New Research

New Research Program & Abstracts

American Psychiatric Association
Annual Meeting • May 17-22, 1997
San Diego, California

Program & Abstracts

PROGRAM
AND
ABSTRACTS ON NEW RESEARCH

IN SUMMARY FORM

150TH ANNUAL MEETING OF THE AMERICAN PSYCHIATRIC ASSOCIATION

SAN DIEGO, CA
May 17-22, 1997

SUBCOMMITTEE ON NEW RESEARCH
OF THE SCIENTIFIC PROGRAM COMMITTEE

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150th Annual Meeting
San Diego, California
May 17-22, 1997

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May 17, 1997

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 1997 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 19, 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 anxiety, schizophrenia, treatment of depression, and genetics. The Young Investigators' Oral/Slide Sessions will begin at 1:00 p.m. on Monday afternoon, followed by a Young Investigators' Poster Session beginning at 3:00 p.m.

The New Research Oral/Slide Sessions will be held Tuesday through Thursday, from 9:00 a.m.-10:30 a.m. Sessions will focus on pharmacology; and mood disorders and premenstrual dysphoric disorders (Tuesday); schizophrenia and depression; and psychopharmacology (Wednesday); treatment techniques, genetics, and geriatric psychiatry; and cross-cultural and minority psychiatry (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 psychopharmacology, somatic therapies, combined pharmacology and psychotherapy, historical questions, and ethics; and addictive disorders, AIDS, violence, forensics, personality dissociative disorders, epidemiology, diagnostics, and treatment techniques (Tuesday); mood and anxiety disorders, premenstrual dysphoric disorder, suicide, managed care, and psychoimmunology; and schizophrenia, biological psychiatry, brain imaging, neurobiology, neuropsychiatry, and research issues (Wednesday); geriatric psychiatry; genetics, consultation-liaison and emergency psychiatry, eating disorders and sixteen smaller topics too numerous to list (Thursday).

The 48 oral/slide papers (including 12 Young Investigators) and 682 poster presentations (including 175 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, II M.D.
Chairperson
New Research Subcommittee of the
Scientific Program Committee

Outside Reviewers for the New Research Program

Hagop S. Akiskal, M.D.
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Carol A. Bernstein, M.D.
Richard A. Bernstein, M.D.
Wade H. Berrettini, M.D.
Rene L. Binder, M.D.
Dan G. Blazer, M.D.
Richard L. Borison, M.D.
William Byerley, M.D.
Joshua W. Calhoun, M.D.
Gabrielle A. Carlson, M.D.
Paula J. Clayton, M.D.
C. Robert Cloninger, M.D.
C. Edward Coffey, M.D.
Joseph T. Coyle, M.D.
Jeffrey L. Cummings, M.D.
Glenn C. Davis, M.D.
Mina K. Dulcan, M.D.
Michael A. Fauman, M.D.
Wayne S. Fenton, M.D.
Michael B. First, M.D.
Arnold J. Friedhoff, M.D.
Abby J. Fyer, M.D.
William M. Glazer, M.D.
Howard H. Goldman, 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.
Donald S. Kornfeld, M.D.
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Robert W. McCarley, M.D.
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Frederic M. Quitkin, M.D.
Peter V. Rabins, M.D.
Mark H. Rapaport, M.D.
Murray A. Raskind, M.D.
Stephen G. Rayport, M.D.
Phillip J. Resnick, 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.
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Ming T. Tsuang, M.D.
Gary J. Tucker, M.D.
Thomas W. Uhde, M.D.
Fred R. Volkmar, M.D.
B. Timothy Walsh, M.D.
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The American Psychiatric Association requires disclosure of the existence of any significant financial interest or other affiliation a presenter has with any commercial product(s) and/or providers of any commercial services 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 acknowledgment in this printed *New Research Program & Abstracts Book*. This policy is intended to openly identify any potential conflict so that members of the audience in an educational activity are able to form their own judgements about the presentation.

The following presenters have indicated a significant financial interest or other affiliation with a commercial supporter of the session and/or with the manufacturer(s) of a commercial product(s) and/or provider of commercial service(s). The presenter's name, the manufacturer's name, and the page number(s) the presenter appears on in this *New Research Program & Abstracts Book* are listed below:

Presenter	Manufacturer(s)	Final Program #
Akiskal, Hagop S.	Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Glaxo Wellcome; Abbott Laboratories	NR408
Albers, Lawrence J.	Wyeth-Ayerst Laboratories	NR281
Albright, Penny	Janssen-Ortho Inc.	NR513
Alpert, Jonathan E.	Eli Lilly and Company	NR643
Ambrosini, Paul J.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR449
Ames, Donna	Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Hoechst-Roussell; Janssen Pharmaceutica and Research Foundation; Abbott Laboratories	NR214
Amsterdam, Jay D.	Wyeth-Ayerst Laboratories	NR451
Arvanitis, Lisa A.	Zeneca Pharmaceuticals Group	NR230, NR232
Asnis, Gregory M.	Eli Lilly and Compony	NR434
Baker, Brian	Eli Lilly and Company, Canada	NR223
Balon, Richard	Bristol-Myers Squibb; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Glaxo Wellcome	NR635
Barbee IV, James G.	Bristol-Myers Squibb; Pharmacia & Upjohn Inc.; SmithKline Beecham Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Glaxo Wellcome; Sano Corporation; Roche Laboratories, a member of the Roche Group; TAP Pharmaceuticals; Ciba Geigy Corporation, Pharmaceuticals Division; Eli Lilly and Company; Novartis Pharmaceuticals Corporation	NR258, NR475
Barge-Schaapveld, Daniela	Solvay Pharmaceuticals, Inc.	NR275
Bauer, Michael	SmithKline Beecham Pharma, Munich	NR110
Berti, Carlo	Pfizer Ltd.	NR252
Black, Donald W.	SmithKline Beecham Pharmaceuticals	NR474
Blomgren, Sharon L.	Eli Lilly and Company	NR188, NR466, NR467
Bondareff, William	Pfizer Inc.	NR678
Brecher, Martin B.	Janssen Pharmaceutica and Research Foundation	NR612
Brescan, Debra W.	Janssen Pharmaceutica and Research Foundation; Pharmacia & Upjohn Inc.	NR257
Brook, Schlomo	Pfizer Inc.	NR584
Buchsbaum, Monte S.	Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Inc.	NR535
Buesching, Don P.	Eli Lilly and Company	NR380
Chatham-Showalter, Peggy E.	Janssen Pharmaceutica and Research Foundation	NR291
Clayton, Anita L.H.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Glaxo Wellcome; Wyeth-Ayerst Laboratories; Bristol-Myers Squibb; SmithKline Beecham Pharmaceuticals	NR502
Coccaro, Emil F.	Eli Lilly and Company; Wyeth-Ayerst Laboratories	NR564
Cohen, Bruce J.	Wyeth-Ayerst Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR343

Presenter	Manufacturer(s)	Final Program #
Cohen, Lee S.	Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; Roche Laboratories, a member of the Roche Group; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR212
Colquett, Phuong	Birch and Davis Associates	NR361
Coplan, Jeremy D.	SmithKline Beecham Pharmaceuticals; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR269, NR481
Cunningham, Lynn A.	Wyeth-Ayerst Laboratories	NR547
Cutler, Neal R.	Novartis Pharmaceuticals Corporation; Hoechst-Roussell	NR516, NR517
Dalheim, Laura J.	Eli Lilly and Company	NR112
Delbressine, Leon P.C.	NV Organon, OSS, Netherlands	NR273
Dewan, Mantosh J.	Ciba Geigy Corporation, Pharmaceuticals Division; SmithKline Beecham Pharmaceuticals; Amersham, Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR295, NR526
Dilea, Clifford	Wyeth-Ayerst Laboratories	NR245
Edgel, Eric T.	Eli Lilly and Company	NR384
Entsuah, Richard	Wyeth-Ayerst Laboratories	NR439
Fava, Maurizio	Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Wyeth-Ayerst Laboratories; SmithKline Beecham Pharmaceuticals; Roche Laboratories, a member of the Roche Group; Glaxo Wellcome; Organon Inc.	NR196, NR255
Fawcett, Jan A.	National Institute of Mental Health; Abbott Laboratories; Bristol-Myers Squibb; Glaxo Wellcome; Eli Lilly and Company; Organon Inc.; Pfizer Inc.; Theodore and Vada Stanley Foundation; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; Zeneca Pharmaceuticals Group; EM Industries, Inc.; Pharmacia & Upjohn Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; American Suicide Foundation; Chicago Consortium for Psychiatric Research; American Association of Suicidology; Psychiatric Research Society; American Society of Clinical Psychopharmacology	NR219, NR220
Feighner, John P.	Wyeth-Ayerst Laboratories	NR419, NR420
Frye, Mark A.	Abbott Laboratories	NR425, NR426
Ghaemi, S. Nassir	Abbott Laboratories	NR482
Gilaberte, Inmaculada	Eli Lilly and Company	NR240
Goldstein, David J.	Eli Lilly and Company	NR191, NR202, NR203
Goldstein, Jeffrey M.	Zeneca Pharmaceuticals Group	NR233
Gomez, Juan-Carlos	Eli Lilly and Company	NR277
Goodnick, Paul J.	Organon Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Abbott Laboratories; Glaxo Wellcome; Wyeth-Ayerst Laborotories; Bristol-Myers Squibb	NR284, NR285
Granneman, Richard	Abbott Laboratories	NR589
Grimm, Scott W.	Zeneca Pharmaceuticals Group	NR251
Grossberg, George T.	Zeneca Pharmaceuticals Group; Somerset; Bristol-Meyers Squibb; Novartis Pharmaceuticals Corporation; Abbott Laboratories; Janssen Pharmaceutica and Research Foundation; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Searle; Parke-Davis, Division of Warner-Lambert Company; Eli Lilly and Company	NR722
Grush, Lynn R.	Eli Lilly and Company	NR447
Haley, Jane C.	Eli Lilly and Company	NR591
Hamner, Mark B.	Abbott Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer, Inc.; Zeneca Pharmaceuticals Group; Otsuka; Janssen Pharmaceutica and Research Foundation	NR575
Hantouche, Elie G.	Eli Lilly and Company, France; Mayoly-Spindler, France; Sanofi, France	NR142, NR495
Hayford, Kara E.	Glaxo Wellcome	NR97
Hellerstein, David J.	Eli Lilly and Company; Wyeth-Ayerst Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR402
Hirschfeld, Robert M.A.	Abbott Laboratories; Bristol-Myers Squibb; Glaxo Wellcome; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; EM Industries; Hoffman LaRoche Inc.; Eli Lilly and Company; Novartis Pharmaceuticals Corporation; SmithKline Beecham Pharmaceuticals	NR372
Hylan, Timothy R.	Eli Lilly and Company	NR388
Kasper, Siegfried	Akzo-Nobel; Lundbeck; Eli Lilly and Company	NR266
Kaye, Walter H.	Dista	NR405

Presenter	Manufacturer(s)	Final Program #
Keck, Jr., Paul E.	Abbott Laboratories; Pfizer, Inc.; Zeneca Pharmaceuticals Group; Janssen Pharmaceutica and Research Foundation; R.W. Johnson Pharmaceutical Research Institute	NR398
Keller, Martin B.	Wyeth-Ayerst Laboratories; SmithKline Beecham Pharmaceuticals; Pharmacia & Upjohn Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Bristol-Myers Squibb; Eli Lilly and Company	NR417
Kelley, Lee A.	Pharmacia & Upjohn Inc.; SmithKline Beecham Pharmaceuticals	NR217
Kelsoe, Jr., John R.	Novartis Pharmaceuticals Corporation	NR406
Kleinberg, David	Janssen Pharmaceutica and Research Foundation	NR599
Koran, Lorrin M.	Solvay Pharmaceuticals, Inc.	NR428, NR429
Kyomen, Helen H.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Wyeth-Ayerst Laboratories	NR666
Lian, Jean	Bristol-Myers Squibb	NR397
Lindenmayer, Jean-Pierre	Novartis Pharmaceuticals Corporation	NR278
Luchins, Daniel J.	Janssen Pharmaceutica and Research Foundation	NR218
Madhusoodanan, Subramoniam	Janssen Pharmaceutica and Research Foundation; Excerpta Medica	NR601
Marcotte, David B.	Parke-Davis, Division of Warner-Lambert Company	NR261
Marder, Stephen R.	Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company; Novartis Pharmaceuticals Corporation; Abbott Laboratories; Lundbeck; McNeil Pharmaceuticals	NR595
Markovitz, Paul J.	Bristol-Myers Squibb	NR222
Martinez, James M.	Abbott Laboratories	NR119
Masand, Prakash S.	Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Inc.; Searle; Wyeth-Ayerst Laboratories; Bristol-Myers Squibb; Abbott Laboratories	NR648
McElroy, Susan L.	Abbott Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Glaxo Wellcome; Alza; Wyeth-Ayerst Laboratories; Parke-Davis, Division of Warner-Lambert Company; Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals	NR345
Mellman, Thomas A.	Bristol-Myers Squibb	NR497
Mendels, Joe	Forest Laboratory; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Novartis Pharmaceuticals Corporation; Bristol-Myers Squibb; SmithKline Beecham Pharmaceuticals; Hoechst-Roussell; Wyeth-Ayerst Laboratories	NR465
Mendelson, Wallace B.	Searle; Bristol-Myers Squibb	NR512
Michelson, David	Eli Lilly and Company	NR189, NR200
Miller, Ivan W.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Bristol-Myers Squibb; Eli Lilly and Company; Organon Inc.	NR416
Nierenberg, Andrew A.	Wyeth-Ayerst Laboratories; Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Organon Inc.; Glaxo Wellcome	NR468
O'Malley, Stephanie S.	DuPont-Merck	NR193
Overo, Kerstin	Lundbeck	NR471
Papp, Laszlo A.	Wyeth-Ayerst Laboratories; Bristol-Myers Squibb; SmithKline Beecham Pharmaceuticals; Interneuron, Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR234
Patten, Christi A.	American Heart Association; California Tobacco Disease Related Research Program	NR22
Perez, Victor	Eli Lilly and Company	NR207
Pfeffer, Cynthia R.	Bristol-Myers Squibb	NR279
Phillips, Katharine A.	Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Inc.; Gate Pharmaceuticals; Eli Lilly and Company	NR483, NR484
Pollack, Mark H.	Bristol-Myers Squibb; Glaxo Wellcome; Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Roche Laboratories, a member of the Roche Group; SmithKline Beecham Pharmaceuticals; Solvay Pharmaceuticals, Inc.; Wyeth-Ayerst Laboratories	NR477
Potkin, Steven G.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR590

Presenter	Manufacturer(s)	Final Program #
Preskorn, Sheldon H.	Abbott Laboratories; Astra/Merck Group, Division of Merck & Co.; Boots; Bristol-Myers Squibb; Glaxo Wellcome; Ciba Geigy Corporation, Pharmaceuticals Division; Eli Lilly and Company; Searle; Hoechst-Roussell; Hoffman LaRoche Inc.; Organon Inc.; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Rhone-Poulenc; Novartis Pharmaceuticals Corporation; SmithKline Beecham Pharmaceuticals; Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn, Inc.; Wyeth-Ayerst Laboratories; Lundbeck; National Psychopharmacology Laboratories	NR224, NR225
Purdon, Scot	Janssen-Ortho Inc.	NR283
Rak, Ihor W.	Zeneca Pharmaceuticals Group	NR249
Rapaport, Mark H.	Solvay Pharmaceuticals, Inc.	NR409, NR410
Rasmussen, Steven A.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Solvay Pharmaceuticals Inc.	NR472
Richelson, Elliott	Bristol-Myers Squibb; Pfizer Inc.; Glaxo Wellcome; Organon Inc.; Wyeth-Ayerst Laboratories	NR248
Rihmer, Zoltan	Lundbeck	NR282
Rogers, Sharon L.	Eisai America Inc.	NR618
Romano, Steven J.	Eli Lilly and Company	NR201
Roose, Steven P.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories	NR209, NR401
Russell, James M.	Pfizer Inc.	NR399
Sanger, Todd	Eli Lilly and Company	NR204
Sechter, Daniel	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR152
Shapira, Nathan A.	R.W. Johnson Pharmaceutical Research Institute	NR101
Siever, Larry J.	Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation; Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Inc.	NR533
Simon, Gregory E.	Eli Lilly and Company	NR455
Speer, Andrew M.	Stanley Foundation; Picker International	NR168
Stahl, Stephen M.	Pharmacia & Upjohn Inc.; Bristol-Myers Squibb; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Glaxo Wellcome; Neurocrine Biosciences, Inc.; Eli Lilly and Company; Forest; Solvay Pharmaceuticals Corporation; Wyeth-Ayerst Laboratories; Janssen Pharmaceutica and Research Foundation; Bayer; Yamanouchi; Roche Laboratories, a member of the Roche Group; Ciba Geigy Corporation, Pharmaceuticals Division; Akzo Nobel; Abbott Laboratories; Organon Inc.; Hoechst-Roussell; Takeda	NR242, NR243
Stewart, Donna E.	Eli Lilly and Company	NR228
Stowe, Zachary N.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Eli Lilly and Company; Wyeth-Ayerst Laboratories	NR192
Sussman, Norman	Organon Inc.; Bristol-Myers Squibb; Eli Lilly and Company; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Wyeth-Ayerst Laboratories; SmithKline Beecham Pharmaceuticals	NR254
Swartz, Conrad M.	Somatics, Inc.	NR237, NR238
Taintor, Zebulon C.	Abbott Laboratories	NR319
Tamburrino, Marijo B.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR413, NR414
Taylor, Leslie V.	Abbott Laboratories; Glaxo Wellcome; Eli Lilly and Company; Organon Inc.; Janssen Pharmaceutica and Research Foundation; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Solvay Pharmaceuticals, Inc.	NR390
Tensfeldt, Thomas G.	Pfizer Inc.	NR571
Thase, Michael E.	Eli Lilly and Company; Wyeth-Ayerst Laboratories; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Bristol-Myers Squibb; Organon Inc.; SmithKline Beecham Pharmaceuticals	NR272
Tohen, Mauricio	Abbott Laboratories; Glaxo Wellcome; Parke-Davis, Division of Warner-Lambert Company; Eli Lilly and Company	NR205, NR206
Tome, Maria B.	SmithKline Beecham Pharmaceuticals	NR86
Tran, Pierre V.	Eli Lilly and Company	NR190
Tucker, Phebe M.	Pharmacia & Upjohn Inc.; Solvay Pharmaceuticals, Inc.; Bristol-Myers Squibb	NR362
Tweedie, Donald J.	Pfizer Inc.	NR570
van Balkom, Anton J.L.M.	Solvay Duphar	NR488
van Kammen, Daniel P.	Eli Lilly and Company; Abbott Laboratories; Janssen Pharmaceutica and Research Foundation; Zeneca Pharmaceuticals Group	NR586, NR587
Versiani, Marcio V.	Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.	NR473

Presenter	Manufacturer(s)	Final Program #
Waldinger, Marcel D.	Solvay Duphar	NR699
Wheatley, David	Feighner Research Institute	NR208
Wilner, Keith D.	Pfizer Inc.	NR572, NR573
Winsberg, Mirene	Abbott Laboratories	NR113
Witztum, Eliezer	Ferring, Malmo, Suleden	NR700
Wolkow, Robert	Pfizer Inc.	NR404
Wong, James Y.W.	Zeneca Pharmaceuticals Group	NR250
Worthington III, John J.	Abbott Laboratories; Glaxo Wellcome; Eli Lilly and Company; Lomex; Roerig Division of the U.S. Pharmaceuticals Group, Pfizer Inc.; Solvay Pharmaceuticals, Inc.; Parke-Davis, Division of Warner-Lambert Company; SmithKline Beecham Pharmaceuticals	NR476
Young, L. Trevor	Abbott Laboratories	NR452
Zaninelli, Rocco M.	SmithKline Beecham Pharma, Munich	NR105
Zarate, Jr., Carlos A.	Janssen Pharmaceutica and Research Foundation	NR211, NR724
Zivkov, Milana V.	NV Organon, OSS, Netherlands	NR274

The following presenters on this year's scientific program failed to return the APA disclosure form. The presenter's name and the program number(s) the presenter appears on in this New Research Program & Abstracts Book are listed below:

Birmes, Philippe J.R. NR81
Cheng, Wen-Hong NR683
Everson, Gregory T. NR642
Ferrando, Laura NR371
Goodkin, Karl NR320
Jimenez, Isabel M. NR107
O'Sullivan, Richard L. NR271
Pandit, Sunila NR111
Simpson, Sabrina R. NR73
Tortora, Guillermo NR114
Yu, Je Chun NR68

NEW RESEARCH

Monday, May 19, 1997, 9:00 a.m.-10:30 a.m.

New Research 1– Poster Session – Special Events Area, Upper Level, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Richard Balon, M.D.

NR1 Gating in Schizophrenia: A Trait-Related Deficit
Arthi Parwani, M.D., Elsa Bartlett, Ed.D., Erica J. Duncan, M.D., Steven H. Madonick, M.D., Phillip B. Chappell, M.D., Rajiv Rajan, M.D.

NR2 The Effect of Mecamylamine on Smoking Patterns in Psychiatric Patients
Christine E. Marx, M.D., Joseph P. McEvoy, M.D.

NR3 Conditional Discrimination Learning in Schizophrenia
Dagmar Maierhofer, M.D., Karl Dantendorfer, M.D., Edith Hofer, M.D., Murat Serim, M.D., Johann Windhaber, M.D., Professor Heinz Katschnig

NR4 Neurological Hard Signs in Schizophrenia
Sanjay S. Chandragiri, M.D., Psyn Sharma, M.D.

NR5 Agnosia of Tardive Dyskinesia in Schizophrenia
Fabien Tremeau, M.D., Xavier Amador, Ph.D., Dolores Malaspina, M.D., Yvan Amodt, M.S., Raymond Goetz, Ph.D., Jack M. Gorman, M.D.

NR6 Measuring Health Status in Older Schizophrenia Patients
Andres F. Sciolla, M.D., Thomas L. Patterson, Ph.D., Jovier D. Evans, Ph.D., M. Jackuelyn Harris, M.D., Dilip V. Jeste, M.D.

NR7 Pilot Trial of Light Treatment for HIV-Associated Sleep Disturbance
Andres F. Sciolla, M.D., Stephen Brown, M.D., J. Hampton Atkinson, Jr., M.D., J. Summers, M.S.W., Igor Grant, M.D., The HNRC Group

Research Funding Poster Session

The Scientific Program Committee in conjunction with the APA Office of Research is sponsoring Posters on research funding being displayed in conjunction with the Young Investigators' Poster Session. Individuals representing federal agencies and private foundations will be available to meet with new, continuing, and potential grantees and other psychiatric investigators to discuss current research grant programs. Representatives listed on page 21.

NR8 Diagnosis and Risk Factors of Depression in Schizophrenia
Rosa Elena Ulloa, M.D., Rogelio Apiquian, M.D., Francisco Paez, M.D., Hector A. Ortega-Soto, M.Sc.

NR9 Plasma HVA in Older Psychotic Patients
Mirela O. Fagarasan, Ph.D., Jonathan P. Lacro, Pharm.D., Paul J. Mills, Ph.D., M. Jackuelyn Harris, M.D., Richard L. Hauger, M.D., Dilip V. Jeste, M.D.

NR10 A Prospective Study of Substance Use Disorders in Schizophrenic Patients
R. Mark Newman, M.D., Peg C. Nopoulos, M.D., Susan J. Oliver, M.D., Nancy C. Andreasen, M.D.

NR11 QEEG During Memory Tasks in Schizophrenia
Duk-In Jon, M.D., Sung H. Lee, M.D., Hong-Schick Lee, M.D., Sung Kil Min, M.D.

NR12 Deficits in Visual Selective Attention in Neuroleptic Naive Psychotic Patients Versus Nonpsychiatric Controls
Glenda MacQueen, M.D., Patricia I. Rosebush, M.D., Steven Tipper

NR13 Language Processing, Thought Disorder and Clinical Symptoms in Schizophrenia
Angel Cienfuegos, M.D., Daniel C. Javitt, M.D., Jorge Barros, M.D., Kevin Moser, Anne-Marie Shelley, Ph.D.

NR14 Neurological Soft Signs in First-Episode Schizophrenia: Schizophreniform Psychosis
Stephen Browne, M.B., Maurice Gervin, M.B., Abbie Lane, M.B., John L. Waddington, Ph.D., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.

NR15 The Clinical Correlates of Quality of Life in First-Episode Schizophrenia/Schizophreniform Psychosis
Stephen Browne, M.B., Maurice Gervin, M.B., Abbie Lane, M.B., John L. Waddington, Ph.D., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.

NR16 Baseline Rate of Spontaneous Dyskinesia in First-Episode Schizophrenia/ Schizophreniform Psychosis in an Urban Area Service
Maurice Gervin, M.B., Stephen Browne, M.B., Abbie Lane, M.B., John L. Waddington, Ph.D., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.

NR17 Effect of Gender on Psychiatric Comorbidity Among Schizophrenic Patients
Sunil Chhibber, M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.S., Ekkehard Othmer, M.D., Ph.D., William F. Gabrielli, Jr., M.D., Charles L. Zaylor, D.O.

NR18 Clozapine Versus Risperidone in Pharmaco-Refractory Schizophrenia: A Preliminary Report
Carsten Konrad, Christoph Schormair, M.D., Petra Ophaus, Uwe Knickelbein, Bernd Eikelmann, M.D.

NR19 Comparisons Between Alcoholics and Social Drinkers
Jung-Sik Lee, M.D., Kwang-Soo Han, M.D., Yoo-Sang Lee, M.D.

NR20 Substance Abuse, Mental Illness and Family History of Substance Abuse
Faye M. Lari, M.D., Lisa B. Dixon, M.D., Jack Scott, Sc.D.

NR21 Interaction of Factors Affecting Hospital Stay of Cocaine Dependents: Comorbidity, Status and Episode
Ashok Jain, M.D., Pedro Ruiz, M.D., Howard Rhoades, Ph.D.

NR22 Changes in Staff Attitudes Toward a Smoke-Free Policy in the Navy Alcohol Rehabilitation Program
Christi A. Patten, Ph.D., John E. Martin, Ph.D., C. Richard Hofstetter, Ph.D., Sandra A. Brown, Ph.D., Nancy A. Braun, Ph.D., Carl D. Williams, B.A.

NR23 Stages of Change as a Predictor of Abstinence Among Alcohol Dependent Subjects in Pharmacotherapy Trials
Carlos A. Hernandez-Avila, M.D., Henry R. Kranzler, M.D., Joseph A. Burleson, Ph.D.

NR24 Improvements in Psychosocial Stages of Development and Defense Styles in Alcoholics During Inpatient Treatment
Paul W. Ragan, M.D., Linda Doty, R.N., Nancy Harnett, Ph.D., Dell Wright, R.N., Sandy Birdsong, R.N., Christopher Geyer, R.N., Susan Squires, R.N.

NR25 Ten-Year Outcomes of Primary and Secondary Men Alcoholics
Saeed A. Shah, M.D., Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Elizabeth J. Nickel, M.S., Jan L. Campbell, M.D., H. Mikel Thomas, M.D.,

NR26 Medical Symptoms Among Alcohol, Cocaine and Heroin Abusers
Ashwin A. Patkar, M.D., Robert Sterling, Ph.D., Edward Gottheil, M.D.

NR27 Mexican Study of First-Episode Psychosis: Temperament and Character
Rogelio Apiquian, M.D., Francisco Paez, M.D., Ma-Elena Medina Mora, Ph.D., Rosa Elena Ulloa, M.D.

NR28 AIDS, Depression and Quality of Life in Black Men
Dwight D. Coleman, M.D., J. Stephen McDaniel, M.D., Peter E. Campos, Ph.D., Eugene W. Farber, Ph.D., James Emshoff, Ph.D., Gary Uhl, Ph.D.

NR29 The Nature of Dissociation: A Transcultural Study About Religion-Related Dissociative Experiences
Paulo J. Negro, Jr., M.D., Mario R. Louza-Neto, M.D.

NR30 Flexible Therapy Versus Traditional Psychotherapy: A Preliminary Study
Manohar K. Shetty, M.D., Salim A Chowdhury, M.D., Robert H. Trivus, M.D., David J. Lynn, M.D., Ronie Titus, M.S.W.

NR31 Paraquet Poisoning and Ethnicity
Gerald Hutchinson, M.D., Manohar K. Shetty, M.D., David J. Lynn, M.D., H. Daisley, Osama M. Saleh, M.D., Koushik Mukherjee, M.D.

NR32 Phobia and Night Terror Associated with Ketamine: How to Avoid Them?
Manohar K. Shetty, M.D., David J. Lynn, M.D., Roopnarine Lalla, M.B., Hamid Razak, M.B., Raj Sarma, M.D.

NR33 Return of Menses in Patients Hospitalized for Anorexia Nervosa
Laurel Mayer, M.D., Evelyn Attia, M.D., B. Timothy Walsh, M.D., Kristin Chally, B.A., Claire Haiman, B.A.

NR34 Low Platelet MAO Associated to Impulsive Behaviors in Eating Disorders
Jose L. Carrasco, M.D., Marina Diaz-Marsa, M.D., Jeronimo Saiz-Ruiz, M.D.

NR35 Sex Differences in Hyperactivity in School-Aged Children
Carol A. Glod, Ph.D., Martin H. Teicher, M.D., Cynthia McGreenery, Ann Polcari, M.S.N., Carl M. Anderson, Ph.D., Judith Holt, R.N.

NR36 The Risk and Protective Factors Scale for Disruptive Behavior Disorders in Preadolescents
Karl J. Looper, M.D., Natalie Grizenko, M.D.

NR37 A Classification of Korean Adolescent Criminals
Eunyoung Oh, M.D., Sookwon Kim, M.D., Sunmi Cho, M.A., Hoyoung Lee, M.D., Choongsoon Lee, M.D., Jihyun Kim, M.D.

NR38 Comorbidity of ADHD and Adolescent Criminals Using TOVA
Myungsoo Lee, M.D., Eunyoung Oh, M.D., Kiyoung Lim, M.D., Keunyoung Park, M.A., Youngki Chung, M.D., Jaisung Noh, M.D.

NR39 Use of Counseling by Pregnant or Postpartum Teens
Jude L. Boyer-Patrick, M.D., Lisa B. Dixon, M.D., Janet D. Woolery, M.D., Phyllis Huff, M.S.W., Joe Turner, M.A.

NR40 Adolescents Semistructured Interview: Interrater and Test-Retest Reliability
Francisco R. De la Pena, M.D., Eduardo Cruz-Elizondo, M.D., Rosa Elena Ulloa, M.D., Margarita Patino, M.D., Arturo Mendizabal, M.D., Gerardo Heinze, M.D.

NR41 Parental Compliance with Psychiatric Referral
John P. Neuhaus, M.D., Linda B. Nahulu, M.D., Deborah Goebert, M.S.

NR42 Vocal Tics in Sydenham's Chorea Patients
Marcos Tomanik Mercadante, M.D., M.Conceicao do Rosar Campos, M.D., Maria J. Dias, M.D., Paul J. Lombroso, M.D., James F. Leckman, M.D., Euripedes C. Miguel, M.D.

NR43 Anorexia and Weight Loss in Children Taking Adderall
Amanda N. Holmes, M.D., Barbara L. Gracious, M.D., Cheryl Preece, M.S., Sheree Atkinson

NR44 Comorbidity and Initial Pharmacotherapy in ADHD
Victoria B. Morgan, M.D., Barbara L. Gracious, M.D., Cheryl Preece, M.S., Sheree Atkinson, Mary Marek, B.S.

NR45 Risperidone Side Effects in Children and Adolescents
Claudia A. Phillips, M.D., Barbara L. Gracious, M.D., Cheryl Preece, M.S., Sheree Atkinson

NR46 Initial Presentations of OCD in Children
Elizabeth A. Schoene, M.D., Helen A. Zaphiris, M.D., Cheryl Preece, M.S., Sheree Atkinson

NR47 A PRN Administration in a Child Inpatient Unit: A Retrospective Study
Alejandra Hallin, M.D., Ronald J. Steingard, M.D., Gordon P Harper, M.D.

NR48 Relationship Between the Psychopathology and the Concentration of Serotonin in Platelet-Rich Plasma of Children with Autistic Spectrum Disorder
Yee-Jin Shin, M.D., Sung Kil Min, M.D.

NR49 Gender-Based Differences in the Presentation of Children and Adolescents to a Psychiatric Emergency Room
Maria T. Cartagena, M.D., Joy L. Kreeger, M.D., Yogesh D. Bakhai, M.D., Wendy L. Weinstein, M.D.

NR50 Seasonal Variations in the Presentation of Children and Adolescents to a Psychiatric Emergency Room
Maria T. Cartagena, M.D., Yogesh D. Bakhai, M.D., Joy L. Kreeger, M.D., Betty Brown, M.D.

NR51 Physician-Assisted Suicide: Medical Students' Perspectives
Ana C. Posada, M.D., Maria Rodill, M.D., Maria D.D. Llorente, M.D.

NR52 Assessing and Improving Neurology Training in General Psychiatry Residencies
Susan M. Maixner, M.D., Ronald C. Albucher, M.D., Michelle Riba, M.D.

NR53 Psychiatric Information Center in Brazil
Yara Azevedo, M.D., Caludio de Novaes Soares, M.D., Ana Maria Almeida, M., Jep Neves, M.D.

NR54 Unexpected Impact of a Client Satisfaction Survey at a Public Mental Health Clinic
Abul Q. Hasan, M.D., David I. Mayerhoff, M.D., Thomas Lysaght, Ph.D.

NR55 Sexual and Racial Discrimination in the Army
Mary B. Cruser, M.D., Elizabeth E. Correnti, M.D., Laura Davidson, Ph.D.

NR56 Outcomes of Housing in Persons with Mental Illness and Substance Use Disorders
Niamh M. Holohan, M.D., Lisa B. Dixon, M.D., Nancy Krauss, L.C.S.W.

NR57 Patients' Characteristics in a Long-Term Hospital
Demetra Pappas, B.S., Rogelio D. Bayog, M.D., Alan I. Green, M.D., David N. Osser, M.D., Howard H. Chang, M.D., Ileana Berman, M.D.

NR58 Primary Care Training: For Psychiatrists?
Cletus S. Carvalho, M.D., Carlos Blanco-Jerez, M.D.

NR59 Non-Specificity of Somatic Depressive Symptoms in Patients Receiving Intensive Cancer Treatment
Jesus Prieto, Jordi Blanch, Jorge Atala, Esteve Cirera, Cristobal Gasto

NR60 Noncompliance in Heart Transplant Patients
Adriana R. Vasquez, M.D., Sheila Towsey, M.D., William N. Friedrich, Ph.D., Christopher McGregor, M.D.

NR61 Seasonal Variation in Mood and Behavior in Chinese Medical Students
Ling Han, M.D., Keqin Wang, M.D., Yiren Cheng, M.D., Zhaoyun Du, M.D., Norman E. Rosenthal, M.D.

NR62 Mental Health Clinicians' Viewpoints of Psychological Wellness Differing by Race
Jeremy A. Herschler, M.D., Lisa B. Dixon, M.D.

NR63 Depression in a Primary Care Setting: Are There Ethnic Differences?
Isabel T. Lagomasino, M.D., Rachel D. McColl, B.A., Rosemarie Mulroy, B.A., Junko Kaji, B.A., Asha I. Parekh, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR64 Suicidal Ideation and Attempts in an Arctic Community
John M. Haggarty, M.D., Zack Z. Cernovsky, Ph.D., Harold Merskey, M.D., Patricio Kermeen, R.N.

NR65 Famotidine: A Supplemental Drug for the Treatment of Schizophrenia
Pinhas N. Dannon, M.D., Elie Lepkifker, M.D., Iulian Iancu, M.D., Reuven Ziv, M.D., Moshe Kotler, M.D., Joseph Zohar, M.D.

NR66 Cholesterol and Suicide Attempts in Panic Disorder and MDD
Pinhas N. Dannon, M.D., Iulian Iancu, M.D., Amir Poreh, Ph.D.

NR67 Pindolol Augmentation for Treating Refractory OCD
Pinhas N. Dannon, M.D., Shmuel Hirschmann, M.D., Iulian Iancu, M.D., Yehuda Sasson, M.D., Leon J. Grunhaus, M.D., Joseph Zohar, M.D.

NR68 Physical Illness Prompting Psychiatric Admission
Je Chun Yu, M.D., O. Soo Han, M.D., In-Ho Park, M.D., Chul Lee, M.D.

NR69 Diagnosing Pancreatic Cancer in Depression: Cost-Benefit Analysis
Carlos Blanco-Jerez, M.D., Cletus S. Carvalho, M.D., Roumen Nikolov, M.D.

NR70 Assessment of Mood Fluctuations in Individual Cases
Jeffrey M. Pyne, M.D., Martin Paulus, M.D., Matthew S. Foley, B.A., Kelly N. Yoo

NR71 Lifetime Psychiatric Comorbidity in a Large Outpatient Clinic
Shakir R. Meghani, M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.S., Ekkehard Othmer, M.D., Ph.D., William F. Gabrielli, Jr., M.D., Marsha R. Read, Ph.D.

NR72 Tryptophan Depletion During Continuous CSF Sampling via Indwelling Lumbar Catheter in Healthy Human Subjects
Linda L. Carpenter, M.D., George Anderson, Ph.D., Christopher J. McDougle, M.D., Paul D. Kirwin, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D.

NR73 Effects of White Matter Hyperintensities on Neuropsychiatric Symptoms in Patients with Alzheimer's Disease
Sabrina R. Simpson, B.A., Alexander P. Auchus, M.D., William M. McDonald, M.D., John L. Woodard, Ph.D., Ralph B. Reed, B.S.E.

NR74 Treating Comorbid Tourette's and OCD with Newer Psychotropics
Parveen Kumar, M.D., Jeffrey A. Ali, M.D.

NR75 Post-Stroke Depression and Location of Lesion: A Systematic Review
Ebrahim Haroon, M.D., Sally J. Vegso, M.S., Pierre B. Fayad, M.D., Robert T. Malison, M.D., Christopher J. McDougle, M.D., George R. Heninger, M.D.

NR76 The Immune Function and Schizophrenia
Juyeon Cho, M.D., Doobyung Park, M.D., Kilhong Lee, M.D.

NR77 Mental Health Service Variations in an HMO
Jonathan C. Lockhart, M.D., Jack D. Burke, Jr., M.D., Raghavan Srinivasan, Ph.D., Nadine Zimmerman, M.S.

NR78 Construct Validity of SF-36 Psychiatric Subscales
Ghazala N. Ahmed, M.D., David Rudd, Ph.D., Kimberly C. Burke, M.S., Cheryl Preece, M.S.

NR79 Suicide Assessment in the Elderly
Lisa Fazzolari, D.O.

NR80 A Self-Injury Motivation Scale: The Characteristics and Motivation of Self-Injurious Behavior
Elizabeth A. Osuch, M.D., Frank W. Putnam, Jr., M.D.

NR81 Mental Defense Mechanisms Predicting PTSD
Philippe J.R. Birmes, M.D., Pierre A. Delpla, M.D., Barbara A. Warner, M.D., Philippe Cadilhac, M.D., Laurent Schmitt, Ph.D.

NR82 Dysfunctional Attitudes and Anger Attacks in Depression
Maya Spillmann, M.D., Andrea R. Kolsky, B.A., Jane K. Burger, B.A., Jonathan E. Alpert, M.D., Joel A. Pava, Ph.D., John D. Matthews, M.D., Maurizio Fava, M.D.

NR83 The Psychiatric Sequelae of Civilian Trauma: A Meta-Analysis
E. Sherwood Brown, M.D., Mark Fulton, M.D., Frederick Petty, M.D., Aidela Wilkeson, M.D.

