchanged. However, re-experience and hyperarousal symptoms were improved although statistically not significant. The depression and anxiety symptoms were more severe among the victims whose accompanied colleagues/friends/relatives died from the accident. The severity of PTSD was positively correlated with the severity of physical injuries and inversely with educational level.

Conclusions: This study shows the high risk of developing PTSD among the victims of the building collapse accident. Severe physical injuries, presence of death of accompanied colleagues/friends/relatives, and lower educational level are important factors that affect the clinical course of PTSD.

NR750 Thursday, May 9, 12 noon-2:00 p.m.

Rehabilitation Readiness Determination in Schizophrenia

Thomas E. Smith, M.D., 21 Bloomingdale Rd, White Plains NY 10605-1504; Scott Trefny, M.A., James W. Hull, Ph.D.

Summary:

Objective: Psychiatric rehabilitation strategies play an important role in the treatment of chronic schizophrenia. In developing a rehabilitation plan, several questions confront the clinician including which skill areas to target for rehabilitation and when in the course of illness to utilize specific rehabilitation strategies. The Rehabilitation Readiness Determination (RRD) interview is designed to answer these questions. This study reports reliability and validity data on this new interview.

Methods: A total of 36 patients with chronic schizophrenia were interviewed using the RRD. These interviews were videotaped and scored by a second trained rater. In addition, all subjects received ratings of positive and negative symptoms. The interview process was repeated three months later, with further data gathered regarding the degree of participation in specific rehabilitation programs.

Results: Interrater reliability was documented for total as well as subscale RRD ratings. Readiness ratings were largely independent of positive and negative symptoms, and did predict participation in rehabilitation activities.

Conclusions: These data support the reliability and validity of a new RRD interview. The RRD interview can play an important role in assessing schizophrenic patients' abilities to participate in and benefit from specific rehabilitation strategies.

NR751 Thursday, May 9, 12 noon-2:00 p.m.

Skills Training for Engagement in After Care: The Community Re-Entry Program

Thomas E. Smith, M.D., Psychiatry, NY Hospital-Cornell, 21 Bloomingdale Rd, White Plains NY 10605-1504; James W. Hull, Ph.D., Sally J. Mackain, Ph.D., Marianne S. Goodman, M.D., Donna T. Anthony, M.D., Mary K. Kentros, M.D.

Summary:

Objective: This is a study of the Community Re-Entry Program, a time-limited skills training module that teaches hospitalized or recently discharged patients skills for engagement with aftercare programs.

Methods: Forty-four patients with chronic psychotic disorders were recruited from consecutive admissions to an inpatient psychiatric unit. The manualized training program consisted of 16 daily small group meetings with topics including defining discharge readiness, identification of symptoms and medication effects, and arranging appropriate aftercare. Assessments of skill levels and positive and negative symptoms were made on admission and upon completion of training, and follow-up data were obtained two weeks post-discharge.

Results: From admission to discharge, positive and negative symptoms diminished and skill levels increased significantly. Post-training skill level was predicted by pre-training skill level and level of participation in the skills training module, indicating a true learning effect. Symptom levels did not predict participation in the program or skill acquisition. Skill level at discharge was also more predictive of two-week post-discharge community adjustment than symptom levels.

Conclusions: The data support the effectiveness of the Community Re-Entry Program. Brief, focused skills training approaches may have an important role in augmenting optimal pharmacotherapy for hospitalized patients with chronic psychotic disorders.

NR752 Thursday, May 9, 12 noon-2:00 p.m.

Evaluating a Community Bereavement Support Group

Nancy C. Maruyama, M.D., Psychiatry, Brown University, 825 Chalkstone Avenue, Providence RI 02908; James Willsey, M.Div., Elinor Collins, R.N.

Summary:

Objective: We sought to assess whether participants in an eight week bereavement support group experienced improvements in measures of grief, psychological symptoms, perceived stress, and social support.

Method: 39 bereaved women and men participated in five groups which met weekly for eight 90-minute sessions. Two mental health professionals co-facilitated the groups structured according to a manual developed here. At the first and last meetings, participants filled out the POMS, the Perceived Stress Scale-10, and the Functional Social Support Questionnaire. Sixteen participants filled out the Texas Revised Inventory of Grief (TRIG) and the Unresolved Grief Index (UGI). Scores were analyzed by paired t-tests. Ten participants dropped out after the first session. Their scores were compared with the baseline scores of subjects who completed the entire group, using a one-way ANOVA.

Results: At eight weeks follow-up, participants reported improvements in stress ($p = .03$), affective ($p = .000$) and confidant social support ($p = .000$), and decreases in psychologic symptoms as measured by the POMS, with decreased total mood disturbance ($p = .000$), depression ($p = .004$), tension ($p = .001$), fatigue ($p = .009$), anger ($p = .007$), and confusion ($p = .000$), and increases in vigor ($p = .014$). Participants reported decreases in grief scores on the TRIG ($p = .000$, $p = .032$,) and the UGI ($p = .05$). The 10 who dropped out scored higher on anger ($F = .008$), with trends toward higher tension ($F = .068$), total mood disturbance ($F = .087$) and lower affective social support ($F = .08$).