NR84 Interruption or Premature Termination of ECT
Kathryn M. Connor, M.D., Andrew D. Krystal, M.D., Richard D. Weiner, M.D., Virginia H. Lindahl, B.A.

NR85 ECT Stimulus Intensity: How Much Is Enough?
Margaret D. Dean, M.D., Andrew D. Krystal, M.D., Richard D. Weiner, M.D., Kathryn M. Connor, M.D., Virginia H. Lindahl, B.A., W. Ryan Massie

NR86 Cost-Benefit of Accelerating the Effect of an Antidepressant
Maria B. Tome, M.D., Michael T. Isaac, M.D.

NR87 Psychiatrists' Perceptions of Religion and Its Association with Life Satisfaction
Sylvia Gheorghiu, M.D., Michael F. Godschalk, M.D., Thomas Mulligan, M.D.

NEW RESEARCH

Monday, May 19, 1997, 1:00 p.m.-2:30 p.m.

New Research 2 - Oral/Slide Session - Room 11A, Upper Level, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

Chp.. Glenn C. Davis, M.D.

NR88	Cocaine Intoxication at Psychiatry Emergency Department Presentation, Hospital Admission and Length of Stay Glenn W. Currier, M.D., Michael H. Allen, M.D.	1:00 p.m.
NR89	Ten-Year Outcomes of Familial Male Alcoholics Sunil Chhibber, M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.S., Barbara J. Powell, Ph.D., Barry I Liskow, M.D., Jan L. Campbell, M.D.	1:15 p.m.
NR90	Are Repeated Episodes of Sydenham's Chorea Associated with Increased Risk of OCD? Fernando R. Asbahr, M.D., Andre B. Negrao, M.D., Jose A. daPaz, M.D., Maria J. Marques-Dias, M.D., Maria H.B. Kiss, M.D., Valentim Gentil, M.D.	1:30 p.m.
NR91	Volumetric Superior Temporal Gyrus Abnormality in Schizotypal Personality Disorder Chandlee C. Dickey, M.D., Martha E. Shenton, Ph.D., Martina M. Voglmaier, Ph.D., Margaret Niznikiewicz, Ph.D., Larry J. Seidman, Ph.D., Robert W. McCarley, M.D.	1:45 p.m.
NR92	An Association Study of Neurotrophin-3 Gene's Polymorphism with Schizophrenia Yu-Sang Lee, M.D., Jin-Hee Han, M.D., Young-Gyu Chai, Ph.D., Hyeong-Seob Kim, M.D., Jung-Sik Lee, M.D., Byung-Hwan Yang, M.D.	2:00 p.m.
NR93	Linkage Disequilibrium Between Bipolar Disorder and Markers on Chromosome 18p11.2 Alan R. Sanders, M.D., Takeo Yoshikawa, M.D., Judith A. Badner, M.D., Wade H. Berrettini, M.D., Elliott S. Gershon, M.D., Sevilla D. Detera-Wadleigh, Ph.D.	2:15 p.m.

NEW RESEARCH

Monday, May 19, 1997, 1:00 p.m.-2:30 p.m.

New Research 3 – Oral/Slide Session – Room 11B, Upper Level, Convention Center

YOUNG INVESTIGATORS' ORAL/SLIDE SESSION

Chp.: Harold Alan Pincus, M.D.

NR94	Neuropsychological Functioning in Panic Disorder Julie Akiko Gladsjo, Ph.D., Mark H. Rapaport, M.D., Rebecca A. McKinney, B.A., Anthony Rabin, M.S., Michelle D. Auerbach, M.S., Lewis L. Judd, M.D.	1:00 p.m.
NR95	A Comparison of the Efficacy of Alprazolam-XR Plus Cognitive-Behavioral Therapy Versus Cognitive-Behavioral Therapy Plus Placebo for Acute Treatment at Three-Month Follow-up Michelle D. Auerbach, M.S., Mark H. Rapaport, M.D., Julie Akiko Gladsjo, Ph.D., Rebecca A. McKinney, B.A., Todd Oliver, M.A., Lewis L. Judd, M.D.	1:15 p.m.
NR96	Trauma Symptoms, Life Stress and Salivary Cortisol in Metastatic Breast Cancer Patients Lisa Butler, Ph.D., Cheryl Koopman, Ph.D., Sandra E. Sephton, M.S., Catherine Classen, Ph.D., David Spiegel, M.D.	1:30 p.m.
NR97	Effectiveness of Wellbutrin for Smoking Cessation for Smokers with a History of Major Depression Kara E. Hayford, M.D., Christi A. Patten, Ph.D., Teresa A. Rummans, M.D., Darrell R. Schroeder, M.S.	1:45 p.m.
NR98	Anemia and Macrocytosis in the Prediction of Serum Folate and B12, and Outcome in Major Depression David Mischoulon, M.D., Jane K. Burger, B.A., Maya K. Spillman, M.D., Andrew A. Nierenberg, M.D., John J. Worthington III, M.D., Maurizio Fava, M.D., Jonathan E. Alpert, M.D.	2:00 p.m.
NR99	Predictors of Treatment Response in Pregnancy and Postpartum Disorders James R. Strader, B.S., Alexis M. Llewellyn, B.A., Zachary N. Stowe, M.D., Charles B. Nemeroff, M.D.	2:15 p.m.

NEW RESEARCH

Monday, May 19, 1997, 3:00 p.m.-5:00 p.m.

New Research 4 – Poster Session – Special Events Area, Upper Level, Convention Center

YOUNG INVESTIGATORS' POSTER SESSION

Moderator.: David M. McDowell, M.D.

NR100 Prevalence of Polypharmacy in Patients on Antidepressants and Its Relation with Drugs and Drug Interaction
Mujeeb U. Shad, M.D., Sheldon H. Preskorn, M.D., Cheryl A. Carmichael, B.B.A.

NR101 Tramadol for Treatment-Refractory OCD
Nathan A. Shapira, M.D., Paul E. Keck, Jr., M.D., Toby D. Goldsmith, M.D., Brian J. McConville, M.D., Patrick J. Haggard, Susan L. McElroy, M.D.

NR102 Methylphenidate and Motor Organization in Children with ADHD
Johanne Renaud, M.D., Michelle Bourassa, M.Ps., Virginia I. Douglas, Ph.D., Gilles Pelletier, M.D., Guy Geoffroy, M.D., Philippe Robaey, M.D.,

NR103 Lamotrigine Treatment and Serotonin Receptor Function
I.S. Shiah, M.D., Lakshmi N. Yatham, Athanasios P. Zis, M.D., Raymond W. Lam, M.D.

NR104 SSRIs Side Effects: Incidence and Management
Carlos Blanco-Jerez, M.D., James J. Daly, M.D.

NR105 Quantitative Assessment of Tremor in Depressed Patients Receiving Lithium Augmented by Paroxetine or Amitriptyline
Rocco M. Zaninelli, M.D., Michael Bauer, M.D., Marc Jobert, Ph.D.

NR106 Effect of Risperidone on Cognitive Function in Schizophrenic Patients: An Open-Label Study
Demetra Pappas, B.S., Nina Leventhal, B.A., Joseph Langlois, M.A., David N. Osser, M.D., Howard H. Chang, M.D., Ileana Berman, M.D.

NR107 Sertraline Treatment of Diabetic Neuropathy
Isabel M. Jimenez, M.D., Paul J. Goodnick, M.D., Adarsh Kumar, Ph.D.

NR108 Ethnicity, Red Blood Cell and Plasma Lithium Concentrations
Richard T. Kotomori, Jr., M.D., Keh-Ming Lin, M.D., Paul Fu, M.D., Mike Smith, M.D.

NR109 Movement Disorder and Functional Impairment in the Middle-Aged and Elderly
John H. Eastham, Pharm.D., Thomas L. Patterson, Ph.D., Enid Rockwell, M.D., Jovier D. Evans, Ph.D., Jonathan P. Lacro, Pharm.D., Dilip V. Jeste, M.D.

NR110 The Safety and Efficacy of Paroxetine and Amitriptyline Augmentation of Lithium in the Treatment of Major Depression
Michael Bauer, M.D., Rocco M. Zaninelli, M.D., Bernd Mueller-Oerlinghause, M.D., Wolfgang Meister, M.D.

NR111 Prescribing Trends of Antidepressants in Bipolar Depression: Phase II
Sunila Pandit, M.D., Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D., Rajesh Narendran, M.D., Alex Madrid, M.A., Eric Tomasini, B.A.

NR112 Olanzapine Crossover in Stable Outpatients
Laura J. Dalheim, M.D., Peter J. Weiden, M.D., Ralph Aquila, M.D., Janet Standard, R.N., Marianne Emanuel, R.N., Annette Zygmunt

NR113 Divalproex in Medication-Naive Bipolar II Depression
Mirene Winsberg, M.D., Sally G. Degolia, M.D., Connie M. Strong, M.S., Terence A. Ketter, M.D.

NR114 Open Multicenter Study with Zoplicone in Insomniac Patients
Guillermo Tortora, M.D.

NR115 Effects of Discontinuing Long-Term Antidepressant Treatment of Major Depression: A Meta-Analysis
Adele C. Viguera, M.D., Ross J. Baldessarini, M.D., Jonathan Friedberg, M.D.

NR116 Risks of Discontinuing Maintenance Treatment in Pregnant Women with Bipolar Disorder
Adele C. Viguera, M.D., Ruta M. Nonacs, M.D., Lee S. Cohen, M.D.

NR117 Risperidone Metabolism and Drug Interaction in Treatment-Refractory Patients
Jayme A. Bork, D.O., Thea Rogers, Pharm D., Peter Wedlund, Ph.D., Wendy Chou, Pharm. D., Jose de Leon, M.D.

NR118 SSRI Interactions with Warfarin
John Snuggs, M.D., William J. Meek, M.D., Cheryl Preece, M.S.

NR119 The Tolerability of Oral Loading of Divalproex Sodium in Acute Mania
James M. Martinez, B.A., James M. Russell, M.D., Robert M.A. Hirschfeld, M.D.

NR120 Survival Analysis of Olanzapine Treatment
Svetlana L.J. Milenkovic, M.D., Neil Conacher, M.D.

NR121 Serotonin Transporter Blocking Properties of Nefazodone Assessed by Measurement of Platelet Serotonin
Meena Narayan, M.D., George Anderson, Ph.D., J. Craig Nelson, M.D.

NR122 Divalproex Treatment of Mania in Elderly Patients
Meena Narayan, M.D., Simona Noaghiul, M.D., J. Craig Nelson, M.D.

NR123 Maladaptive Schemas and Axis II Personality Traits in Survivors of Sexual Abuse with PTSD
Naureen Atiullah, M.D., Caron Zlotnick, Ph.D., M. Tracie Shea, Ph.D., Katy Amory, B.A.

NR124 Deficits of Recall in Depressed Patients: Evidence for a Subcortical Dysfunction in Major Depression
P.H. Fossati, M.D., Be Deweer, Ph.D., Na Raoux, Ph.D., J.F. Allilaire, M.D.

NR125 Preliminary Analysis of a Self-Report Questionnaire of Affective Temperament
Rustin R. Berlow, M.D., Mauro V. Mendlowicz, M.D., Jose Montes, M.D., Mark H. Rapaport, M.D., John R. Kelsoe, Jr., M.D., Hagop S. Akiskal, M.D.

NR126 Psychotic Depression as a Separate Entity
Marcelo F. Mello, Ph.D., Helio Elkis, Ph.D., Vania Baggio, M.D., Monica G. Cereser, M.D.

NR127 Kindling Effect in Bipolar Disorder
Diego J. Palao, M.D., Myriam Cavero, M.D., Inma Jodar, Ph.D., Manuel M. Marquez, M.D., Carlos Lopez, M.D.

NR128 The Recognition and Diagnosis of Bipolar II Disorder
Phillip W. Antunes, M.D., Jack D. Burke, Jr., M.D., Kimberly C. Burke, M.S., Cheryl Preece, M.S., Sheree Atkinson

NR129 Frontal Cognitive Deficit and Psychomotor Retardation
Paul Jacques, M.D., Philippe Baruch, M.D., Sophie Lemlin, Ph.D.

NR130 Gabapentin for Mood Instability Associated with Migraine
Turai S. Kumaran, M.D., Manohar K. Shetty, M.D., David J. Lynn, M.D.

NR131 Affective Symptoms from Corticosteroids: A Hypothesis for Bipolar Disorder
E. Sherwood Brown, M.D., Trisha Suppes, M.D., David A. Khan

NR132 Catecholamine Depletion in Euthymic Subjects with a History of Major Depression
Robert M. Berman, M.D., Helen L. Miller, M.D., Angela C. Cappiello, M.D., Amit Anand, M.D., Dan A. Oren, M.D., Dennis S. Charney, M.D.

NR133 Analysis of Psychomotor Function Using Q-Sort Methodology
Shragit Glassman, M.D., Neil Westrich, M.D., Michael Bagby, Ph.D., Kathryn Parker, Anthony J. Levitt, M.D.

NR134 The Anticonvulsant Lamotrigine in Treatment-Resistant Manic-Depressive Illness
Jonathan Sporn, M.D., Gary S. Sachs, M.D.

NR135 Suicidal Ideation During Pregnancy
Cassandra P. Morabito, M.Ed., Lee S. Cohen, M.D., Jennie W. Bailey, B.A., Mary H. Collins, M.D., Jerrold F. Rosenbaum, M.D.

NR136 A Comparison of Obstetrical Complication Rates Among Bipolar Subgroups
Claudia F. Baldassano, M.D., Una Jain, B.A., Amy E. Shriver, B.A., Gary S. Sachs, M.D.

NR137 Chronic Choline Administration Does Not Increase Brain Choline:Creatine
Christina M. Demopulos, M.D., Perry F. Renshaw, M.D., Gary S. Sachs, M.D., Una Jain, B.A., Andrew L. Stoll, M.D., Amy E. Shriver, B.A.

NR138 Antidepressant Withdrawal-Induced Mania
Amy E. Shriver, B.A., Claudia F. Baldassano, M.D., Christina M. Demopulos, M.D., Una Jain, B.A., Gary S. Sachs, M.D.

NR139 Anger Attacks in Bipolar Depression Versus Unipolar Depression
Una Jain, B.A., Vinita C. Leslie, M.A., Bronwyn R. Keefe, B.A., Gary S. Sachs, M.D., Maurizio Fava, M.D.

NR140 SAD Treatment: Light Box Versus Dawn Simulator, A.M. Versus P.M.
Paul Desan, M.D., Christine J. Truman, B.A., Una Jain, B.A., Claudia F. Baldassano, M.D., Dina R. Hirshfeld, Ph.D., Gary S. Sachs, M.D.

NR141 Comorbidity of Social Phobia and Personality Disorders
Antonio E. Nardi, M.D., Ivan Figueira, M.D., Marcio V. Versiani, M.D.

NR142 Discontinuation of Long-Term Benzodiazepine Use: Predictive Model of Success in a Double-Blind, Controlled-Study
Elie G. Hantouche, M.D., Luc Jacob, M.D., Denis Comet, M.D., Professor Julien-Dan Guelfi

NR143 Prevalence of Psychopathology in Families of Patients with OCD
Kurt K. Hubbard, B.A., Andrew Shack, M.A., Juliana R. Lachenmeyer, Ph.D., Regina Ucello, B.A., Kevin B. Handley, M.A.

NR144 The Effect of CCK-4 in Social Phobia and OCD
Martin A. Katzman, M.D., Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., F. Vaccarino, Ph.D., Margaret A. Richter, M.D.

NR145 Effects of Citalopram Treatment on Behavioral, Cardiovascular and Neuroendocrine Response to CCK Tetrapeptide Challenge in Panic Disorder Pts
Jakov Shlik, M.D., Anu Aluoja, M.A., Veiko Vasar, M.D., Eero Vasar, M.D., Toomas Podar, M.D., Jacques Bradwejn, M.D.

NR146 Psychiatric Diagnoses of Veterans Seeking Treatment in a Trauma Recovery Unit
Cenk Tek, M.D., Stephen F. Bono, Ph.D., Pedro E. Martinez, M.D.

NR147 Dissociative Symptomatology in Patients with OCD and PTSD
Munazzah Khawaja, M.D., Teresa A. Pigott, M.D., James M. Martinez, B.A., Dennis L. Murphy, M.D., Sheila M. Seay, M.A., Jean P. Goodwin, M.D.

NR148 Sensory Phenomena in Sydenham's Chorea
M. Yanki Yazgan, M.D., Ayse Arman, M.D., Sennur Zaimogl, M.D., Mefkure Eraksoy, M.D.

NR149 Age of Onset of OCD as a Predictive Factor of Response to Clomipramine
Roseli Gedanke Shavitt, M.D., M.Conceicao do Rosar Campos, M.D., Euripedes C. Miguel, M.D.

NR150 Early-Onset OCD: A Different Subtype
M. Conceicao do Rosar Campos, M.D., Roseli Gedanke Shavitt, M.D., Marcos Tomanik Mercadante, M.D., Euripedes C. Miguel, M.D.

NR151 Implicit and Explicit Memory for Threatening Stimuli in Panic Disorder Patients
Rebecca A. McKinney, B.A., Julie Akiko Gladsjo, Ph.D., Mark H. Rapaport, M.D., Michelle D. Auerbach, M.S., Anthony Rabin, M.S., John Lucas, Ph.D.

NR152 Comparison of Sertraline and Fluoxetine on Quality of Life in Depressed Outpatients
Daniel Sechter, Sylvie Troy

NR153 Evaluation of Dreams in Combat-Related PTSD
Karin F. Esposito, M.D., Amparo B Benitez, D.O., Thomas A. Mellman, M.D.

NR154 Impact of Alprazolam on Neuropsychological Functioning in Panic Disorder
Julie Akiko Gladsjo, Ph.D., Mark H. Rapaport, M.D., Rebecca A. McKinney, B.A., Anthony Rabin, M.S., Michelle D. Auerbach, M.S., Lewis L. Judd, M.D.

NR155 A Study of the Sampoong Disaster Survivors in Korea
Byung-Joo Ham, M.D., Min Soo Lee, M.D., Dong-Il Kwak, M.D., Joon-Sang Lee, M.D.

NR156 Hypochondriasis as an Obsessive-Compulsive Spectrum Disorder
Martin Aigner, M.D., Ulrike Demal, Ph.D., Werner Zitterl, M.D., Michael Bach, M.D.

NR157 Temporal Relationship Between Alexithymia and Somatization During Inpatient Treatment
Michael Bach, M.D., Ulrike Lupke, Ph.D., Ralph Schaible, Ph.D., Detlev O. Nutzinger, M.D.

NR158 Screening for DSM-IV Somatoform Disorders in Chronic Pain Patients
Michael Bach, M.D., Martin Aigner, M.D., Sandra Krones, Anna Spacek, M.D., Hans-Georg Kress, M.D.

NR159 The Gene Encoding Tryptophan Hydroxylase Is Intact in SAD, OCD, Anorexia Nervosa and Alcoholism
Ling Han, M.D., Norman E. Rosenthal, M.D., David Nielsen, Ph.D., Markku I. Linnoila, M.D., David S. Goldman, M.D., Kimberly Jefferson, B.S., Walter H. Kaye, M.D., Dennis L. Murphy, M.D., Anil K. Malhotra, M.D., Giovouuc Cosseuo, M.D., Marty Altemus, M.D., Matti Virkkunen, M.D., Alexandro Rotondo, M.D., David Picker, M.D., Julie Humphries, M.D.

NR160 Stimulant Effects on Acoustic Startle in ADD
Arthi Parwani, M.D., Michal Kunz, M.D., Lenard A. Adler, M.D., Elsa Bartlett, Ed.D., Erica J. Duncan, M.D., Rajiv Rajan, M.D.

NR161 Relationships Among Psychopathology, Gender and Monoamine Metabolism in Chronic Schizophrenia
Dae-Yeob Kang, M.D., John Poole, Ph.D., Sophia Vinogradov, M.D., Jason Willis-Shore, B.A., Faith Corwin, Ph.D., Margeaux Lieberman, B.A., Elysa Marco, B.A.

NR162 Responses to Clonidine and Pre- and Post-Menopausal Women
Ann M. Woo-Ming, M.D., Robert L. Trestman, M.D., Andrew Aronson, M.D., Larry J. Siever, M.D.

NR163 Low Cholesterol and Violence
Rizwan M. Mufti, M.D., Richard Balon, M.D., Cynthia Arfken, Ph.D.

NR164 Prolactin Levels of Premenopausal Women Treated with Risperidone and Conventional Neuroleptics
Renuka Ananthamoorthy, M.D., Giovanni Caracci, M.D.

NR165 Behavioral and Biological Effects of Acute Depletion of Plasma Tryptophan in Patients with Alcoholism and in Normal Volunteers
Wendol A. Williams, M.D., Daniel W. Hommer, M.D., Susan Shoaf, Ph.D., David S. Goldman, M.D., Christopher Geyer, R.N., Markku I. Linnoila, M.D.

NR166 Differences of Eye Tracking Pattern in Schizophrenia, Affective and Schizoaffective Disorders: A Lab Investigation Using Electrooculography
Ingo Gerdsen, M.D.

NR167 Hemispheric Asymmetry of Benzodiazepine Receptor Binding Sites in Schizophrenia: A Study with I-Iomazenil SPECT
Ingo Gerdsen, M.D., Joerg Pinkert, M.D., Liane Oehme, M.A., Bettina Ripke, M.A., Klaus Zoephel, M.D., U. Neumann, M.D.

NR168 New Windows into Bipolar Illness: Serial Perfusion MRI Scanning in Rapid-Cycling Bipolar Patients
Andrew M. Speer, M.D., Vidya H. Upadhyaya, M.D., Daryl E. Bohning, Ph.D., S. Craig Risch, M.D., Diana J. Vincent, Ph.D., Mark S. George, M.D.

NR169 Neuroimaging in Geriatric Psychiatry: A Review
Srinivasan S. Pillay, M.D., Scott L. Rauch, M.D., Perry F. Renshaw, M.D., Stephanie L. Rose, B.A.

NR170 MRI/Event-Related Potential Abnormalities in First-Episode Psychosis
Yoshio Hirayasu, M.D., Martha E. Shenton, Ph.D., Dean F. Salisbury, Ph.D., Chandlee C. Dickey, M.D., Iris A. Fischer, B.A., Robert W. McCarley, M.D.

NR171 Relationships Between Corpus Callosum Size, Cingulate Gyrus Metabolic Rate and Symptoms of Schizophrenia
Jack E. Downhill, Jr., M.D., Monte S. Buchsbaum, M.D., M. Mehmet Haznedar, M.D., Tse Chung Wei, Ph.D., Jacqueline Spiegel-Cohen, M.S.

NR172 Temporal Lobe Volume in Schizotypal Personality Disorder and Schizophrenia
Jack E. Downhill, Jr., M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, M.B., Stacey Barth, M.S., Sonia Lees-Roitman, M.S., Melissa Nunn, B.S., Larry J. Siever, M.D.

NR173 The Clonidine Challenge Test in Depression: A PET Study in Women
Cynthia H. Fu, M.D., Gregory M. Brown, M.D., Shitij Kapur, M.D., Alan Wilson, Ph.D., Sylvain Houle, M.D.

NR174 Goal-Oriented Cognitive-Behavior Therapy in a Group Setting for Treatment of Late-Life Depression
Ellen J. Klausner, Ph.D., John F. Clarkin, Ph.D., Lisa Speilman, Ph.D., George S. Alexopoulos, M.D., Christopher Pupo, B.A., Robert C. Abrams, M.D.

NR175 Acute Dystonia in Two Demented Patients
Thomas M. Magnuson, M.D., William J. Burke, M.D., William H. Roccaforte, M.D., Steven P. Wengel, M.D.

NR176 Use of Mood Agents in Bipolar Geriatric Patients
Diana R. Sanderson, M.D., Sudeep Chakravorty, M.D., Michele T. Pato, M.D.

NR177 White Matter Lesions in Elderly Depressed Subjects
Eric J. Lenze, M.D., Yvette I. Sheline, M.D., Dewitte Cross, M.D., Daniel Lin, B.S., Michael Vannier, M.D.

NR178 A Survey of Depression Knowledge/Understanding in Nursing Home Aides
Luis G. Allen, M.D., Blaine S. Greenwald, M.D., Anjan Chatterjee, M.D., Donald H. Gemson, M.D.

NR179 T2 Signal Intensities in Alzheimer's Disease
Ramin V. Parsey, M.D., K. Ranga Krishnan, M.D.

NR180 Clinical Implications of Comorbid Antisocial BPD in Older Patients with Substance Use Disorders
Trevia F. Hayden, M.D., Joseph G. Liberto, M.D., Edward Shearin, Ph.D., Paul E. Ruskin, M.D.

NR181 Temperament and Treatment Response in Major Depressive Disorder
Julie R. Newman, Scott E. Ewing, D.O., Rachel D. McColl, B.A., Joseph S. Borus, B.A., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Maurizio Fava, M.D.

NR182 Effect of Crisis Treatment on Functional Improvement
Douglas R. Dolnak, D.O., Mark H. Rapaport, M.D., William B. Hawthorne, M.D.

NR183 Effectiveness of a Psychiatric Pain Clinic
John V. Anooshian, M.D., Jon M. Streltzer, M.D., Deborah Goebert, M.S.

NR184 The Arizona Sexual Experience Scale: Validity and Reliability
Cynthia A. McGahuey, A.A., Alan J. Gelenberg, M.D., Cindi A. Laukes, M.F.A., Rachel Manber, Ph.D., Kathy M. McKnight, B.S., Francisco A. Moreno, M.D., Pedro L. Delgado, M.D.

NR185 ECT Outcome of Dually Diagnosed Patients
Judy S. Uy, M.D., Ramanbhai C. Patel, M.D., Ali Khadivi, Ph.D.

NR186 Aminophylline Lengthens Short Seizures During ECT
Liat Stern, M.D., Pinhas N. Dannon, M.D., Shmuel Hirschmann, M.D., Daniela Amytal, M.D., Leon J. Grunhaus, M.D.

NR187 Anxiogenic Effects of Naloxone Hydrochloride and Sodium Lactate in Normal Volunteers
Smit S. Sinha, M.D., Donald F. Klein, M.D.

Research Funding Poster Session

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

David Shore, M.D., NIMH, Division of Clinical and Treatment Research; Richard K. Fuller, M.D., NIAAA, Division of Clinical and Prevention Research; Tim Condon, Ph.D., NIDA, Office of Science Policy and Communications; Stephen Zukin, M.D., NIDA, Division of Clinical and Services Research; John R. Feussner, M.D., Department of Veterans Affairs, Washington, DC; Thomas B. Horvath, M.D., Veterans Administration, Washington, DC; Earnestine Vanderveen, Ph.D., National Institute on Alcohol Abuse and Alcoholism; Robert M. Post, M.D., National Alliance for the Mentally Ill; Constance E. Lieber, National Alliance for Research on Schizophrenia and Depression.

Not Attending, Sending Information Only

Ronald Abeles, Ph.D., NIA, Behavioral and Social Research Program; Peter Greenwald, M.D., NCI, Division of Cancer Prevention and Control.

NEW RESEARCH

Tuesday, May 20, 1997, 9:00 a.m.-10:30 a.m.

New Research 5 – Oral/Slide Session – Room 11A, Upper Level, Convention Center

PSYCHOPHARMACOLOGY

Chp.: Richard Balon, M.D.

NR188 SSRI Dose Interruption Study: Interim Data — 9:00 a.m.
Sharon L. Blomgren, M.D., William Krebs, Ph.D., Michael Wilson, M.S., Richard Ascroft, R.Ph., Maurizio Fava, M.D., Jerrold F. Rosenbaum, M.D.

NR189 Optimal Length of Continuation Therapy: A Prospective Assessment During Fluoxetine Long-Term Treatment of MDD — 9:15 a.m.
David Michelson, M.D., Frederick W. Reimherr, M.D., Charles M. Beasley, Jr., M.D., Michael Wilson, M.S.

NR190 Olanzapine Versus Risperidone in the Treatment of Schizophrenia and Other Psychotic Disorders — 9:30 a.m.
Pierre V. Tran, M.D., Gary D. Tollefson, M.D., Susan Hamilton, M.S.

NR191 Effects of First Trimester Fluoxetine Exposure on the Newborn — 9:45 a.m.
David J. Goldstein, M.D., Lois A. Corbin, R.N., Karen L. Sundell, B.S.

NR192 Placental Passage of Antidepressants — 10:00 a.m.
Zachary N. Stowe, M.D., Alexis M. Llewellyn, B.A., James R. Strader, B.S., C.D. Kilts, Ph.D., James C. Ritchie, Ph.D., Charles B. Nemeroff, M.D.

NR193 Naltrexone in the Treatment of Nicotine Dependence: A Preliminary Study — 10:15 a.m.
Stephanie S. O'Malley, Ph.D., Suchitra Krishnan-Sarin, Ph.D., Borislav Meandzija, M.D.

NEW RESEARCH

Tuesday, May 20, 1997, 9:00 a.m.-10:30 a.m.

New Research 6 – Oral/Slide Session – Room 11B, Upper Level, Convention Center

MOOD DISORDERS AND PREMENSTRUAL DYSPHORIC DISORDERS

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

NR194 Prospective Assessment of Mood Disorders in HIV Infection — 9:00 a.m.
Paula Bird, M.S.N., Jane Leserman, Ph.D., Diana O. Perkins, M.D., Susan G. Silva, Ph.D., Dwight L. Evans, M.D., Robert N. Golden, M.D.

NR195 Prevalence of Dysthymia in Primary Care — 9:15 a.m.
Meir Steiner, M.D., Gina Browne, Ph.D., Jacqueline Roberts, M.Sc., Edward J. Dunn, Ph.D., Barbara A. Bell, M.D., Ellen Jamieson, M.Ed.

NR196 Treatment Response in Dysthymic Patients With and Without a History of MDD — 9:30 a.m.
Maurizio Fava, M.D., A. John Rush, M.D., Richard C. Shelton, M.D., Michael E. Thase, M.D., Lorrin M. Koran, M.D.

NR197 Ten-Year Cumulative Probability of Recurrence After Recovery from an Index Episode of MDD — 9:45 a.m.
Timothy I. Mueller, M.D., Andrew C. Leon, Ph.D., Martin B. Keller, M.D., David A. Solomon, M.D., Jean Endicott, Ph.D., Meredith Warshaw, M.S.S.

NR198 Treatment of Premenstrual Dysphoric Disorder with Sertraline During the Luteal Phase: A Randomized, Double-Blind Placebo-Controlled Crossover Trial — 10:00 a.m.
Steven A. Young, M.D., Peyton H. Hurt, M.D., David M. Benedek, M.D., Robin S. Howard, M.A.

NR199 A Controlled-Study of Light Therapy in Premenstrual Dysphoric Disorder — 10:15 a.m.
Raymond W. Lam, M.D., Diana Carter, M.B., Shaila Misri, M.D., Annie Kuan, B.A., Lakshmi N. Yatham, Athanasios P. Zis, M.D.

NEW RESEARCH

Tuesday, May May 20, 1997, 12 noon-2:00 p.m.

New Research 7 – Poster Session – Special Events Area, Upper Level, Convention Center

PSYCHOPHARMACOLOGY, SOMATIC THERAPIES, COMBINED PHARMACOLOGY AND PSYCHOTHERAPY, HISTORICAL QUESTIONS, AND ETHICS

Moderator: Elisa Triffleman, M.D.

NR200 Abrupt Discontinuation of Fluoxetine: A Randomized, Placebo-Controlled Study
David Michelson, M.D., Roland Onawala, Ph.D., Charles M. Beasley, Jr., M.D.

NR201 Fluoxetine Versus Desipramine in Depressed Females with Advanced Cancers
Steven J. Romano, M.D., Rosalinda Tepner, R.Ph., Michael Wilson, M.S.

NR202 Effectiveness of Fluoxetine Therapy in Bulimia Nervosa Regardless of Baseline Depression
David J. Goldstein, M.D., Michael Wilson, M.S., Richard Ascroft, B.S.

NR203 Effect of Fluoxetine Therapy on Weight in Depressed Geriatric Patients
David J. Goldstein, M.D., Charles M. Beasley, Jr., M.D., Michael Wilson, M.S.

NR204 Olanzapine Versus Haloperidol in the Treatment of First-Episode Psychosis
Todd Sanger, Ph.D., Gary D. Tollefson, M.D., Jeffrey A. Lieberman, M.D., Mauricio Tohen, M.D.

NR205 Gender Differences in the Response of Olanzapine Versus Haloperidol in the Treatment of First-Episode Psychosis
Mauricio Tohen, M.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D.

NR206 Olanzapine Versus Haloperidol in the Treatment of Schizoaffective Bipolar Patients
Mauricio Tohen, M.D., Todd Sanger, Ph.D., Gary D. Tollefson, M.D., Susan L. McElroy, M.D.

NR207 Fluoxetine Plus Pindolol in Unipolar Major Depression
Victor Perez, M.D., Inmaculada Gilaberte, M.D., Douglas Faries, Dolors Puigdemont, M.D., Enric Alvarez, M.D., Francesc Artigas, Ph.D.

NR208 A Randomized, Double-Blind Comparison of Mirtazapine and Fluoxetine in Patients with Major Depression
David Wheatley, M.D., Charlotte Kremer, M.D.

NR209 Fluoxetine Safety in Patients with Heart Disease
Steven P. Roose, M.D., Alexander H. Glassman, M.D., Evelyn Attia, M.D., Sally Woodring, R.N., Elsa Giardina, M.D., J. Thomas Bigger, Jr., M.D.

NR210 Early Morning, Short-Acting Beta-Blockers as Treatment for Winter Depression
Christina C. Norman, M.A., David S. Schlager, M.D.

NR211 Olanzapine Response in Acute Schizophrenia, Schizoaffective Disorder and Psychotic Mood Disorders
Carlos A. Zarate, Jr., M.D., Rajesh Narendran, M.D., Alex Madrid, M.A., Arielle Berman, B.Sc., James Greaney, Pharm.D., Max Sederer, B.A.

NR212 Perinatal Outcome Following Fluoxetine Exposure: A Preliminary Report
Lee S. Cohen, M.D., Lynn R. Grush, M.D., Jennie W. Bailey, B.A., Jerrold F. Rosenbaum, M.D.

NR213 Pindolol Acceleration of SSRI Antidepressants: A Six-Month Study
Michael T. Isaac, M.D., Maria B. Tome, M.D.

NR214 Treatment-Resistant Schizophrenia: Efficacy of Risperidone Versus Haloperidol
Donna Ames, M.D., William C. Wirshing, M.D., Barringer D. Marshall, Jr., M.D., Michael F. Green, Ph.D., Susan R. McGurk, Ph.D., Jim Mintz, Ph.D., Stephen R. Marder, M.D.

NR215 Loss of Initial Response to Risperidone Treatment
Jennifer L. Francis, B.S., Michael S. Shutty, Ph.D., Robert A. Leadbetter, M.D.

NR216 (3H)RY-80, A Selective Radioligand for GABA-A Receptors with Alpa-5 Subunits
Rona J. Hu, M.D., Christine Cook, B.S., Stephen Hurt, Ph.D., Ruiyan Liu, Ph.D., James M. Cook, Ph.D., Phil Skolnick, Ph.D.

NR217 Personality and SSRI Treatment
Lee A. Kelley, M.D., Marian Hjelmfelt, Ph.D., Arthur Goodwin, M.S.

NR218 Continuity of Medication in a Mental Health System
Daniel J. Luchins, M.D., Randy Malan, R.Ph., Patricia Hanrahan, Ph.D., John Harris, M.A.

NR219 A Meta-Analysis of Anxiety/Agitation in Double-Blind Clinical Trials of Mirtazapine
Jan A. Fawcett, M.D.

NR220 An Open-Label Study of Nefazodone in General Psychiatric Practices: Treatment of Depression with a Focus on Anxiety, Sleep and Sexual Function
Jan A. Fawcett, M.D., John M. Zajecka, M.D., Frederick W. Reimherr, M.D., Susan G. Kornstein, M.D., Frances E. Borian, R.N., John R. Ieni, Ph.D., Darlene N. Jody, M.D.

NR221 Steroselective Excretion of Fluoxetine and Norfluoxetine in Breast Milk and Neonatal Exposure
John Kim, M.S., Shaila Misri, M.D., K. Wayne Riggs, Ph.D., Deirdre M. Ryan, M.B., Diana Carter, M.B., Dan W. Rurak, D.Phil.

NR222 An Open Trial of Once Versus Twice Daily Nefazodone
Paul J. Markovitz, M.D., Susan C. Wagner, M.A.

NR223 Effects of Fluoxetine on Interpersonal Sensitivity in Depressed Outpatients
Brian Baker, M.B., Paul Sandor, M.D., David Newman, M.D., Miney Paquette, P. Dorian, M.D., C. Shapiro, M.D., M.J. Irvine, D.Phil.

NR224 Once-Daily Dosing of Nefazodone for the Treatment of Depression in Patients Previously Stabilized on Twice Daily Dosing
Sheldon H. Preskorn, M.D., Ryan D. Magnus, M.D., Paul J. Markovitz, M.D., Stephen M. Stahl, M.D., Frances E. Borian, R.N., Suha Hamid, Pharm.D., John R. Ieni, Ph.D., Darlene N. Jody, M.D.

NR225 Sertraline Does Not Inhibit Cytochrome P450 (CYP) 3A-Mediated Drug Metabolism in Vivo
Sheldon H. Preskorn, M.D., Jeffrey A. Alderman, Ph.D., David J. Greenblatt, M.D., Dale W. Horst, Ph.D.

NR226 Immediate Crossover from Fluoxetine to Mirtazapine
Ryan D. Magnus, M.D., Kelli Omo, R.N., Mujeeb U. Shad, M.D., Sheldon H. Preskorn, M.D.

NR227 Genetics of Impulsivity and Novelty Seeking
Christopher Reist, M.D., Daiga M. Helmeste, Ph.D., Ryan Vu, Dominic Tran, Siu Wa Tang, M.D.

NR228 Neurodevelopment of Children Exposed In Utero to Antidepressant Drugs
Donna E. Stewart, M.D., Irena Nulman, M.D., Gideon Koren, M.D., Joanne Rouet, Ph.D., Jacob Wolpin, Ph.D., H. Alan Gardner, M.D., Jochen Theis, M.D., Nathalie Kulin, B.Sc.

NR229 Incidence of Sexual Dysfunction in Normal Volunteers on Fluvoxamine Therapy
Anne N. Nafziger, M.D., Angelica Goss-Bley, Joseph S. Bertino, Jr., Pharm.D., Angela D.M. Kashuba, Pharm.D.

NR230 The Long-Term Efficacy and Safety of Quetiapine
Lisa A. Arvanitis, M.D., Ihor W. Rak, M.D.

NR231 Efficacy, Safety and Tolerability of Quetiapine in Elderly Subjects with Psychotic Disorders
Marc Cantillon, M.D., Lisa A. Arvanitis, M.D.

NR232 The Atypical Profile of Quetiapine Is Supported by Its Lack of Sustained Elevation of Plasma Prolactin Concentrations
Lisa A. Arvanitis, M.D., Jeffrey M. Goldstein, Ph.D.

NR233 Quetiapine, a Promising New Antipsychotic Agent: Overview of Safety and Tolerability
Jeffrey M. Goldstein, Ph.D., Lisa A. Arvanitis, M.D.

NR234 Low-Dose Venlafaxine Treatment in Panic Disorder
Laszlo A. Papp, M.D., Smit S. Sinha, M.D., Jeremy D. Coplan, M.D., Jack M. Gorman, M.D.

NR235 Finding and Treating Depression in Alzheimer's Patients: A Study of the Effects on Patients and Caregivers
Eric A. Pfeiffer, M.D., Dorothy Baxter, M.P.H., Betty Candelora, M.P.H.

NR236 Clozapine-Induced Gastrointestinal Symptoms
Maria D.D. Llorente, M.D., Mercedes Gonzalez-Blanco, M.D., Brandon Boswell, B.A.

NR237 ECT Pulsewidth 0.5 Millisecond is More Efficient than 1.0 Millisecond Stimuli
Conrad M. Swartz, M.D., David T. Manly, M.D.

NR238 Betaxolol Is Effective for Anxiety Disorders
Conrad M. Swartz, M.D., Everett C. Simmons, M.D.

NR239 The Relative Efficacy of New and Atypical Neuroleptics in Chronic Psychiatric Inpatients
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D.

NR240 Method to Assess a Fast Antidepressant Action
Inmaculada Gilaberte, M.D., Victor Perez-Sola, M.D., Douglas Faries, Domenec Serrano, M.D., Francesc Artigas, Ph.D., Enric Alvarez, M.D.

NR241 Cost-Effectiveness of Clozapine: A Retrospective Study
Prabir K. Mullick, M.D., Raj Sarma, M.D., Manohar K. Shetty, M.D., Koushik Mukherjee, M.D., David J. Lynn, M.D., Jack Merchant, R.N.

NR242 Tolerability of Mirtazapine Used in High or Low Initial Dose
Stephen M. Stahl, M.D., Charlotte Kremer, M.D., Roger Pinder, Ph.D.

NR243 Meta-Analysis of Randomized, Double-Blind Placebo Controlled Studies of Mirtapapine Versus Amitriptyline
Stephen M. Stahl, M.D., Milana V. Zivkov, M.D.

NR244 Sertraline Treatment of Panic Disorder: Combined Results from Two Placebo-Controlled Trials
Robert B. Pohl, M.D., Cathryn M. Clary, M.D., Robert Wolkow, M.D.

NR245 Bioavailability and Pharmacokinetics of an Extended Release (ER) Formulation of Venlafaxine
Clifford Dilea, Pharm.D., Steven Troy, M.S., Cathie Leister, M.S., Patrick D. Martin, M.D.

NR246 Charleston, SC: Drug Interactions Surveillance Program
C. Lindsay DeVane, Pharm.D., John S. Markowitz, M.D., Harry S. Gill, Ph.D., S. Craig Risch, M.D.

NR247 Serum Cholesterol in Patients with OCD During Treatment with Behavior Therapy and Fluvoxamine Versus Placebo
Helmut Peter, M.D., Susanne Tabrizian, Iver E. Hand, M.D.

NR248 Studies on Positive and Negative Mirtazapine at Some Human Brain Receptors
Elliott Richelson, M.D., Terry Souder, Joann Acuna

NR249 Overview of the Efficacy of Quetiapine
Ihor W. Rak, M.D., Lisa A. Arvanitis, M.D.

NR250 The Effect of Phenytoin and Cimetidine on the Pharmacokinetics of Quetiapine
James Y.W. Wong, Ph.D., Barbara J. Ewing, Ph.D., Per T. Thyrum, M.D., Chiao Yeh, Ph.D.

NR251 In Vitro Prediction of Potential Metabolic Drug Interactions for Quetiapine
Scott W. Grimm, Ph.D., Karen R. Stams, B.S., Khanh Bui, Ph.D.

NR252 Sertraline Efficacy in Elderly Patients Suffering from Major Depression
Carlo Berti, Dr., K Wilson, A. Whitehead

NR253 Clozapine in Schizophrenia with Comorbid OCD
Michael Poyurovsky, M.D., Abraham Weizman, M.D.

NR254 Mirtazapine Versus Amitriptyline in Relapse Prevention
Norman Sussman, M.D., Charlotte Kremer, M.D.

NR255 The Emergence of Adverse Events Following Venlafaxine Extended Release (ER) Discontinuation
Maurizio Fava, M.D., Rosemarie Mulroy, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D.

NR256 The Effects of Risperidone Versus Haloperidol on Frontal Lobe Functioning in Treatment-Resistant Schizophrenia
Susan R. McGurk, Ph.D., Michael F. Green, Ph.D., William C. Wirshing, M.D., Donna Ames, M.D., B.D. Marshall, M.D., Stephen R. Marder, M.D., Henry Koehn, B.S.

NR257 Risperidone and Glucose Tolerance
Debra W. Brescan, M.D., Luis F. Ramirez, M.D.

NR258 Buspirone Augmentation of Nefazodone in Depression
James G. Barbee IV, M.D., John M. Zajecka, M.D., Susan G. Kornstein, M.D., Frances E. Borian, R.N., Suha Hamid, Pharm.D., Darlene N. Jody, M.D.

NR259 Ginkgo Biloba Extract in Schizophrenic Patients
Ileana Berman, M.D., Demetra Pappas, B.S., Nina Leventhal, B.A., Robert D. Sigadel, M.D., Charu K. Patel, M.D.

NR260 Trends in the Use of SSRIs at Nine Department of Veterans Affairs Facilities
John C. Voris, Pharm.D.

NR261 Gabapentin: An Effective Therapy for Patients with Bipolar Affective Disorder
David B. Marcotte, M.D., Leeanne Fogleman, M.H.A., Neila Wolfe, M.S., Ruth Nemire, Pharm.D.

NR262 A Controlled Study of Bromocriptine and Placebo in Treating Neuroleptic-Induced Amenorrhea
Baiquan Zhang, M.D.

NR263 Effect of Penfluridol on Positive and Negative Symptoms of Schizophrenia
Baiquan Zhang, M.D., Guifang Zhao, M.D.

NR264 Risperidone in Adolescents with Psychosis and Mood Disorders
Herman A. Tolbert, M.D., Henry A. Nasrallah, M.D., Nicholas Votolato, R.P.H., Noelle K. Gehm, B.S.

NR265 Acute Effect of Paroxetine and Amitriptyline on the Psychomotor Performance in Healthy Volunteers
Chang Yoon Kim, M.D., Seong Yoon Kim, M.D., Chul Lee, M.D., In-Ho Park, M.D., O. Soo Han, M.D.

NR266 Mirtapapine Versus Amitriptyline and Placebo in the Treatment of Severely Depressed Patients
Siegfried Kasper, M.D.

NR267 Cross-Over Comparison of CYP2D6 Inhibition: Insignificant Effect of Venlafaxine Compared to Sertraline, Paroxetine and Fluoxetine
Y.W. Francis Lam, Pharm.D., Cara L. Alfaro, Pharm.D., Larry Ereshefsky, Pharm.D., Joseph A. Simpson, M.D., Jess D. Amchin, M.D.

NR268 Outcome of Risperdone Treatment in Alzheimer's Disease Patients with Psychotic Symptoms and Behavioral Disturbances
Arnaldo E. Negron, M.D., Andrew C. Coyne, Ph.D.

NR269 Low-Growth Hormone After Clonidine in Adversely-Reared Primates
Jeremy D. Coplan, M.D., Eric Smith, Ph.D., Ronald Trost, M.D., David E. Scharff, M.D., Jack M. Gorman, M.D., Leonard Rosenblum, M.D.

NR270 Clozapine to Olanzapine Conversion: Preliminary Results
Barbara G. Haskins, M.D., Robert A. Leadbetter, M.D., Michael S. Shutty, Ph.D., Jennifer L. Francis, B.S., Jack W. Barber, M.D., Kenneth H. Brasfield, Pharm.D.

NR271 Venlafaxine Treatment of Trichotillomania: An Open Series of Ten Cases
Richard L. O'Sullivan, M.D., Nancy J. Keuthen, Ph.D., Dayami Rodriguez, B.A., Paige Goodchild, B.A., Gary A. Christenson, M.D., Scott L. Rauch, M.D.

NR272 A Double-Blind, Placebo-Controlled Trial of Once-Daily Venlafaxine Extended Release (ER) in Outpatients with Major Depression
Michael E. Thase, M.D.

NR273 Characterization and Inhibition of Human Cytochrome P450 Enzymes Involved in the In Vitro Metabolism of Mirtazapine
Leon P.C. Delbressine, Ph.D., Sheldon H. Preskorn, M.D., Dale W. Horst, Ph.D.

NR274 Remission Rates During Short-Term Treatment with Mirtazapine
Milana V. Zivkov, M.D., Charlotte Kremer, M.D.

NR275 The Pharmaco-Economic Profile of Fluvoxamine in Recurrent Depression
Daniela Barge-Schaapveld, M.Sc.

NR276 Effects of Divalproex on 5HT-1A Receptor Function
Lakshmi N. Yatham, I.S. Shiah, M.D., Athanasios P. Zis, M.D., Raymond W. Lam, M.D.

NR277 Olanzapine in Treatment-Refractory Schizophrenia
Juan-Carlos Gomez, M.D., Joaquin Martin, M.D., Enrique Garcia Bernardo, M.D., Victor Peralta, M.D., Enrique Alvarez, M.D., Manuel Gurpegui, M.D.

NR278 Cognitive Profile and Soft Signs in Clozapine Versus Risperidone Treatment
Jean-Pierre Lindenmayer, M.D., Adel Iskander, M.D., Fotini-Sonia Apergi, Mohan Park, M.D.

NR279 Buspirone Treatment of Aggressive Child Inpatients
Cynthia R. Pfeffer, M.D.

NR280 Naltrexone as a Treatment for Repetitive Self-Injurious Behavior: Efficacy Over One Year
Augusta S. Roth, M.D., Robert B. Ostroff, M.D., Ralph E. Hoffman, M.D.

NR281 Pharmacokinetic Effects of Venlafaxine on Imipramine Metabolism
Lawrence J. Albers, M.D., Christopher Reist, M.D., Daiga M. Helmeste, Ph.D., Siu Wa Tang, M.D.

NR282 Selegiline-Citalopram Combination for Patients with Parkinson's Disease and Depression
Zoltan Rihmer, M.D., Maria Satori, M.D.

NR283 Nonverbal Learning Improvement in Schizophrenia After Eight Weeks of Risperidone: Preliminary Evidence for Right Hemisphere Changes from the
Scot Purdon, Ph.D.

NR284 Weight Change During Mirtazapine Therapy
Paul J. Goodnick, M.D., Charlotte Kremer, M.D., Peggy Wingard, M.D.

NR285 Lack of Typical SSRI Adverse Effects and Sexual Dysfunction with Mirtazapine Is Related to Specific Blockade of 5HT2 and 5HT3 Receptors
Paul J. Goodnick, M.D., Milana V. Zivkov, M.D.

NR286 Haemodynamic Control During ECT Treatments
Mustafa M. Husain, M.D., Lewis A. Stool, M.D., Michael N. Avramov, M.D., W. Fu, M.D., Paul W. White, M.D.

NR287 EEG-Monitoring of ECT: First Results with the Fast-Fourier-Frequency- Analysis
Here W. Folkerts, M.D., G. Wagner, M.D., S. Theysohn

NR288 The Effects of ECT on Quantified EEG
James S. Lawson, Ph.D., Donald W. Brunet, M.D., Nicholas J. Delva, M.D.

NR289 A Naturalistic Review of Maintenance ECT
Barry A. Kramer, M.D.

NR290 Challenges in Using the Medical Outcome Scale for Mental Health Clinic Outpatients
Susan D. Wiley, M.D.

NR291 Longitudinal Risperidone Use and Side-Effects in an Urban Mental Health Clinic
Peggy E. Chatham-Showalter, M.D., Maureen MacFarland, R.N., Ralph A. Primelo, M.D.

NR292 Fluvoxamine Therapy for Schizophrenia Patients with OCD
Pinkhas Sirota, M.D., Ilya Reznik, M.D.

NR293 Therapist-Patient Sexual Relations: Result of a National Survey
Alex Aviv, M.D., Yoseph Levine, M.D., Nili Speiser, M.A., Avner Elizur, M.D.

NR294 Front-Loading Ambulatory Care for Bipolar Disorder
Mark S. Bauer, M.D., Linda McBride, M.S.N., Nancy Shea, R.N., Christopher Gavin, B.S.

NR295 Cost of Care by a Psychiatrist Versus Split Treatment
Mantosh J. Dewan, M.D.

NR296 The Perception of Effectiveness: Physician Use of Lobotomy in a California State Hospital, 1947-1954
Joel T. Braslow, M.D.

NR297 Practice of ECT in Veterans Affairs Medical Centers
Jagannathan Srinivasaraghavan, M.D., Richard D. Weiner, M.D.

NEW RESEARCH

Tuesday, May 20, 1997, 3:00 p.m.-5:00 p.m.

New Research 8 – Poster Session – Special Events Area, Upper Level, Convention Center

ADDICTIVE DISORDERS, AIDS, VIOLENCE, FORENSICS, PERSONALITY, DISSOCIATIVE DISORDERS, EPIDEMIOLOGY, DIAGNOSTICS, AND TREATMENT TECHNIQUES

Moderator: Richard Balon, M.D.

NR298 Neuroendocrine Effects of Intravenous Meta-Chlorophenylpiperazine in Three 4-Methylenedioxymethamphetamine Users
Una D. McCann, M.D., Melissa M. Mertl, B.A., Dennis L. Murphy, M.D., Robert M. Post, M.D., George A. Ricaurte, M.D.

NR299 Comparison of Morphine and Methadone Maintenance in Pregnant Opiate Addicts
Petra Etzersdorfer, M.D., Gabriele Fischer, M.D., Harald Eder, Reinhold Jagsch, M.A.G., Kathrin Schmidl-Mohl, M.D., Wolfgang Gombas, M.D.

NR300 Buprenorphine Maintenance in Pregnant Opiate Addicts
Gabriele Fischer, M.D., Kathrin Schmidl-Mohl, M.D., Petra Etzersdorfer, M.D., Harald Eder, Reinhold Jagsch, M.A.G., Wolfgang Gombas, M.D.

NR301 Effect of Varying Methadone Doses on Heroin Use
Chandresh Shah, M.D., Adonis Sfera, M.D., Lena Simitian, Pharm.D.

NR302 Gene Coding for D2 Dopamine Receptor and Addiction
Philip A.P.M. Gorwood, M.D., Jean Ades, M.D., Philippe Batel, M.D., Pierre Sokoloff, Ph.D., Jean C. Schwartz, Ph.D., Josue Feingold, M.D.

NR303 Patterns of Drug Use Risk in Psychiatric Patients
Ihsan M. Salloum, M.D., Dennis C. Daley, M.S.W., Jack R. Cornelius, M.D., Levent Kirisci, Ph.D.

NR304 Assessment of the Role of Kindling Mechanism and Somatic Disorders in Development and Course of Alcohol Withdrawal Delirium
Marcin Wojnar, M.D., Artur Cedro, M.D., Zdzislaw Bizon, Ph.D., Agata Orlow, M.D.

NR305 The Alcohol Insensitivity Index: Pilot Study of a Potential Phenotypic Measure
Thomas P. Beresford, M.D., David B. Arciniegas, M.D., John Hewitt, Ph.D.

NR306 Heavy Alcohol Use and Cardiac Surgery Outcome
Catherine Villanueva, Ph.D., Adrianne Casebeer, M.A., Laurie Shroyer, Ph.D., Frederick L. Grover, M.D., Karl Hammermeister, M.D., Thomas P. Beresford, M.D.

NR307 Alcoholic Liver Disease and Liver Transplantation: A Survey of United States Programs
Thomas P. Beresford, M.D., David B. Arciniegas, M.D., James Everhart, M.D.

NR308 Cocaine as a Risk Factor for Neuroleptic-Induced Acute Dystonia
Peter N. van Harten, M.D., Jan C. van Trier, M.D., Ernst H. Horwitz, M.D.

NR309 Coexistence of Tardive Dyskinesia, Parkinsonism and Akathisia and Tardive Dystonia: Their Prevalence and Inter-Relationships
Peter N. van Harten, M.D., Hans W. Hoek, M.D., Glenn E. Matroos, M.D.

NR310 Treatment of Depressed Alcoholics
Alec Roy, M.D.

NR311 Ego Defense Mechanisms in Korean Male Cigarette Smokers
Sang Keun Chung, M.D., Ik-Keun Hwang, M.D., Hong Bai Eun, M.D., Young Chul Chung, M.D.

NR312 Alcoholism and Depression in the Community
Jin Pyo Hong, M.D., Maeng Je Cho, M.D., Yang Sook Ha, Ph.D., Chang Yoon Kim, M.D., Gun Hee Lee, Ph.D.

NR313 Platelet 5HT-2 Receptor in Alcohol Use Disorder
Young Chul Chung, M.D., Hong Bai Eun, M.D., Ik-Keun Hwang, M.D., Sang Keun Chung, M.D.

NR314 Naltrexone Effects on Lorazepam Challenge in Alcoholics
Ede Frecska, M.D., Robert Hitzemann, Ph.D., Maria Taylor, R.N., Paula Cerveny, N.P., Kathleen Piscani, R.N., Laurel Weissman, R.Ph.

NR315 Social Consequences of Substance Abuse: The Impact of Comorbid Psychiatric Disorders: A Prospective Study of a Nation-Wide Sample of Treatment Seeking
Kristinn Tomasson, M.D., Per Vaglum, M.D.

NR316 Sertraline with Naltroxene Versus Naltrexone Alone in the Treatment of Alcohol Dependence
Conor K. Farren, M.D., Dana Catapano, B.A., Stephanie S. O'Malley, Ph.D.

NR317 Stages of Change Among Cocaine Dependent Schizophrenic Patients
Lisa J. Roberts, M.A., Andrew L. Shaner, M.D., G. Alan Marlatt, Ph.D., Jeffery N. Wilkins, M.D.

NR318 Caffeine and Nicotine Use Around Alcohol Withdrawal in Veterans Diagnosed with Alcohol Dependence
James J. Kim, M.D., Hedy E. Tasbas, M.D., Jagannathan Srinivasaraghavan, M.D.

NR319 Dissociative Phenomena in MICA Inpatients
Zebulon C. Taintor, M.D., A. Jonathan Porteus, M.A.

NR320 HIV-1-Induced Cognitive Impairment Is Associated with Total But Not Free p24 Antigen Level
Karl Goodkin, M.D., Frances Wilkie, Ph.D., Benedetto Vitiello, M.D., J. Hampton Atkinson, M.D., Peter N.R. Heseltine, M.D., Daniel Feaster, M.S.

NR321 Neurocognitive Decline in HIV-1 Infection: Relationship to Cortisol
Susan G. Silva, Ph.D., Eric D. Jackson, B.S., Jane Leserman, Ph.D., Diana O. Perkins, M.D., Robert N. Golden, M.D., Dwight L. Evans, M.D.

NR322 Stress and Social Conflict Predict Major Depression in HIV-Infected Men
Jane Leserman, Ph.D., Diana O. Perkins, M.D., Susan G. Silva, Ph.D., Paula Bird, M.S.N., Dwight L. Evans, M.D., Robert N. Golden, M.D.

NR323 An Open Trial of Nefazodone in HIV-Positive Outpatients with Major Depression
Andrew J. Elliott, M.D., Peter P. Roy-Byrne, M.D.

NR324 AIDS Patients' Preferences About Advance Directives
Cheryl A. Kennedy, M.D., James Hill, Ph.D., Debra Kantor, Ph.D., Scott Matthews, Kari O'Connell

NR325 Depression Among AIDS Patients in a Nursing Home
Leonid Bilenkin, B.S., Gopalakrishna K. Upadhya, M.D., Ali Khadivi, Ph.D., Rogelio Thomas, M.D.

NR326 Psychiatrist Outreach to Homebound AIDS Patients
Lawrence B. Jacobsberg, M.D., Robert P. Parkin, M.D., David C. Lindy, M.D., Neil Pessin, Ph.D.

NR327 The Progression of HIV Knowledge, Attitudes and Behavior of Drug and Alcohol Outpatients Through Treatment
Thomas M. Brady, M.S., Joseph A. Flaherty, M.D., Norman S. Miller, M.D.

NR328 Assessment of Asymptomatic HIV Patients with the Computerized Neuropsychological Test Battery
John Herrera, Ph.D., Amy Veroff, Ph.D., John J. Sramek, Pharm.D., Stanford S. Jhee, Pharm.D., Claudette Francis, R.N., Neal R. Cutler, M.D.

NR329 Physicians in a Residence Program: Evaluation of a Substance Abuse Training Approach Using Simulated Patients
Frances R. Levin, M.D., Patricia Owen, Ph.D., Edward Rabinowitz, M.D., Nicholas A. Pace, M.D.

NR330 Buprenorphine for Opioid Detoxification in a Private Practice Setting
Richard B. Resnick, M.D., Marc Galanter, M.D., William Matikiewicz, M.D., Elaine Resnick, M.S.W.

NR331 Influence of Addictions Treatment on Perceived Problem and Need for Treatment of Substance Use Disorders and Mental Illness Among Dually
Jill RachBeisel, M.D., Lisa B. Dixon, M.D., Jean Gearon, Ph.D.

NR332 Sequential 5HT Assessments in Cocaine Addicts After Cocaine Discontinuation
Laure B. Buydens-Branchey, M.D., Marc H. Branchey, M.D.

NR333 Utilization of Consultation Services in an Addiction Unit
Vasant P. Dhopesh, M.D., Bruce J. Berg, M.D., Elmer Yu, M.D., Gerald A. Groves, M.D.

NR334 State-Dependent Personal Memories During Intoxification Reported by Patients with Alcoholism
Richard J. Esposito, M.S., Ralph E. Hoffman, M.D., Marc I. Rosen, M.D., Rockholz Peter, M.S.S.W.

NR335 Toxicological and Psychosocial Profile of Ecstasy Abusers and Non-Abusers in Military Conscripts
Julio Bobes, M.D., Pilar A. Saiz, Ph.D., Maria P. Gonzalez, Ph.D., Manuel Bousono-Garcia, M.D., Jose R. Perez-Carral, M.D.

NR336 Quality of Life in 274 Schizophrenic Outpatients Undergoing Risperidone Maintenance Treatment
Julio Bobes, M.D., Miguel Gutierrez, M.D., Juan Gibert, Ph.D., Maria P. Gonzalez, Ph.D., Marisa Herraiz, M.D., Antonio Fernandez, M.D.

NR337 The Association Between Animal Cruelty and Psychiatric Disorders
Roman Gleyzer, M.D., Alan R. Felthous, M.D., Charles E. Holzer III, Ph.D.

NR338 Newborn Murder in Maternity Wards: A Report of Three Cases and a Discussion on the Definition of Neonaticide
Marcio Gekker, M.D., Mauro V. Mendlowicz, M.D., Katia Mecler, M.D., Talvane M. de Moraes, Mark H. Rapaport, M.D.

NR339 A Case-Control Study on the Sociodemographic Characteristics of a Sample of Fifty-Five Neonaticide Women
Mauro V. Mendlowicz, M.D., Mark H. Rapaport, M.D., Talvane M. de Moraes, Katia Mecler, M.D., Marcio Gekker, M.D.

NR340 Psychosis and Criminal Behavior: Implications for Risk Assessment and Dispositional Planning
Debra A. Pinals, M.D., Stephen G. Noffsinger, M.D.

NR341 A Descriptive Study on the Psychiatric Aspects of Fifty-Five Cases of Neonaticide
Talvane M. de Moraes, Mauro V. Mendlowicz, M.D., Mark H. Rapaport, M.D., Katia Mecler, M.D., Marcio Gekker, M.D.

NR342 Correlates of Aggression in Male Prisoners
Eulon R. Taylor, M.D., Pamela M. Diamond, Ph.D., Eugene W. Wang, M.S., Lue E. Herrington, M.S.

NR343 Coercion in Medical and Psychiatric Admissions: An Empirical Study
Bruce J. Cohen, M.D., Steven K. Hoge, M.D.

NR344 Impulsivity Related to Suicide Attempts and Self-Aggression in Mentally Disordered Offenders
Francisco Paez, M.D., Alberto G. Lopez, M.D., Rogelio Apiquian, M.D., Humberto Nicolini

NR345 Intermittent Explosive Disorder: A Preliminary Report of 17 Cases
Susan L. McElroy, M.D., Cesar A. Soutullo, M.D., DeAnna A. Beckman, M.S.W., Paul E. Keck, Jr., M.D., Purcell Taylor, Jr., Ed.D.

NR346 Chronicity in PTSD and Predictors of Course of PTSD in Patients with Comorbid Anxiety Disorders
Caron Zlotnick, Ph.D., Meredith Warshaw, M.S.S., M. Tracie Shea, Ph.D., Jennifer Allsworth, B.A., Teri B. Pearlstein, M.D., Martin B. Keller, M.D.

NR347 A New Screening Measure for Domestic Violence
David P. Bernstein, Ph.D., Edward A. Walker, M.D., Judith Stein, Ph.D., Martha A. Medrano, M.D., Murray B. Stein, M.D.

NR348 5HT Response to Trauma and Axis II Disorders
David P. Bernstein, Ph.D., Larry J. Siever, M.D., Rachel Yehuda, Ph.D., Robert A. Grossman, M.D.

NR349 Physiological Response to Trauma and Subsequent PTSD: A Prospective Study
Arieh Y. Shalev, M.D., Tali Sahar, M.A., Sara Freedman, M.A., Tuvia Peri, Natali Glick, M.D., Dalia Brandes, Scott P. Orr, Ph.D., Roger K. Pitman, M.D.

NR350 Children as Homicide Victims in Homicide-Suicide Events
Maria D.D. Llorente, M.D., Donna Cohen, Ph.D., Carl Eisdorfer, M.D., Maria A. Gadia, M.D.

NR351 Neuroleptics in Nursing Homes: Outcome of Discontinuation
Edwin J. Olsen, M.D., Maria D.D. Llorente, M.D., Oscar Leyva, M.D., John Lewis, Ph.D.

NR352 Psychosocial Stressors Among Homeless Children: Relationship to Child Mental Health Problems
Bonnie T. Zima, M.D., Regina Bussing, M.D., Marina Bystritsky, M.A., Barbara J. Genovese, M.A., Thomas R. Belin, Ph.D.

NR353 Childhood Maltreatment in Psychiatric Inpatients
Taruna Ahluvalia, M.A., David L. Pogge, Ph.D., David P. Bernstein, Ph.D., Susan R. Borgaro, M.A., John M. Stokes, Ph.D.

NR354 Violently Injured Patients and the Development of PTSD
Sheila J. Eaton, Ph.D., John D. Mesaros, M.D., Shiyoko Slate, B.A., Manuel E. Tancer, M.D., Thomas W. Uhde, M.D.

NR355 Cost of Incidents of Aggression in a Large Metropolitan State Hospital
Mohammed Y. Alam, M.D., Asif A. Aleem, Daniel J. Luchins, M.D., Patricia Hanrahan, Ph.D.

NR356 Valproate in Impulsivity and Violent Behavior in Psychiatric Emergency Hospital
Luis D. Mosca, M.D., Jorge L. Coppola, M.D., Juan P. Licciardo, M.D.

NR357 Psychophysiologic Assessment of Breast Cancer Patients and Witnesses
Douglas M. Lanes, M.D., Stephanie K. Williston, M.S.Ed., Scott P. Orr, Ph.D., Roger K. Pitman, M.D.

NR358 5HT-Related Genes and Impulsive Aggression in Personality Disorders
Antonia S. New, M.D., Joel Gelernter, M.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

NR359 Gulf Veterans Seeking Department of Defense Care: Relationship to Gender, Absenteeism and Combat Stressors
Charles C. Engel, Jr., M.D., Robert J. Ursano, M.D., Charles D. Magruder, M.D.

NR360 Examination of Family Environment Characteristics Among Couples Involved in Abusive Relationships
Charles D. Magruder, M.D., Phuong Colquett, M.A., David Cowan, Ph.D., Robert Mays, Ph.D.

NR361 An Examination of Stress and Social Resources Among Abusive and Non-Abusive Couples in a Military Population
Phuong Colquett, M.A., Charles D. Magruder, M.D., David Cowan, Ph.D., Robert Mays, Ph.D.

NR362 Terrorism in Oklahoma City: Predictors of Distress
Phebe M. Tucker, M.D., Warren Dixon, Ph.D., Gwen Allen, M.S.W., Betty Pfefferbaum, M.D., Sara Jo Nixon, Ph.D., Amar N. Bhandary, M.D.

NR363 Psychiatric Consequences of Ethic Cleansing: One Year After Resettlement
Dolores Vojvoda, M.D., Stevan M. Weine, M.D., Daniel F. Becker, M.D., Leslie Hyman, M.S.W., Dori Laub, M.D., Steven Lazrove, M.D., Thomas H. McGlashan, M.D.

NR364 Relationships and Psychiatric Disorders
Robert Kohn, M.D., Caron Zlotnick, Ph.D., Gabor I. Keitner, M.D.

NR365 Epidemiological Study of ADHD in an Egyptian Sample
Mohamed H. Ghanem, M.D., Maissa N. Farid, M.D., Hayam K. Nazif, M.D., Nancy I. Abu-El-Maaty, M.D.

NR366 Prevalence of PTSD in a Community Sample of Older Adolescents
Steven P. Cuffe, M.D., Cheryl L. Addy, Ph.D., Carol Z. Garrison, Ph.D., Jennifer L. Waller, Ph.D., Kirby L. Jackson, A.B., Robert E. McKeown, Ph.D.

NR367 Use of the Beck Depression Inventory with French Children
Fabien Durif, M.D., Veronique Gentil, M.D., Jean P. Raynaud, Ph.D., Laurent Schmitt, M.D.

NR368 Enhancing the Effects of Acupuncture Detoxification with Clonidine in Acute Heroin Withdrawals
Cheng-Jen Chen, M.D., Alexander Babayants, M.D.

NR369 Seasonal Variation in Bipolar Disorder in Appalachia
Hazel E.A. McBride, Ph.D., Geoffrey S. Duckworth, M.D., Joselito B. Morales, M.D., Roy S. Price, M.S.W.

NR370 Memory and Physostigmine in Personality Disorders
Andrea Bergman, Ph.D., Philip D. Harvey, Ph.D., Harold W. Koenigsberg, M.D., Bonnie J. Steinberg, M.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

NR371 Treatment Influence on Axis I and Axis II Disorders
Laura Ferrando, Emmanuelle Weiller, Julio Bobes, M.D., J. Gibert, G. Saiz, Y. Lecrubier

NR372 Stability of Personality Disorders with Treatment for Chronic Depression
Robert M.A. Hirschfeld, M.D., James P. McCullough, Ph.D., James M. Russell, M.D., Martin B. Keller, M.D.

NR373 Applicability of Personality Disorder Criteria to Hospitalized Adolescents: An Internal Consistency Evaluation
Daniel F. Becker, M.D., Carlos M. Grilo, Ph.D., Leslie C. Morey, Ph.D., Martha Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

NR374 Fate of Borderline Psychopathology: Nine-Year Follow-Up Study in Japan
Norimasa Ikuta, M.D., Kuninao Minakawa, M.D., Yuko Miyake, Ph.D., Naoki Moriya, M.D., Ken Murakami, M.D., Aya Nishizono-Maher, M.D.

NR375 A Partially Heritable Oppositional Factor Predicts Adult Antisocial Symptoms Separately from a Conduct Factor in an Adoption Study
Douglas R. Langbehn, M.D., Remi J. Cadoret, M.D., William R. Yates, M.D., Edward P. Troughton, B.A., Mark A. Stewart, M.D.

NR376 Cognitive Impulsivity and Behavioral Abnormalities in Patients with Personality Disorder
Sonia Lees-Roitman, M.S., Philip D. Harvey, Ph.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

NR377 Money Management for Mentally Ill Individuals
Patricia Hanrahan, Ph.D., Daniel J. Luchins, M.D., Kendon J. Conrad, Ph.D., Michael D. Matters, Ph.D., Courtenay E. Savage, M.A., Marc S. Shinderman, M.D.

NR378 The Austen Riggs Follow-Along Study: A Preliminary Report on Dynamic and Descriptive Change
J. Christopher Perry, M.D., Eric M. Plakun, M.D., Ann Grief, Ph.D., Patricia Kelly-Chalfonte, Ed.M., Stephen Beck, M.Psy., Rachel Lefebvre, M.Psy.

NR379 Treatment of Substance Abusing Schizophrenic Patients: Two-Year Progress Report
Andrew P. Ho, M.D., John W. Tsuang, M.D., Andrew L. Shaner, M.D.

NR380 Medical Cost Offset in Depressed Primary Care Patients in Two Health Maintenance Organizations
Don P. Buesching, Ph.D., Timothy R. Hylan, Ph.D.

NR381 Modification of EEG Sleep Parameters Under ECT in Drug-Resistant Major Depressives: Preliminary Results of Correlation with Clinical Improvement
Renate Eiber, M.D., Michel Tiberge, M.D., Jean-Michel Loustalan, M.D., Laurent Schmitt, M.D., Michel Escande, M.D.

NR382 Neurometric EEG Predicts Pharmacotherapeutic Outcome in Depressed Outpatients: A Prospective Trial
Stephen C. Suffin, M.D., Nick M. Gutierrez, M.D., Sarla Karan, M.D., David Aurua, M.D., W. Hamlin Emory, M.D., Arthur Kling, M.D.

NR383 Outcomes of Psychiatric Hospitalization: 1988-96
Paul B. Lieberman, M.D., Stephen A. Wiitala, Ph.D., Elliott E. Binette, M.A., Sandra McCormick, M.S.W., Stephanie Goyette, M.S.

NR384 Economic Outcomes Associated with Initial Treatment
Eric T. Edgel, Pharm.D., Timothy R. Hylan, Ph.D.

NR385 Post Discharge Medication Compliance in Adolescent Psychiatric Inpatients
Anne Lloyd, David L. Pogge, Ph.D., William P. Horan, M.A., John M. Stokes, Ph.D., Susan R. Borgaro, M.A., Philip D. Harvey, Ph.D.

NR386 A Double-Blind, Placebo-Controlled Study on Gradual Withdrawal of Antiparkinsonian Medication in Chinese Schizophrenia Patients
Alfred Hin Tat Pang, M.D., Gabor S. Ungvari, M.D., Helen F.K. Chiu, M.D., Linda C.W. Lam, M.D., Dicky W.S. Chung, M.D., Tony Leung, M.Sc.

NR387 Immediate Naltrexone Decreases in Alcohol Intake Urges as Predictor of a Good Outcome
Jorge F. Perez-Cruet, M.D., Tomislav Iricanin, M.D.

NR388 Comparisons of Antidepressant Prescribing and Use Patterns in Privately Insured and Medicaid Populations
Timothy R. Hylan, Ph.D., Cathy A. Melfi, Ph.D., Anita J. Chawla, Ph.D., William H. Crown, Ph.D., Thomas W. Croghan, M.D., Don P. Buesching, Ph.D.

NR389 Combined ECT and Neuroleptic Therapy in Treatment-Resistant Schizophrenia
Worrawat Chanpattana, M.D., Ronnachai Kongsakon, M.D., Wanchai Buppanheran, M.D.

NR390 Telephone/Computer Administered Prime-MD
Leslie V. Taylor, M.D., Kenneth A. Kobak, Ph.D., Susan L. Dottl, Ph.D., John H. Greist, M.D., James W. Jefferson, M.D., Diane Burroughs, B.A.

NR391 Preliminary Test-Retest Reliability of the Structured Clinical Interview for DSM-IV Children Diagnoses
Frederick J. Matzner, M.D., Raul R. Silva, M.D., Matthew Silvan, Ph.D., Mizanur Chowdury, M.D., Lisa Nastasi

NR392 Prevalence of Kraepelin's Paraphrenia in a Psychiatric Hospital
Berta Rios, M.D., Natividad Vicente, M.D., Enriqueta Ochoa, M.D.

NR393 Dissociative Symptoms and Aggression in Outpatients
Margaret L. Kaplan, Ph.D., Miriam Ehrensaft, M.A., William Sanderson, Ph.D., Scott Wetzler, Ph.D., Gregory M. Asnis, M.D.

NEW RESEARCH

Wednesday, May 21, 1997, 9:00 a.m.-10:30 a.m.

New Research 9 – Oral/Slide Session – Room 11A, Upper Level, Convention Center

SCHIZOPHRENIA AND DEPRESSION

Chp.: Wayne S. Fenton, M.D.

NR394 Effects of Amphetamine on Working Memory in Schizotypal Personality Disorder — 9:00 a.m.
Richelle M. Kirrane, M.D., Robert L. Trestman, M.D., Michael J. Serby, M.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

NR395 Diurnal Dopamine Rhythm in Non-Psychotic Relatives of Schizophrenic Probands — 9:15 a.m.
Farooq Amin, M.D., Adriana E. Stroe, M.D., Oladele Adebogun, M.D., Jeremy Silverman, Ph.D., Christopher J. Smith, B.S., Peter J. Knott, Ph.D., Larry J. Siever, M.D., Kenneth L. Davis, M.D.

NR396 Symptom Dimensions and Psychosocial Outcome in Schizophrenia — 9:30 a.m.
Beng-Choon Ho, M.D., Peg C. Nopoulos, M.D., Arndt Stephan, Ph.D., Michael A. Flaum, M.D., Sue Oliver, M.S., Nancy C. Andreasen, M.D.

NR397 Nefazodone Treatment of Depression Requires Less Use of Concomitant Anxiolytic and Sedative/Hypnotic Drugs — 9:45 a.m.
Jean Lian

NR398 The Efficacy of Ziprasidone in the Treatment of Positive, Negative and Depressive Symptoms of Schizophrenia — 10:00 a.m.
Paul E. Keck, Jr., M.D., Edmund P. Harrigan, M.D., Karen R. Reeves, M.D.

NR399 The Economic Impact of the Treatment of Depression — 10:15 a.m.
James M. Russell, M.D., Stan Finklestein, M.D., Paul Greenberg, M.Sc., Ernst Berndt, Ph.D., Andrew Baker, M.P.A., Martin B. Keller, M.D.

NEW RESEARCH

Wednesday, May 21, 1997, 9:00 a.m.-10:30 a.m.

New Research 10 – Oral/Slide Session – Room 11B, Upper Level, Convention Center

PSYCHOPHARMACOLOGY

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

NR400 Infant Outcome After Sertraline Exposure — 9:00 a.m.
Alexis M. Llewellyn, B.A., Zachary N. Stowe, M.D., Charles B. Nemeroff, M.D.

NR401 Paroxetine Versus Nortriptyline in Ischemic Disease — 9:15 a.m.
Steven P. Roose, M.D., Bruce Pollack, M.D., John Kennedy, M.D., J. Craig Nelson, M.D., James McCafferty, M.D., Ivan Gergel, M.D.

NR402 Dysthymia: An Outcome Study of Combined Group Therapy and Medication Treatment Versus Medication Treatment Alone — 9:30 a.m.
David J. Hellerstein, M.D., Suzanne A.S. Little, M.A., Sarai Batchelder, Ph.D., Lisa Wallner Samstag, M.A., Richard N. Rosenthal, M.D., Arnold Winston, M.D.

NR403 Compliance of Naltrexone in the Treatment of Alcohol Dependence — 9:45 a.m.
Kee Namkoong, M.D., Conor K. Farren, M.D., Patrick O'Connor, M.D., Stephanie S. O'Malley, Ph.D.

NR404 A Placebo-Controlled Trial of Sertraline Treatment for Pediatric OCD — 10:00 a.m.
Robert Wolkow, M.D., John S. March, M.D., Allan Z. Safferman, M.D., Joseph Biederman, M.D.

NR405 Relapse Prevention with Fluoxetine in Anorexia Nervosa: A Double-Blind Placebo-Controlled Study — 10:15 a.m.
Walter H. Kaye, M.D., Theodore E. Weltzin, M.D., L.K. George Hsu, M.D., Mae S. Sokol, M.D., Claire Mc Conaha, B.S.N., Katherine H. Plotnicov, Ph.D.