Conclusions: These findings demonstrate improvement of grief, psychological symptoms, increases in sense of social support, and decreases in stress in a heterogeneous group of individuals participating in bereavement support groups. Although the lack of a control group does not allow one to attribute the improvements to the intervention, the data underscore the fact that the groups do not harm bereaved individuals by increasing distress, grief, and stress. Furthermore, it is unlikely that the improvements particularly in the symptoms of grief, could occur in such a short period of time. The lack of follow-up on those who dropped out is a limitation. Nevertheless, the findings suggest that participants with high anger, tension, total mood disturbance, and low social support should be enrolled in a separate intervention.

NR753 Thursday, May 9, 12 noon-2:00 p.m.

Effects of Psychodynamic Therapy in Schizophrenic Patients

Prof. Vittoris Volterra, Institute of Psychiatry, University of Bologna, Viale Pepolis, Bologna 60100, Italy; Diana De Ronchi, M.D., Gabriella Belelli, Mirella Ruggeri, M.D., Antonella Lunardi, M.D.

Summary:

Objective: 1) to determine, over a one-year follow-up, the relative effectiveness of group and individual psychotherapy (plus haloperidol 2 mg/day) compared to drug only treatment (haloperidol, 10 mg/day) for schizophrenic patients; 2) to analyze the role of psychotherapy in the outcome of schizophrenia; 3) to isolate the more specific effects of psychotherapy on schizophrenic patients.

Method: Forty patients who met DSM-III criteria for schizophrenia and with a recent onset (six months) were included in this study and were randomly assigned to a group or individual ($n = 22$) one-year treatment with insight-oriented therapy plus haloperidol 2

mg/day or drug therapy alone (n = 18). Assessments were performed at the end of the run-in period (baseline), six, and 12 months after the beginning of the treatments. Severity of schizophrenia was assessed by the Brief Psychiatric Rating Scale, the Clinical Global Impressions Scale for Severity (CGI-S). The Clinical Global Impressions Scale for Improvement (CGI-I), the Symptom Checklist (SCL-90), the SADD, and the Zung scale were also used. The study protocol was approved by the ethics committees and informed consent was obtained from all patients.

Results: Thirty patients had completed the 12 weeks of treatment and were included in the analysis. Sociodemographic characteristics of the two treatment groups were very similar (mean age = 25 ± 4, 9 women and 21 men); no statistically significant difference was found in the baseline scores of the CGI, while patients treated with psychotherapy reported higher mean values on the BPRS at the baseline. Overall improvement at CGI and improvement in the BPRS items of anxiety, conceptual disorganization, depressive mood, motor retardation, blunted affect, and excitement was higher in patients in the groups treated with psychotherapy plus neuroleptics. Differences between group and individual psychotherapy will be discussed in detail.

Conclusions: Many studies found that psychodynamic treatment for schizophrenia failed to exert any beneficial effect on outcome and Strupp have pointed out that psychotherapy can sometimes lead to deleterious effects. Stone reported that 20% of the patients who received psychodynamic therapy committed suicide. In our study we observed in psychotherapy treated patients an improvement on depressive symptoms and on suicidal ideation; furthermore, we noticed that psychodynamic treatment can have beneficial effects for patients with high levels of anxiety. Mueser wrote that "The evidence that psychodynamic treatment worsens the outcome of schizophrenia is indirect and debatable" and our preliminary data suggest that some schizophrenic patients may benefit from psychodynamic treatment.

NR754 Thursday, May 9, 12 noon-2:00 p.m.

Testimony Psychotherapy in Bosnian Refugees: An Open Trial

Alma Dzubur Kulenovic, M.D., Division Clin Serv, State of Ill Ctr, Ste 6-400, 100 West Randolph St., Chicago IL 60601; Stevan M. Weine, M.D., Ivan Pavkovik, M.D.

Summary:

Objective: To describe the clinical effectiveness of the testimony method of psychotherapy as a treatment intervention in a pilot study with a group of adult traumatized refugees.

Method: Eight Bosnian refugees (4 men and 4 women; mean age = 43 years) who gave informed consent participated in testimony psychotherapy (averaging five sessions). They received standardized assessments for symptoms of PTSD (PTSD Symptom Scale) and depression (Beck Depression Inventory), traumatic events (Communal Trauma Events Inventory), coping with traumatic memories (Traumatic Memory Coping Scale), GAF, and prior psychiatric history, administered both prior to treatment and at the conclusion of the final treatment session.

Results: The post-treatment assessments demonstrated notable decreases in PTSD diagnosis (100% to 62.5%), PTSD symptom severity (26.5 to 15.8; p = .001), and PTSD hyperarousal cluster positive symptoms (3.5 to 2.4; p = .007). There were small decreases in PTSD hyperarousal cluster positive symptoms, PTSD avoidance cluster positive symptoms, and depressive symptoms, and small increases in GAF and traumatic memory coping that did not reach statistical significance.

Conclusions: This pilot study with Bosnian survivors of genocide suggests that testimony psychotherapy may lead to substantial improvements in PTSD when assessed at the completion of treatment. For these subjects, it appears that by joining with witnessing professionals to tell and document their trauma story in all its enormity and complexity, survivors advance on a path toward recovery. Further studies with more subjects and extended longitudinal follow-up are warranted.

NR755 Thursday, May 9, 12 noon-2:00 p.m.

A Dose-Response Study of Acupuncture Detoxification for Acute Heroin Withdrawal Symptoms

Cheng-Jen Chen, M.D., Psychiatry, East Orange VAMC, 447 Washington Ave, Washington Townshi NJ 07675-4013; Alexander Babayan, M.D.

Summary:

Objective: Acupuncture has been used in heroin detoxification. However, there are few dose-response studies available to clearly indicate which patient will benefit from the treatment. We have discovered a technique that can treat patients who suffer from acute heroin withdrawal symptoms with the same sets of acupoints. We report a study to show how the effect of this treatment varies according to the level of abuse.

Method: Thirty-seven consecutively admitted heroin addicts in a VA psychiatric inpatient unit were treated with the technique that consisted of a 30-minute body-acupuncture and a five-day press-needle mediated ear acupuncture. Each patient got only one or two treatments during the course of detoxification. Withdrawal symptoms were recorded with a symptom checklist for three days. Patients were divided into four groups according to their self-reported daily dosages of heroin abused.

Results: Eight out of nine (88.9%) patients who abused one to two bags of heroin per day had successful response. Eight out of 12 (66.7%) patients who abused three to four bags per day were successfully treated. Four out of eight (50%) patients who abused five to six bags per day were successfully treated. Only one out of eight (12.5%) patients who abused more than 6 bags of heroin per day was successfully treated.

Conclusions: Acupuncture in heroin detoxification is like any other detoxification modality. Each has its own indications and limitations. Mild to moderate heroin abusers seem to be the best group for acupuncture detoxification.

NR756 Thursday, May 9, 12 noon-2:00 p.m.

Parameters Predicting Extended Full Leather Restraints

Jagannathan Srinivasaraghavan, M.D., Psychiatry, VA Med Ctr, 400 Fort Hill Avenue, Canandaigua NY 14424; Linda Kossow, M.S.N.

Summary:

Objective: There is wide variation in the management of major disruptive behaviors of psychiatric inpatients across the U.S. Commonly utilized methods include medications, seclusion, and restraints either alone or in combination. This study aims to delineate characteristics of patients placed in full leather restraints (FLR) and parameters predicting extended FLR.

Design: Retrospective chart review.

Setting: Long-term care V.A. medical center with 756 beds (334 psychiatric beds).

Subjects: All patients placed in FLR during the study period from January to June 1994.

Methods: From available medical records, the following data are collected: age, sex, height, weight, marital status, competency, admission status, and diagnosis. Based on the longest episode of restraints, the patients were placed in one of the following groups. 1) < 12 hours 2) 12 hours– <24 hours 3) 24 hours– <72 hours 4) 72 hours or more.

Results: There were 32 patients placed in full leather restraints in six months involving 50 episodes. Age ranged from 34 to 79 with a mean of 50.29 years. All but two were whites, 18 single, 20 voluntary, and 20 competent. While there was wide variety of Axis I and II diagnoses, there was no statistically significant pattern. Length of restraints and weight of patient showed r = 0.2168 (2 tail) p .01.

Conclusions: Patients perceived to be intimidating were more likely to stay longer in full leather restraints.

NR757 Thursday, May 9, 12 noon-2:00 p.m.

Prediction of Drug Interactions with Olanzapine Through the Use of In Vitro Methodologies

Barbara J. Ring, M.S., Drug Disposition, Eli Lilly and Co, Lilly Corporate Center DC0925, Indianapolis IN 46285; Shelly N. Binkley, B.S., Mark Van den Branden, John Catlow, B.S., Thomas J. Lindsay, M.S., Steven A. Wrighton, Ph.D.

Summary:

The ability of olanzapine in vitro to inhibit the metabolism catalyzed by five cytochromes P450 was examined. These studies found that olanzapine is a non-competitive inhibitor of CYP3A (Ki = 491 μM); a competitive inhibitor of CYP2D6 (Ki = 89 μM); a non-competitive inhibitor of CYP2C9 (Ki = 715 μM); a non-competitive inhibitor of CYP2C19 (Ki = 920 μM); a competitive inhibitor of CYP1A2 (Ki = 38 μM). Assuming a plasma concentration of olanzapine of 0.2 μM, the calculated maximal percent inhibition of these P450s by olanzapine was < 0.7%.