NEW RESEARCH

Wednesday, May 21, 1997, 12 noon-2:00 p.m.

New Research 11 – Poster Session – Special Events Area, Upper Level, Convention Center

MOOD AND ANXIETY DISORDERS, PREMENSTRUAL DYSPHORIC DISORDER, SUICIDE, MANAGED CARE, AND PSYCHOIMMUNOLOGY

Chp.: Marian I. Butterfield, M.D.

NR406 Support for the Dopamine Transporter as a Possible Susceptibility Locus for Bipolar Disorder
John R. Kelsoe, Jr., M.D., A. Dessa Sadovnick, Ph.D., Helgi Kristbjarnarson, M.D., Patricia Bergesch, Zofi Mroczkowski-Parker, Mark H. Rapaport, M.D., Pamela Flodman, M. Anne Spence, Ph.D., Ronald A. Remick, M.D.

NR407 Health-Related Quality of Life and Early Treatment Response in Depression
Jeffrey M. Pyne, M.D., Kelly N. Yoo, Shahrokh Golshan, Ph.D., Robert M. Kaplan, M.D.

NR408 Assessment of Affective Temperament in BP-I Disorder: Preliminary Data from a French Multicenter Study "EPIMAN"
Hagop S. Akiskal, M.D., Elie G. Hantouche, M.D., Jean-Philippe Fraud, M.D., Jean-Michel Azorin, M.D., Marc Bourgedis, M.D.

NR409 The Immune Immodulating Effects of Lithium in Normal Volunteers
Mark H. Rapaport, M.D., Lewis L. Judd, M.D.

NR410 The Characterization and Treatment of Patients with Minor Depression and Subsyndromal Depressive Symptoms
Mark H. Rapaport, M.D., Lewis L. Judd, M.D.

NR411 The Course of Bipolar Disorder During Pregnancy
Verinder Sharma, M.D., Karen M. Kueneman, B.A., Bhooma Bhayana, M.D., Pierre Mattar

NR412 Hopelessness in Outpatients with MDD
Barbara J. Cannon, M.D., Rosemarie Mulroy, B.A., Michael W. Otto, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D.

NR413 Depression Screening: Ham-D Compared with Prime-MD
Marijo B. Tamburrino, M.D., Rollin W. Nagel, M.A., Denis J. Lynch, Ph.D., Mary Kay Smith, M.D., Osman M. Ali, M.D., Raj A. Narayan

NR414 Prime-MD Depression Screening: Anxiety Comorbidity
Marijo B. Tamburrino, M.D., Mary Kay Smith, M.D., Denis J. Lynch, Ph.D., Rollin W. Nagel, M.A., Raj A. Narayan, Osman M. Ali, M.D.

NR415 Manual-Based Group Therapy for Bipolar Disorder
Linda McBride, M.S.N., Mark S. Bauer, M.D., Catherine E. Chase, D.O., Gary S. Sachs, M.D.

NR416 Disability in the Chronically Depressed
Ivan W. Miller, Ph.D., James M. Russell, M.D., Michael E. Thase, M.D., Andrew Baker, M.P.A.

NR417 Sertraline Maintenance Therapy in Chronic Depression
Martin B. Keller, M.D., James H. Kocsis, M.D., James P. McCullough, Ph.D., George A. Trapp, M.D., Alan F. Schatzberg, M.D., Michael E. Thase, M.D.

NR418 Predictors of Service Use in Bipolar Disorder
Christopher Gavin, B.S., Nancy Shea, R.N., Linda McBride, M.S.N., Mark S. Bauer, M.D.

NR419 A Fixed-Dose Comparison of Citalopram Versus Placebo
John P. Feighner, M.D., Ronald R. Fieve, M.D., John S. Carman, M.D., Lynn A. Cunningham, M.D., Gerri Schwartz, Ph.D.

NR420 Effects of Extended Release (ER) Venlafaxine on Anxiety in Patients with Major Depression
John P. Feighner, M.D., Richard Entsuah, Ph.D., Mary K. McPherson, M.S.

NR421 Differential Female and Male Cerebral Glucose Metabolism Abnormalities in Depression
Timothy A. Kimbrell, M.D., Terence A. Ketter, M.D., Robert T. Dunn, M.D., John T. Little, M.D., Mark A. Frye, M.D., Robert M. Post, M.D.

NR422 Effects of Prior Course of Illness on the Neuropsychological Functioning of Patients with Bipolar Disorder
Syed O. Ali, B.S., Earlian E. Smith-Jackson, R.N., Gabriele S. Leverich, M.S.W., Ellen G. Connell, Robert M. Post, M.D., Kirk D. Denicoff, M.D.

NR423 Psychosensory Symptoms in Patients with Bipolar Disorder
Syed O. Ali, B.S., Kirk D. Denicoff, M.D., Terence A. Ketter, M.D., Earlian E. Smith-Jackson, R.N., Robert M. Post, M.D.

NR424 Cognitive Side-Effects of Lithium, Carbamazepine and Their Combination in Patients with Bipolar Disorder
Kirk D. Denicoff, M.D., Syed O. Ali, B.S., Earlian E. Smith-Jackson, R.N., Allan F. Mirsky, M.D., Robert M. Post, M.D.

NR425 Thyroid Potentiation in Affective Illness
Mark A. Frye, M.D., Kirk D. Denicoff, M.D., David A. Luckenbaugh, M.A., Timothy A. Kimbrell, M.D., Robert T. Dunn, M.D., Robert M. Post, M.D.

NR426 Thyroid Stimulating Hormone and Suicidality in Refractory Mood Disorders
Mark A. Frye, M.D., Gabriele S. Leverich, M.S.W., Amy L. Danielson, B.A., Ann M. Callahan, M.D., Timothy A. Kimbrell, M.D., Robert T. Dunn, M.D.

NR427 Anhedonia and Regional Cerebral Metabolism in Affective Disorders
Robert T. Dunn, M.D., Timothy A. Kimbrell, M.D., John T. Little, M.D., Mark A. Frye, M.D., Mark W. Willis, M.Eng., Robert M. Post, M.D.

NR428 OCD in an HMO: Prevalence, Treatment and Costs
Lorrin M. Koran, M.D., Jeanne L. Leventhal, M.D., Bruce Fireman, M.S., Alice Jacobson, M.S.

NR429 Preventing Relapse in Chronic Depressions
Lorrin M. Koran, M.D., Charles Debattista, M.D., Christine Smith, M.D., Robert H. Howland, M.D., Susan G. Kornstein, M.D.

NR430 Alcohol Abuse and Bipolar Disorder: Family History
Jose de Leon, M.D., Fernando Mosquera, M.D., Ana Gonzalez-Pinto, M.D., Miguel Guiterrez, M.D., Juan L. Figuerido, M.D., Purification Lopez, M.D.

NR431 Psychosis and Bipolar Disorder
Jose de Leon, M.D., Ana Gonzalez-Pinto, M.D., Fernando Mosquera, M.D., Miguel Gutierrez, M.D., Jose L. Perez de Heredia, M.D., Jesus Ezcurra, M.D.

NR432 The Relationship Between Head Injuries, Depression and Suicidality in Appalachia
Geoffrey S. Duckworth, M.D., Hazel E.A. McBride, Ph.D., Joselito B. Morales, M.D., Roy S. Price, M.S.W.

NR433 Risperidone for Bipolar Symptoms in the Developmentally Disabled
Mary C. Chapman, George Woodley, M.D., Barkhat U. Kahn, M.D.

NR434 Depression Awareness in Mental Health Professionals
Gregory M. Asnis, M.D., Elizabeth John, M.D., Shehzad Kamran, M.D., William Sanderson, Ph.D.

NR435 The Altman Self-Rating Mania Scale (ASRM)
Edward Altman, Psy.D., Donald Medeker, Ph.D., James L. Peterson, B.A., John M. Davis, M.D.

NR436 Personality Variables in Response to Antidepressants
Michael T. Isaac, M.D., Maria B. Tome, M.D.

NR437 Study of the ECT Influence in the rCBF by HMPAO-SPECT
Edorta Elizagarate, Maria Artamendi, M.D., Ana Gonzalez-Pinto, M.D., Julia Cortes, M.D., Ignacio Alonso, M.D., Miguel Gutierrez, M.D.

NR438 Prevalence of Mood Disorders in Hungary
Erika Szadoczky, M.D., Zsuzsanna Papp, Jozsef Vitray, Zoltan Rihmer, M.D., Janos Iuredy, Ph.D.

NR439 Benefit-Risk Analysis Between Venlafaxine XR and Venlafaxine
Richard Entsuah, Ph.D.

NR440 Prevalence and Significance of Catatonic Symptoms in Mania
Stephanie Kruger, M.D., Peter Braunig, M.D., Gerald Shugar, M.D.

NR441 Severity of Illness in Mania and Schizophrenia
David B. Schnur, M.D., Scott P. Smith, M.A., Adam D. Smith, Ph.D., Michael Obuchowski, Ph.D., Barbara Cornblatt, Ph.D., Sajid Hussain, M.D.

NR442 Gender-Based Differences in Depressive Symptoms
Dale A. D'Mello, M.D., Anne M. Miller, D.O., John R. Meyers, M.D., Dominic V. Barberio, D.O., Donald Athearn, R.N., Rafael Villicana

NR443 Memory Processes and Executive Functions in Depression and Schizophrenia
Gilles Amar, M.D., P.H. Fossati, M.D., Na Raoux, Ph.D., J.F. Allilaire, M.D.

NR444 Anger Attacks in French Depressed Patients
Pauline Morand, M.D., Guy Thomas, Ph.D., Maurice Ferreri, M.D., Jouvent Roland, Ph.D.

NR445 Hormonal Responses to D-Fenfluramine in Depression: Evidence for Decreased Serotonin Function
Fabrice Duval, M.D., M. Claude Mokrani, Ph.D., Humberto Correa, M.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D.

NR446 DST Status and Dopamine Function in Psychotic Depression
Fabrice Duval, M.D., M. Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D., Humberto Correa, M.D.

NR447 Diagnostic Validity in Pregnancy
Lynn R. Grush, M.D., Lee S. Cohen, M.D., Jennie W. Bailey, B.A., Paula Tyack, Ph.D., Jerrold F. Rosenbaum, M.D.

NR448 Family Influences on Outcome in Bipolar Illness
Deborah A. Perlick, Ph.D., John F. Clarkin, Ph.D., JoAnne Sirey, Ph.D., Annette Zygmunt

NR449 Irritable and Depressed Mood: Are They Synonymous?
Paul J. Ambrosini, M.D., Gary M. Meyers, M.D., Michael D. Bianchi, M.D., Claudia Metz, M.D.

NR450 Predictors of Early Recovery in Outpatient Depression
JoAnne Sirey, Ph.D., Barnett S. Meyers, M.D., Martha L. Bruce, Ph.D., Deborah A. Perlick, Ph.D., Patrick Raue, Ph.D., George S. Alexopoulos, M.D.

NR451 Randomized, Double-Blind Placebo-Controlled Comparison of Once Daily Versus Twice Daily Venlafaxine in MDD
Jay D. Amsterdam, M.D., Mady Hornig-Rohan, M.D., Mary Hooper, B.A., Jess D. Amchin, M.D.

NR452 Gabapentin in Bipolar Depression: A Case Series
L. Trevor Young, M.D., Janine Robb, B.Sc.N., Irene Patelis-Siotis, M.D., Cathy MacDonald, R.N., Russell T. Joffe, M.D.

NR453 A Test of the Phase-Shift Hypothesis of SAD
James Kurtz, M.D., Mark S. Bauer, M.D., Russell Poland, Ph.D.

NR454 Rapid-Cycling Bipolar Disorder: Does Homozygosity for the COMT Low Activity Allele Represent a Risk Factor for the Development of Rapid-Cycling?
Sabine E. Veit, M.D., Gianni L. Faedda, M.D., Herbert M. Lachman, M.D., Demitri F. Papolos, M.D.

NR455 Anxiety, Insomnia and Antidepressant Selection
Gregory E. Simon, M.D., John Heilegenstein, M.D., Wayne J. Katon, M.D.

NR456 WITHDRAWN

NR457 A Double-Blind, Placebo-Controlled Study of Sertraline in the Treatment of Outpatients with Dysthymia
Arun Ravindran, M.B., Robert Wiseman, Ph.D.

NR458 A Double-Blind Study of Sertraline and Moclobemide in the Treatment of Outpatients with Atypical Depression
Paul R. Latimer, M.D., Robert Wiseman, Ph.D., Guangrui Zhu, Ph.D.

NR459 Does Severity of Depression Influence Treatment Utilization or Adherence to Guidelines?
Sagar V. Parikh, M.D., Elizabeth Lin, Ph.D., Sidney Kennedy, M.D., Paula N. Goering, Ph.D.

NR460 Reversed Neurovegetative Symptoms of Depression: A Community Study of Ontario
Robert O. Levitan, M.D., Alain D. Lesage, M.D., Sagar V. Parikh, M.D., Paula N. Goering, Ph.D., Sidney Kennedy, M.D.

NR461 The Seasonality of Bulimic Symptoms in Seasonal Depressives and Healthy Controls
Anthony J. Levitt, M.D., Alan Kaplan, M.D., Robert O. Levitan, M.D., Susan Dickens

NR462 The Chronological Relationship Between the Onset of Dysthymia and Major Depression Impacts on Outcome
Anthony J. Levitt, M.D., Russell T. Joffe, M.D., Stephen Sokolov, M.D.

NR463 Longitudinal Study of 5HT Function in Depression
Robert N. Golden, M.D., Amy D. Heine, M.S., Robert D. Ekstrom, M.A., Joseph M. Bebchuk, M.D., Martha E. Leatherman, M.D., James C. Garbutt, M.D.

NR464 Growing Old and the Risk of Major Depression
Robert E. Roberts, Ph.D., George A. Kaplan, Ph.D., William J. Strawbridge, Ph.D., Sarah J. Shema, B.S.

NR465 Citalopram in the Treatment of Moderate to Severe Depression
Joe Mendels, M.D., Ari Kiev, M.D., Louis F. Fabre, Jr., M.D., Gerri Schwartz, Ph.D.

NR466 The Course of Psychomotor Agitation During Pharmacotherapy of Depression: Analysis from Double-Blind Controlled Trials
Sharon L. Blomgren, M.D., Gary D. Tollefson, M.D., Mary E. Sayler, M.S.

NR467 Fluoxetine Therapy in Depression in the Older Patient: Effects on Anxiety, Agitation and Insomnia
Sharon L. Blomgren, M.D., Rosalinda Terner, R.Ph., Michael Wilson, M.S.

NR468 Residual Symptoms in Responders to Fluoxetine
Andrew A. Nierenberg, M.D., Bronwyn R. Keefe, B.A., Vinita C. Leslie, M.A., Jonathan E. Alpert, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR469 Motor Activity and Variation of Mood in Depression
Matthias R. Lemke, M.D., Alesia Broderick, M.S., Martin Zeitelberger, M.D., Wolfgang Hartmann, M.D.

NR470 Enhanced Corticotropin Response to Corticotropin-Releasing Hormone as a Predictor of Mania in Euthymic Bipolar Patients
Eduard Vieta, M.D., Maria J. Martinez-De-Osaba, M.D., Francesc Colom, Ph.D., Aurora Otero, M.D., Cristobal Gasto

NR471 Citalopram Versus Amitriptyline in Depressed Elderly
Kerstin Overo, D.Sc.

NR472 Previous SSRI Treatment and Efficacy of Sertraline for OCD: Combined Analysis of Four Multicenter Trials
Steven A. Rasmussen, M.D., Lee Baer, Ph.D., David Shera, Ph.D.

NR473 The Clonazepam Switch to Sertraline in Panic Disorder
Marcio V. Versiani, M.D., Egidio Nardi, M.D., Sandra Pinto, Ph.D.

NR474 Hoarding Predicts Poor Response in OCD
Donald W. Black, M.D., Patrick O. Monahan, M.S., Gerard P. Clancy, M.D., Peggy B. Baker, M.D., Janelle M. Gabel, R.N.

NR475 A Follow-Up Study of DSM-III-R GAD with Syndromal and Subsyndromal Major Depression
James G. Barbee IV, M.D., Charles K. Billings, Jr,, M.D., Nancy B. Bologna, Ph.D., Mark H. Townsend, M.D.

NR476 Long-Term Experience with Clonazepam in Patients with Panic Disorder
John J. Worthington III, M.D., Mark H. Pollack, M.D., Georges Moroz, M.D., Michael W. Otto, Ph.D., Renee McLean, B.A., Jerrold F. Rosenbaum, M.D.

NR477 Multi-Dimensional Outcome and Quality of Life in Panic Disorder: The Effects of Sertraline Treatment
Mark H. Pollack, M.D., Robert Wolkow, M.D., Cathryn M. Clary, M.D.

NR478 Nefazodone in the Treatment of Social Phobia
Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Jonathan Oakman, Ph.D., Steve Collins, M.D.

NR479 Shyness and Behavioral Inhibition in Anxiety Disorders
Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Jonathan Oakman, Ph.D.

NR480 Symptom Structure in OCD: Factor Analytic Evidence for Subgroups
Laura J. Summerfeldt, M.A., Margaret A. Richter, M.D., Martin M. Antony, Ph.D., Veronika M. Huta, B.Sc., Richard P. Swinson, M.D.

NR481 Plasma Anti-5HT and 5HT Antibodies Raised in Panic Disorder
Jeremy D. Coplan, M.D., Hadassah Tamir, M.D., Denise Calaprice, Marybeth J. De Jesus, B.A., Laszlo A. Papp, M.D., Jack M. Gorman, M.D.

NR482 Adjunctive Treatments in Bipolar and Schizoaffective Disorder: Comparisons of Risperdone, Conventional Neuroleptics or Clonazepam Combined with Mood
S. Nassir Ghaemi, M.D., Frederick K. Goodwin, M.D.

NR483 Personality Traits and Disorders in Body Dysmorphic Disorder
Katharine A. Phillips, M.D., Susan L. McElroy, M.D.

NR484 Prevalence of Body Dysmorphic Disorder in Dermatology Patients
Katharine A. Phillips, M.D., Raymond Dufresne, M.D., Caroline Wilkel, M.D., Carmella Vittorio, M.D.

NR485 The Brown Assessment of Beliefs Scale: Reliability and Validity
Jane L. Eisen, M.D., Katharine A. Phillips, M.D., Lee Baer, Ph.D., Douglas A. Beer, M.D., Katherine D. Atala, M.D., Steven A. Rasmussen, M.D.

NR486 Insight in Body Dysmorphic Disorder Versus OCD
Jane L. Eisen, M.D., Katharine A. Phillips, M.D., Steven A. Rasmussen, M.D., Douglas Luce

NR487 Long-Term Prognosis of Panic Disorder
Hisanobu Kaiya, M.D., Yoshikazu Miyamae, M.A., Noriya Ishida, M.D.

NR488 Cognitive-Behavioral Therapy Versus the Combination with Fluvoxamine in the Treatment of OCD
Anton J.L.M. Van Balkom, M.D., Else De Haan, Ph.D., Patricia Van Oppen, Ph.D., Ph. Spinhoven, Ph.D., C.A.L. Hoogduin, M.D., R. Van Dyck, M.D.

NR489 Are Anger Attacks in Unipolar Depression a Variant of Panic Disorder?
Joyce R. Tedlow, M.D., Vinita C. Leslie, M.A., Bronwyn R. Keefe, B.A., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR490 Correlates of Hypochondriacal Tendencies in Panic Disorder with Agoraphobia
Vladan Starcevic, M.D., Goran Bogojevic, M.D., Smiljka Popovic-Deusic, M.D.

NR491 Low Serum Beta-Endorphin Levels in Panic Disorder
Lucia Perez-Costillas, M.D., Manuel Gurpegui, M.D., Esperanza Ortega, M.D.

NR492 Repetitive Behaviors of OCD and Tourette's Syndrome
Euripedes C. Miguel, M.D., Lee Baer, Ph.D., Barbara J. Coffey, M.D., Scott L. Rauch, M.D., James F. Leckman, M.D., Michael A. Jenike, M.D.

NR493 Psychotic Symptoms in PTSD
Daniella David, M.D., Gary S. Kutcher, Ph.D., Elizabeth I. Jackson, M.D., Thomas A. Mellman, M.D.

NR494 Alcohol and the Pituitary in Hippocampal Volume Loss in PTSD
David B. Arciniegas, M.D., Thomas P. Beresford, M.D., Donald C. Rojas, Ph.D., Jeanelle Sheeder, B.A., Peter D. Teale, M.S.E.E., Martin L. Reite, M.D.

NR495 Repetitive Assessment of Impulsivity in a Cohort of 155 Patients with OCD: Twelve-Month Prospective Follow-Up
Elie G. Hantouche, M.D., Myriam L. Bouhassira, M.D., Marc L. Bourgeois, M.D.

NR496 PTSD in Community Samples: A Measurement Problem
Carol S. Fullerton, Ph.D., Robert J. Ursano, M.D., Brian Crowley, M.D., Richard S. Epstein, M.D., Karrie J. Craig, Ph.D., Andrew S. Baum, Ph.D.

NR497 Pilot Study of Nefazodone for Chronic PTSD and Related Sleep Disturbance
Thomas A. Mellman, M.D., Daniella David, M.D., Lydia Barza

NR498 Personality Disorders and Temperament and Character in PTSD
Jose J. Almanza, M.D., Francisco Paez, M.D., Marcos Hernandez, M.D., Genaro Barajas, M.D., Sergio Altamirano, M.D., Humberto Nicolini

NR499 Stability of Temperament in Panic Disorder Patients
Manuel Gurpegui, M.D., Lucia Perez-Costillas, M.D.

NR500 Compulsive Behavior in GAD and OCD
Mark H. Townsend, M.D., Karen Weissbecker, Ph.D., James G. Barbee IV, M.D., Daniel K. Winstead, M.D.

NR501 Cortisol Circadian Rhythms During the Menstrual Cycle and with Sleep Deprivation in Premenstrual Dysphoric Disorder and Normal Control Subjects
Suryabanu Javeed, M.D., Barbara L. Parry, M.D., Richard Haugher, M.D., Paul Cloptim, M.S.

NR502 PMS, Premenstrual Dysphoric Disorder, and Diurnal Variation in 5HIAA Levels
Anita L.H. Clayton, M.D., Adrienne E.R. Sheldon-Keller, Ph.D., Catherine A. Leslie, M.D.

NR503 Effects of Antidepressants: EEG Sleep Studies in Depressed Patients During Dothiepin Treatment
Seung Chul Hong, M.D., Jin-Hee Han, M.D., Sung-Pil Lee, M.D.

NR504 Age Differences in Behaviors Leading to Completed Suicide
Yeates Conwell, M.D., Paul Duberstein, Ph.D., Christopher Cox, Ph.D., Jack Herrmann, M.S., Eric D. Caine, M.D.

NR505 Completed Suicide and Remitted Alcoholism
Paul Duberstein, Ph.D., Yeates Conwell, M.D., Dorrie-Sue Barrington, B.S., Jack Herrmann, M.S., Christopher Cox, Ph.D., Eric D. Caine, M.D.

NR506 Predisposition to Suicide Attempts in Appalachia
Joselito B. Morales, M.D., Hazel E.A. McBride, Ph.D., Geoffrey S. Duckworth, M.D., Roy S. Price, M.S.W.

NR507 Variation in Suicide Risk Among Bipolar Families
Sylvia G. Simpson, M.D., Dean F. MacKinnon, M.D., Melvin G. McInnis, M.D., Francis J. McMahon, M.D., J. Raymond DePaulo, Jr., M.D.

NR508 Decreased Risk of Suicide in Clozapine Treated Patients with Schizophrenia: A Retrospective Cohort Study
Michael J. Reinstein, M.D., Kathleen D. Colombo, B.S.N., Lynne E. Jones, R.N., Sangarapillai C. Mohan, M.D.

NR509 Precarious Job Integration in Self-Attempters: A French Preliminary Report
Francoise Chastang, M.D., I. Dupont, Patrice Rioux, M.D., V. Kovess, E. Zarifian

NR510 Inducible Nitric Oxide Synthase in the Brain
Ma-Li Wong, M.D., Amer Al-Shekhlee, M.D., Peter B. Bongiorno, B.Sc., Samuel M. McCann, M.D., Philip W. Gold, M.D., Julio Licinio, M.D.

NR511 The Immune Function and MDD
Doobyung Park, M.D., Juyeon Cho, M.D., Aeja Park, M.D.

NR512 Insomnia and Its Impact: A Survey of Enrollees at Five U.S. Managed Care Organizations
Wallace B. Mendelson, M.D., Hind T. Hatoum, Ph.D., Chris Kania, M.S., Sheldon X. Kong, Ph.D., Josephine Wong, Pharm.D.

NR513 Long-Term Health Care Resource Utilization and Cost Before and After Initiation of Risperidone Treatment in Patients with Chronic Schizophrenia
Penny Albright, Ph.D., David L. Keegan, M.D., Patricia M. Vandenbygaart, M.Sc.

NEW RESEARCH

Wednesday, May 21, 1997, 3:00 p.m.-5:00 p.m.

New Research 12 – Poster Session – Special Events Area, Upper Level, Convention Center

SCHIZOPHRENIA, BIOLOGICAL PSYCHIATRY, BRAIN IMAGING, NEUROBIOLOGY, NEUROPSYCHIATRY, AND RESEARCH ISSUES

Chp.: Mark H. Rapaport, M.D.

NR514 Independence of Affect Expression and Affect Recognition in Schizophrenia
Richard J. Shaw, M.D., Melissa Dong, M.A., Kelvin O. Lim, M.D., Murray Alpert, Ph.D., Enrique R. Pouget, B.A.

NR515 A Clinical Lab for Psychiatry: Vocal Acoustic Measures of Flat Affect and Alogia
Murray Alpert, Ph.D., Enrique R. Pouget, B.A., Richard J. Shaw, M.D., Melissa Dong, M.A., Kelvin O. Lim, M.D.

NR516 A Bridging Study of Once Daily Iloperidone in Schizophrenia Patients
Neal R. Cutler, M.D., James E. Shipley, M.D., Jerome F. Costa, M.D., Laura Zumpano, Mindy F. Gellock, Jameel Hourani, D.O., Stanford S. Jhee, Pharm.D., John J. Sramek, Pharm.D.

NR517 A Bridging Study of Once-Daily MDL 100,907 in Schizophrenia Patients
Neal R. Cutler, M.D., Linda Elkins, Ph.D., Lutrecia Church, M.A., Jerome F. Costa, M.D., John J. Sramek, Pharm.D.

NR518 Computerized Assessment of Psychosis Severity Questionnaire
Robert G. Stern, M.D., Ronald G. Fudge, Ph.D., James Crichton, M.A., Cecile E. Sison, Ph.D., Benedict J. Connolly, M.A., Miklos F. Losonczy, M.D.

NR519 Speech Processing Impairments Associated with Hallucinated Voices in Schizophrenia
Ralph E. Hoffman, M.D., Donald M. Quinlan, Ph.D., Jill Rapaport, M.S., Helen Sayward, M.A., Carolyn M. Mazure, Ph.D.

NR520 Schizophrenic Relapse in Medication-Complaint and Non-Complaint Patients
Jose L. Ayuso-Gutierrez, M.D., Beatriz Paya, M.D., Margarita Saenz, M.D., Julia Del Rio, M.D.

NR521 Risperidone Versus Conventional Neuroleptics in Forensic Hospital Patients
Patrick J. Devitt, M.D., Prakash S. Masand, M.D.

NR522 Alcohol Metabolism in Three Different Aldehyde Dehydrogenase 2
Sy-Ueng Luu, M.D., Ming-Fang Wang, M.S., Shih-Jiun Yin, Ph.D.

NR523 Additive Effect of Dopaminergic Genes in OCD with Tics
Humberto Nicolini, Beatriz Camarena, B.Sc., Carlos Cruz, Ph.D., Francisco Paez, M.D.

NR524 Thyroid Hormones and ADHD

Peter Hauser, M.D., Rosa Soler, Francoise Brucker-Davis

NR525 Serial Correlation of CSF HVA and 5-HIAA in Healthy Humans Undergoing Sequential CSF Sampling for Over Thirty Hours
Mitchel A. Kling, M.D., Michael D. De Bellis, M.D., Thomas D. Geracioti, Jr., M.D., Dennis L. Murphy, M.D., Philip W. Gold, M.D.

NR526 Clinical and Neuropsychological Improvement Unrelated to SPECT Changes in OCD
Mantosh J. Dewan, M.D., John F. Tanquary, M.D., Prakash S. Masand, M.D., Robert Sprafkin, Ph.D., F. Deaver Thomas, M.D., N.M. Szeverenyi, Ph.D., Leslie F. Major, M.D.

NR527 Lithium Therapy and Hyperparathyroidism
Marion E. Wolf, M.D., Mary Holland, R.P.H., Don Grant, R.P.H., Janet M. Mosnaim, Sandra Dempsey, M.D.

NR528 Reversed Circadian Rhythm in Gerbils May Shed Light on Some Sleep and Mood Disorders
John D. Hallonquist, Ph.D., Penny Gray-Allan, B.Sc., Terry Lao, B.A., Rod Wong, Ph.D.

NR529 D-fenfluramine Challenge Test in Acute Schizophrenia
Pavel Mohr, M.D., Jiri Horacek, M.D., Lucie Motlova, M.D., Jan Libiger, M.D., Pal Czobor, Ph.D.

NR530 Catechol O-Methyltransferase and Tryptophan Hydroxylase Genotypes in Violent Schizophrenia Patients
Pavel Mohr, M.D., Karen A. Nolan, Ph.D., Herbert M. Lachman, M.D., Jan Volavka, M.D.

NR531 Amygdala Volume and Glucose Metabolic Rate in Autism and Asberger's Disorder
M. Mehmet Haznedar, M.D., Monte S. Buchsbaum, M.D., Inbahl Heth, B.A., Tse Chung Wei, Ph.D., Patrick Hof, M.D., Eric Hollander, M.D.

NR532 Cavum Septi Pellucidi in Schizophrenia Spectrum Disorders
M. Mehmet Haznedar, M.D., Monte S. Buchsbaum, M.D., Jonathan Schwartz, B.S., Erin A. Hazlett, M.B., Jacqueline Spiegel-Cohen, M.S., Larry J. Siever, M.D.

NR533 PET Studies and Fenfluramine in Impulsive Patients
Larry J. Siever, M.D., Monte S. Buchsbaum, M.D., Antonia S. New, M.D., Erin A. Hazlett, M.B., Elizabeth Sevin, B.S.

NR534 Frontal Lobe and Startle Eye-Blink Deficits in Schizophrenia
Erin A. Hazlett, M.B., Monte S. Buchsbaum, M.D., M. Mehmet Haznedar, M.D., Melissa Biren, B.A., David B. Schnur, M.D.

NR535 Diffusion Tensor Analysis of White Matter Pathways in Schizophrenia
Monte S. Buchsbaum, M.D., Cheuk Y. Tang, M.S., Erin A. Hazlett, M.B., Dongfeng Lu, Ph.D., Jacqueline Spiegel-Cohen, M.S., Scott W. Atlas, M.D.

NR536 Memorization Strategy and CBF
Igor I. Galynker, M.D., Vanessa Cahn, B.A., Christie Ieronimo, B.A., D. Howard Finestone, M.D., Fukiat OngSeng, M.D., Eamon Dutta, M.D., Dragos Serseni, M.D.

NR537 Diminution of CBF After Caffeine: Clinical Evaluation by Means of Neurospect
Aida T. Ruiz, M.D., Ismael G. Mena, M.D., Sonia G. Neubauer, M.D., Jacqueline T.

Cornejo, M.D., Carmen M. Thomas, M.D., Tony Strickland, M.D.

NR538 SPECT in Schizophrenics with Positive Versus Negative Symptoms
Mohamed H. Ghanem, M.D., Mostafa Kamel, M.D., Adel Sadek, M.D., Mohamed El-Banouby, M.D., Salma Kwalil, M.D.

NR539 Outpatient Antidepressant Responders Have Lower Paralimbic Regional Cerebral Glucose Metabolism than Inpatient Nonresponders
Brenda E. Benson, B.S., Timothy A. Kimbrell, M.D., Terence A. Ketter, M.D., John T. Little, M.D., Robert T. Dunn, M.D., Robert M. Post, M.D.

NR540 The Cerebellum, Vermis and Brainstem in Schizophrenia: An MRI Study
James J. Levitt, M.D., Robert M. Donnino, B.A., Martha E. Shenton, Ph.D., Ronald Kikinis, M.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

NR541 Midline Cerebral Structures in Schizophrenic Patients: A MRI Study
Professor Giuseppe Bersani, Dr. Cristiana Silvestrini, Dr. Angela Iannitelli, Dr. Pietro Cipriano, Dr. Catia Zucca, Paolo Pancheri, M.D.

NR542 Obstetric Complications, Age at Onset and Autistic Dimension in Male Schizophrenic Patients
Professor Giuseppe Bersani, Ives Taddei, Piero Venturi, Paolo Pancheri, M.D.

NR543 A PET Study of Traumatic Response in PTSD
Stephen K. Brannan, M.D., Paul Ingmundson, Ph.D., Mark Alfano, Ph.D., Alexander L. Miller, M.D., Helen Mayberg, M.D., Peter Fox, M.D.

NR544 Toward Localization of Thalamic Pathology in Schizophrenia
William M. Byne, M.D., Liesl Jones, Ph.D., Eileen Kemether, M.D., V. Haroutunian, Ph.D., Kenneth L. Davis, M.D.

NR545 Effects of Anabolic Steroids on Lymphocyte Beta-Adrenergic and Serotonin Receptor mRNA Levels in Male Normal Volunteers
Tong-Ping Su, M.D., Christopher Hough, Ph.D., David R. Rubinow, M.D., De-Maw Chuang, Ph.D.

NR546 Enkephalin Gene Expression After NMDA Receptor Hypofunction Induced by Acute Ketamine
Andrea de Bartolomeis, M.D., Luigi Aloj, M.D., Giovanni Muscettola, M.D.

NR547 A Double-Blind, Placebo-Controlled Comparison of Venlafaxine and Venlafaxine Extended Release (ER) in Outpatients with Major Depression
Lynn A. Cunningham, M.D.

NR548 Evidence for a Casual Relationship Between Phantom Limb Pain and Cortical Reorganization in Arm Amputees
Wolfgang Larbig, M.D.

NR549 Personality Correlates of Response to CCK-4 in Healthy Males
Diana Koszycki, Ph.D., Jacques Bradwejn, M.D.

NR550 Respiratory Response to CCK-4 in Healthy Subjects

Jacques Bradwejn, M.D., Jean-Marc Legrand, M.D., Diana Koszycki, Ph.D., Jason H.T. Bates, Ph.D., Michel S. Bourin, M.D.

NR551 Trauma and HPA Axis Activity in BPD and Normal Controls
Robert A. Grossman, M.D., Rachel Yehuda, Ph.D., Larry J. Siever, M.D.

NR552 Reproducibility of ACTH Secretory Response to Corticosteroid Withdrawal and Corticotropin Releasing Hormone and Naloxone Stimulation in Healthy Humans
David A. Graeber, M.D., Richard I. Dorin, M.D., E. Jonathan Lisansky, M.D., Brian B. Roberts, M.D., Clifford R. Qualls, Johannes D. Veldhuis

NR553 The Relationship Between the Amygdala and the Midbrain Dopamine System: Implications for Schizophrenia
Julie L. Fudge, M.D., Suzanne N. Haber, Ph.D.

NR554 The Phenomenology of Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections
Susan J. Perlmutter, M.D.

NR555 The Sunnybrook Stroke Study: A Prospective Study of Depressive Symptoms and Functional Outcome
Nathan Herrmann, M.D., Sandra E. Black, M.D., Joanne Lawrence, R.N., Christine Szekely, M.A., John P. Szalai, Ph.D.

NR556 EEG Evidence of Hemispheric Activation with Contralateral Visual Field Stimulation
Fredric Schiffer, M.D., Carl M. Anderson, Ph.D., Martin H. Teicher, M.D.

NR557 Bedside Neuropsychiatric Findings in Adults with ADHD
Joseph P. Horrigan, M.D., L. Jarrett Barnhill, Jr., M.D.

NR558 Lithium and Neuroleptics in Combination: The Spectrum of Neurotoxicity
Stephen A. Goldman, M.D.

NR559 Minor Depression Following Traumatic Brain Injury: A One-Year Longitudinal Study
Ranjan Dahiya, M.D., Robert G. Robinson, M.D., Sergio Paradiso, M.D.

NR560 Social Impairment and Recovery from Stroke
Kengo Shimoda, M.D., Robert G. Robinson, M.D.

NR561 Slower Reaction Time in Schizophrenia: Relationship to Clinical Symptoms and Cerebral Dysfunction
Jason Willis-Shore, B.A., Sophia Vinogradov, M.D., John Poole, Ph.D., Beth A. Ober, Ph.D., Greg Shenaut, Ph.D.

NR562 Gepirone Extended Release (ER) Compared to Placebo in the Treatment of Outpatients with Major Depression
Cal K. Cohn, Ph.D., Louis F. Fabre, Jr., M.D.

NR563 Psychometric Validation and Reliability Testing of a State Scale of Dissociation
Christa Kruger, M.Med., Chris J. Mace, M.B.

NR564 Intermittent Explosive Disorder: Revised Criteria for Aggression Research

Emil F. Coccaro, M.D., Richard J. Kavoussi, M.D., Mitchell E. Berman, Ph.D., Lauren Y. Weinberg, M.S., Barrie Franklin, Ph.D., Jennifer D. Lish, Ph.D.

NR565 Prescribing Practices: Trazodone
John W. Goethe, M.D., Bonnie L. Szarek, R.N.

NR566 Effect of Concept Formation Training on the Performance of the Wisconsin Card Sorting Test in Schizophrenic Patients
Young-Nam Park, M.D., Hee Choel Kim, M.D., Sung Mi Kim, M.D.

NR567 Personality and Symptom Dimensions in Psychoses
Manuel J. Cuesta, M.D., Victor Peralta, M.D., Francisco Caro, M.D., Alfredo Martinez

NR568 MRI and Neruopsychological Measures in Schizophrenia: Partial Least Squares Analysis
Paul G. Nestor, Ph.D., John Barnard, Ph.D., Brian F. O'Donnell, Ph.D., Martha E. Shenton, Ph.D., Ronald Kikinis, M.D., Ferenc A. Jolesz, M.D.

NR569 Outcome Measures in Initially Untreated Psychosis
David J. Meagher, M.B., John L. Waddington, Ph.D., James Mullaney, M.D., John J. Quinn, M.B., Patrice Murphy, M.B.

NR570 Ziprasidone Metabolism and Cytochrome P450 Isoforms
Donald J. Tweedie, Ph.D., Chandra Prakash, Ph.D., Amin K. Kamel, M.D., D. Cui, Robert D. Whalen, M.D., Jeffrey J. Miceli

NR571 Steady State Pharmacokinetics of Ziprasidone in Healthy Old and Young Volunteers
Thomas G. Tensfeldt, M.S., Keith D. Wilner, Ph.D., Barbara Baris, Terry A. Smolarek, Ph.D., Ryan Z. Turncliff, B.A., Wayne A. Colburn, Ph.D.

NR572 Effects of Cimetidine or Maalox on Ziprasidone Pharmacokinetics
Keith D. Wilner, Ph.D., Robert A. Hansen, Carol J. Folger, Geoffroy Pierre

NR573 Lack of CYP2D6 Inhibition by Ziprasidone in Healthy Volunteers
Keith D. Wilner, Ph.D., Steven Demattos, B.S., Richard J. Anziano, M.S., Glen Apseloff, M.D., Nicholas Gerber, M.D.