Kinetic analyses of olanzapine oxidative metabolism yielded Clint (Vmax/Km) values that indicated N-desmethyl (NdM) olanzapine and N-oxide (N-O) olanzapine should be formed at similar rates whereas formation of 2-hydroxymethyl (2-OH) olanzapine is substantially lower. Experiments utilizing human liver samples and cDNA expressed enzymes indicated that CYP2D6 mediates 2-OH olanzapine formation; CYP1A2 mediates NdM olanzapine formation; and flavin-containing monooxygenase (FMO3) mediates N-O olanzapine formation. Although not detected in vivo, 7-hydroxy (7OH) olanzapine was formed in vitro. 7OH olanzapine formation correlated with CYP1A2 activities and was formed by cDNA expressed CYP1A2. Therefore, perturbations in 2-OH olanzapine formation would be expected to have minimal impact on olanzapine clearance since this route of metabolism is relatively minor. The potential exists for drug-drug interactions with CYP1A2 substrates, inhibitors, and inducers. Agents that alter the activity of FMO3 may perturb the N-oxidation route of olanzapine metabolism.

NR758 Thursday, May 9, 12 noon-2:00 p.m.

Computer Documentation at the Patient's Side

James J. Strain, M.D., Psychiatry, Mt. Sinai School of Med, 1 Gustave Levy Place, New York NY 10029; Jeffrey S. Hammer, M.D., George Fulop, M.D.

Summary:

Introduction: Resident training requires understanding computer technology, point of care documentation, and means to immediately access essential literature. The resident needs structured screening instruments, diagnostic alerts, structured questionnaires, medical drug-psychotropic drug alerts, access to pertinent random control trial results, compliance data, and patient outcomes. This report demonstrates a new software in a handheld computer that can be integrated with institutional databases. In addition, on-site queries of archival data from clinical encounters and access to new literature by modem place the user in contact with the 6,000–7,000 scientific reports published daily.

Organization of the Software: Patient archieval data, dictionaries for CPT's, DRGs DSM-IV, ICD-10, drugs, laboratory studies, diagnostic scales are part of the software database. Menu driven report generation for the consultant's profile of cases, progress notes, medical record chart note, graphs of pertinent data, visits, medical record to diskette for the patient's use, and questionnaire and query builder are inherent features. The software is integrated with specialized and institutional databases: 1) utilizing the health level 7 (HL7), 2) integrative and translating protocol to relate with the hospital and other institutional systems.

Intelligent Agents - Recurrent Critical Searches: "Intelligent Agents" augment the work of the C-L psychiatrist by accessing information, e.g., laboratory values, pertinent literature on an ongoing basis without the physician's need to initiate and over-see the search.

Conclusion: Hand-held computerized "point of care" - one time data entry, diagnostic and treatment lexicons, and automatic report writing in this system decrease the documentation time by 50% and provide a computerized record for the medical chart, thereby making the hardware and software cost effective, as well as creating an electronic record for immediate retrieval. Radio frequency wireless downloading to the main or office computer obviates the need for secretarial or data entry personnel.

NR759 Thursday, May 9, 12 noon-2:00 p.m.

Computer-Assisted Behavior Therapy for OCD

John H. Greist, M.D., Research and Education, Dean Foundation, 8000 Excelsior Dr Ste 302, Madison WI 53717-1914; Lee Baer, Ph.D., Isaac M. Marks, M.D., Kenneth A. Kobak, M.S.W., Keith W. Wenzel, B.S., Susan L. Dottl, Ph.D.

Summary:

Behavior therapy (BT), in the form of exposure and ritual prevention (E&RP) has been well established in controlled trials as an effective treatment for obsessive compulsive disorder (OCD). Compared to the SRIs, BT treatment gains are maintained longer following treatment discontinuation. However, increased recognition of OCD and limited availability of behavior therapists makes BT difficult to obtain, and when available, the cost is high. This open, pilot study evaluated a computer based self-assessment and self-help BT program (BT STEPS™) for OCD. BT STEPS™ uses Interactive Voice Response (IVR) technology via TouchTone telephone and an accompanying manual to help patients develop and implement a treatment plan, perform E&RP sessions, and monitor their progress. Forty patients (19 females, 21 males) from three sites participated in the core 12-week trial, with up to 22 weeks' additional access to BT STEPS™. Significant improvements were found in patients' YBOCS scores ($p < .02$), discomfort for specific triggers ($p < .008$), functioning in work and social situations ($p < .008$), and depression ($p < .02$). Patients who performed more E&RP sessions experienced greater improvement in YBOCS scores ($p < .001$). Seventy-seven percent of the patients who completed two or more E&RP sessions reported being "much improved" or "very much improved."

NR760 Thursday, May 9, 12 noon-2:00 p.m.

Satisfaction As a System Performance Indicator in Persons with Schizophrenia

Barbara M. Rohland, M.D., Psychiatry, University of Iowa, 200 Hawkins Drive 2887 UPP, Iowa City IA 52242; Douglas R. Langbehn, M.D., James E. Rohrer, Ph.D.

Summary:

Objective: The purpose of this study is to determine if self-report of satisfaction is a useful indicator of system performance in persons with schizophrenia.

Method: A survey was mailed to 2,535 adults who received mental health services under the 1993 Iowa Medicaid fee-for-service program. The sample population was stratified by diagnosis and included 833 (32.9%) persons with schizophrenia. The survey measured self-reported satisfaction with mental health services and quality of life in several functional domains.

Results: Of 2,535 adult surveys sent, 886 (34.9%) were returned including 300 responses (33.9%) from persons with schizophrenia. Among the seven diagnostic groups surveyed, persons with schizophrenia reported high levels of satisfaction with their mental health status, mental health services, economic status, occupational status, and residential status. However, they had more hospitalizations, were more likely to receive SSDI, and were less likely to live independently compared to persons in other diagnostic categories.

Conclusions: In persons with schizophrenia, satisfaction is not a useful measure of clinical or functional status. Therefore, self-report of satisfaction cannot be used as a sole indicator of service quality in this group. The impact of service reduction in persons with schizophrenia should be monitored by measures other than self-report of satisfaction.

NR761 Thursday, May 9, 12 noon-2:00 p.m.

Pharmacoeconomic Evaluation of Risperidone in Schizophrenia

Ronald F. Cookson, Ph.D., Medical Dept, Janssen-Cilag Ltd., PO Box 79, Saunderton, Buckinghamshire HP144UJ, United Kingdom; Julian F. Guest, Ph.D., Warren M. Hart, M.Sc.

Summary:

Objectives: To examine the cost implications of long-term risperidone use.

Method: Direct costs to United Kingdom health care providers were applied to results from a two-year Swedish resource utilization study of 31 patients with chronic schizophrenia. Costs incurred during two years of treatment (R_1 and R_2) were compared with those from the year before risperidone treatment (R_0).

Patients: Mean age = 38 years; time since diagnosis of schizophrenia = 17 years; number of previous hospital admissions = 10.7.

Results: Mean PANSS scores fell from 86.7 $\pm$ 16.6 at R_0 to 59.9 $\pm$ 19.3 at R_1 and 55.4 $\pm$ 17.5 at R_2 ($p < 0.001$). Mean hospital stay decreased from 171.8 $\pm$ 150.3 days in R_0 to 118.9 $\pm$ 147.0 days in R_1 ($p < 0.02$). Residential accomodation use increased from 28.4 $\pm$ 82.6 to 84.7 $\pm$ 143.3 days, respectively. Total mean cost per patient fell from £22,362 in R_0 to £21,174 in R_1. In 18 patients followed for two years, mean cost per patient was £22,682 in R_0, £19,828 in R_1, and £12,402 in R_2. Most reductions were due to decreased hospital stay. The model was robust for prices ranging from £75 to £175 per hospital stay.

Conclusions: The findings suggest that switching patients to treatment with risperidone results in clinical improvements that may reduce costs to health care providers. Savings are largely due to decreased hospitalization and offset the increased costs of drug treatment and residential accomodation.

NR762 Thursday, May 9, 12 noon-2:00 p.m.

Cognitive Impairment As a Predictor of Psychiatric Length of Stay

Zinoviy Gutkovich, M.D., Psychiatry, Beth Israel Med Ctr, First Avenue at 16th Street, New York NY 10003; Christian Miner, Ph.D., Jennifer Rosenblum, Sc.B., Igor I. Galynker, M.D.

Summary:

We have recently reported that brief neuropsychological screening at the time of admission to an acute psychiatric unit was useful in predicting the length of inpatient hospital stay (LOS). (1). The purpose of this study was to replicate our findings in a new patient population and to attempt to improve the predictive value of the original model by incorporating the severity of psychiatric illness and new demographic variables. Thirty-two patients admitted consecutively to a general psychiatric unit were administered the Mini-Mental State Examination (MMSE), the Trail-Making Tests A and B (TMA and TMB), and the visual reproduction subtest (VR) of the Wechsler Memory Scale within 72 hrs of their admission. A computerized psychiatric severity index (CPSI) was calculated by retrospective chart review (2). The data were analyzed using a hierarchical stepwise regression model. The best fitting model derived from the previous study (1) showed modest predictive validity (Pearson $R = .48$ $p < .01$). TMA and CPSI were the strongest predictors of LOS accounting together for 59.9% of variance in LOS. For the combined sample of 41 patients from (1) and the current 32-patient group, the neuropsychological tests accounted for 20.4% of outcome variance. The results of this study support our previous finding that LOS is related to cognitive impairment. Cognitive testing combined with ratings for the severity of psychiatric illness at the time of admission to a psychiatric hospital could be useful in predicting LOS.

NR763 Thursday, May 9, 12 noon-2:00 p.m.

Effectiveness of the PRIME-MD in the Primary Care Setting: A Clinical Trial with Three Levels of Support

Marcia T. Valenstein, M.D., Psychiatry, University of Michigan, 2215 Fuller Road 116C, Ann Arbor MI 48105; Gregory W. Dalack, M.D., Sara R. Figueroa, M.D., Frederic C. Blow, Ph.D., Alan B. Douglass, M.D.

Summary:

Objective: The efficacy of the PRIME-MD, a screening instrument for psychiatric disorders that combines a patient questionnaire and a structured interview, has been demonstrated under research conditions in primary care. This study evaluated the effectiveness of the PRIME-MD in a general medical clinic, under support conditions more likely to be achievable in clinical practice.