NR574 Working Memory Dysfunction in Schizophrenia
Anne-Marie Shelley, Ph.D., Daniel C. Javitt, M.D., Herbert G. Vaughan, Ph.D.

NR575 Cardiovascular Safety of Sertindole
Mark B. Hamner, M.D., Chris Silber, M.D., Rita Driscoll, M.D., Mack Randall, B.S.

NR576 The Nicotine Patch, Smoking and Schizophrenia
Gregory W. Dalack, M.D., James H. Meador-Woodruff, M.D.

NR577 No Evidence for Autoimmunity in Schizophrenia
Pinkhas Sirota, M.D., Yoav Cori, M.D., Talia Hahn, Ph.D., Amichai Schattner, M.D.

NR578 The Relationship Between Changes in Schizophrenic Symptoms and Cognitive Deficits During Treatment with an Atypical Neuroleptic
Howard H. Chang, M.D., Ileana Berman, M.D., Demetra Pappas, B.S., Nina Leventhal, B.A., Rogelio D. Bayog, M.D., Joseph Langlois, M.A.

NR579 Neuropsychology of Mood Disorder and Schizophrenia
Joseph Ventura, Ph.D., William McMullan, Ph.D., Barry H. Guze, M.D., Lorie Humphrey, Ph.D., Michael J. Gitlin, M.D.

NR580 PRN Medication and Seclusion Use in Chronic Psychiatric Inpatients
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D.

NR581 A Psychiatry Primary Care Clinic and Hospital Stay
Patricio R. Escalona, M.D., Ervin W. Lewis, M.D., Bruce Washburne, David A. Graeber, M.D.

NR582 Oral-Facial Dyskinesia in Chronic Institutional Schizophrenic Inpatients
Rebecca E. Adams, M.D., Michael J. Parrella, Ph.D., Leonard White, Ph.D., William M. Byne, M.D., Philip D. Harvey, Ph.D.

NR583 Empirical Definition of Subtypes of Schizophrenia
Leonard White, Ph.D., Philip D. Harvey, Ph.D., Sonia Dollfus, M.D.

NR584 The Tolerability and Efficacy of Intramuscular Ziprasidone
Schlomo Brook, M.D., Rachel Swift, M.D., Edmund P. Harrigan, M.D.

NR585 QEEG Topographic Maps in Psychiatric and Neurological Groups
Donald W. Brunet, M.D., Susan J. Adams, M.B., Marguarita Criollo, M.D., Howard Galin, M.A., James S. Lawson, Ph.D., Duncan J. MacCrimmon, M.D.

NR586 The Role of Immune Measures in Schizophrenic Behavior
Daniel P. van Kammen, M.D., Cathy G. McAllister, Ph.D., Mary E. Kelley, M.S., Aleksander A. Mathe, M.D., Walter A. Brown, M.D., Jeffrey K. Yao, Ph.D.

NR587 Medication Effects on Negative Symptoms in Schizophrenia
Daniel P. van Kammen, M.D., Mary E. Kelley, M.S.

NR588 A One-Year Prevalence Study of Schizophrenia on Reunion Island in the Indian Ocean
Philip A.P.M. Gorwood, M.D., Marion Leboyer, M.D., Maurice Jay, M.D., Josue Feingold, M.D.

NR589 Population Pharmacokinetics of Sertindole
Richard Granneman, M.D., Sheckman Wong, Ph.D., Patricia Wozniak, Ph.D., Chris Silber, M.D., Randall Mack, B.S.

NR590 Efficacy and Safety of Once-Daily Dosing with Risperidone in Patients with Schizophrenia
Steven G. Potkin, M.D.

NR591 A Cost-Effectiveness Clinical Decision Analysis Model for Schizophrenia
Jane C. Haley, Cynthia Palmer, M.Sc., Dennis Revicki, Ph.D., Laura A. Genduso, Susan Hamilton, M.S.

NR592 Metabolic Rate in Kraepelinian Versus Non-Kraepelinian Schizophrenia
Lina S. Shihabuddin, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, M.B., Johannes Schroeder, M.D., M. Mehmet Haznedar, M.D., Kenneth L. Davis, M.D.

NR593 Left Ventricular Size Increases with Age and Is Associated with Reduced Parietal and Occipital Cortical Metabolic Rate in Schizophrenia
Adarsh K. Gupta, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, M.B.

NR594 Skills Training for Substance Abusing Schizophrenics
Andrew L. Shaner, M.D., Lisa J. Roberts, M.A., Thad Eckman, Ph.D., Jeffery N. Wilkins, M.D.

NR595 The Clinical Actions of Risperidone: Factor Analysis of Data from the North American Trial
Stephen R. Marder, M.D., John M. Davis, M.D., Guy Chouinard, M.D.

NR596 Attention and Information Processing Deficits in Schizophrenia: Correlates with Clinical Syndromes
Elton T.C. Ngan, M.D., Peter F. Liddle, Ph.D.

NR597 Depressive Symptoms in Recent-Onset Schizophrenia Patients Are Associated with a Family History of Depression
Kenneth L. Subotnik, Ph.D., Keith Nuechterlein, Ph.D., Robert F. Asarnow, David L. Fogelson, M.D., Michael J. Goldstein, Ph.D., Jim Mintz, Ph.D.

NR598 Long-Term Treatment of Elderly Psychotic Patients with Risperidone
Michael Davidson, M.D.

NR599 Prolactin Levels and Adverse Events in Patients Treated with Risperidone
David Kleinberg, Martin B. Brecher, M.D., John M. Davis, M.D.

NR600 The Reduced Response of Auditory Steady-State 40HZ in Schizophrenia
Jun Soo Kwon, M.D., Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D., Ronald J. Gurrera, M.D., Robert W. Greene, M.D., Yoshio Hirayasu, M.D.

NR601 Risperidone in Elderly Patients with Psychotic Disorders
Subramoniam Madhusoodanan, M.D., Ronald Brenner, M.D., John W. Kasckow, M.D., Mark E. Kunik, M.D., Amando Negron, M.D., Nunzio Pomara, M.D.

NR602 Haloperidol Improves Memory in Schizophrenia
Daniel N. Allen, Ph.D., Mark W. Gilbertson, Ph.D., Ethan Barry, B.A., Daniel P. van Kammen, M.D., John A. Gurklis, Jr., M.D.

NR603 Visuospatial Working Memory in Schizotypal Personality Disorder
Sonia Lees-Roitman, M.S., Richard S.E. Keefe, Ph.D., Vivian Mitropoulou, M.S., Rachel DuPre, B.A., Larry J. Siever, M.D.

NR604 Gender Differences in Acute Schizophrenic Symptoms
Julie M. Hannon, B.A., Michael Obuchowski, Ph.D., Alyson Andreasen, B.S., Scott P. Smith, M.A., Chris Smith, B.S., David B. Schnur, M.D., Barbara Cornblatt, Ph.D.

NR605 Antipsychotics Affect Suicidality in Schizophrenia
Carolyn Heimberg, M.D., Richard R. Owen, Jr., M.D., Lynn Mason, R.N., Ellen P. Fischer, Ph.D.

NR606 Glial Architecture of Human Cortex: Implications for Neurocognition in Schizophrenia
Bruce Quinn, M.D., William M. Byne, M.D., Laurie S. Conklin, B.S., Kenneth L. Davis, M.D.

NR607 Schizotypal Personality Disorder: A Replication of Cognitive Deficits
Martina M. Voglmaier, Ph.D., Larry J. Seidman, Ph.D., Dean F. Salisbury, Ph.D., Richard Rhodes, B.S., Robert W. McCarley, M.D.

NR608 Volumetric Comparisons of the Cingulate Gyrus in Patients with Schizophrenia and Controls
Patricia A. Fodor, M.D., Jeanelle Sheeder, B.A., Donald C. Rojas, Ph.D., Peter D. Teale, M.S.E.E., Jack Simon, M.D., Martin L. Reite, M.D.

NR609 The Thalamus in Schizophrenia: Failure to Replicate Reduced Volume
David B. Arciniegas, M.D., Jeanelle Sheeder, B.A., Donald C. Rojas, Ph.D., Peter Teele, M.S.E.E., Martin L. Reite, M.D.

NR610 Predictors of Suicidality in Schizophrenia
Naveed Iqbal, M.D., Bruce J. Schwartz, M.D., Edward McGraw, B.A., Stephen Daniel, Ph.D., Syed R. Ahmed, M.D., Faiq A. Hameedi, M.D.

NR611 Working Memory Dysfunction in Schizophrenics
Eduardo A. Leiderman, M.D., Sergio A. Strejilevich, M.D., Carlos A. de Lajonquiere, M.D.

NR612 Tolerability and Cardiovascular Safety of Risperidone
Martin B. Brecher, M.D., Philippe Lemmens, Ph.D., Bart van Baelen,

NEW RESEARCH

Thursday, May 22, 1997, 9:00 a.m.-10:30 a.m.

New Research 13 – Oral/Slide Session – Room 11A, Upper Level, Convention Center

TREATMENT TECHNIQUES, GENETICS, AND GERIATRIC PSYCHIATRY

Chp.: Wayne S. Fenton, M.D.

NR613 A Study of Treatment Outcome Comparing Dysthymia and Non-Dysthymia Diagnoses in Brief Psychotherapy — 9:00 a.m.
Lisa Wallner Samstag, M.A., David J. Hellerstein, M.D., J. Christopher Muran, M.D., Arnold Winston, M.D.

NR614 OCD, Response to SSRIs and the Serotonin Transporter Gene — 9:15 a.m.
Margaret A. Richter, M.D., James L. Kennedy, M.D., Elizabeth Billett, B.Sc., A. Heils, Ph.D., K. Peter Lesch, M.D.

NR615 CCK-B Receptor Gene Alleles Associated with Panic Disorder — 9:30 a.m.
James L. Kennedy, M.D., Diana Koszycki, Ph.D., Martin A. Katzman, M.D., Nicole A. King, B.Sc., Jacques Bradwejn, M.D.

NR616 Identification of a Putative Alzheimer's Disease Risk Locus on the X-Chromosome — 9:45 a.m.
George S. Zubenko, M.D., J. Scott Stiffler, B.S., Hugh B. Hughes, M.S., Mark R. Hurtt, M.D.

NR617 Late-Life Depression and Service Use in Primary Care — 10:00 a.m.
Barnett S. Meyers, M.D., M. Philip Luber, M.D., Mary E. Charlson, M.D., Pamela G. Williams-Russo, M.D., Tara DiDomenico, M.A., James Hollenberg, M.D.

NR618 Donepezil (E2020) Improves Cognition and Function in Patients with Mild to Moderately Severe Alzheimer's Disease: Results from Phase III Trials — 10:15 a.m.
Sharon L. Rogers, Ph.D., Richard C. Mohs, Ph.D., Lawrence T. Friedhoff, M.D.

NEW RESEARCH

Thursday, May 22, 1997, 9:00 a.m.-10:30 a.m.

New Research 14 – Oral/Slide Session – Room 11B, Upper Level, Convention Center

CROSS-CULTURAL AND MINORITY PSYCHIATRY

Chp.: Donald F. Klein, M.D.

NR619 Homicidal Behavior and Schizophrenia in Finland — 9:00 a.m.
Markku E.J. Eronen, M.D., Pirkko Rasanen, Ph.D., Panu Hakola, Ph.D., Jari Tiihonen, Ph.D.

NR620 A Sixth-Month Parasuicide Prospective Study in the Emergency Room of a French General Hospital — 9:15 a.m.
Francoise Chastang, M.D., I. Dupont, Patrice Rioux, M.D., V. Kovess, E. Zarifian

NR621 PTSD in Survivors of Rwanda's 1994 War — 9:30 a.m.
Athanase Hagengimana, M.D., John Mburu, M.D., Rachel Kangethe, M.D., David Ndetei, M.D., Lawson R. Wulsin, M.D.

NR622 Mental Disorders in a French Follow-Up Study of Rape Victims — 9:45 a.m.
Jean-Michel Darves-Bornoz, M.D., Fabrice Pierre, M.D., Christian Berger, M.D., Jacques Lansac, M.D., Andree DeGiovanni, M.D., Philippe Gaillard, M.D.

NR623 The Relationship Between PTSD and Trauma-Related Disorders and ymptomatology Among Incarcerated Women — 10:00 a.m.
Caron Zlotnick, Ph.D.

NR624 Correlates of ADHD in the Quebec Child Mental Health Survey — 10:15 a.m.
Philippe Lageix, Lise Bergeron, Ph.D., Jean-Marie Honorez, Ph.D., Jean-Pierre Valla, M.D.

NEW RESEARCH

Thursday, May 22, 1997, 12 noon-2:00 p.m.

New Research 15 – Poster Session – Special Events Area, Upper Level, Convention Center

GERIATRIC PSYCHIATRY, GENETICS, CONSULTATION-LIAISON AND EMERGENCY PSYCHIATRY, EATING DISORDERS, PLUS SIXTEEN SMALLER TOPICS

Chp.: Dilip V. Jeste, M.D.

NR625 Clinical Correlates of Mental Retardation in a County Hospital's Psychiatric Emergency Room
Shashi Berdia, M.D., David I. Mayerhoff, M.D., Jacob K. Ninan, M.D.

NR626 Risperidone in the Treatment of Gilles de la Tourette's Syndrome
Mara Stamenkovic, M.D., Shird Schindler, M.D., Harald Aschauer, M.D.

NR627 How to Diagnose and Treat ADHD in Children and Adults
Sanjay Jasuja, M.D.

NR628 Self-Perception Profile in Children with Leukemia: Self Versus Parent Report
Valsamma Eapen, Ph.D., Tom Revez, M.D., Chris Mpofu, M.D., Tewfik Daradkeh, M.B.

NR629 Obsessive-Compulsive Symptoms in Probands with OCD and Tourette's Syndrome
Valsamma Eapen, Ph.D., David L. Pauls, Ph.D., Mary M. Robertson, M.D.

NR630 Impact of Tics on Social Adaptation in Tourette's Disorder
Dinohra M. Munoz, M.D., Raul R. Silva, M.D., E. Steven Dummit III, M.D., Frederick J. Matzner, M.D., Daniel M. Medeiros, M.D., Thomas Hollenbach, Ph.D.

NR631 Childhood Sexual Abuse in Medical Students
Barbara A. Warner, M.D., Jerald Kay, M.D., Ronald J. Markert, M.D., William M. Klykylo, M.D., David G. Bienenfeld, M.D., Paulette M. Gillig, M.D.

NR632 The Impact of House Officer Rotation on Patient Care
Robert B. Daroff, Jr., M.D.

NR633 Schizophrenia or Strangeness Disorder: An Alternative Name
Isaac Charam, M.D.

NR634 Integration of Psychiatry: Designing a Problem-Based Medical Curriculum
Mohammed K. Al-Haddad, M.D.

NR635 Discrimination in Residency Applicant Selection?
Richard Balon, M.D., Rizwan M. Mufti, M.D., Mark T. Williams, M.D., Michelle Riba, M.D.

NR636 A Survey of State Financing of Psychiatry Residency Programs
Deborah A. Banazak, D.O., Jed G. Magen, D.O.

NR637 The Internet in Continuing Psychiatric Education
Rima Styra, M.D., Ivan Silver, M.D., Stephen Pogorski, Ph.D.

NR638 Patients' Experiences of a Representative Payee Program
Lisa B. Dixon, M.D., Nancy Krauss, L.C.S.W., Jack Scott, Sc.D., Scot W. McNary, M.A.

NR639 Medical Inpatient Utilization of Recurrently Readmitted Veterans
Nancy A. McCarthy, M.D.

NR640 Adolescent Substance Abuse Prevention
John F. Aruffo, M.D., Debra L. Hollis, B.A., A.J. Naylor, B.A., Roger A. Webb, Ph.D.

NR641 Persistence of Depressive Illness in Primary Care Patients with Major Depression: Is a Coexisting Anxiety Disorder a Risk Factor?
Bradley N. Gaynes, M.D., Kathryn M. Magruder, Ph.D., Barbara Burns, Ph.D., W.E. Broadhead, M.D., Grayson S. Norquist, M.D.

NR642 Alcohol Dependent Liver Graft Recipients: A Controlled, Three-Year Follow-Up
Gregory T. Everson, M.D., Gayatri Bharadhwaj, M.D., David B. Arciniegas, M.D., Thomas P. Beresford, M.D.

NR643 The Relationship Between Major Depression and Cardiovascular Disease: Is Homocysteine a Link?
Jonathan E. Alpert, M.D., Isabel T. Lagomasino, M.D., Andrea R. Kolsky, B.A., Teodoro Bottiglieri, Ph.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR644 Adjustment Disorder in Hospitalized Cancer Patients Receiving Bone Marrow Transplantation
Jesus Prieto, Jorge Atala, Jordi Blanch, Cristobal Gasto, Esteve Cirera

NR645 Middle-Aged Women with Heart Disease Have Greater Depressive Symptoms
Stephen L. Stern, M.D., David J. Frid, M.D., Anne Fish, Ph.D., Tilmer O. Engebretson, Ph.D., Charles F. Emery, Ph.D., Jo Ann Homan, M.S.

NR646 Identification of Domestic Violence Among Hospitalized Patients: Utilization of a Screening Questionnaire by a Psychiatric C/L Service
Stephanie K. Stern, M.D., James J. Strain, M.D.

NR647 Psychopathology Following Cardioverter-Defibrillator Implantation
Scott J. Crow, M.D., Marcia Justic, M.S.N., JoAnne Collins, B.S.N., Robert Goetz, Stuart Adler, M.D., Barbara Praus

NR648 Treatment of Delirium with Risperidone
Prakash S. Masand, M.D., Rose-Marie Sime, M.D., Anil Sipahimalani, M.D.

NR649 Screening for Anxiety and Depression in Women with Breast Cancer
Rosalind G. Hoffman, M.D., David K. Payne, Ph.D., Mary Jane Massie, M.D., Maria Theodoulou, M.D.

NR650 Recognition and Management of Psychiatric Distress in Ethnically Diverse Primary Care Patients
Henry Chung, M.D., Peter J. Guarnaccia, Ph.D., Jean Teresi, Ph.D., Tracey Goldstein, M.S., Mark Olfson, M.D., Barnett S. Meyers, M.D.

NR651 Acculturation, Psychiatric Distress and Major Depression in Ethnically Diverse Primary Care Patients
Henry Chung, M.D., Peter J. Guarnaccia, Ph.D., Mark Olfson, M.D., Barnett S. Meyers, M.D., Jean Teresi, Ph.D., Tracey Goldstein, M.S.

NR652 Older Hispanic Men: At Risk for Untreated Depressive Symptoms?
Irene E. Ortiz, M.D., Ernest J. Dole, Pharm.D., Andrew Allen, M.S., Linda J. Romero, M.D., Robert D. Lindeman, M.D.

NR653 Ethnicity and Anxiety Surrounding Breast Cancer Screening Mammography in an Urban Center
Theresa M. Miskimen, M.D., Arthur T. Meyerson, M.D., Haftan M. Eckholdt, Ph.D., Beverly R. Delaney, M.D.

NR654 African-American Women with Breast Cancer
Ruth M. Lamdan, M.D., Kathryn Taylor, Ph.D., Bonnie O'Connor, Ph.D., Jamie Siegel, M.D., Karen Moran, B.S.

NR655 Bosnian Student Survivors at Home and in Exile: A Comparative Study
Stevan M. Weine, M.D., Slobodan Loga, M.D., Ismet Ceric, M.D., Vladimir Gruden, M.D., Alma Dzubur Kulenovic, M.D., Zorana Kusevic, M.D., Ines Matijas, B.S., Amer Smajkic, M.D., Ivan Pavkovic, M.D.

NR656 Evidence of Genetic Linkage of Antisocial Alcoholism to the 5HT-1B Gene
Jaakko Lappalainen, M.D., Jeffrey C. Long, Ph.D., Norio Ozaki, M.D., H. Naukkarinen, Michael S. Eggert, M.D., Matti Virkkunen, M.D., Markku I. Linnoila, M.D., David S. Goldman, M.D.

NR657 18q Locus for Comorbid Bipolar and Panic Disorder
Dean F. MacKinnon, M.D., Jianfeng Xu, Ph.D., Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., O. Colin Stine, Ph.D., Melvin G. McInnis, M.D., J. Raymond DePaulo, Jr., M.D.

NR658 MDD: Are Genetic and Environmental Contributions Different in Men and Women?
Laura J. Bierut, M.D., Andrew Heath, D.Phil., Kathleen K. Bucholz, Ph.D., Stephen H. Dinwiddie, M.D., Pamela A.F. Madden, Ph.D., Dixie J. Statham, Michael P. Dunne, Ph.D., Nicholas G. Martin, Ph.D.

NR659 Systematic Search for Molecular Variants of Catechol-O-Methyltransferase Gene and Association Study with Schizophrenia
Chia-Hsiang Chen, M.D., Yue-Ru Lee, B.S., Kwang-Jen Hsiao, Ph.D.

NR660 Familial Aggregation of Psychiatric Disorders in Schizophrenic Probands
Aida T. Ruiz, M.D., Rafael C. Blanco, M.D., Jaime T. Santander, M.D., Adriana B. San Martin, M.D.

NR661 ApoE Gene Variants and Drug-Induced Cognitive Toxicity in the Elderly
Nunzio Pomara, M.D., Hla Tun, M.D., Dennis Deptula, Ph.D., David J. Greenblatt, M.D.

NR662 D2 Dopamine Gene Receptor Allele and Reward Dependence-Attachment
Robert G. Ruegg, M.D., James E. Lee, M.D., William H. Wilson, Ph.D.

NR663 Cerebrovascular Risk Factors in Older Depressives: Testing a Small Vessel Brain Disease Model of Pathogenesis
Jeffrey M. Lyness, M.D., Eric D. Caine, M.D., Christopher Cox, Ph.D., Deborah A. King, Ph.D., Yeates Conwell, M.D., Telva E. Olivares, M.D.

NR664 P300 Latency, Prefrontal Dysfunction and Antidepressant Treatment of Geriatric Depression
Balkrishna Kalayam, M.D., Robert C. Young, M.D., George S. Alexopoulos, M.D., Wilfred Van Gorp, Ph.D., Kathryn Lockwood, Ph.D., Colette Gonzales, M.A.

NR665 Inverse Nortriptyline Dose-Response Relationships in Dementia
Joel E. Streim, M.D., David O. Oslin, M.D., Suzanne DiFilippo, R.N., Thomas B. Cooper, M.D., Ira R. Katz, M.D.

NR666 Estrogen Therapy Decreases the Frequency of Physically Aggressive Behaviors in Severely Demented Elderly Patients
Helen H. Kyomen, M.D., Andrew Satlin, M.D., Jeanne Y. Wei, M.D.

NR667 Neuropsychological Functioning and MRI Signal Hyperintensities in Geriatric Depression
Elisse Kramer-Ginsberg, Ph.D., Blaine S. Greenwald, M.D., K. Ranga Krishnan, M.D., Leaane Popali, Charles Auerbach, Ph.D., Neil Kremen, M.D., Peter M. Aupperle, M.D.

NR668 Neuroanatomical Localization of Magnetic Resonance Hyperintensities of Geriatric Depression
Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., K. Ranga Krishnan, M.D., Manzar Ashtari, Ph.D., Neil Kremen, M.D., Peter M. Aupperle, M.D., Charles Auerbach, Ph.D., Mahendra C. Patel, M.D.

NR669 Apathy and Activities of Daily Living in Geriatric Depressed Patients With and Without CT-Scan Identified White Matter Disease
Melissa Jenkins, Ph.D., Paul F. Malloy, Ph.D., Stephen P. Salloway, M.D., Robert Kohn, M.D., Robert J. Westlake, M.D., Debbie Javorsky, M.A.

NR670 Clinical Significance of White Matter Hyperintensities on MRI in Geriatric Depression
Robert J. Westlake, M.D., Melissa Jenkins, Ph.D., Paul F. Malloy, Ph.D., Stephen P. Salloway, M.D., Robert Kohn, M.D., Katarina Luketela, Ph.D.

NR671 Clinical Utility of the Dementia Rating Scale for Evaluation of Patients with Stroke and Non-Alzheimer's Dementia
Ronald Cohen, Ph.D., Melissa Jenkins, Ph.D., Katarina Luketela, Ph.D.

NR672 A Stress-Diathesis Model of Spousal/Consortial Homicide-Suicide in the Aged
Donna Cohen, Ph.D., Maria D.D. Llorente, M.D., Julie Malphurs, M.A., Carl Eisdorfer, M.D.

NR673 Increased Medical Utilization in High Anxiety Sensitivity Elderly
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.

NR674 Usefulness of Alzheimer's Disease Assessment Scale Late Version for Distinguishing Levels of Function in Advanced Alzheimer's Dementia Patients
Karen L. Dahlman, Ph.D., Philip D. Harvey, Ph.D., Richard C. Mohs, Ph.D.

NR675 Hopelessness and Suicide Attempts in Elderly Patients with Major Depression
Yeates Conwell, M.D., Paul Duberstein, Ph.D., Larry Seidlitz, Ph.D., Christopher Cox, Ph.D., Eric D. Caine, M.D.

NR676 Personality Disorders Predicts Functional Decline in Elderly Depressives
Robert C. Abrams, M.D., Lisa A. Spielman, Ph.D., Ellen J. Klausner, Ph.D., George S. Alexopoulos, M.D.

NR677 Effects of Normal Aging on ACTH Response to Corticotropin-Releasing Hormone
Brian B. Roberts, M.D., David A. Graeber, M.D., E. Jonathan Lisansky, M.D., Richard I. Dorin, M.D., Clifford R. Qualls, Johannes D. Veldhuis

NR678 Sertraline Treatment of Behavioral Disturbances in Demented Older Adults
William Bondareff, M.D., Ill-Woo Han, M.D., Ellen Richter, Ph.D., Laurie La Bree, M.S., Doris Bass, M.S.W.

NR679 Caregiver Status in Late-Life Depression
Nancy Turret, M.S.W., Steven P. Roose, M.D., Davangere P. Devanand, M.D., Harold A. Sackeim, Ph.D.

NR680 Principle Component Analysis of Positive and Negative Syndrome Scale in Dementia
Igor I. Galynker, M.D., Alexander Prikhojan, M.D., Naomi Vilkas, B.A., Richard N. Rosenthal, M.D.

NR681 The Cognitive Effect of Risperidone in Elderly Schizophrenic Patients: A Pilot Double-Blind Comparison Study with Haloperidol
Ileana Berman, M.D., Edward R. Allan, M.D., Demetra Pappas, B.S., Cecile E. Sison, Ph.D., Amalia Merson, M.D.

NR682 Geropsychiatric Day Hospital: Successful Utilizers Versus Inpatient Recidivists
David Klahr, M.D., Eileen Rosendahl, Ph.D., Suzanne Paolucci, A.C.S.W., Blaine S. Greenwald, M.D.

NR683 Pupil Dilation Test: A Potential Marker for Alzheimer's Disease?
Wen-Hong Cheng, M.S., Wenwei Yan, M.D.

NR684 Career Soldiers' Attitudes Toward Homosexuals
Elizabeth E. Correnti, M.D., Laura Davidson, Ph.D., Mary B. Cruser, M.D.

NR685 Influence of Disease Severity on Self-Perceived Mental and Physical Health in Schizophrenic and Neurotic Patients
Bernd Eikelmann, M.D., Klaus Berger, M.D., Dirk Richter, Ph.D., Thomas Reker, M.D.

NR686 Enhanced Dexamethasone Responsivity in Female Veterans with PTSD
M. Michele Murburg, M.D., Susan Ballagh, M.D.,

NR687 Social Support, Coping Style, Stress Perception and Depressive Symptoms in the Patients Whose Esophageal Manometry and Gastroesophagea Reflux Tests
Sang-Yeol Lee, M.D., Min-Cheol Park, M.D., Suck-Chei Choi, M.D., Yong-Ho Nah, M.D.

NR688 Gender Bias in Psychiatric Texts
Raphael J. Leo, M.D., Maria T. Cartagena, M.D.

NR689 Investigation of Perimenstrual History Among Climateric Patients: Steiner's PMS Questionnaire, Test-Retest
Caludio de Novaes Soares, M.D., Osvaldo P. Almeida, Ph.D.

NR690 Assessment of Prevalence of Eating Disorders Among Rural Adolescents
Merry N. Miller, M.D., Ruth D. Verhegge, R.D., Barney E. Miller, Ph.D.

NR691 The Role of Temperamental Traits in Determining the Association of Heavy Drinking and Bulimia-Like Behavior in College
Dean D. Krahn, M.D., Candace L. Kurth, Ph.D., Adam Drewnowski, Ph.D., Edith Gomberg, Ph.D., Cynthia Pomerleau, Ph.D., Ovide Pomerleau, Ph.D.

NR692 Individual Versus Group Formats for Symptom-Focused Therapy of Bulimia Nervosa: Comparative Efficacy
Philippe Lageix, Howard Steiger, Ph.D., Sheila Jabalpurwala, Ph.D.

NR693 Clinical and Demographic Characteristics of Active Duty Inpatients with Eating Disorders: A Retrospective Study
Anita M. Nusbaum, M.D., Vicki A. Alberts, M.D.

NR694 Comorbidity of Eating Disorders and Personality Disorders in Japan
Ken Murakami, M.D., Tetsuro Tachi, M.D., Teruhisa Washizuka, M.D., Keizou Murotsu, Ph.D., Yuko Miyake, Ph.D., Norimasa Ikuta, M.D.

NR695 Cortisol and Catecholamine in Childhood PTSD
Michael D. De Bellis, M.D., Boris Birmaher, M.D., Andrew S. Baum, Ph.D., Frank J. Jenkins, Ph.D., Neal D. Ryan, M.D.

NR696 Are Anxious Children Smaller than Others?
E. Steven Dummit III, M.D., Raul R. Silva, M.D.

NR697 Validation of a New Depression Scale for Adolescents
Fabien Durif, M.D., Veronique Gentil, M.D., Jean P. Raynaud, Ph.D., Laurent Schmitt, M.D.

NR698 Gender Differences in Adolescent's Coping Strategies
Fabien Durif, M.D., Veronique Gentil, M.D., Jean P. Raynaud, Ph.D., Laurent Schmitt, M.D.

NR699 Treatment of Primary Premature Ejaculation: A Model for Investigation of SSRI-Induced Sexual Side Effects
Marcel D. Waldinger, M.D.

NR700 Continuous Treatment with Long-Acting Gonadotropin-Releasing Analog Triptoelin for Males with Severe Paraphilias
Eliezer Witztum, M.D., Ariel Rosler, M.D.

NR701 The Use of a 5HT 2a/2c and a2 Antagonist (Mianserin) in the Treatment of Sexual Dysfunction Induced by SSRIs
Dov Aizenberg, M.D., Zvi Zemishlany, M.D., Shay Gur, M.D., Abraham Weizman, M.D.

NR702 The Prevalence of Sexual Disorders in Tourette's Syndrome
J. Paul Fedoroff, M.D., Andrew Weeks, M.A., Paul Sandor, M.D.

NR703 Psychiatric Syndromes in Persian Gulf War Veterans: An Association of Handling Dead Bodies with Somatoform Disorders
Lawrence A. Labbate, M.D., Etzel Cardena, Ph.D., Michael Roy, M.D., Charles C. Engel, Jr., M.D.

NR704 Application of DSM-IV to Patients with Pain
Steven A. King, M.D.

NR705 Quantitative Morphology of the Caudate Nucleus in Boys with ADHD
Seog W. Kong, M.D., Jung Seop Lee, M.D., Kang-E M. Hong, M.D.

NR706 Personality Functioning in Adolescent Psychopathology
Susan R. Borgaro, M.A., David L. Pogge, Ph.D., John M. Stokes, Ph.D., Joel Lord, Ph.D.

NR707 Valproate Response Versus Blood Levels in Autistic and Pervasive Developmental Disorder Not Otherwise Specified Adolescents
Jessica A. Hellings, M.D., Sunil Chhibber, M.D., Earl R. Kilgore, Psy.D., Elizabeth J. Nickel, M.S.

NR708 PTSD Symptoms in Adolescent Survivors of Ethnic Cleansing: Results from a One-Year Follow-Up Study
Daniel F. Becker, M.D., Stevan M. Weine, M.D., Dolores Vojvoda, M.D., Thomas H. McGlashan, M.D.

NR709 Personality Traits in Adolescent Conduct Disorder
Ashley Bennett, B.A., Susan R. Borgaro, M.A., David L. Pogge, Ph.D., John M. Stokes, Ph.D., Joel Lord, Ph.D.

NR710 Lateralization of Cognitive Impairment in Adolescent Psychopathology
David L. Pogge, Ph.D., Susan R. Borgaro, M.A., Anne Lloyd, M.A., John M. Stokes, Ph.D., Philip D. Harvey, Ph.D.

NR711 Effectiveness of Day Treatment for Children with Severe Behavior Problems: Five-Year Follow-Up
Natalie Grizenko, M.D.

NR712 Diagnostic Validity in Childhood Depression
Michele Zaccario, M.A., Susan R. Borgaro, M.A., Julie Krauss, B.A., John M. Stokes, Ph.D., David L. Pogge, Ph.D.

NR713 Effects of Targeted Assertive Outreach in Patients with Schizophrenia and Substance Use Disorders
Richard N. Rosenthal, M.D., Christian Miner, Ph.D., David J. Hellerstein, M.D.

NR714 Autobiographical Memory and Mood Disorders in Heroin Addicts
Renate Eiber, M.D., Laurent Schmitt, M.D., Philippe Cadilhal, M.D.

NR715 Growth Hormone Treatment in Anorexia Nervosa
Kelly K. Hill, M.D., John Bucuvalas, M.D., Craig McClain, M.D., R. Krycio, Ph.D., Mary P. Alfaro, M.S., Michael J. Maloney, M.D.

NR716 Suicidality and Eating Disorders: Epidemiology in a Canadian Community Sample
David S. Goldbloom, M.D., Cathy Spegg, M.B.A., Paul E. Garfinkel, M.D., Elizabeth Lin, Ph.D., Paula N. Goering, Ph.D., Allan S. Kaplan, M.D.

NR717 5HT-1A Challenge Study: Test Meal Response
Barbara E. Wolfe, Ph.D., Eran D. Metzger, M.D., David C. Jimerson, M.D.

NR718 Treatment and Six-Year Course of Binge Eating Disorder
Manfred M. Fichter, M.D., Norbert Quadflieg, Ph.D., Winfried Rief, Ph.D.

NR719 Decreased Plasma Leptin Levels in Bulimia Nervosa
Timothy D. Brewerton, M.D., Michael D. Lesem, M.D., Adele Kennedy, M.D., W. Timothy Garvey, M.D.

NR720 Very Low Calorie Diet Combined with Cognitive-Behavioral Therapy in the Treatment of Obese Patients with Binge Eating Disorders
Martina de Zwaan, M.D., James E. Mitchell, M.D., Melissa P. Mussell, Ph.D., Ross Crosby, Ph.D.

NR721 Changes in Sympathetic Activity and Metabolic Rate in Patients with Anorexia Nervosa During Refeeding Treatment
Susan K. Schultz, M.D., Philippe van de Borne, M.D., Erling Anderson, Ph.D., Tim Ruffin, R.C.P.T., Lou Ann Vogel, R.R.T., Virend K. Somers, M.D.

NR722 Sertindole Treatment in Elderly Patients with Dementia
George T. Grossberg, M.D., Neal R. Cutler, M.D., Chris Silber, M.D., Jan O'Neil, B.S., Randall Mack, B.S.

NR723 Amyloid Beta Protein Concentration in CSF Decreases with Advancing Severity of Alzheimer's Dementia
Steven C. Samuels, M.D., Jeremy Silverman, Ph.D., Deborah B. Marin, M.D., Steven Younkin, M.D., Elaine Peskind, M.D., David Greenberg, M.D.

NR724 Use of Risperidone in the Elderly
Carlos A. Zarate, Jr., M.D., Ross J. Baldessarini, M.D., Arthur J. Siegel, Ataru Nakamura, M.D., Jane McDonald, Lou Ann Muir-Hutchinson

NR725 Decision-Making Capacity in the Elderly
Stephen L. Pinals, M.D., Neal R. Cutler, M.D., Steven Steiner, M.D., Ashok J. Bharucha, M.D., Roland J. Polinsky, M.D., Debra A. Pinals, M.D., Albert Enz, Ph.D., Andrew Satlin, M.D., Linda Mancione, Jameel Hourani, D.O., John J. Sramek, Pharm.D.

NR726 Effect of Alzheimer's Disease Severity on Functional Failure in Different Brain Regions: Assessed by Parametric Visual Stimulation During PET
Marc J. Mentis, M.D., Gene Alexaneer, Ph.D., Barbara Levine, M.D., Kavita Prasad, M.D., Pietro Pietrini, M.D., Mark Schapiro, M.D.

NR727 Serial Cognitive Testing of Chronic Psychiatric Patients
Eric S. Cole, Ph.D., Cheryl K. Cantrell, M.D.

NR728 CBT Versus Supportive Therapy in Social Phobia: A Controlled Study
Jean A. Cottraux, M.D., Ivan Note, M.D., Eliane Albuisson, M.D., Sainan Yao, M.D., Nathalie Etkmedjian, M.D., Isabelle Jalencques, M.D.

NR729 Are Psychiatry Residents Biased Against Cognitive-Behavior Therapy?
Ari E. Zaretsky, M.D.

NR730 Are Dependency and Self-Criticism Risk Factors for MDD?
Ari E. Zaretsky, M.D., Maurizio Fava, M.D., Katharine Davidson, B.A., Joel A. Pava, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D.

NR1 Monday, May 19, 9:00 a.m.-10:30 a.m.

Gating in Schizophrenia: A Trait-Related Deficit

Arthi Parwani, M.D., Department of Psychiatry, New York VAMC, 423 East 23rd Street, New York NY 10010; Elsa Bartlett, Ed.D., Erica J. Duncan, M.D., Steven H. Madonick, M.D., Phillip B. Chappell, M.D., Rajiv Rajan, M.D.

Summary:

Objective: Schizophrenics show deficits in sensory gating as measured by prepulse inhibition of the acoustic startle response (PPI). Since the neural pathways and pharmacology of PPI are well characterized, studies in this area may further our understanding of the pathophysiology of schizophrenia (Braff, 1992). The goal of this investigation is to further characterize PPI deficits in schizophrenia, and to test the hypothesis that these deficits are trait- rather than state-linked.

Method: PPI was measured in 17 male schizophrenics (9 acutely psychotic inpatients and 8 stable outpatients) and in 17 age-matched normal controls. Schizophrenics were rated for positive and negative symptoms at the time of testing.

Results: Schizophrenics showed deficient PPI compared to normals. Among the schizophrenics, acutely psychotic inpatients and stable, remitted outpatients did not differ in percent PPI. Three acutely psychotic inpatients who were retested when stable showed no consistent improvement in PPI deficits. PPI did not correlate with severity of positive or negative symptoms.

Conclusion: In accordance with the findings of Braff and Geyer et al., these results suggest that schizophrenics have impaired central inhibitory mechanisms as measured by PPI. The results support our hypothesis that these deficits are trait- rather than state-linked.

NR2 Monday, May 19, 9:00 a.m.-10:30 a.m.

The Effect of Mecamylamine on Smoking Patterns in Psychiatric Patients

Christine E. Marx, M.D., Department of Psychiatry, Duke University Medical Center, PO Box 3837, Durham NC 27710; Joseph P. McEvoy, M.D.

Summary:

Objective: Smoking prevalence rates are higher in certain psychiatric populations than in the general population (70% to 80% in patients with schizophrenia or mania, 90% in patients with substance abuse). Mecamylamine, a central nicotinic receptor antagonist, increases *ad lib* smoking in a dose-dependent manner in normal smokers. We are examining the effects of mecamylamine on smoking in patients with schizophrenia, mania, and substance abuse.