Method: Rates of PRIME-MD completion, psychiatric diagnosis, and new clinical interventions were assessed under four support conditions: PRIME-MD not available (NA), patient questionnaire administered by designated non-clinic staff (NCS), questionnaire administered by nursing staff (RN), and questionnaire administered and screened by non-clinical staff with written prompts to internists to follow up (SP). We report on the first 972 patients.

Results: The support conditions had a significant effect on completion rates of the PRIME-MD structured interview ($x^2 = 23.42$, $p < .001$), the rate of psychiatric diagnosis ($x^2 = 8.77$, $p < .05$), and new interventions by primary care providers ($x^2 = 7.93$, $p < .05$). Relative likelihood of structured interview completion under SP condition compared to NCS or RN was 2.2 and 1.43. Relative likelihood of identifying a psychiatric diagnosis under SP condition compared NCS, RN, or NA was 1.33, 1.47, and 2.1. The relative likelihood of a new clinical intervention in the SP condition compared to NCS, RN, or NA was 2.43, 1.41, and 2.57.

Conclusion: We conclude that the effectiveness of the PRIME-MD in "real-world" clinic settings depends significantly on the support provided for administration. Our data describe the magnitude of this effect and permit calculation of the marginal costs of assigning psychiatric diagnoses and initiating new clinical interventions in primary care.

NR764 Thursday, May 9, 12 noon-2:00 p.m.

Screening for Pschiatric Disorders in Primary Care: Patient Acceptance Versus Physician Reluctance

Mark Zimmerman, M.D., Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence RI 02903; Bruce Horowitz, M.D., Jill I. Mattia, M.A.

Summary:

Purpose: To examine medical patients' attitudes toward being screened for psychiatric disorders, and to determine how accurate are primary care physicians' perceptions of patients' willingness and expectations about addressing mental health issues.

Methods: More than 1,600 patients in three primary care settings were asked to complete two short questionnaires. The first, the SCREENER, inquires about current DSM-IV Axis I disorders. The second is a brief multiplechoice questionnaire which asks the patients about their attitudes to being asked the questions in the SCREENER, and their thoughts and expectations about discussing mental health problems with their doctor. No site differences were found with respect to patients' responses; they were therefore treated as a single cohort. In addition, 45 family practitioners in Rhode Island were shown the SCREENER, and asked to predict the percentage of patients that would choose each response on the patient acceptability questionnaire.

Results: Patients experienced much less negative affect toward mental health screening than the physicians predicted they would. The physicians predicted that 90.0% of patients would be embarrassed by answering the questions on the screening questionnaire, whereas only 13.3% of the patients reported embarrassment ($p < .001$). Similarly, the physicians predicted that 85% to 90% of patients would be annoyed, upset, or uncomfortable answering the questions, markedly higher than the 12% to 20% frequencies found in the patients. Physicians also underestimated the percentage of patients who believed it would be easy to talk to their primary care physician about mental health issues (39% vs 91%, $p < .001$).

Conclusions: Patients are ready and willing to discuss mental health issues with their primary care provider, which may include filling out a brief screening questionnaire. This willingness and acceptability was identical across the different sociodemographic and geographic groups studied. Primary care physicians vastly underestimated the patients' acceptance, willingness, and expectations with regard to dealing with mental health issues.

NR765 Thursday, May 9, 12 noon-2:00 p.m.

A Study of Family Stress and Service Needs at the Time of Psychiatric Hospitalization

Marilyn J. Wedenoja, M.S.W., Psychiatry, University of MI Med Ctr, 1500 East Med Ctr Dr B2910, Ann Arbor MI 48109; David L. Neal, M.S.W.

Summary:

Introduction: By understanding the specific stresses, strains, and service needs identified by family caregivers, mental health professionals can effectively and empathically build partnerships with families of persons with severe mental illness. Often the month directly preceding admission to an inpatient psychiatric unit is a time of stress for both the patient and family. This survey focused on family caregivers' experiences, appraisals, and service priorities during this vulnerable period, with the eventual goal of increasing collaboration between family caregivers and mental health professionals.

Methods: Fifty-six family caregivers were interviewed shortly following their relative's admission for inpatient psychiatric services using the Family Burden Interview Schedule, the Family Service Satisfaction Scale, and measures of the caregivers' pre-admission stressors and utilization of services. Only the primary caregiver in each family was included in the sample. The hospitalized relative included patients primarily with a diagnosis of schizophrenia or severe affective disorder.