Method: We have so far recruited 11 patients with schizophrenia, 6 with mania, and 8 with substance abuse. Patients received capsules containing either 0, 5, or 10 mg mecamylamine, in random sequence, double-blind. Each patient participated in two-hour *ad lib* smoking sessions. We measured expired carbon monoxide (CO) levels and plasma nicotine levels at the end of the sessions.

Results: There was a dose-dependent increase in expired CO in all three diagnostic groups, but this increase appears to be more pronounced in patients with schizophrenia. In patients with schizophrenia, mania, and substance abuse, mean percent increases in expired CO were 45.1%, 22.7%, and 18.4%, respectively. Mean percent increases in nicotine levels are pending.

Conclusions: Early evidence from our ongoing study suggests that schizophrenic patients may be more susceptible to nicotinic receptor blockade.

NR3 Monday, May 19, 9:00 a.m.-10:30 a.m.

Conditional Discrimination Learning in Schizophrenia

Dagmar Maierhofer, M.D., Department of Psychiatry, University Clinic, Waehringer Guertel 18-20, Wien AU 1090, Austria; Karl Dantendorfer, M.D., Edith Hofer, M.D., Murat Serim, M.D., Johann Windhaber, M.D., Professor Heinz Katschnig

Summary:

Introduction: In schizophrenia (SZ) abnormalities in brain morphology and/or function have been described for such different brain areas as the frontal lobes, the temporal lobes, the basal ganglia, the parietal lobes, and the corpus callosum. Equally heterogenous have been the neuropsychological deficits found with standardized test batteries. Two of the most difficult to control factors in testing cognitive functions were the influence of patients' motivation and attention on test results. Recent reports suggest that memory and learning deficits seem to be more specific to SZ than previously accepted. Conditional discrimination learning based on eyelid conditioning has been shown to be selectively sensitive in testing temporal lobe function and has the advantage of making minimal demands on attentional capacities and motivation.

Methods: In our ongoing study, an eyelid conditional discrimination learning task is used to examine healthy controls and two groups of SZ patients (DSM-III-R paranoid type SZ with predominant positive symptoms and disorganized type with predominant thought disorders). The occurrence of the first conditioned response (FCR) and response frequency to reinforced (CRR) and unreinforced trials (CRU) are quantified.

Results: Seventeen controls showed a FCR after 5 ± 2,25 trials as well as a frequency of 32% ± 5,5% CRRs and 14% ± 3% CRUs. Two paranoid type SZ patients tested up to now, showed high rates of CRRs as well as CRUs (CRR/CRU; 23%/25% and 29%/21%). The two disorganized type patients showed low rates of CRRs and CRUs (CRR/CRU; 2%/4% and 4%/4%). All four patients had the FCR on unreinforced trials and three of them showed delayed FCRs (trials 9, 14, 17) compared to controls.

Conclusions: Our preliminary data suggest that while paranoid as well as disorganized type schizophrenics show reduced discrimination learning capacity, the two subgroups might be differentiated by conditioned response frequencies probably due to differences in temporal lobe functions. (Supported by grant no. 5657 Jubiläumsfonds der Österr. Nationalbank.)

NR4 Monday, May 19, 9:00 a.m.-10:30 a.m.

Neurological Hard Signs in Schizophrenia

Sanjay S. Chandragiri, M.D., Department of Psychiatry, SUNY Stony Brook, Health Sciences Center/T10-020, Stony Brook NY 11794; Psyn Sharma, M.D.

Summary:

Objective: This study focused on neurological hard signs in schizophrenia.

Method: Forty consecutive patients who met DSM-III-R criteria for schizophrenia, 30 consecutive patients who met DSM-III-R criteria for bipolar affective disorder, and 30 normal controls were selected as subjects. All subjects received a thorough standard neurological examination. The findings on neurological examination were rated on a 79-item protocol (Woods, et al, 1986). Signs that were considered to be due to medication effect or a known neurologic condition were excluded.

Results: On pairwise comparison schizophrenic subjects had more neurological signs than those with bipolar affective disorder and normal controls. The difference between subjects with bipolar affective disorder and normal controls was not significant.

Within the group of schizophrenic subjects, there was a significant relationship of neurological hard signs to duration of illness, negative symptoms, nonparanoid subtypes, and female sex.

Conclusions: Neurological hard signs, reflective of brain pathology, are prevalent among schizophrenic patients and vary within subgroups.

NR5 Monday, May 19, 9:00 a.m.-10:30 a.m.

Agnosia of Tardive Dyskinesia in Schizophrenia

Fabien Tremeau, M.D., Forenar, 27 Rue-Du 4 RSM, Rouffach NY 68250, France; Xavier Amador, Ph.D., Dolores Malaspina, M.D., Yvan Amodt, M.S., Raymond Goetz, Ph.D., Jack M. Gorman, M.D.

Summary:

Lack of insight into psychiatric symptoms and agnosia of tardive dyskinesia (TD) are two striking phenomena observed in schizophrenia that have only recently been studied rigorously and remain poorly understood. Moreover, correlations between them have not previously been studied systematically.

Methods: Twenty-two subjects with TD and schizophrenia, and nine with TD and schizoaffective disorder participated. TD localization and intensity were rated with the Abnormal and Involuntary Movement Scale, and awareness of each abnormal movement was recorded. Insight was measured with the Scale to Assess Unawareness in Mental Disorders (SUMD). Degree of handedness was assessed with a modified Handedness Survey.

Results: Unawareness of TD was highly correlated with poor insight into psychiatric symptoms (correlation coefficient: 0.44; $p = 0.018$) and with degree of right handedness (0.48; $p = 0.007$). No indication that agnosia of TD is a unilateral function in the brain was found.

Conclusion: This is the first study to show that awareness of psychiatric symptoms and awareness of neurological symptoms such as TD are not two independent functions in schizophrenia, and that they share some similar mechanisms. The correlation between agnosia of TD and the degree of right handedness is consistent with the fact that awareness depends on the degree of lateralization of the brain.

NR6 Monday, May 19, 9:00 a.m.-10:30 a.m.

Measuring Health Status in Older Schizophrenia Patients

Andres F. Sciolla, M.D., Department of Psychiatry, VA Medical Center, 3350 La Jolla Village Drive, San Diego CA 92161; Thomas L. Patterson, Ph.D., Jovier D. Evans, Ph.D., M. Jackuelyn Harris, M.D., Dilip V. Jeste, M.D.

Summary:

Objective: The Medical Outcomes Study (MOS) 36-item short form health survey (SF-36) is one of the most commonly used outcome measures in medicine. To our knowledge, the SF-36 has not been systematically studied in schizophrenia, particularly in older patients.

Method: Subjects were 70 outpatients with schizophrenia and 45 normal comparison subjects, ranging in age from 45 to 79. Subjects underwent a comprehensive neuropsychiatric evaluation, which included the self-reported SF-36 and other standardized clinical, psychosocial, and neuropsychological assessments.

Results: Patients had significantly higher scores in five of the eight SF-36 subscales as compared to normal subjects: energy, social functioning, emotional well-being, role limitations due to emotional problems, and general health (F values 5.7 to 35.9, all p's < .03). The most significant associations of the general health score were with measures of psychopathology, positive symptoms, and depression (Pearson's r values −.32 to −.40, all p's < .01).

Comment: Self-reported health status and disability were worse in older schizophrenia patients than in normal subjects in several domains. In the schizophrenia group, severities of disability and psychopathology were correlated. The MOS SF-36 may be a useful instrument for outcome studies of schizophrenia.

NR7 Monday, May 19, 9:00 a.m.-10:30 a.m.

Pilot Trial of Light Treatment for HIV-Associated Sleep Disturbance

Andres F. Sciolla, M.D., Department of Psychiatry, VA Medical Center, 3350 La Jolla Village Drive, San Diego CA 92161; Stephen Brown, M.D., J. Hampton Atkinson, Jr., M.D., J. Summers, M.S.W., Igor Grant, M.D., The HNRC Group

Summary:

Objective: Standard therapies for HIV-associated sleep disturbance are often ineffective or poorly tolerated. Our previous work suggested that light treatment might alleviate sleep disturbance in HIV disease.

Method: Six HIV+ men without DSM-III-R current diagnosis whose global score in the Pittsburgh Sleep Quality Index (PSQI) was 6 or more (clinically significant sleep disturbance), were randomly assigned to either bright light (light boxes, > 2,000 lux) or dim red light (<50 lux) for one hour every evening for two weeks. Mean age/range of age and CD4 lymphocyte counts were 36.8/29-51 and 299/7-578, respectively. A modified PSQI was administered at baseline and at the end of each of the treatment weeks.

Results: Four subjects on bright light reported a 35% mean drop in their PSQI scores (range 0% to 56%); scores from subjects on red light remained basically unchanged. None of the participants experienced undesirable side effects. Two participants on bright light wanted to continue to use the lights.

Comment: Further research on the efficacy of light treatment for HIV-associated sleep disturbance seems warranted. The effect size observed is of note given the low dose and duration of light exposure. Tolerance was quite good.

NR8 Monday, May 19, 9:00 a.m.-10:30 a.m.

Diagnosis and Risk Factors of Depression in Schizophrenia

Rosa Elena Ulloa, M.D., Clinical Research, Institute of Mexican Psych, Calzada Mexico Xochmilco 101, Mexico City 14370, Mexico; Rogelio Apiquian, M.D., Francisco Paez, M.D., Hector A. Ortega-Soto, M.Sc.

Summary:

Objective: This study was designed to compare demographic data, number of relapses within the last year, and treatment between depressed schizophrenic and nondepressed schizophrenic patients to find risk factors for depression.

Method: We recruited 62 patients with schizophrenia. A diagnosis of depression was assessed with the WHO's Composite International Diagnostic Interview (CIDI) and symptom severity was measured with PANSS and CDS. Demographic data, relapses, and treatment were registered.

The Calgary Depression Scale (CDS) scores were higher in the depressed patients than in the nondepressed patients ($t = 2.13$, df 15,p + 0.03). We found 80% of specificity with CDS score of eight.

Results: CDS scores were correlated with positive ($r = 0.37$, $p = 0.01$), general ($r = 0.56$, $p = 0.001$), and total ($r = 0.41$, $p = 0.04$) subscales of the PANSS. Single marital status is a risk factor for depression in these patients ($p = 0.05$).

Conclusion: Psychotic symptoms and single marital status could be related to depression in our schizophrenic patients.

NR9 Monday, May 19, 9:00 a.m.-10:30 a.m.

Plasma HVA in Older Psychotic Patients

Mirela O. Fagarasan, Ph.D., Psychiatry, Univ. of Calif/San Diego, 3359 La Jolla Village Drive, La Jolla CA 92161; Jonathan P. Lacro, Pharm.D., Paul J. Mills, Ph.D., M. Jackuelyn Harris, M.D., Richard L. Hauger, M.D., Dilip V. Jeste, M.D.

Summary:

Background: Plasma HVA (pHVA) is believed to be an important peripheral marker of dopaminergic activity. The findings with pHVA in young adult schizophrenic patients have been variable. We did not find a systematic study of pHVA in older schizophrenic patients. Below we present an interim analysis from an ongoing study.

Subjects and methods: We examined pHVA by HPLC with electrochemical detection in 28 middle-aged and elderly subjects who received comprehensive clinical evaluation. There were 15 patients with DSM-III-R schizophrenia, six with other psychotic disorders, and seven normal comparison subjects. The assessments included SCID for DSM-III-R, Brief Psychiatric Rating Scale (BPRS) for psychopathology, and Mini-Mental State Examination (MMSE) for global cognitive impairment. Plasma was drawn in the morning in subjects who were stable psychopathologically and pharmacologically.

Results: The mean (± SD) pHVA in schizophrenic patients [7.4 ± 3.4 ng/ml] was significantly greater than that in normal subjects [4.0 ± .9] ($p = .006$, t-test), and was not significantly greater than that in other psychotic patients [6.1 ± 1.8] ($p = .1$). In the schizophrenic group, pHVA did not correlate with age or neuroleptic dose, but tended to correlate with BPRS total ($r = -.51$, $p = .06$) and with MMSE total ($r = -.47$, $p = .08$).

Comment: Our preliminary results suggest that pHVA may be associated with severity of psychopathology and cognitive impairment in older schizophrenic patients.

NR10 Monday, May 19, 9:00 a.m.-10:30 a.m.

A Prospective Study of Substance Use Disorders in Schizophrenic Patients

R. Mark Newman, M.D., Department of Psychiatry, University of Iowa, 2911 JPP/200 Hawkins Drive, Iowa City IA 52245; Peg C. Nopoulos, M.D., Susan J. Oliver, M.D., Nancy C. Andreasen, M.D.

Summary:

Objective: Numerous studies have revealed that substance use disorders occur frequently in schizophrenic patients. However, few studies have examined the natural history of substance use disorders in this population. This study assessed the frequency over time of substance use disorders among schizophrenic patients.

Methods: We studied a group of 65 individuals with schizophrenia spectrum disorders who were either first episode or recent onset psychosis. We examined the rate and stability of comorbid substance use disorders in these individuals over five years.

Results: At intake 32.3% had a lifetime history of a substance use disorder (16.9% with abuse and 15.4% with dependence) and 7.7% of this group had a current substance use disorder (3.1% with abuse and 4.6% with dependence). At yearly intervals to 60 months, we assessed for any active substance use disorder and found that the rate never exceeded 3%.

Conclusions: These findings suggest that in this rural Iowa sample, despite a significant past history of substance use disorders, the rates of substance use disorders over time were low. This suggests a pattern of substance use disorders that are associated with early phase of the illness or antedate it, but remits as the psychotic illness becomes more chronic.

NR11 Monday, May 19, 9:00 a.m.-10:30 a.m.

QEEG During Memory Tasks in Schizophrenia

Duk-In Jon, M.D., Department of Psychiatry, Yonsei University, 134 Shinchon-Dong SeoDaeMoon, Seoul, Korea; Sung H. Lee, M.D., Hong-Schick Lee, M.D., Sung Kil Min, M.D.

Summary:

Objective: Under the hypothesis that activated brain regions of patients with schizophrenia differ from those of normals during memory tasks, this study was aimed to investigate topographic changes related to memory functions in schizophrenia.

Method: Subjects consisted of 20 unmedicated patients with schizophrenia and 19 normal controls who were matched for age, sex, and handedness. Quantitative EEG (QEEG) with 32 channels was recorded with eyes open in a resting condition (EEG1) and during computerized verbal encoding (EEG2) and recognition (EEG3) tasks.

Results: Pairwise comparison showed that the alpha activity of normals significantly increased from EEG1 to EEG2 in the parietal region and from EEG1 to EEG3 in all regions except both frontal regions, while those of patients with schizophrenia did not change. The beta activity of normals significantly increased from EEG1 to EEG2 in both temporal regions and from EEG1 to EEG3 in the frontal, temporal, and parietal regions, while those of patients with schizophrenia significantly increased only in the parieto-occipital region.

Conclusions: These results suggest the possibility of a different memory process for visually presented words between patients with schizophrenia and normals. It may be concluded that the frontal lobe, temporal lobe, and thalamus were not appropriately activated during memory tasks in schizophrenia.

NR12 Monday, May 19, 9:00 a.m.-10:30 a.m.

Deficits in Visual Selective Attention In Neuroleptic Naive Psychotic Patients Versus Nonpsychiatric Controls

Glenda MacQueen, M.D., Department of Psychiatry, McMaster University, 1200 Main West, RM 3G15, Hamilton Ontario L8N 3Z5, Canada; Patricia I. Rosebush, M.D., Steven Tipper

Summary:

Objective: To examine deficits of selective attention in patients with acute psychosis.

Method: Twenty (14 males) neuroleptic-naive psychotic subjects, age = 24 +/- 7.0 (mean +/- SD), BPRS = 43 +/- 9.8, and GAS = 37 +/- 9.9, and 20 controls completed a test of selective attention called negative priming (NP) in which the effect of a distractor on trial N was examined by requiring subjects to attend to the distractor on trial N + 1.

Results: Subjects with psychosis had response times and error rates that were comparable to controls, while demonstrating markedly reduced levels of NP (8 msec versus 33 msec for controls, $t = 2.08$, df (19), $p < 0.05$). There was a correlation ($r^2 = 0.159$, df (19), $p < 0.05$) between BPRS score and reduction in NP such that patients with higher BPRS scores demonstrated less NP.

Conclusions: Patients with acute psychosis secondary to various etiologies have reduced levels of NP, suggesting an impairment in selective attention. The extent to which NP was reduced is comparable to the reduction observed in patients with chronic schizophrenia (MacQueen, Goldberg & Tipper, 1996); additional subjects are being recruited to determine whether the presence

of psychosis independent of ultimate diagnosis can account for impairment in this attention process.

NR13 Monday, May 19, 9:00 a.m.-10:30 a.m.

Language Processing, Thought Disorder and Clinical Symptoms in Schizophrenia

Angel Cienfuegos, M.D., Department of Psychiatry, Albert Einstein/Bronx Psyc Ctr, 1500 Waters Place, Bronx NY 10461; Daniel C. Javitt, M.D., Jorge Barros, M.D., Kevin Moser, Anne-Marie Shelley, Ph.D.

Summary:

This study examined the performance of 40 chronic schizophrenic patients on an echoic memory task for synthetic tones and a lexical decision task, with phonological and semantic priming. Patients were also assessed on the Thought, Language and Communication (TLC) Index for thought disorder and the Positive and Negative Syndrome Scale (PANSS).

In the echoic memory task there was a decay in performance with increasing SOA (stimulus onset asynchrony). In the lexical decision task, patients were asked to state if the target, presented visually, was a word or a non-word. There were 200 msec-delay and 400 msec-delay conditions. Patients had a longer reaction time (RT) for non-word targets than for word targets. Priming was present in both semantic and phonological modalities. Semantic priming was the same for both delay and non-delay conditions; phonological priming was greater in the delay condition. There was a correlation between phonological and semantic priming in both conditions. Although there is a trend toward an inverse relationship between total score of TLC and percentage of correct answers on the lexical decision task ($p = 0.059$), preliminary analysis shows no significant correlation between priming effects and TLC scores. A correlation between TLC scores and the PANSS positive subscale ($p = 0.013$) appeared.

NR14 Monday, May 19, 9:00 a.m.-10:30 a.m.

Neurological Soft Signs in First-Episode Schizophrenia: Schizophreniform Psychosis

Stephen Browne, M.B., Cluain Mhuire Family Ctr, Stanley Research Unit, Newtown Pk Ave Blackrock, Dublin, Ireland; Maurice Gervin, M.B., Abbie Lane, M.B., John L. Waddington, Ph.D., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.

Summary:

Objectives: To investigate the clinical correates of neurological soft signs (NSS).

Method: First-episode schizophrenia/schizophreniform psychosis patients were assessed at presentation (where feasible, neuroleptic naive) using the Neurological Evaluation Scale (NES), Condensed Neurological Examination (CNE), Positive and Negative Syndrome Scale (PANSS), and the Structured Clinical Interview for DSM-IV diagnosis (SCID).

Results: 48 subjects (35 M, 13 F, mean age 25.8 ± 8.0) were included. There was no gender difference in NES ($p = 0.72$) and Rossi ($p = 0.52$) scores. NSS were independent of PANSS scores but were inversely related to number of years spent in education ($p < 0.04$) on both scales. Neuroleptic-naive patients ($n = 24$) did not differ from minimally treated patients (< 1 month treatment; $n = 24$) in terms of NES ($p = 0.50$) or Rossi ($p = 0.70$) scores.

Conclusions: Neurological soft signs are present in individuals presenting with a first episode of schizophrenia and are independent of age, gender, medication status, or level of symptomatology. Although potential confounders must be considered, the association between lower educational level and NSS could possibly be explained by a neurodevelopmental model.

NR15 Monday, May 19, 9:00 a.m.-10:30 a.m.

The Clinical Correlates of Quality of Life in First-Episode Schizophrenia/Schizophreniform Psychosis

Stephen Browne, M.B., Cluain Mhuire Family Ctr, Stanley Research Unit, Newtown Pk Ave Blackrock, Dublin, Ireland; Maurice Gervin, M.B., Abbie Lane, M.B., John L. Waddington, Ph.D., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.

Summary:

Objectives: To assess the quality of life of individuals with a first episode of schizophrenia/schizophreniform psychosis and its clinical correlates.

Method: Patients presenting with first-episode schizophrenia/schizophreniform psychosis were assessed using the Quality of Life Scale (QLS), Positive and Negative Syndrome Scale (PANSS), Global Assessment of Functioning Scale (GAF), Premorbid Adjustment Scale (PAS), and the Structured Clinical Interview for DSM-IV diagnosis (SCID). Duration of untreated psychosis was ascertained by interview.

Results: 46 subjects (35M, 11F, mean age 25.6 ± 7.6) were included. The mean total QLS score (60.8 ± 23.0) was independent of age and gender. The total QLS score was negatively correlated with duration of untreated psychosis ($r = -0.48$, $p = 0.01$), PAS score ($r = -0.32$, $p = 0.02$), and PANSS score ($r = -0.28$, $p = 0.03$) and positively correlated with the GAF score ($r = 0.33$, $p = 0.02$)

Conclusions: Patients with a first episode of schizophrenia have an impaired quality of life that is related to the duration of untreated psychosis, poorer premorbid adjustment, severity of symptomatology, and level of functioning.

NR16 Monday, May 19, 9:00 a.m.-10:30 a.m.

Baseline Rate of Spontaneous Dyskinesia in First-Episode Schizophrenia/Schizophreniform Psychosis in an Urban Area Service

Maurice Gervin, M.B., Cluain Mhuire Family Ctr, Stanley Research Unit, Newtown Pk Ave Blackrock, Dublin, Ireland; Stephen Browne, M.B., Abbie Lane, M.B., John L. Waddington, Ph.D., Conall Larkin, M.B., Eadbhard O'Callaghan, M.B.

Summary:

Objective: To determine the baseline rate of spontaneous dyskinesia in a representative sample of patients with first-episode schizophrenia/schizophreniform psychosis presenting to a defined catchment area service (165,000).

Method: Patients with a first episode of schizophrenia/schizophreniform psychosis (DSM-III-R) were examined at the time of presentation and where possible were neuroleptic naive, for the presence of abnormal involuntary movements using the Abnormal Involuntary Movements Scale (AIMS).

Results: 62 subjects (40M, 22F, mean age = 27.8 ± sd 9.4) presented over a 2.8-year period; 66% were neuroleptic naive and the remainder had been treated for less than one month. Four patients satisfied Schooler Kane criteria for spontaneous dyskinesia, giving a baseline rate of 6.5%. Patients with spontaneous dyskinesia did not differ from those without (26.5 ± 13.7 vs 27.9 ± 9.2) in terms of age, but had spent significantly ($p < 0.02$) fewer years of schooling (10.5 ± 1.7 vs 13.5 ± 2.5).

Conclusions: Spontaneous dyskinesia may be more common in first-episode schizophrenia than previously suggested and, more speculatively, may even be associated with poorer premorbid cognitive functioning. This supports the view that involuntary movements may be intimately related to the pathophysiology of schizophrenia and not purely a side effect of treatment.

NR17 Monday, May 19, 9:00 a.m.-10:30 a.m.

Effect of Gender on Psychiatric Comorbidity Among Schizophrenic Patients

Sunil Chhibber, M.D., Department of Psychiatry, Kansas University Medical Ctr, 3901 Rainbow Boulevard, Kansas City KS 66160; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.S., Ekkehard Othmer, M.D., Ph.D., William F. Gabrielli, Jr., M.D., Charles L. Zaylor, D.O.

Summary:

Objective: Recent studies from the community and clinic have shown that the rate of comorbid psychiatric syndromes is surprisingly high when contemporary, criterion-referenced, diagnostic instruments are employed. Moreover, the presence of multiple co-occurring psychiatric syndromes is associated with greater impairment and dysfunction, a more malignant outcome, and higher utilization of treatment resources. Little information is available about the range of comorbid psychiatric syndromes in patients suffering from schizophrenia; even less information exists about the influence of gender on the range of comorbid syndromes in schizophrenia.

Method: During a five-year period, 1,458 patients new to the Kansas University Outpatient Psychiatry Clinic were administered the structured Psychiatric Diagnostic Interview and other research procedures before they were seen by the treating physician. Of these, 192 or 13.2% satisfied both DSM-III and Feighner criteria for schizophrenia; 121 were female and 71 were male. The ratio of male to female schizophrenic patients did not differ from the ratio of male to female patients in the total sample.

Results: Using inclusive diagnostic criteria, we found that the lifetime prevalence of comorbid psychiatric syndromes was very high among this schizophrenic sample; only 26 of the schizophrenic patients (13.5%) satisfied criteria for schizophrenia only. The total number and prevalence of the comorbid syndromes was higher in the schizophrenic sample than in the total sample for both males and females. The rank order of the prevalence of lifetime syndromes was similar in the total sample and in the schizophrenic subsample. Moreover, the rank order of the additional psychiatric syndromes among the male and female schizophrenic patients corresponded to the rank order of the same syndromes in the male and female patients of the total sample. Gender differences across the co-occurring syndromes were similar for all disorders except major depression; both male and female schizophrenic patients reported equally high levels of depression (67.6% vs 72.7%). No gender differences were found across the 46 specific psychotic symptoms that were reviewed. As reported by others, the number of co-occurring syndromes was associated with increasing disability and treatment utilization.

Conclusions: Psychiatric comorbidity is especially high among both male and female schizophrenic patients, a phenomenon that should not be ignored in research and treatment studies in the future.

NR18 Monday, May 19, 9:00 a.m.-10:30 a.m.

Clozapine Versus Risperidone in Pharmaco-Refractory Schizophrenia: A Preliminary Report

Carsten Konrad, Friedrich-Wilhelm Weber Str 30, Muenster 48026, Germany, Christoph Schormair, M.D., Petra Ophaus, Uwe Knickelbein, Bernd Eikelmann, M.D.

Summary:

Background: Pharmaco-refractoriness is a major problem in the treatment of schizophrenic patient. We investigated drug response to either risperidone or clozapine in patients who had failed to respond to other antipsychotics.

Methods: Sixty-one inpatients with schizophrenia (ICD-10 criteria) who previously failed two or more trials of antipsychotic drugs over at least three weeks were assigned by their individual psychiatrist to risperidone (n = 37) or clozapine (n = 24) and observed for six weeks. PANSS, BPRS, CGI, and EPS rating scales were performed by an independent blinded observer as well as NOSIE and SWN-self-rating scales by nursing staff and patients, respectively. Wilcoxon signed-ranks tests were conducted within each group comparing weeks two and six to baseline.

Results: Patients in both groups improved significantly on total scores for CGI, BPRS, and PANSS, as well as on positive syndrome and general psychopathology scales (PANSS). Only the risperidone group showed significant improvement on PANSS negative syndrome and NOSIE index scores. EPS scores also decreased significantly. Patients' self-rating scores showed significantly increased function in six domains for risperidone-treated patients, but only in two for clozapine-treated patients.

Conclusions: Our preliminary findings suggest that risperidone may be at least as effective as clozapine in improving symptoms and subjective well-being of treatment-refractory inpatients with schizophrenia.

NR19 Monday, May 19, 9:00 a.m.-10:30 a.m.

Comparisons Between Alcoholics and Social Drinkers

Jung-Sik Lee, M.D., Department of Psychiatry, Yong-In Mental Hospital, 4 Sangha-Ri Kusung-Myun/Yongin, Si, Kyunggi-Do 449-910, Korea; Kwang-Soo Han, M.D., Yoo-Sang Lee, M.D.

Summary:

Objective: In this study, the authors attempted to identify differences between patients with alcohol dependence and social drinkers and correlations in emotional state, self-percept, family environment, and social support.

Methods: The subjects were 30 male patients with alcohol dependence (DSM-IV) and age-, sex-, and education-matched 30 male social drinkers. They filled out several questionnaires after they had recovered from acute intoxication (two weeks from admission date): Beck Depression Inventory, the State Trait Anxiety Scale, Self-Percept Scale, Family Environmental Scale, and Social Support Scale. Two psychiatrists diagnosed the patients by DSM-IV and examined the patients through NAST (Korean version of MAST).

Results: Alcoholic patients were more depressed and more anxious than social drinkers. Alcoholic patients perceived themselves and their family environment more negatively than social drinkers. Alcoholic patients reported fewer social supports than social drinkers. There were considerable correlations among these scales.

Conclusions: The authors suggest that cognitive-behavioral therapy focused on these differences would play an important role in treatment and relapse prevention of alcoholic patients.

NR20 Monday, May 19, 9:00 a.m.-10:30 a.m.

Substance Abuse, Mental Illness and Family History of Substance Abuse

Faye M. Lari, M.D., Department of Psychiatry, University of Maryland, 645 W Redwood Street, Baltimore MD 21201; Lisa B. Dixon, M.D., Jack Scott, Sc.D.

Summary:

Objective: We compared family history of substance abuse and associated factors in two patient groups: 1) individuals with a substance use disorder (SUD) only; and 2) those with a dual diagnosis (DD) of mental illness and substance use.

Methods: Twenty-five patients consecutively admitted to a substance abuse treatment program in each group (N = 50) were assessed with a chart review. Background characteristics and

admission Addiction Severity Index family history data and problem severity scores were recorded.

Results: DD patients were more likely than SUD only patients to have a positive family history of substance abuse (PFHSA)($p < .02$), to be unemployed ($p = .05$), and to have more severe family ($p < .001$) and drug ($p \leq .001$) problems. Patients with a PFHSA had more severe family ($p < .05$) and drug problems ($p < .01$), and were less likely to be employed ($p < .01$) than patients without PFHSA. In multivariate analyses, a mental disorder was predictive of worse family and drug problems; a family substance history predicted worse family and employment problems.

Conclusion: This study shows a complex interactive relationship between mental illness, patient substance use, and family substance abuse. It underlines the importance of considering family substance abuse in the management of dual diagnosis patients.

NR21 Monday, May 19, 9:00 a.m.-10:30 a.m.

Interaction of Factors Affecting Hospital Stay of Cocaine Dependents: Comorbidity, Status and Episode

Ashok Jain, M.D., Department of Psychiatry, University of TX/Houston, 1300 Moursund Avenue, #162, Houston TX 77030; Pedro Ruiz, M.D., Howard Rhoades, Ph.D.

Summary:

Objective: This study examines the interaction of various factors and their influence on hospitalization of cocaine dependent patients.

Methods: A total of 1,200 admissions with the discharge diagnosis of cocaine dependence were categorized equally in voluntary, involuntary, male, and female. We studied the correlation of the length of stay (on a weekly basis) with comorbidity, number of episodes, gender, and status.

Results: Among the comorbid (38.42%) patients, 26.37% were comorbid with other substance abuse or alcohol dependence, 6.27% with mood disorders, and 4.79% with psychotic disorders. Regarding episodes, 55.38% patients had one episode, 18.61% had two, while 26.21% had more than two episodes. Most of the cocaine and substance dependent patients had earlier drop out than alcoholism and mood disorder patients, who tend to have longer hospital stays; also more were experiencing their first episode.

Discussion: The highly significant shift of more patients belonging to cocaine dependence as episodes increase could reflect cocaine dependents becoming hard addicts while initially starting with comorbidity of alcoholic/mood disorders. The unusual underrepresentation of mood disorder is worth exploring. In contrast to recent literature this study emphasizes the need for vigilant screening of substance abusers at detoxification centers and then referring them to psychiatric centers for presence of any significant psychopathology.

NR22 Monday, May 19, 9:00 a.m.-10:30 a.m.

Changes in Staff Attitudes Toward a Smoke-Free Policy in the Navy Alcohol Rehabilitation Program

Christi A. Patten, Ph.D., Department of Psychology, Mayo Clinic, 200 First Street, SW, Rochester MN 55905; John E. Martin, Ph.D., C. Richard Hofstetter, Ph.D., Sandra A. Brown, Ph.D., Nancy A. Braun, Ph.D., Carl D. Williams, B.A.

Summary:

The feasibility of smoke-free alcohol treatment units is a topic of recent interest. This study examined changes in staff attitudes toward a smoke-free policy in the Navy Alcohol Rehabilitation program (NARC), which is located in San Diego, CA. The staff were administered a survey two months before and six months after policy implementation. The response rate for the initial staff survey was 60.6% (86 of 142). Overall, 98.8% of staff considered smoking to be an addiction and 81.3% favored the implementation of the smoke-free policy. However, current smokers were significantly less likely (33.3%) than former (94.3%) or never smokers (91.2%) to favor the implementation of the policy ($p < 0.001$). The response rate to the survey given six months after implementation of the smoke-free policy was 77.0% (104 of 135). Overall, 84.6% of staff indicated that the NARC should remain smoke free. Current smokers were significantly less likely to indicate that the NARC should remain smoke free (44.4%) than former (87.5%) or never smokers (95.7%) ($p < 0.001$). Those in recovery from alcohol/drugs were also less likely to favor the policy compared to those who were not in recovery (77.1% vs. 93.5%; $p = 0.02$). Of note, 71.3% of staff reported that the smoke-free policy was associated with an increase in negative behavior incidents including angry outbursts, and resistance and violations of the policy among smoking patients. Despite these observations, 84.6% of staff recommended that other CD treatment facilities be smoke free.

NR23 Monday, May 19, 9:00 a.m.-10:30 a.m.

Stages of Change as a Predictor of Abstinence Among Alcohol Dependent Subjects in Pharmacotherapy Trials

Carlos A. Hernandez-Avila, M.D., Department of Psychiatry, University of Conn Hlth Ctr, 263 Farmington Avenue, Farmington CT 06030; Henry R. Kranzler, M.D., Joseph A. Burleson, Ph.D.

Summary:

Method: Using a longitudinal prospective design, we examined abstinence rates at treatment endpoint and at six-month posttreatment follow-up among 134 alcohol-dependent patients participating in one of two 12-week, placebo-controlled, pharmacotherapy trials. Hierarchical logistic regression was used to distinguish drinking versus abstinence as a function of baseline demographic, behavioral, and psychological predictors, and stages of change. Predictors were required to show significance both in their model χ^2 improvement and final Wald test.

Results: At treatment endpoint, older males, younger females, treatment completers, and subjects with low levels of depressive symptoms were more likely to be abstinent. During posttreatment follow-up, treatment condition was significant, with active medication recipients being more likely to remain abstinent. With respect to stages of change, individuals with higher scores on the Action subscale were more likely to be abstinent during treatment and, to a lesser degree, during the posttreatment period.

Conclusions: Although the stages of Precontemplation, Contemplation, and Maintenance were not associated with abstinence, Action, subjects' readiness to act to change, in conjunction with age, gender, depressive symptoms, and assignment to an active pharmacological agent, significantly contributed to the model.

NR24 Monday, May 19, 9:00 a.m.-10:30 a.m.

Improvements in Psychosocial Stages of Development and Defense Styles in Alcoholics During Inpatient Treatment

Paul W. Ragan, M.D., NIAAA/LCS, Bldg 10 Rm 3B19, 9000 Rockville Pike, Bethesda MD 20892; Linda Doty, R.N., Nancy Harnett, Ph.D., Dell Wright, R.N., Sandy Birdsong, R.N., Christoper Geyer, R.N., Susan Squires, R.N.

Summary:

We have previously reported on a group of 34 alcoholics who, during inpatient treatment, demonstrated significant decrement in

measures of psychosocial development and ego defenses compared with age- and gender-matched controls. We have expanded the sample size to include 85 actively drinking alcoholics (51 men, 34 women, mean age ± SD = 40 ± 8 y) who met DSM-III-R criteria for alcohol dependence. Twenty-six comparison subjects (13 men, 13 women, mean age 37 ± 11 y) served as controls who had no lifetime axis I or II diagnoses and no first-degree relatives with any substance dependence. Alcoholics completed psychosocial development (MEPSI, MPD) and defense style (DMI, DSQ) questionnaires at admission and after three weeks of sobriety. Alcoholics were administered and scored significantly higher on the Schedule for Recent Experience compared with controls: 786 ± 540 vs 280 ± 263 ($p < .001$). After three weeks of treatment, this larger sample of patients demonstrated significant improvement in six of eight MEPSI scales, in three of five DMI scales, and in the neurotic and immature scales of the DSQ. Unlike our previous findings, the alcoholics showed significant improvement in self-reports of psychosocial developmental and ego defensive style functioning, which most likely reflects short-term recovery from both the toxicity of alcohol and relief from chaotic environments. Severe alcoholics may need sufficient time for recovery of some ego functioning prior to maintaining sobriety in an outpatient setting.

NR25 Monday, May 19, 9:00 a.m.-10:30 a.m.

Ten-Year Outcomes of Primary and Secondary Men Alcoholics

Saeed A. Shah, M.D., Department of Psychiatry, Kansas University Med Ctr, 3901 Rainbow Blvd., Kansas City KS 66160; Elizabeth C. Penick, Ph.D., Barbara J. Powell, Ph.D., Elizabeth J. Nickel, M.S., Jan L. Campbell, M.D., H. Mikel Thomas, M.D.

Summary:

Objective: In this 10-year, naturalistic outcome study of alcoholism, we wanted to determine whether patients with major depression beginning prior to alcoholism (primary depression) differed in any clinically significant way from patients whose depression began after the onset of abusive drinking (secondary depression).

Methods: From a large sample of 360 hospitalized VA alcoholic men who were extensively investigated at intake into the study and systematically evaluated one and 10 years later, we selected a subsample of 97 (27%) who also satisfied inclusive DSM-III-R criteria for major depression but not mania or a sustained psychosis. Forty-one of these 97 were eliminated: 28 with co-occurring antisocial personality disorder (ASP) and 13 patients for whom 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 patients were then divided into three subgroups for comparative purposes: (1) Primary Depressed Alcoholic (N = 23). Onset of depression preceded the onset of alcoholism by at least two years. (2) Concurrent Depressed Alcoholic (N = 13). Onset of depression and alcoholism began within plus-or-minus one year of each other. (3) Secondary Depressed Alcoholic (N = 20). Onset of depression followed the onset of alcoholism by at least two years.

Results: At intake into the study, no differences were found across a wide range of variables. 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 comorbidity did not distinguish the three subgroups. One year later, only two of the 56 patients were lost to the study. Although the entire sample improved significantly with respect to abusive drinking, no one-year differences were found on multiple outcome measures. Ten years later, all of the original 56 patients were re-evaluated; 16 of the patients (29%) had died. Again, outcome measures including abstinence rates, drinking sequelae, treatments received, psychiatric severity, and ratings of psychosocial functioning were comparable across the three groups.

Conclusion: The results of this long-term outcome study question the clinical utility of distinguishing primary and secondary depression in non-ASP male alcoholics.

NR26 Monday, May 19, 9:00 a.m.-10:30 a.m.

Medical Symptoms Among Alcohol, Cocaine and Heroin Abusers

Ashwin A. Patkar, M.D., Department of Psychiatry, Jefferson Medical College, 1201 Chestnut Street, 15th Flr, Philadelphia PA 19107; Robert Sterling, Ph.D., Edward Gottheil, M.D.

Summary:

Objectives: Substance abuse is associated with various medical complications and carries a high morbidity. We investigated whether there were any differences in medical symptoms attributable to the use of alcohol, cocaine, or heroin.

Methods: The subjects were admissions to the outpatient alcohol and drug treatment programs affiliated with a university hospital. Substance abuse was diagnosed according to DSM-III-R. Medical symptoms were assessed by a 134-item self-report questionnaire (MILCOM).

Results: A total of 343 subjects were studied (alcohol = 101, cocaine = 113, opiate = 108, and others = 21). Cocaine abusers reported significantly fewer absolute number of symptoms than alcohol and heroin abusers ($p < 0.005$). Furthermore, significant differences were observed across cardiovascular ($p < 0.005$), neurological ($p < 0.003$), mood ($p < 0.01$), musculoskeletal ($p < 0.003$), digestive ($p < 0.018$), and dermatologic ($p < 0.004$) symptoms, with cocaine abusers reporting the least and alcohol abusers reporting the most symptoms. Women and Caucasians also reported significantly more mood, neurologic, nose/throat, and digestive symptoms.

Conclusions: First, cocaine abusers report fewer symptoms, even those related to cardiovascular and neurological systems, than do heroin and alcohol abusers. Second, there seems to be sex-related and race-related differences in the frequency of symptoms reported.

NR27 Monday, May 19, 9:00 a.m.-10:30 a.m.

Mexican Study of First-Episode Psychosis: Temperament and Character

Rogelio Apiquian, M.D., Clinical Research, Institute of Mexican Psych, Calzada Mexico Xochmilco 101, Mexico City 14370, Mexico; Francisco Paez, M.D., Ma-Elena Medina Mora, Ph.D., Rosa Elena Ulloa, M.D.

Summary:

Different personality traits and disorders have been associated with psychotic patients and they are known to affect course and be related with poor premorbid adjustment.

Objective: We compared temperament and character between patients with first-episode psychosis and a control group of subjects without psychiatric illness.

Method: We recruited 50 first-episode psychotic patients and 269 control subjects. Psychiatric diagnoses were assessed with the SCAN system; symptom severity was measured with the PANSS. Premorbid adjustment and psychosocial functioning were evaluated with specific scales. The patients and control group were examined with the Temperament and Character Inventory (TCI).

Results: Forthy-eight percent (N = 24) of the patients were male. The mean age was 28 years (SD = 10.1). Patients were classified as having schizophrenia (N = 18), affective psychotic disorders

(N = 17), or nonaffective psychotic disorders (N = 16). The patients showed an elevation in the harm avoidance (18.4 vs 12.6,t = 5.10,df 311, p = 0.001), in self-transcendence (20.6 vs 16.4,t = 4.09,df 311, p = 0.001), and diminution in self-directedness (26.1 vs 29.9,t = 2.25,df 311, p = 0.02) scales of the TCI. These TCI dimensions correlated with poor premorbid adjustment(r = 0.38, p = 0.01) and social functioning (r = 0.39 p = 0.01).

Conclusion: A personality disturbance was indicated by the low counts on the self-directedness scale.

NR28 Monday, May 19, 9:00 a.m.-10:30 a.m.

AIDS, Depression and Quality of Life in Black Men

Dwight D. Coleman, M.D., Department of Psychiatry, Emory University Sch of Med, 341 Ponce de Leon Avenue, SE, Atlanta GA 30308; J. Stephen McDaniel, M.D., Peter E. Campos, Ph.D., Eugene W. Farber, Ph.D., James Emshoff, Ph.D., Gary Uhl, Ph.D.

Summary:

While African Americans represent only 13% of the general U.S. population, they represent 1/3 of all AIDS cases. This trend is particularly true in Georgia where AIDS rates for blacks are twice those of whites. Although HIV infection rates continue to increase disproportionately among blacks, limited data currently describe the extent of psychiatric morbidity among HIV-positive black individuals. Depression, a complication that can affect numerous domains including quality of life, HIV risk behavior, and survival, remains a critical area of study within the HIV-affected black community. Moreover, black men with AIDS have been postulated to manifest an increased risk of depression and suicide.

The Emory Center for AIDS Mental Health Services is one of 11 national sites participating in a four-year, SAMHSA-funded demonstration project examining psychiatric morbidity, quality of life, and mental health service needs among HIV positive individuals. To date, 1/3 of the total Emory participants (N = 320) are black men. Current screening data reveal that 62.4% of the participants have major depression and 19% have dysthymia. We will present data from this ongoing study describing demographic characteristics, depressive symptoms (measured by the CIDI), quality of life (measured by the HIV-PARSE), and risk behaviors in HIV positive black men. We will discuss these findings and their HIV disease correlates in the context of culturally sensitive treatment.

NR29 Monday, May 19, 9:00 a.m.-10:30 a.m.

The Nature of Dissociation: A Transcultural Study About Religion-Related Dissociative Experiences

Paulo J. Negro, Jr., M.D., Department of Psychiatry, University of TX Hlth Sci Ctr, 7703 Floyd Curl Drive, San Antonio TX 78284; Mario R. Louza-Neto, M.D.

Summary:

Objectives: Dissociative behaviors are well described in the literature, but usually in pathological populations. We studied dissociative behaviors such as spiritual possession, automatic writing, and out of the body experiences in a cultural setting in which those behaviors are sanctioned and adaptive. To our knowledge, this is the first quantitative transcultural study of such nature.

Method: Seventy-two subjects from a prominent religious center in São Paulo, Brazil, surveyed for religiosity, social support, happiness, dissociative experiences related to their religious practices, Cloninger's personality scale (TPQ), and ratings in the Dissociative Experience Scale in situations related and unrelated to the religious setting. The hypotheses of the study include: 1) presence of high degree of happiness and satisfaction in spite of prominent dissociative behavior, 2) absence of history of child abuse, 3) mastering of the dissociative experiences associated with training, and 4) association between dissociative behavior and reward dependency score at Cloninger's personality scale.

Results: 1) happiness: 67.8% (SD. 18.5) in a visual analogic scale; 2) sexual abuse: reported in only four out of 62 valid scores; 3) good social support and work history; 4) good social control of dissociative behavior; 5) substantial dissociative behavior related to the religious practices (spiritual incorporation: 4.6 events; hearing spirits: 2.9 events; automatic writing: 1.0 events; psychophony: 2.8 events in 30 days; spiritual incorporation: 46 min; hearing spirits: 18 min; automatic writing: 35 min; psychophony: 35 min per week); 6) general DES profile: between 10% and 35%; 7) DES scores: significant higher values for scores in situations outside the religious setting than in situations linked to religious practices in the items 18, 21, 22, 24; 8) correlation between training and social control of the dissociative behavior (Spearman r = 0.49 p = 0.0001); 9) correlation between reward dependency and dissociative behavior (Spearman r = 0.22 p = 0.045).

Conclusions: The behavior partially modeled by the social matrix. Such findings argue partially for the sociocognitive model of dissociation and point to limitations of ego psychology theories of dissociation and toward the conceptualization of dissociative identity disorder as a culture-bound syndrome.

NR30 Monday, May 19, 9:00 a.m.-10:30 a.m.

Flexible Therapy Versus Traditional Psychotherapy: A Preliminary Study

Manohar K. Shetty, M.D., Department of Psychiatry, St. Francis Medical Center, 410-B Glen Malcolm Drive, Glenshaw PA 15116; Salim A Chowdhury, M.D., Robert H. Trivus, M.D., David J. Lynn, M.D., Ronie Titus, M.S.W.

Summary:

Introduction: Psychotherapy is an accepted form of treatment for various mental health disorders. Concepts and utilization of traditional psychotherapies, including psychoanalysis, have changed over time due to multiple factors including cost. This has lead to our idea of Flexible Psychotherapy, an electric form of treatment whereby more emphasis is given to the patient's here and now, providing an existential, empathic approach.

Methods: Twenty-five patients were chosen from two groups. The first group received traditional psychotherapy of an interpersonal or psychodynamic type. The second group was treated with Flexible Psychotherapy as described on the poster. These patients were followed for one year with various parameters monitored and rated.

Results: There were no drop-outs in the Flexible Therapy group compared with a drop-out rate of 4% in the traditional therapy group. Compliance with medication was 80% in both groups; hospitalization was 4% in the Flexible Therapy group as compared with 8% in the traditional group. Flexible Therapy patients also showed significant improvement in social functioning and absence of regression.

Conclusion: Although we must be cognizant of price-based costing in designing and utilizing a therapeutic modality, therapeutic outcome, in terms of patient's level of functioning, is of paramount importance. Flexible Therapy appears to satisfy both of these goals and warrants further study.

NR31 Monday, May 19, 9:00 a.m.-10:30 a.m.

Paraquet Poisoning and Ethnicity

Gerald Hutchinson, M.D., Department of Psychiatry, St. Francis Medical Center, 410-B Glen Malcolm Drive, Glenshaw PA 15116; Manohar K. Shetty, M.D., David J. Lynn, M.D., H. Daisley, Osama M. Saleh, M.D., Koushik Mukherjee, M.D.

Summary:

Introduction: Suicide by organophosphorous compounds is rare in the United States. This is the most common method in South Asia and some Caribbean nations, where one sees a significant number of South Asians. We tried to understand the reasons why South Asians, though living in the Caribbean, still use this painful method.

Method: This prospective study was done at General Hospital, Trinidad, West Indies. The patients admitted after organophosphorous compound ingestion were interviewed. The different methods of suicide based on the ethnic background were computed.

Results: There was a disproportionate increase in suicides by organophosphorous compounds in the South Asian immigrant population. It was also realized that the patients who tried to kill themselves by this method did not realize the lethality of the substance.

Conclusion: The exact reasons for ingesting organophosphorous compounds for attempted suicide in this ethnic group are still being investigated. However, the easy access is a factor since they are used as herbicides. The absence of knowledge of the potential lethality of this substance was the cause for increased incidence. The educational methods used in Sri Lanka indicate that an understanding regarding the lethality of this substance will reduce the incidence of organophosphorous ingestion and suicide rate.

NR32 Monday, May 19, 9:00 a.m.-10:30 a.m.

Phobia and Night Terror Associated with Ketamine: How to Avoid Them?

Manohar K. Shetty, M.D., Department of Psychiatry, St. Francis Medical Center, 410-B Glen Malcolm Drive, Glenshaw PA 15116; David J. Lynn, M.D., Roopnarine Lalla, M.B., Hamid Razak, M.B., Raj Sarma, M.D.

Summary:

Introduction: Ketamine, a highly potent analgesic related to phencyclidine, is used to induce general anesthesia. In this study we looked at the relationship between development of phobia and night terrors in children after repeated ketamine anesthesia.

Method: In this retrospective study the behaviors of children requiring repeated ketamine anesthesia for burn dressings and escherectomy were observed. The extent of burns, number of times they had ketamine anesthesia, and its effects on their behavior over a period were observed. Behaviors were compared after giving long-acting benzodiazepines preoperatively.

Results: Children developed night terrors after repeated ketamine administration. They also developed a specific phobia for the ER, ER attendants, and gurneys. Intensity was proportional to the amount of physical injury and the stimulation in the ER. There was a decrease in phobia and night terrors after the use of long-acting benzodiazepines as preoperative sedation.

Discussion: Though ketamine is known to produce dissociative states, the behaviors observed were over days after ketamine administration, which becomes a significant clinical entity when children had to be taken to OR multiple times. We advocate a higher dose of long-acting benzodiazepines be given preoperatively to prevent phobias and night terrors in children.

NR33 Monday, May 19, 9:00 a.m.-10:30 a.m.

Return of Menses in Patients Hospitalized for Anorexia Nervosa

Laurel Mayer, M.D., Department of Psychiatry, NY State Psychiatric Institute, 722 W 168th Street/Unit 86, New York NY 10032; Evelyn Attia, M.D., B. Timothy Walsh, M.D., Kristin Chally, B.A., Claire Haiman, B.A.

Summary:

Objective: To examine the relationship between weight and return of menses among women with anorexia nervosa.

Method: Charts of 97 female inpatients meeting DSM-IV diagnostic criteria for anorexia nervosa were reviewed. Historical information, diagnostic subtype, percent ideal body weight (%IBW) on admission, weekly, and at return of menses were recorded. If amenorrhea persisted, %IBW on discharge was noted. Statistical analysis was performed on 46 charts from which reliable data were available.

Results: Menses resumed in 12 of 46 (26%) subjects. Mean %IBW for subjects whose menses returned was 89.5% versus 82.0% for those in whom menses did not ($p < 0.001$). Of 12% of those who gained to ≥90% IBW, 61.5% regained their menses. Those who remained <90% IBW regained their menses ($p < 0.001$). The frequency of resumption of menses among women gaining to ≥90% IBW was significantly greater compared to the frequency among those who gained from 80% to 84% IBW (chi-square = 7.67, df = 1, $p < 0.01$). The difference between the groups achieving 85% to 89% and ≥90% IBW did not reach statistical significance (chi-square = 1.17, df = 1, $p < 0.3$).

Conclusions: Resumption of menses correlates strongly with weight gain, although multiple factors likely contribute. Treatment for patients with anorexia nervosa should aim to restore weight to ≥90% IBW.

NR34 Monday, May 19, 9:00 a.m.-10:30 a.m.

Low Platelet MAO Associated to Impulsive Behaviors in Eating Disorders

Jose L. Carrasco, M.D., Department of Psychiatry, Medical School, AV Campo Charro S/N, Salamanca 37007, Spain; Marina Diaz-Marsa, M.D., Jeronimo Saiz-Ruiz, M.D.

Summary:

The relationship between impulsivity and eating disorders has not yet been clarified. While some patients show dysfunctional hormone response to serotonergic challenges and respond to anti-impulsive serotonergic drugs, other patients do not. An association between bulimic, but not anorectic, symptoms and impulsive personality traits has been postulated. Decreased platelet MAO, a marker of impulsive traits, has been scarcely studied.

Sixty-two normal-weight patients with eating disorders (32 anorexia nervosa, 25 bulimia nervosa, and five eating disorders NOS), according to DSM-IV, and a control group of 24 age-matched women, were studied with personality interviews and questionnaires, including Cloninger's TCI, EPQ, Karolinska and Barrat impulsivity scales, and SCID-II. Platelet MAO activity was measured in all patients following an isotopic method with C-14 benzylamine as substrate.

Preliminary results show no difference in MAO activity between patients and controls. Binge-eating behaviors in the different subgroups are significantly associated with low platelet MAO ($p < 0.01$) and are correlated with impulsive personality traits.

Impulsivity might be related to some behaviors associated with eating disorders.

NR35 Monday, May 19, 9:00 a.m.-10:30 a.m.

Sex Differences in Hyperactivity in School-Aged Children

Carol A. Glod, Ph.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Martin H. Teicher, M.D., Cynthia McGreenery, Ann Polcari, M.S.N., Carl M. Anderson, Ph.D., Judith Holt, R.N.

Summary:

Attention-deficit hyperactivity disorder (ADHD) is estimated to affect 6% of children, predominantly males. Our hypothesis was that ADHD was equally prevalent in boys and girls, but that teachers were more likely to detect symptoms in boys. The final sample consisted of 698 first and second graders (371 M; 327 F). Children completed a 15 minute continuous performance test (CPT) at school, while head movements were tracked using an infrared motion analysis system, which in previous studies discriminated ADHD from normal with 93% accuracy (Teicher et al, 1996). Teachers completed Connor's and Iowa ratings. The activity and attention scores were not normally distributed. There was a large bell-shaped component in which about 95% of the population fell, and there was a second smaller distribution outside the normal range, which indicates the presence of a discrete abnormal population. The primary question was whether girls and boys had the same prevalence of abnormalities. Using absolute gender-neutral criteria we found no significant gender differences. For example, 14 girls (4.4%) and 22 boys (6.2%) were objectively hyperactive (cut-off criteria >50 cm^2, head movement area; Fisher Exact Test = 0.391). In contrast, teacher's rated only nine (2.7%) girls and 44 (11.9%) boys as symptomatic on the Conners Teacher Rating Scale (Fisher exact = 0.000003). The majority of girls identified by teachers as abnormal were also hyperactive on objective measures. In contrast, the majority of identified boys had good capacity to sit still and pay attention. This raises the possibility that their school-related difficulties may be due to other psychiatric causes.

NR36 Monday, May 19, 9:00 a.m.-10:30 a.m.

The Risk and Protective Factors Scale for Disruptive Behavior Disorders in Preadolescents

Karl J. Looper, M.D., Department of Psychiatry, McGill University, 4131 Cote Des Neiges #14, Montreal PQ H3H 1X1, Canada; Natalie Grizenko, M.D.

Summary:

The disruptive behavior disorders, including attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder (CD), are among the most common disorders in childhood. Studies have shown a 40% persistence of ADHD at 10-year follow-up, and associations of 25% with antisocial disorder and substance abuse disorder in adulthood. The high prevalence and consequences of these disorders require early identification and intervention for children at risk of developing a disruptive behavior.

The Risk and Protective Factors Scale for Disruptive Behavior Disorders (RPS-DBD) (Grizenko, Looper, Pawliuk, 1997) is a 34-item scale categorized by biological, psychological, and social subgroups. The RPS-DBD is the only scale that is designed to identify children at risk for developing disruptive behavior disorders. The development and description of the scale will be presented, as well as the results of a reliability and validity study of the RPS-DBD with a group of 120 preadolescents (Looper, Grizenko, 1997). The validity of the scale is demonstrated by its ability to discriminate between diagnosis and no-diagnosis groups, and correlations with the Revised Child Behavior Checklist (Achenbach). The internal consistency (alpha 0.62 to 0.84), interrater reliability (kappa 0.57 to 1.0), and test-retest reliability (Pearson 0.58 to 1.0) will also be discussed.

NR37 Monday, May 19, 9:00 a.m.-10:30 a.m.

A Classification of Korean Adolescent Criminals

Eunyoung Oh, M.D., Department of Psychiatry, Ajou University, 5 Wonchon-Dong, Paldal-Gu, Suwon, Kyunggi-Do 442380, South Korea; Sookwon Kim, M.D., Sunmi Cho, M.A., Hoyoung Lee, M.D., Choongsoon Lee, M.D., Jihyun Kim, M.D.

Summary:

Objective: This study was conducted to classify the personality characteristics of Korean adolescent criminals using MMPI and to compare the frequency and type of criminal behaviors among the classified group.

Method: The subjects were 35 randomly selected, 15- to 22-year-old male Korean adolescent criminals without major psychiatric illnesses, who were administered the Minnesota Multiphasic Personality Inventory (MMPI).

Results: The 13 standard scales were subjected to cluster analysis resulting in two clusters of the original sample. Both clusters showed high scores in scale 4(Pd). There was no significant statistical difference between clusters, but cluster aA (n = 19) had more frequency of acting out behavior and showing unusual behavior in social context than cluster B (n = 16) (T-test, p.01). There were no significant statistical differences in frequency and type of criminal behavior between the two clusters.

Conclusions: These results suggest that the personality characteristics of male adolescent criminals are not homogeneous.

NR38 Monday, May 19, 9:00 a.m.-10:30 a.m.

Comorbidity of ADHD and Adolescent Criminals Using TOVA

Myungsoo Lee, M.D., Department of Psychiatry, Ajou University, 5 Wonchon-Dong, Paldal-Gu, Suwon, Kyunggi-Do 442380, South Korea; Eunyoung Oh, M.D., Kiyoung Lim, M.D., Keunyoung Park, M.A., Youngki Chung, M.D., Jaisung Noh, M.D.

Summary:

Objective: The goal was to investigate the possibility of comorbidity between conduct disorder and ADHD in South Korea, using TOVA.

Method: We enforced TOVA on 46, 15- to 22-year-old male Korean adolescents attending Suwon reformatory school, who met DSM-IV criteria for conduct disorder. The same task was applied to 18 normal controls consisting of 14- to 18-year-old males in middle or high school.

Results: Two-sample t-test revealed that the omission ($T[1,62] = 3.70$, $p < .001$) and the commission scores ($T[1,62] = 2.34$, $p < .05$) were significantly different between the two groups, but the response time and variability were not significantly different.

Conclusions: The results showed that the conduct disorder group had problems of inattention and impulsivity when compared with the normal control group. We can assume that the conduct disorder is closely related to ADHD.

Comments: This is an ongoing study with more subjects and controls being added, so we expect to get more statistically significant data over time.

NR39 Monday, May 19, 9:00 a.m.-10:30 a.m.

Use of Counseling by Pregnant or Postpartum Teens

Jude L. Boyer-Patrick, M.D., Department of Psychiatry, University of Maryland, 7329 Kerry Hill Court, Columbia MD 21045-5024; Lisa B. Dixon, M.D., Janet D. Woolery, M.D., Phyllis Huff, M.S.W., Joe Turner, M.A.

Summary:

Objective: The counseling needs and psychological status of single, pregnant, and/or postpartum high school girls are largely unknown. We assessed feelings of depression, use of street drugs and alcohol, and past utilization of counseling services among

girls voluntarily attending a high school for pregnant and postpartum teens.

Methods: As part of a school-wide needs assessment, we anonymously surveyed 110 students at a special inner-city high school. Questions included counseling history, current symptoms of depression, and drug use. Virtually all active students (96% African American, mean age 16.4 [SD 1.3], 49% currently pregnant) participated.

Results: Almost half of the girls (N = 49 (46%)) reported a "counseling" experience; 37% of those in counseling had seen a psychiatrist or psychologist. Approximately one-third of the girls reported feeling nervous or down in the dumps at least some of the time. A history of counseling was associated with recent substance use ($p < .02$), reported willingness to discuss sadness with a counselor ($p < .01$), and greater total affective symptoms (trend). Only 15% reported that they would talk about physical or sexual abuse in counseling.

Conclusion: This study suggests the importance of counseling services for pregnant or postpartum teenage girls. However, issues of trust need to be addressed in order for these girls to discuss critical personal problems.

NR40 Monday, May 19, 9:00 a.m.-10:30 a.m.

Adolescents Semistructured Interview: Interrater and Test-Retest Reliability

Francisco R. De la Pena, M.D., Department of Psychiatry, Univ of AZ Health Science Cntr, 4324 N. Rillito Cre., Tucson AZ 85719; Eduardo Cruz-Elizondo, M.D., Rosa Elena Ulloa, M.D., Margarita Patino, M.D., Arturo Mendizabal, M.D., Gerardo Heinze, M.D.

Summary:

Semistructured interviews are a basic necessity for any investigation in psychiatry. We designed a semistructured clinical interview based on other instruments such as the K-SADS, ISC, DISC, and SCAN. The ASI was designed according to DSM-IV criteria to explore internalized and externalized disorders, psychotic, and substance abuse disorders. The goals of the study were to establish the inter-rater and test-retest (one week) reliability of the ASI. The adolescents were evaluated in the second contact with the Instituto Mexicano de Psiquiatria, conjointly with the mother or father after informed consent was obtained. The evaluation was made in 60 to 90 minutes. Two clinicians were present at the interview; one asked the questions and assessed, while the other only assessed. Both were blind to each other's diagnosis. The test-retest was made by different clinicians. The sample was integrated with 80 outpatients. The kappa values for the inter-rater study were as follows: major depressive disorder (MDD) 0.92, dysthymic disorder (DD) 0.81, attention deficit disorder (ADD) 0.75, conduct disorder (CD) 0.97, and substance abuse (SA) 0.90. The kappa values for the test-retest study were as follows: MDD 0.59, DD 0.49, ADD 0.78, CD 0.85, and SA 0.65. This is the first worldwide study of an adolescent semistructured clinical interview in Spanish.

NR41 Monday, May 19, 9:00 a.m.-10:30 a.m.

Parental Compliance with Psychiatric Referral

John P. Neuhaus, M.D., Department of Psychiatry, University of Hawaii, 1356 Lusitana Street, 4th Flr, Honolulu HI 96813; Linda B. Nahulu, M.D., Deborah Goebert, M.S.

Summary:

Children and adolescents seen in the emergency department (ED) or in the general hospital as part of a child-psychiatry consultation service are often a high-risk group who need intervention to help prevent further morbidity or self-harm.

Objective: This study will examine the compliance rates and associated factors for psychiatric follow-up of children and adolescents seen in the ED or general hospital setting.

Method: One hundred twenty children and adolescents were seen by the child psychiatric consult-liaison team in 1996. Patient and parent demographics as well as psychiatric profile and follow-up information were abstracted. The psychiatric profile included such variables as the precipitating circumstances, diagnosis, active and past psychiatric treatment, medications, and disposition. Follow-up information was confirmed at the two primary referral sites by chart review. A brief survey was mailed to parents to assess satisfaction, impressions, and follow-up.

Results: The factors affecting parental compliance with the follow-up regime are examined. Parental satisfaction, parental impression, and frequent ED use are assessed as interfering with compliance, and medication and previous or current psychiatric treatment as improving compliance.

Conclusions: The effectiveness of consultation work is dependent, in part, upon the achievement of follow-up. This study has identified factors related to follow-up noncompliance that can be used to implement safeguards that will ensure aftercare.

NR42 Monday, May 19, 9:00 a.m.-10:30 a.m.

Vocal Tics in Sydenham's Chorea Patients

Marcos Tomanik Mercadante, M.D., Department of Psychiatry, Sao Paulo University, Rua Dr Ovidio Pires de Campos, Sao Paulo SP 05403-010, Brazil; M. Conceicao do Rosar Campos, M.D., Maria J. Dias, M.D., Paul J. Lombroso, M.D., James F. Leckman, M.D., Euripedes C. Miguel, M.D.

Summary:

Background: Sydenham chorea (SC) is a neuropsychiatric disorder that is a late sequela of a streptococcal infection. A higher incidence of obsessive-compulsive symptoms (OCS) and obsessive-compulsive disorder (OCD) have been documented in SC patients. OCD has also been described more frequently in patients with Tourette's syndrome (TS) and there are several lines of research suggesting that some forms of OCD may represent a variant expression of TS. The present study was undertaken to determine whether vocal tics, in addition to obsessive-compulsive symptoms, were present in SC patients.

Method: Nineteen children with SC and seven children with rheumatic fever (RF) were evaluated. The RF patients were diagnosed according to Jones criteria. Psychiatric and neurological evaluations were performed on all patients. The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiological version, Yale-Brown Obsessive Compulsive Scale, and Yale Global Tics Severity Scale were administered to all patients.

Results: The SC sample showed 14 patients with vocal tics (73.68%) and 10 patients with OCS (52.63%). The RF sample showed four patients with OCS (57.14%) and none with vocal tic.

Conclusions: The finding of vocal tics in these patients suggests that tics as well as OCS are found more frequently in children with Sydenham's chorea.

NR43 Monday, May 19, 9:00 a.m.-10:30 a.m.

Anorexia and Weight Loss in Children Taking Adderall

Amanda N. Holmes, M.D., Department of Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Barbara L. Gracious, M.D., Cheryl Preece, M.S., Sheree Atkinson

Summary:

Objective: The purpose of this study is to evaluate the relationship between appetite suppression and weight loss in children aged 12 years and younger prescribed Adderall for management of attention deficit hyperactivity disorder (ADHD).

Methods and Materials: A retrospective chart review using electronic medical records was conducted for children diagnosed with ADHD and prescribed Adderall during 1995 and 1996 at Scott and White Clinic. Information was collected on demographics, height and weight, other medications prescribed, and initial and maximum dose. When possible, follow-up information was collected at 12 months or until the drug was discontinued.

Results: Fifty percent of the subjects prescribed Adderall experienced neither weight loss nor anorexia on doses of 10-20 mg daily. One subject experienced anorexia on 20 mg daily, two patients had weight loss only (both 0.7 kg/4 months, 20 and 25 mg daily), and two patients experienced weight loss and anorexia (1.5 kg/5 weeks and 1.7 kg/8 weeks, both 20 mg daily). Follow-up results as well as results for age-matched controls prescribed Ritalin are presented in the final manuscript.

Conclusions: Initial results suggest that Adderall, like other stimulants, has significant anorectic properties that make monitoring growth parameters important for clinicians prescribing this drug.

NR44 Monday, May 19, 9:00 a.m.-10:30 a.m.

Comorbidity and Initial Pharmacotherapy in ADHD

Victoria B. Morgan, M.D., Department of Psychiatry, Scott & White, 2401 South 31st Street, Temple TX 76508; Barbara L. Gracious, M.D., Cheryl Preece, M.S., Sheree Atkinson, Mary Marek, B.S.

Summary:

Objective: This retrospective chart review explores the effects that gender or a comorbid psychiatric disorder might have on initial choice of psychoactive medication in a population of latency-aged children with a new diagnosis of attention deficit hyperactivity disorder (ADHD) using DSM-IV criteria.

Methods and Materials: The sample (n = 51) included male and female children ages 5 to 12 years, selected from all new psychiatric evaluations in a semirural multispeciality hospital with a new diagnosis of ADHD. Data on comorbid psychiatric illness and pharmacologic therapy were collected through electronic medical record reviews by trained staff.

Results: The sample was 77% male. Only 35% of these patients had no comorbid psychiatric disorder identified. The remaining cases had at least one comorbid condition. Methylphenidate (59%), pemoline (15%), and imipramine (15%) were the most common medications prescribed initially.

Conclusions: One factor that should be considered when choosing the most appropriate medication for children diagnosed with ADHD is a comorbid psychiatric illness. Other factors that may play a role in the pharmacological treatment of ADHD include gender and race.

NR45 Monday, May 19, 9:00 a.m.-10:30 a.m.

Risperidone Side Effects in Children and Adolescents

Claudia A. Phillips, M.D., Department of Psychiatry, Scott and White, 2401 South 31st Street, Temple TX 76508; Barbara L. Gracious, M.D., Cheryl Preece, M.S., Sheree Atkinson

Summary:

Introduction: The purpose of this study is to compare the side-effect profile of risperidone with that of other neuroleptics in a child and adolescent population.

Methods and Materials: A review of electronic medical records for 65 children and adolescents under the age of 18 prescribed neuroleptics was performed by the Division of Child and Adolescent Mental Health, Department of Psychiatry, Scott and White Clinic and Hospital in Temple, Texas. Charts were assessed for side effects including extrapyramidal symptoms, anticholinergic effects, weight gain, sedation, alteration in mood, endocrine effects, and orthostatic hypotension as reported by the patient, parent, and/or physician. Additional data recorded included age, race, gender, indication for the neuroleptic, diagnoses, initial and maximum doses, dose changes, duration of treatment, and any additional medications.

Results: Initial analyses revealed that 45% of the patients prescribed risperidone experienced side effects as compared with 43% prescribed haloperidol and 17% prescribed thioridazine. Complete analyses address the type of side effects and their duration.

Conclusions: Risperidone may not have a more favorable side-effect profile when compared with other neuroleptics in a clinical child and adolescent population. Further studies are needed to quantify side effects objectively.

NR46 Monday, May 19, 9:00 a.m.-10:30 a.m.

Initial Presentations of OCD in Children

Elizabeth A. Schoene, M.D., Department of Psychiatry, Scott & White, 2401 South 31st Street, Temple TX 76508; Helen A. Zaphiris, M.D., Cheryl Preece, M.S., Sheree Atkinson

Summary:

Objective: This study examines early symptoms and presentations of a pediatric population eventually diagnosed with obsessive-compulsive disorder (OCD) in an attempt to assist with better recognition of OCD and aid in its early diagnosis.

Methods and Materials: Patients were selected from all new referrals for evaluation performed in a semirural child and adolescent psychiatry clinic during 1995. Using an electronic medical record database at Scott and White Clinic in Temple, Texas, charts were reviewed for children ages 5 through 18. Children were included in the study if they received a new, probable, or provisional diagnosis of OCD. A trained reviewer used a computer-generated data collection sheet to gather information on demographics, reasons for referral, comorbid diagnoses, and treatments.

Results: Seventeen new cases of OCD were diagnosed in the clinic in 1995. Mean age at time of diagnosis was 10 years. Reasons for referral included mood symptoms (50%), combined mood and anxiety symptoms (17%), anxiety symptoms only (8%), psychotic symptoms (8%), and other symptoms (17%).

Conclusions: Initial results suggest children with OCD commonly present with symptoms resembling other psychiatric disorders. This may delay initiation of appropriate pharmacologic and/or psychotherapeutic interventions.

NR47 Monday, May 19, 9:00 a.m.-10:30 a.m.

A PRN Administration in a Child Inpatient Unit: A Retrospective Study

Alejandra Hallin, M.D., 20 Chapel Street, Apt. C709, Brookline MA 02146-5468; Ronald J. Steingard, M.D., Gordon P. Harper, M.D.

Summary:

The use of prn medications in a inpatient unit is common. However, research on this topic is sparse. The purpose of this review was to assess the use of prn medications on child/adolescent inpatients, looking for factors such as sex, race, time of administration, and length of stay that may predict that use. The charts of

92 patients who were consecutively admitted over six months to a child inpatient unit in an academic setting were reviewed. The use of all prn psychotropic medications was recorded. A total of 43 (46%) patients received at least one prn administration. There were 375 prn administrations. Age, sex, time of the administration, and length of stay were poor predictors of the number of prn administered; race impacted on the total number of doses received. Implications for practice and further research are discussed.

NR48 Monday, May 19, 9:00 a.m.-10:30 a.m.

Relationship Between the Psychopathology and the Concentration of Serotonin in Platelet-Rich Plasma of Children with Autistic Spectrum Disorder

Yee-Jin Shin, M.D., Early Developmental Study, University of Colorado, 4200 East 9th Street, Denver CO 80262; Sung Kil Min, M.D.

Summary:

Objective: This research was designed to find the relationship between the abnormalities of the serotonergic system and the autistic psychopathology in autistic children and atypically autistic children, who have similar but milder autistic symptoms.

Method: We compared the concentrations of serotonin (5-HT) in platelet-rich plasma (PRP) between autistic, atypically autistic, and control groups. The psychopathology of infantile autism, measured by Childhood Autism Rating Scale (CARS), was correlated with the concentrations of 5-HT in PRP in the autism or atypical autism group. We diagnosed children as having autism and atypical autism who fulfilled DSM-III-R criteria of autistic disorder and pervasive developmental disorder not otherwise specified, respectively. The subjects of this study were 48 autistic patients, 14 atypically autistic patients, and 38 control children, and the concentration of 5-HT was measured by using HPLC-ECD method.

Results: 1.) The concentration of PRP 5-HT of patients with atypical autism and autism was significantly higher than that of control children, and patients with atypical autism showed the highest level. 2.) The concentration of PRP 5-HT was related to the eighth CARS item, abnormal auditory responsiveness, in the autistic group. But there was no significant correlation in the atypical autism group.

Conclusion: These results suggest that both autism and atypical autism are related to an abnormality of the serotonergic system, and the high level of 5-HT is related to the symptom of abnormal auditory responsiveness in children with infantile autism.

NR49 Monday, May 19, 9:00 a.m.-10:30 a.m.

Gender-Based Differences in the Presentation of Children and Adolescents to a Psychiatric Emergency Room

Maria T. Cartagena, M.D., Department of Psychiatry, SUNY Buffalow ECMC, 462 Grider Street, Buffalo NY 14215; Joy L. Kreeger, M.D., Yogesh D. Bakhai, M.D., Wendy L. Weinstein, M.D.

Summary:

Objective: To examine whether any gender based differences exist in the patterns of presentation of children and adolescents in a psychiatric emergency room.

Method: The frequency with which children, ages one to 17, presenting to the Comprehensive Psychiatric Emergency Room (CPEP) at the Erie County Medical Center in Buffalo, New York, was calculated. The time period examined was from June 1, 1994, through May 31, 1996. The cases were separated into two age groups, ages 0 to 12 years and 13 to 17 years, and examined by gender and ethnic origin.

Results: A total of 1,974 visits by children ages 0 to 17 occurred within the 24-month period. Of those cases, 943 (47.8%) were males and 1,031 (52.2%) females. In the 0 to 12 years age group, a total of 289 (66.4%) males and only 146 (33.6%) females were observed. Conversely, in the 13 to 17 years age group only 654 (42.3%) male cases were seen compared with 885 (57.3%) female cases. This trend was consistent during most months (79.2%). The cases were also examined with regard to diagnosis and the hour of day during which the patients presented. Results are currently pending further analysis.

Conclusion: The study demonstrates an interesting newly described trend in the presentation of children to psychiatric emergency rooms.

NR50 Monday, May 19, 9:00 a.m.-10:30 a.m.

Seasonal Variations in the Presentation of Children and Adolescents to a Psychiatric Emergency Room

Maria T. Cartagena, M.D., Department of Psychiatry, SUNY Buffalow ECMC, 462 Grider Street, Buffalo NY 14215; Yogesh D. Bakhai, M.D., Joy L. Kreeger, M.D., Betty Brown, M.D.

Summary:

Objective: To determine if seasonal trends exist in the presentation of children and adolescents to a psychiatric emergency room.

Methods: The frequency of presentation by children and adolescents ages 0 to 18 years to the Comprehensive Psychiatric Emergency Program (CPEP) at the Erie County Medical Center in Buffalo, New York, between January 1, 1991, and December 31, 1994, was examined. Frequencies were calculated every two months for all four years and separated into three age groups: 0 to 6 years, 7 to 12 years, and 13 to 18 years.

Results: Over four years 4,043 cases were seen. Across all age groups, the largest number of cases presented during March/April (800, 20%) and the fewest number of cases presented during July/August (578, 14%). Similarly, in both the 7 to 12 year and the 13 to 18 year age groups, the largest number of cases presented during March/April (19, 22%), (587, 19%). The fewest numbers presented in July/August (115, 13%) (492, 16%). In children 0 to 6 years, the largest number of cases also presented during March/April (23, 20%). However, the fewest number presented during May/June (16, 13.6%). The statistical significance is pending further analysis.

Conclusion: Based on preliminary analyses, a distinct pattern of presentation to the psychiatric emergency room exists in the child and adolescent population. This pattern is most consistent in school-age children.

NR51 Monday, May 19, 9:00 a.m.-10:30 a.m.

Physician-Assisted Suicide: Medical Students' Perspectives

Ana C. Posada, M.D., Department of Psychiatry, University of Miami/VAMC, 1201 NW 16th Street, Miami FL 33125; Maria Rodill, M.D., Maria D.D. Llorente, M.D.

Summary:

Introduction: This study examined views of medical students regarding suicide, including physician-assisted suicide (PAS), determined life events that influence these views; and evaluated the impact of ethnicity, gender, and religion on these attitudes.

Methods: Randomly chosen groups of senior medical students were asked to complete an anonymous survey that solicited demographic information; opinions about suicide, life-sustaining treatments, and PAS; and experiences that influenced these opinions. Frequency distributions were calculated.

Results: A total of 102 surveys were completed (97% response). Data showed that 71.5% believed suicide to be acceptable, but

only 58.8% agreed with PAS; 38.2% would participate in PAS. Reasons given by those that would not participate included: 27% against beliefs, 25% not MD role, 21.6% feel it's homicide, 7% illegal. Demographic differences were found. Those opposed to PAS: 54% of women v. 34% of men; 53% of foreign-born v. 36% U.S.-born; 52% of Christians v. 22% of Jews v. 33% of those without religious affiliation. Also, 80% of students with personal experiences with suicide were opposed to PAS.

Conclusions: Foreign-born, female medical students with religious affiliations are the least likely to agree with PAS. Medical school curricula should offer students positive experiences with elderly and terminally ill patients and instruction in adequate pain management. Discussions in ethics courses should include PAS and what experiences influence one's opinion.

NR52 Monday, May 19, 9:00 a.m.-10:30 a.m.

Assessing and Improving Neurology Training in General Psychiatry Residencies

Susan M. Maixner, M.D., Department of Psychiatry, University of Michigan, 2215 Fuller Road, Ann Arbor MI 48105; Ronald C. Albucher, M.D., Michelle Riba, M.D.

Summary:

Objective: Our study assesses the adequacy of neurology training for general psychiatry residents by measuring residents' subjective and objective neurological proficiencies.

Method: Thirty-two psychiatry residents were surveyed about perceived levels of competency in 24 neurologic or neuropsychiatric conditions. Mean proficiencies were compared by residency year, and to recommended standards. Also, consecutive Psychiatry Residency In-Training Examination (PRITE) scores of 39 residents were analyzed for trends in neurology and psychiatry subscores throughout residency.

Results: Residents who recently completed their neurology training reported the highest levels of neurological aptitude. There was a gradual decay in self-assessed competency over each year, with the lowest scores reported by the senior class. This was despite significant improvement in neurology subsection scores on the PRITE for the fourth-year residents in our program ($F = 3.77$; $p = 0.03$). Psychiatry subsection PRITE scores also significantly improved for each year of training ($F = 52.79$; $p = 0.0001$).