Results: Sixty-seven percent of the caregivers rated their pre-admission global stress level as "extremely" or "very" stressed. The stressor rated the most stressful was observing the effect of the psychiatric illness on their relative, defined in the literature as "empathic pain". Eighty percent of the caregivers consulted with their relative's mental health professional during the year preceding admission, and gathered additional information from television, newspapers, and magazines. Twenty-seven percent of this sample were involved with a family self-help group. Close to half of the caregivers were living in the same household with their relative and an independent T-test analysis found no significant difference in terms of worry, caregiving, or stress levels between those in the same or separate households. In evaluating service satisfaction with mental health professionals during the year preceding admission, caregivers were least satisfied with receiving practical caregiving advice. Only 4% reported feeling blamed by the community-based professional for their relative's psychiatric condition, a marked decrease from blaming attitudes toward families previously reported. Regarding inpatient services, caregivers expressed the most interest in information about their relative's treatment and condition, and participating in planning and decision-making.

Conclusion: The caregiver's primary focus on their relative's needs and condition during this period of crisis, similar to family response to other types of medical crises, has implications for approaching and engaging family members during hospitalization. The greatest worry was for their relative's future, and indicates a need for this topic to be specifically addressed in family meetings, as well as involving the family in planning for the future. More information and practical advice about caring for and supporting a relative with a severe psychiatric illness is also needed.

NR766 Thursday, May 9, 12 noon-2:00 p.m.

Barriers to Equity in Mental Health Services Provision to Children and Adolescents

Alan J. Flisher, M.B., Child Psychiatry, Columbia University, 722 West 168th Street, Unit 43, New York NY 10032; Rachel A. Kramer, D.Sc., Rene C. Grosser, Ph.D., Sherryl H. Goodman, Ph.D., Stevan Greenwald, M.A., Sarah M. Horowitz, Ph.D., William E. Narrow, M.D., Christina Hoven, Ph.D.

Summary:

Objective: To document the extent and correlates of unmet need for psychiatric services in a community sample of children and adolescents.

Method: Data were obtained from the 1,285 parent/youth pairs interviewed at four sites in the USA in the NIMH Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) Study. Unmet need was defined as the presence of psychopathology with no recent psychiatric treatment.

Results: 232 (18.1%) youth had unmet need. Adjusting for demographic variables, logistic regression revealed that unmet need was significantly ($p < 0.05$) associated with: not having health insurance; being on public assistance; parental psychopathology; perception of poor mental health by the parent and child; poor school grades; difficulty in arranging transport to mental health facilities; uncertainty about where to go for help; concern that the child would be hospitalized or removed without parental consent; and parental beliefs that treatment would not help, would take up too much time or be inconvenient, or that the child would want to solve the problem unassisted or would refuse to attend.

Conclusion: Equity in mental health service provision to children and adolescents would be facilitated by addressing the above correlates of unmet need for services.

NR767 **Thursday, May 9, 12 noon-2:00 p.m.**

Patterns of Service Utilization and Correlates in a Psychiatric Outpatient Clinic

Barnett S. Meyers, M.D., Psychiatry, NY Hospital-Cornell, 21 Bloomingdale Road, White Plains NY 10605; JoAnne Sirey, Ph.D., Patrick Raue, Ph.D., Deborah A. Perlick, Ph.D., Tara Di Domenico, M.A., George S. Alexopoulos, M.D.

Summary:

Objective: To describe the patterns of service utilization of patients seeking psychiatric treatment at a university-based outpatient clinic.

Method: 60 individuals comprise the initial sample of an ongoing investigation of the treatment of major depression and service use. Prior to evaluation, subjects were administered the CES-D and MINI International Neuropsychiatric Interview to measure symptoms, and reported on use of medical and psychiatric services in the last three months using the Comprehensive Service Use form.

Results: Most patients used outpatient services prior to admission. A majority used outpatient psychological services (62%), with 42% using intensive services such as hospitalization or emergency room visits. Service users did not differ in gender, marital status, education, or employment status. Level of distress on the CES-D and major depression reported on the MINI were not associated with service use.

Remarkably, 15% of the admissions used 62% of the outpatient visits and 52% of the intensive services reported by this sample. Characteristics of these individuals are reported.

Conclusion: Most admissions had sought psychiatric services recently. Level of emotional distress and standard sociodemographic measures do not distinguish those who used services. A small proportion of newly admitted outpatients account for the majority of recent outpatient services.

NR768 **Thursday, May 9, 12 noon-2:00 p.m.**

Daily Left Prefrontal Repetitive Transcranial Magnetic Stimulation in Outpatient Depression: Initial Results of a Double-Blind Placebo Controlled Crossover Trial

Mark S. George, M.D., Radiology, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425; Eric M. Wassermann, M.D., Wendol A. Williams, M.D., Timothy A. Kimbrell, M.D., John T. Little, M.D., Mark Hallett, M.D., Robert M. Post, M.D.

Summary:

Background: Animal models of depression and open trials in treatment-resistant patients have indicated that prefrontal repetitive transcranial magnetic stimulation (rTMS) might have antidepressant activity.

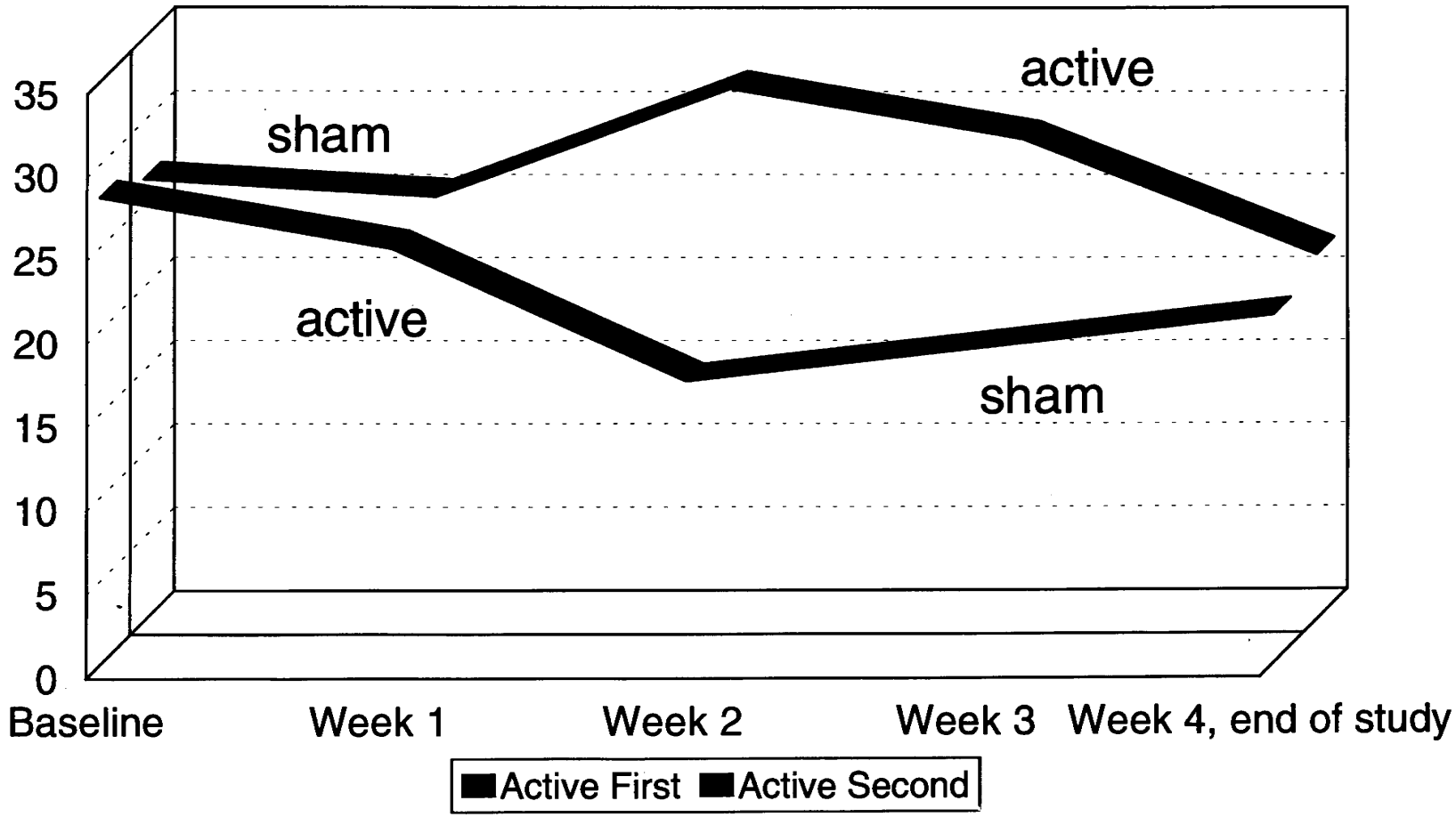
Methods: We organized a double-blind, sham controlled, crossover study of daily left prefrontal rTMS in moderately depressed non-refractory outpatients. To date, six adult women (five unipolar depressed, one bipolar II; mean entry Hamilton Depression Rating of 27.8 (3.0 SD) have completed both legs (randomized two weeks active, two weeks sham) of the study (rTMS parameters - 80% motor threshold, 20 Hz, 2secs x 20 over 20 minutes every morning). For sham, the coil was applied nontangentially to the scalp.

Results: During the active phase, mean Hamilton scores decreased 7.2 points (5DF, $t = 1.8$, $p = .11$, two-tailed paired t-test), while during the two-week placebo phase they decreased by one point. Directly comparing the Hamilton scores at the end of active versus placebo phase showed that active rTMS had a significantly greater antidepressant effect (6.1 mean diff, 5DF, $t = 4$, $p < 0.01$, two-tailed paired t-test). No adverse side effects were noted.

Conclusions: These initial placebo-controlled results indicate that daily left prefrontal rTMS has antidepressant activity in moderately depressed outpatients.

Ongoing Double-Blind Crossover Study

Active or Sham, L Prefrontal 20 2sec 20 Hz 80%MT over 20 minutes



28-item Hamilton, 6 depressed outpatients (3 in each series)

AUTHOR INDEX

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

X

Y

Z

American
Psychiatric
Association

1400 K STREET, N.W.
WASHINGTON, D.C. 20005

PRINTED IN U.S.A