Conclusions: Psychiatric residents in our program felt less secure in their neurologic clinical abilities despite an expanding knowledge base in neurology and neuropsychiatry. Additional neurologic or neuropsychiatric clinical experiences later in residency training may enhance self-confidence in this important area of training.

NR53 Monday, May 19, 9:00 a.m.-10:30 a.m.

Psychiatric Information Center in Brazil

Yara Azevedo, M.D., Department of Psychiatry, University S. Paulo, Rua Jose Maria Liboa 1060 AP21, Sao Paulo SP 01423001, Brazil; Caludio de Novaes Soares, M.D., Ana Maria Almeida, M., Jep Neves, M.D.

Summary:

Background: Some of the recent literature in psychiatric education pointed out that efforts need to be directed at developing mental health consultation services in order to expand knowledge and skills of community care providers, professionals, and physicians.

Objective: To describe the development and organization of a psychiatric information center in a third-world country and its one-year results.

Methods: Population and health professionals have access by a toll-free number (55-11-2804562). Calls are received and answered by a staff of four psychiatrists.

Results: More than 1,300 calls had been answered during the first year; 63% of the inquires were made by physicians, 18% by other health professionals, and 19% by the general population. We analyze professional inquiries concerning psychopharmacology management of patients and general information in psychiatry. This service provides knowledge in the assessment and management of psychiatric disorders for health professionals (physicians, social workers, psychologists, nurses) as well as parents and other interested people.

Conclusion: Information and consultation centers play an important role in continuing education programs for health professionals.

NR54 Monday, May 19, 9:00 a.m.-10:30 a.m.

Unexpected Impact of a Client Satisfaction Survey at a Public Mental Health Clinic

Abul Q. Hasan, M.D., Department of Psychiatry, NCMC, 2201 Hempstead Turnpike, East Meadow NY 11554; David I. Mayerhoff, M.D., Thomas Lysaght, Ph.D.

Summary:

In keeping with the increased use of consumer satisfaction as an important index of quality in health care, a client satisfaction survey was undertaken at the mental health clinic of a large county hospital. Like many public hospitals, budget cutbacks had rendered the facility lacking in resources to improve the physical plant or to hire staff. What remained was a diminished and overworked but dedicated staff.

The main part of our survey was the distribution of a two-page questionnaire (with 10 questions) to all clinic patients. The questionnaire was so prepared that it would reflect not only the treatment rendered but also how comfortable the clients felt in coming to the clinic. A total of 116 clients (out of a total 850) completed the survey. Unexpectedly, the results were extremely favorable and complimentary of the care provided by the staff. Sixty-four (55.2%) of the clients were fully satisfied with all aspects of the clinic experience, while 16 of the clients (13.8%) expressed dissatisfaction with the appearance and maintenance of the setting.

What began as a project undertaken with considerable anxiety about our self-image turned out to be an instrument of valuable criticism and a vehicle for an unexpected boost in morale.

NR55 Monday, May 19, 9:00 a.m.-10:30 a.m.

Sexual and Racial Discrimination in the Army

Mary B. Cruser, M.D., Department of Psychiatry, Eisenhower Army MC, Fort Gordon GA 30905; Elizabeth E. Correnti, M.D., Laura Davidson, Ph.D.

Summary:

Objective: This study of career soldiers stationed at two major Army bases assessed how service members who have served at least 10 years on active duty perceive sexual and racial discrimination in the military.

Method: Questionnaires were distributed to 400 subjects who agreed to participate in a comprehensive survey of attitudes and military experiences. Equal numbers of men and women were enrolled and 248 returned the questionnaires. Subjects discussed personal experiences of sexual and racial discrimination and responded to questions regarding their perceptions of how much of a problem these are for the military. A subgroup of participants were interviewed by the researchers.

Results: Racial discrimination was reported by 20% of the sample; 35% of non-Caucasians reported it and 10% of white subjects felt they had experienced reverse discrimination. Sexual discrimi-

nation was reported by 33% of the women; 49% said they had been sexually harassed. Men, regardless of race, were evenly divided as to whether sexual or racial discrimination was the larger problem for the military. Nonwhite women reported that racial discrimination was a greater problem than sexual discrimination, but white women reported the opposite.

Conclusion: Career soldiers feel racial and sexual discrimination to be significant problems for the Army; race and gender influence their perceptions.

NR56 Monday, May 19, 9:00 a.m.-10:30 a.m.

Outcomes of Housing in Persons with Mental Illness and Substance Use Disorders

Niamh M. Holohan, M.D., Department of Psychiatry, University of Maryland, 701 West Pratt, Baltimore MD 21201; Lisa B. Dixon, M.D., Nancy Krauss, L.C.S.W.

Summary:

Objectives: This study assessed the impact of dual diagnosis (DD) of substance use on housing outcomes in persons with severe mental illness (SMI) receiving Assertive Community Treatment (ACT).

Methods: Clinical staff recorded each patient's nightly housing location and reasons for moves in 70 ACT patients. DD and non-DD patients were compared on total and quarterly summaries of number and types of housing moves and locations.

Results: DD patients had significantly more total moves ($p < 0.05$) and more moves in the first ($p < 0.05$) and second ($p < 0.02$), but not third and fourth quarters. Moves for DD patients were less likely to be in the direction of permanent housing ($p < 0.05$). DD patients spent more days on the street ($p < 0.05$) but did not differ from non-DD patients in other types of housing used. Moves for DD patients were more likely to originate or end in independent community settings.

Conclusions: A baseline substance abuse disorder had an adverse impact on housing stability, but this effect seemed to diminish with time and ongoing treatment with ACT.

NR57 Monday, May 19, 9:00 a.m.-10:30 a.m.

Patients' Characteristics in a Long-Term Hospital

Demetra Pappas, B.S., Taunton State, Harvard Medical School, 60 Hodges Avenue, Taunton MA 02780; Rogelio D. Bayog, M.D., Alan I. Green, M.D., David N. Osser, M.D., Howard H. Chang, M.D., Ileana Berman, M.D.

Summary:

In the process of developing a research and evaluation unit as part of a state hospital, we looked at the characteristics of patients hospitalized at our chronic care institution over a specific period of time. We collected data from a total of 142 charts. Of these 142 patients, 97 were male and 45 were female. We found gender differences in patients' diagnosis with male patients being diagnosed with schizophrenia and schizoaffective disorder more frequently than women. Women, however, were diagnosed with an affective disorder more often than men. Selecting only patients with schizophrenia or schizoaffective disorder, we found no statistically significant gender differences in the age of illness onset or severity of symptoms at admission; however, age seemed to predict higher BPRS scores. Since schizophrenia equally affects men and women, our findings suggest that compared to females, males with schizophrenia are more likely to require long-term institutionalization. Previous findings that have shown that women with schizophrenia may indeed have a better outcome than men, may explain our results. In addition, we found that age was a predictor of symptom severity in our chronically hospitalized patients. Since there were no significant age differences in the level of hostility or depression and thus no differences in the potential risk to hurt self or others, we wonder whether clinicians will be more comfortable treating patients in the community as they become familiar with the patient's symptoms with time.

NR58 Monday, May 19, 9:00 a.m.-10:30 a.m.

Primary Care Training: For Psychiatrists?

Cletus S. Carvalho, M.D., Department of Psychiatry, St. Vincent's Hospital, 101 West 15th Street, #3-OS, New York NY 10011-6745; Carlos Blanco-Jerez, M.D.

Summary:

Objective: This project presents data obtained from a survey sent out to practicing psychiatrists, in an effort to assess how extensive primary care training for psychiatrists should be.

Method: A questionnaire was mailed to 73 psychiatrists of a major teaching hospital in New York. The questionnaire asked psychiatrists what they felt a "well-trained psychiatrist" should do for adult patients with 25 different sets of symptoms or laboratory findings, before these patients were referred to another physician. Four options were given: 1) perform physical exam, 2) order diagnostic tests, 3) treat the condition, and 4) none of these. More than one response could be checked off.

Results: A 41.09% response rate was obtained; 6.6% responders felt that the "well-trained psychiatrist" should perform a physical exam, 9.5% indicated diagnostic tests should be ordered, 2.3% indicated treatment should be administered, and 84.3% indicated that none of the above should be done before a referral is made. This survey was a pilot to a planned mailing of a similar questionnaire to psychiatrists nationwide.

Conclusion: Although there is growing interest in improving primary care training in our specialty, a disparity exists between perceived and proposed needs to address this important issue.

NR59 Monday, May 19, 9:00 a.m.-10:30 a.m.

Non-Specificity of Somatic Depressive Symptoms in Patients Receiving Intensive Cancer Treatment

Jesus Prieto, Department of Psychiatry, Hospital D'Olot, Mulleres S/N, Olot 17800, Spain; Jordi Blanch, Jorge Atala, Esteve Cirera, Cristobal Gasto

Summary:

Objective: This study analyzes the appropriateness of DSM-IV criteria in diagnosing major depression in a group of cancer patients hospitalized for bone marrow transplantation.

Method: A consecutive series of 170 patients were evaluated on admission and weekly until discharge. We used structured clinical interviews and DSM-IV criteria for diagnosis. We compared at each assessment the frequency of symptoms reported by depressed and nondepressed patients.

Results: At initial evaluation and prior to cancer treatment, every symptom was significantly more frequent in the depressed group except for psychomotor agitation. In the next three assessments, depressed mood, loss of interest or pleasure, feeling worthless or guilty, and suicidal ideation were the only symptoms found to be significantly more common in depressed patients at each interview. When excluding somatic symptoms attributed to cancer-related factors, five patients (3%) were assigned a diagnosis of major depressive episode. This prevalence rate increased to 20% (34 patients) when these excluded symptoms were considered as psychiatrically significant.

Conclusion: After initiating cancer treatment, somatic depressive symptoms are found to be nonspecific in the diagnosis of major depressive episode. DSM-IV criteria can lead to underdiagnosis of major depressive episode in this clinical setting.

NR60 Monday, May 19, 9:00 a.m.-10:30 a.m.

Noncompliance in Heart Transplant Patients

Adriana R. Vasquez, M.D., Department of Psychiatry, Mayo Clinic, Rochester MN 55905; Sheila Towsey, M.D., William N. Friedrich, Ph.D., Christopher McGregor, M.D.

Summary:

Objective: To determine the degree of noncompliance in heart transplant patients.

Method: Retrospective review of patients who had been transplanted between 1991 and 1996 who could participate in a multidisciplinary, pretransplantation evaluation and survived at least six months posttransplant, and were over the age of 18. These patients were rated pretransplant by the transplant coordinator most familiar with the patient who rated the patients on degree of knowledge about their illness, motivation for transplantation, family support, financial and insurance concerns, concerns about medication side effects, history of noncompliance, problematic relationships with authority figures, and optimism about transplant outcome. Posttransplant, the patients were rated with respect to compliance with medication, exercise, and diet, nicotine use, and attendance at outpatient appointments.

Results: Thirty-four patients were studied (ages 24 to 70)—five females, 29 males. Of the noncompliant, five were males and four were females. Twenty-four males and one female of our study population were compliant.

Conclusions: A small percentage of our patients were noncompliant. We will discuss factors related to noncompliance in our population of patients and in other studies. We will also make recommendations for future research.

NR61 Monday, May 19, 9:00 a.m.-10:30 a.m.

Seasonal Variation in Mood and Behavior in Chinese Medical Students

Ling Han, M.D., c/o Dr. Goldman, NIH/NIAAA lab of Neurogen., 12420 Parklawn Drive, Rockville MD 20851; Keqin Wang, M.D., Yiren Cheng, M.D., Zhaoyun Du, M.D., Norman E. Rosenthal, M.D.

Summary:

Objectives: The main goal of this first report on seasonality from China is to evaluate the prevalence of seasonal changes in mood and behavior among Chinese medical students.

Method: During early March 1996, 1,358 medical students were surveyed with a Chinese version of the Seasonal Pattern Assessment Questionnaire (SPAQ) and Beck Depression Inventory (BDI) in Jining, China. Fourteen days later, 124 subjects were retested with the same questionnaires.

Results: The mean global seasonality scores (GSS) of the sample is 8.3 (SD = 3.6); 81.7% of the subjects reported some problems with the changing seasons. Summer difficulties were more prevalent than winter difficulties by a ratio of 3:2, with estimated prevalences of summer-SAD and subsyndromal-SAD of 4.4% and 8% as compared with the corresponding winter figures of 2.4% and 5.7%. The test-retest correlation coefficients was 0.65 for GSS ($v = 124$, $p < 0.001$). A significant positive correlation of 0.176 ($v = 1345$, $p < 0.0001$) is observed between GSS and BDI scores.

Conclusions: These results suggest that seasonal problems are common in China, but the predominance of summer difficulties stands in contrast to most Western studies and is consistent with the only other published study performed in Asia.

NR62 Monday, May 19, 9:00 a.m.-10:30 a.m.

Mental Health Clinicians' Viewpoints of Psychological Wellness Differing by Race

Jeremy A. Herschler, M.D., Department of Psychiatry, University of Maryland, 302 N Chapel Gate Lane, Apt B, Baltimore MD 21229-2426; Lisa B. Dixon, M.D.

Summary:

Objective: Research is increasingly revealing the importance of considering culture and race in understanding the process and outcomes of mental health treatment. We compared viewpoints of white and nonwhite mental health clinicians regarding what constitutes psychological wellness.

Methods: Twenty-six mental health clinicians of differing backgrounds were surveyed regarding their beliefs about what behaviors and defense mechanisms are consistent with psychological wellness. Whites ($N = 18$) and nonwhites ($N = 8$) were compared.

Results: Nonwhite clinicians were less likely to rate the defense mechanisms of fantasy ($p < .01$), introjection, ($p < .05$), projection ($p < .02$), and undoing ($p < .01$) as signs of wellness when compared with white clinicians. Nonwhite clinicians were also less likely to agree that "satisfying one's needs" ($p < .05$), winning ($p = .05$), and "participation" ($p = .05$) are indicative of psychological wellness. The overall group correctly identified defense mechanisms considered in the literature to be most mature.

Conclusion: This preliminary study suggests that white and nonwhite mental health clinicians characterize psychological wellness differently. If replicated, these differences could have important implications for clinical treatment. More research is necessary.

NR63 Monday, May 19, 9:00 a.m.-10:30 a.m.

Depression in a Primary Care Setting: Are There Ethnic Differences?

Isabel T. Lagomasino, M.D., Department of Psychiatry, Massachusetts General Hosp, 15 Parkman/ACC 815, Boston MA 02114; Rachel D. McColl, B.A., Rosemarie Mulroy, B.A., Junko Kaji, B.A., Asha I. Parekh, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Objective: We examined differences in the prevalence and phenomenology of depression among primary care patients of different ethnic groups.

Population and Methods: A total of 1,022 patients aged 18 years or older presenting to a primary care clinic in an ethnically diverse, urban community were asked to complete the Beck Depression Inventory (BDI); 542 did so, of which 428 completed every question. Patients with scores ≥ 16 were asked to participate in a diagnostic interview using the Structured Clinical Interview for DSM-III-R-Patient Edition (SCID-P).

Results: Among completers, Hispanics had higher mean scores than whites on the BDI (13.2 ± 12.7 v. 8.8 ± 8.4; $p < .0002$) and more Hispanics had scores ≥ 16 (31.8% v. 17.4%; $p < .0008$). Hispanics scored significantly higher than other groups on BDI subscales of affect and performance, self-denigration, and physiological function, and were more often worried about physical problems. Based on BDI and SCID-I/P results, the estimated prevalence of major depressive disorder in the clinic population was 5.7–13.5% (3.1–7.9% for whites; 9.3–19.3% for Hispanics).

Conclusions: Depressive symptoms appear to be highly prevalent across different ethnic groups in primary care settings.

NR64 Monday, May 19, 9:00 a.m.-10:30 a.m.

Suicidal Ideation and Attempts in an Arctic Community

John M. Haggarty, M.D., Department of Psychiatry, University Western Ontario, 31 Winding Way Cresent, London Ontario N6V 3E8, Canada; Zack Z. Cernovsky, Ph.D., Harold Merskey, M.D., Patricio Kermeen, R.N.

Summary:

A random, household survey was conducted in an Inuit community to assess prevalence of suicidal ideation and attempts. Data were gathered using a four-item self-report questionnaire (in English or Inuktitut) dealing with thoughts of killing oneself in the past week, suicide attempts, plans to kill oneself, and wish to die within the last six months.

The sample consisted of 111 Inuit (50 men, 61 women). Ages ranged from 14 to 77 (mean 35.5, SD = 16.0). A total of 43.6% of those responding had thought of committing suicide in the previous week, while 52.9% reported a wish to die in the previous six months. Of 100 respondents to our question about recent attempts, 30% attempted suicide within the preceding six months; 16% (n = 16) have attempted suicide more than once. Men and women were not significantly different (chi-square, $p > .05$) on any of the four items. Younger persons more frequently reported a wish to die ($r = .30$, $p = .002$) and thoughts about killing themselves ($r = .37$, $p < .001$) than did their older counterparts. Compared with U.S. prevalence data for suicide attempts within a past year (only 0.6% of 720 respondents), the rates found in our study are alarming and among the highest self-reported rates in the psychiatric literature.

NR65 Monday, May 19, 9:00 a.m.-10:30 a.m.

Famotidine: A Supplemental Drug for the Treatment of Schizophrenia

Pinhas N. Dannon, M.D., Department of Psychiatry, Chaim Sheba Medical Center, Tel Hashomer 52621, Israel; Elie Lepkifker, M.D., Iulian Iancu, M.D., Reuven Ziv, M.D., Moshe Kotler, M.D., Joseph Zohar, M.D.

Summary:

Objective: To assess the effect of famotidine as a supplemental drug to high-potency neuroleptics in the treatment of chronic schizophrenia.

Methods: Eleven (10 male and one female) partial responder schizoprenic patients were included in this open-label study. Forty mg famotidine was added at bedtime dosage in the first week and 60 mg for the remaining three weeks. Response to treatment was assessed separately every week by two investigators (inter-rater reliability 0.94) using the SAPS, SANS, HAMD-17, and CGI. Statistical analysis was performed by student t-test and ANOVA with repeated measures.

Results: The patients showed an improvement in all scales during the second week, according to the student t-test ($p < 0.01$). After four weeks the mean scores were found to be significantly lower by the two-tailed Wilcoxon test ($p = 0.033$), as well as ANOVA with repeated measures ($p < 0.001$).

Conclusions: This preliminary study suggests that famotodine is indeed effective as an adjunctive drug to high-potency neuroleptics in the treatment of schizophrenia. However, larger, double-blind studies are needed to confirm these results.

NR66 Monday, May 19, 9:00 a.m.-10:30 a.m.

Cholesterol and Suicide Attempts in Panic Disorder and MDD

Pinhas N. Dannon, M.D., Department of Psychiatry, Chaim Sheba Medical Center, Tel Hashomer 52621, Israel; Iulian Iancu, M.D., Amir Poreh, Ph.D.

Summary:

Objectives: The study examined the cholesterol levels of patients with major depressive (MD) and panic (PD) disorders and their relationship to previous suicide attempts.

Methods: Total cholesterol levels among 53 PD outpatients with or without agoraphobia, and 50 depressed outpatients, matched for pertinent demographic variables, were compared. History of suicide attempts was obtained by interviewing the patients and confirmed via medical files. Cholesterol levels were obtained from a single laboratory. Data were analyzed using SPSS 6.1 for Windows.

Results: PD patients without agoraphobia ($n = 27$) had significantly lower cholesterol levels than the depressed patients ($n = 50$) ($t = 2.25$, $p < 0.002$). Additionally, the MDD patients attempted suicide more often than the PD sample ($t = 3.12$, $p < 0.05$). Finally, ANOVA indicated no significant correlation between suicide attempts and cholesterol levels among members of the two groups.

Conclusions: The present study is partially consistent with earlier reports regarding the possible role of cholesterol as an intervening variable in the understanding of mental illness. Additional studies with larger samples are necessary to further elucidate and validate our findings.

NR67 Monday, May 19, 9:00 a.m.-10:30 a.m.

Pindolol Augmentation for Treating Refractory OCD

Pinhas N. Dannon, M.D., Department of Psychiatry, Chaim Sheba Medical Center, Tel Hashomer 52621, Israel; Shmuel Hirschmann, M.D., Iulian Iancu, M.D., Yehuda Sasson, M.D., Leon J. Grunhaus, M.D., Joseph Zohar, M.D.

Summary:

Objective: To determine the efficacy of pindolol as an augmentation strategy to paroxetine in the treatment of refractory obsessive-compulsive disorder (OCD) patients.

Method: Eleven refractory OCD patients treated for 18.4 ± 2.2 weeks with 60 mg/d paroxetine in an open manner were assigned to a double-blind, placebo-controlled pindolol (2.5 mg x 3/d) augmentation. Patients were evaluated biweekly for a six-week period with the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), Hamilton Anxiety Scale (HM-Anx), and Montgomery Asberg Depression Scale (MADRS). Two-tailed t-test and Mann-Whitney U test were used to analyze the scores.

Results: Four parameters were examined: compulsions, obsessions, anxiety, and depression. Augmentation with pindolol demonstrated significant improvement on the compulsion scale (paired t-test $p < 0.035$, Mann-Whitney U test $p < 0.05$), and marginally significant on the obsession scale (paired t-test $p < 0.07$, Mann-Whitney U test $p < 0.08$). There were no significant differences on the anxiety and the depression scales.

Conclusions: Results of this preliminary study demonstrated statistical tendency to beneficial therapeutic effect in refractory OCD, although the mean decrease in Y-BOCS was less than 25%.

NR68 Monday, May 19, 9:00 a.m.-10:30 a.m.

Physical Illness Prompting Psychiatric Admission

Je Chun Yu, M.D., Department of Psychiatry, Asan Medical Center, Song-Pa/PO Box 145, Seoul, South Korea; O. Soo Han, M.D., In-Ho Park, M.D., Chul Lee, M.D.

Summary:

The purpose of this study was to investigate the frequency and characteristics of causal physical illnesses that prompted psychiatric admission and utilization of neuroimaging studies in diagnosing the undetected physical illnesses of patients who were admitted to the psychiatric ward in a general hospital.

A total of 2,374 patients were admitted to the psychiatric ward of Asan Medical Center between January 1990 and March 1996. By searching computerized hospital data bases and retrospective chart review, it was determined in 33 patients (1.4%) hidden and undiagnosed physical illness had been the sole and exclusive cause of initial psychiatric symptoms, which had prompted psychiatric admission.

Among these causal physical illnesses, brain tumors and central nervous system infections accounted for 18.2% (N = 6). Other brain diseases (i.e. multiple sclerosis, TLE, cerebral venous thrombosis, vestibular neuronitis) and tumors other than brain, and endocrine diseases accounted for 12.1% (N = 4). Neurocysticercoses accounted for 6.1% (N = 2). The initial psychiatric diagnosis was major depressive disorders (N = 10, 30.3%), schizophrenia and other psychotic disorders (N = 7, 21.2%), conversion disorders (N = 6, 18.2%), somatoform disorders (N = 4, 12.1%), and anxiety disorders (N = 3, 9.1%). Two-thirds of the patients (N = 22, 66.7%) were diagnosed for the causal physical illnesses within the first week of psychiatric admission; however, four out of 33 subjects (12.1%) were diagnosed after discharge. The method of diagnosing causal physical illnesses was 30.3% (N = 10) by brain MRI and 6.1% (N = 2) by brain CT.

NR69 Monday, May 19, 9:00 a.m.-10:30 a.m.

Diagnosing Pancreatic Cancer in Depression: Cost-Benefit Analysis

Carlos Blanco-Jerez, M.D., Department of Psychiatry, Columbia University, 722 West 168th Street, Box 81, New York NY 10032; Cletus S. Carvalho, M.D., Roumen Nikolov, M.D.

Summary:

Objective: To determine whether a work-up in pancreatic cancer is warranted in patients presenting with depression.

Method: A cost-benefit analysis of this work-up was performed. We estimated the probability of pancreatic cancer in patients with depression. The cost of diagnosis and treatment of pancreatic cancer was then calculated. This was compared with the benefit of the treatment of pancreatic cancer.

Result: In patients presenting with depression the cost of diagnosing and treating pancreatic cancer is 56 times greater than the benefit of treating it.

Conclusion: For patients presenting with depression and no other associated symptoms, a work-up for pancreatic cancer is not warranted.

NR70 Monday, May 19, 9:00 a.m.-10:30 a.m.

Assessment of Mood Fluctuations in Individual Cases

Jeffrey M. Pyne, M.D., Department of Psychiatry, UCSD, 9500 Gilman Drive MC 0603, La Jolla CA 92093; Martin Paulus, M.D., Matthew S. Foley, B.A., Kelly N. Yoo

Summary:

The statistical analysis of mood fluctuations in patients with unipolar depression is in its infancy. Recently, a simple self-administered rating scale for assessing the severity of manic and depressive symptoms, the Internal State Scale (ISS), was introduced by Bauer et al. The ISS is characterized by reasonable test/retest reliability, internal consistency, and content or predictive validity. This scale was given to a number of psychiatric inpatients at the Mental Health Clinical Research Center at the San Diego Veterans Affairs Medical Center to determine whether patients in a current major depressive episode exhibit significant daily mood fluctuations. Two patients were selected based on their DSM-IV diagnosis obtained by consensus using a SCID-IV interview. Daily ratings for these patients were available for four and six weeks, respectively. The degree of fluctuation was assessed for the Activation, Depression, Well-being, and Perceived Conflict subscales of the ISS using the coefficient of variation method. This technique quantifies the deviation of the observed score relative to the overall mean subscale score. The results indicate that patients with identical DSM-IV mood disorder diagnosis exhibit significant differences in daily mood fluctuations. Thus, daily assessment of mood fluctuation may provide important information for treatment planning.

NR71 Monday, May 19, 9:00 a.m.-10:30 a.m.

Lifetime Psychiatric Comorbidity in a Large Outpatient Clinic

Shakir R. Meghani, M.D., Department of Psychiatry, Kansas University Medical Ctr, 3901 Rainbow Boulevard, Kansas City KS 66160; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.S., Ekkehard Othmer, M.D.,Ph.D., William F. Gabrielli, Jr., M.D., Marsha R. Read, Ph.D.

Summary:

Objective: Studies of psychiatric comorbidity are becoming increasingly important as the widespread prevalence of co-occurring psychiatric syndromes is recognized both in community and clinic samples. Psychiatric comorbidity has been associated with increased suffering, poorer outcomes, and greater utilization of treatment resources. Comprehensive broad-spectrum studies of psychiatric comorbidity, using contemporary criterion-referenced instruments, are typically found associated with community epidemiological studies or specific clinic populations, such as alcoholics. Less systematic information is available about the range of psychiatric comorbidity that exists in general psychiatric outpatient clinics.

Methods: This study utilized the structured Psychiatric Diagnostic Interview to examine the psychiatric comorbidity and other characteristics of 1,458 new patients entering the psychiatric outpatient clinic of a large midwestern teaching hospital over a five-year period.

Results: As true in other studies, the lifetime prevalence of co-occurring syndromes was high. The mean number of psychiatric syndromes (out of 15) was 2.01; 55% of the patients satisfied inclusive diagnostic criteria for two or more syndromes. The rank order of the prevalence of the psychiatric syndromes in this study closely resembled the rank order found in community studies of men and women, except that the absolute prevalence of the disorders in this study was higher for both sexes. Virtually all gender, age, and age-of-onset differences commonly reported by community samples were replicated in this clinic sample. For multiple-syndrome patients, age of onset of any psychiatric illness varied according to the syndrome combination. The relationships between the co-occurring disorders was clearly nonrandom. Certain disorders clustered together. Moreover, the clustering of positive syndromes differed for men and women. Especially striking was the asymmetrical relationships found between pairs of disorders that help explain some epidemiological inconsistencies contained in the older clinical literature.

Conclusions: Our study suggests that the phenomenon of psychiatric comorbidity will, of necessity, play a major role in the continuing development of nosological psychiatric systems and mental health treatment guidelines in the future.

NR72 Monday, May 19, 9:00 a.m.-10:30 a.m.

Tryptophan Depletion During Continuous CSF Sampling via Indwelling Lumbar Catheter in Healthy Human Subjects

Linda L. Carpenter, M.D., Department of Psychiatry, CMHC-Research Unit, 24 Park Street, 3rd Floor, New Haven CT 06519; George Anderson, Ph.D., Christopher J. McDougle, M.D., Paul D. Kirwin, M.D., Lawrence H. Price, M.D., George R. Heninger, M.D.

Summary:

Objective: The tryptophan depletion paradigm has been employed to investigate mood and behavioral effects of acutely lowering plasma tryptophan (and presumably brain serotonin) through administration of a special diet and/or amino acid drink. Our goal was to test the assumption that a corresponding fall in central levels of tryptophan and serotonin (measured by its major metabolite, 5-HIAA) occurs during the standard execution of this method in healthy adult subjects.

Method: Five healthy subjects (three males, two females) completed the protocol, which included a one-day low-tryptophan diet and a tryptophan-free amino acid drink. Lumbar puncture was performed with an indwelling lumbar catheter connected to a pump and fraction collector. CSF was aspirated continuously for a 14-hour period (before, during, and after the drink), with fractions removed every 15 minutes. Plasma samples were simultaneously obtained.

Results: CSF tryptophan levels were highly correlated with plasma tryptophan levels, falling a mean of 88% and 92% from baseline, respectively. CSF nadirs were reached several hours after plasma nadirs. CSF 5-HIAA dropped modestly (24% to 41%, mean 31% change from baseline), with lowest levels observed eight to 12 hours after the amino acid drink.

Conclusion: CSF indices of serotonin production and metabolism parallel those changes measured in blood, but occur later. Efforts to measure CSF serotonin (5-HT) are underway. These data provide further validation for the tryptophan depletion paradigm.

NR73 Monday, May 19, 9:00 a.m.-10:30 a.m.

Effects of White Matter Hyperintensities on Neuropsychiatric Symptoms in Patients with Alzheimer's Disease

Sabrina R. Simpson, B.A., Department of Neurology, Wesley Woods Health Center, 1841 Clifton Road, NE, Atlanta GA 30329; Alexander P. Auchus, M.D., William M. McDonald, M.D., John L. Woodard, Ph.D., Ralph B. Reed, B.S.E.

Summary:

Objective: To study the effects of brain MRI hyperintensities on clinical features of Alzheimer's disease (AD).

Methods: Brain MRI scans from 51 subjects with probable AD (NINCDS-ADRDA criteria) were reviewed. Severity of periventricular hyperintensities (PVH) and deep white matter hyperintensities (DWMH) were determined using a 0-3 point rating scale (Fazekas et al., 1987). We also determined the presence or absence of psychotic symptoms (hallucinations, delusions), affective symptoms (depressed, anxious mood), and severity of dementia (MMSE, DRS scores) from chart review. The relationship between presence or absence of psychotic symptoms and severity of PVH was investigated using the Mann-Whitney U test. The same analysis was used to investigate the relationship between affective symptoms and severity of DWMH. Multiple regression analysis was used to relate both PVH and DWMH to dementia severity.

Results: There were no significant relationships (all P values > .05) between the severity of PVH and the presence of psychotic symptoms, or between PVH and DWMH and dementia severity. However, the subjects with affective symptoms had more severe DWMH than subjects without these symptoms ($p = .051$).

Conclusions: Structural pathology involving deep cerebral white matter may be a contributing factor in the pathogenesis of affective symptoms in AD.

NR74 Monday, May 19, 9:00 a.m.-10:30 a.m.

Treating Comorbid Tourette's and OCD with Newer Psychotropics

Parveen Kumar, M.D., Department of Psychiatry, School of Medicine, 2500 N. State Street, Jackson MS 39216; Jeffrey A. Ali, M.D.

Summary:

Recently it has been postulated that Tourette's disorder and obsessive-compulsive disorder may share a common genetic diathesis. Indeed, studies indicate that the comorbidity of the two disorders ranges between 28% and 62%. Haloperidol and pimozide, both dopamine antagonists, are commonly used in treating Tourette's, while the serotonin reuptake inhibitors fluvoxamine and fluoxetine are FDA approved for treating OCD. No established treatment approach for comorbid Tourette's and OCD exists.

We report the successful use of risperidone in the treatment of three patients with comorbid Tourette's and OCD. Use of this medication produced mixed results in patients with only Tourette's disorder, and failed to help patients with a diagnosis of OCD alone. Our patients were evaluated with the BPRS, YBOCS, BDI, and Hopkins Tic Scales before, during, and after treatment. In the responders, significant changes in YBOCS and Hopkins Tic Scale scores as well as in clinical presentation were noted. A possible explanation for risperidone's efficacy may lie in the fact that it is both a dopamine and a serotonin antagonist. Further studies are needed to clarify this proposed mechanism of action.

NR75 Monday, May 19, 9:00 a.m.-10:30 a.m.

Post-Stroke Depression and Location of Lesion: A Systematic Review

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Summary:

Objective: Post-stroke depression may be a useful model to understand the neurobiology of depression in patients without stroke. We conducted a systematic review of the role of location of brain lesion on the development of post-stroke depression.

Methods: All papers identified on MEDLINE that reported on clinico-pathological correlations of post-stroke depression were stratified until the heterogeneity among them was reduced to insignificant levels. The relative risk ratios from different studies were combined to yield pooled relative risk ratios, which were compared between selections and with the null value. Publication bias was studied using "funnel plot" analysis.

Results: In contrast to many of the previous reports, interhemispheric differences in the location of lesion (i.e., right vs. left) did not increase the risk of depression following stroke. Anterior/posterior and cortical/subcortical location did appear to increase the risk of depression.

Discussion: This systematic, quantitative review identified findings that are different from those previously reported. Validation of these findings by further studies will be required before extending them to the understanding of depression among patients without stroke.

NR76 Monday, May 19, 9:00 a.m.-10:30 a.m.

The Immune Function and Schizophrenia

Juyeon Cho, M.D., Department of Psychiatry, Chung-Ang University Hospital, 82-1 Phil-Dong Chung-Gu, Seoul, Korea; Doobyung Park, M.D., Kilhong Lee, M.D.

Summary:

Objective: The objectives of this study were to investigate 1) the differences of the immune function between schizophrenia and healthy normal controls, 2) the correlation between the severity of symptoms and immune functions in schizophrenia, and 3) the differences of the immune function between subgroups of schizophrenia (positive, negative) and controls.

Method: The subjects were 30 patients who met the DSM-IV criteria for schizophrenia. Thirty-two healthy adults were recruited for control. The following immunological functions were observed in the patients on admission and controls at the same day: WBC, lymphocyte subpopulations (T-, B-, CD4+-, CD8+ cell, CD4+/CD8+ cell ratio), NK cell count and percentage, serum IgG, A, M levels, total hemolytic complement activity. The schizophrenia was classified into positive and negative symptom groups by the Positive and Negative Syndrome Scale on sampling day. The severity of symptoms was assessed by using the Brief Psychiatric Rating Scale on each day of immunological examinations.

Results: No significant difference was observed by measuring several immunological functions from schizophrenic patients and controls. The severity of symptoms was significantly positively correlated with Ig A, the number and the percentage of total lymphocyte, whereas it was negatively correlated with the number of CD8+ cell. In the positive symptom group, the percentage of T cells and the number of CD8+ cells were significantly reduced and Ig M was increased compared with controls. In the negative symptom group, the number and the percentage of NK cells were decreased compared with controls.

Conclusions: These results suggest that alterations in immune system in schizophrenia do not appear to be a specific biological correlate of this disorder, but may be associated with symptom severity and may occur in subgroups of schizophrenia patients.

NR77 Monday, May 19, 9:00 a.m.-10:30 a.m.

Mental Health Service Variations in an HMO

Jonathan C. Lockhart, M.D., Department of Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Jack D. Burke, Jr., M.D., Raghavan Srinivasan, Ph.D., Nadine Zimmerman, M.S.

Summary:

Objective: This initial report from a new regional mental health database examines the use of mental health and nonmental health services in a 120,000-member HMO in terms of geographic distribution and specialty of provider.

Methods and Materials: The researchers collected detailed information about health services used by anyone assigned a mental health diagnosis during calendar year 1995. A geographical information system was also constructed using the residential zip code of each patient.

Results: Out of 9,668 patients, 50% were never seen by a mental health specialist. When subdivided into rural and urban counties, 50% and 59% of patients in two rural counties saw no mental health specialist. In the urban county where the HMO is based, 45% of patients saw no mental health provider. Overall, patients who had seen a mental health specialist used nonmental health services 1.6 times as much as those who had not seen a mental health specialist.

Conclusions: Approximately half of the patients with a mental health diagnosis in this study were not seen by a mental health specialist during 1995. This result is true in both the rural and urban setting. These patients also used significantly less nonmental health services. Similar analyses have also been applied to a public mental health system.

NR78 Monday, May 19, 9:00 a.m.-10:30 a.m.

Construct Validity of SF-36 Psychiatric Subscales

Ghazala N. Ahmed, M.D., Department of Psychiatry, Scott & White, 2401 South 31st Street, Temple TX 76508; David Rudd, Ph.D., Kimberly C. Burke, M.S., Cheryl Preece, M.S.

Summary:

Objective: The purpose of this study was to explore construct validity of the Rand Health Survey 1.0 among a sample of psychiatric inpatients. This was accomplished by examining correlations between selected scales on the Rand Health Survey and the Minnesota Multiphasic Personality Inventory (MMPI).

Methods: During 1996, all patients admitted to the psychiatric inpatient unit at Scott and White Hospital in Temple, Texas, completed the Rand Health Survey upon admission. A subset of those patients (n = 39) also completed the MMPI at admission. Scores on the F-scale, depression, psychasthenia (anxiety), schizophrenia, and mania scales were correlated with the scales on the Rand Health Survey.

Results: Although not influenced by general distress and dysphoria, the psychiatric subscales of the Rand Health Survey were significantly related to a range of symptom constellations including somatic complaints, depression, and anxiety. All subscales were found to be significantly correlated with the psychasthenia (anxiety) scales.

Conclusions: Although there is some evidence to support construct validity of the Rand Health Survey among this sample, the incremental validity is poor. As a result, we recommend the use of the overall measure of general mental health.

NR79 Monday, May 19, 9:00 a.m.-10:30 a.m.

Suicide Assessment in the Elderly

Lisa Fazzolari, D.O., Department of Psychiatry, Hershey Medical Center, 500 University Drive, Hershey PA 17033-0850

Summary:

Objective: To determine risk factors associated with suicide attempts in geriatric patients with diagnosis of depression.

Method: A retrospective chart review of a three-month period for geriatric inpatients with diagnosis of depression (N = 38). Patients were separated into three groups: (1) suicide attempts (N = 3); (2) suicidal ideation (N = 11); and (3) no suicidal ideation (N = 24).

Results: All three patients who made a suicide attempt were male, had a history of depression, and experienced anhedonia. Two of the three had a history of past suicide attempt, alcohol abuse, and serious medical illnesses. The average hospital length of stay was 17 days. In comparing those with suicidal ideation to those without suicidal ideation, there were no significant differences in risk factors for suicide attempt. Average hospital length of stay was 12.3 and 13 days, respectively.

Conclusions: In this study, suicide attempters were more likely to be male and have a history of suicide attempt and alcohol abuse. In patients with suicidal ideation and no suicidal ideation, there were no differences in risk factors for suicide attempt. The average hospital length of stay was longer for those who attempted suicide than for those with suicidal ideation and those without suicidal ideation.

NR80 Monday, May 19, 9:00 a.m.-10:30 a.m.

A Self-Injury Motivation Scale: The Characteristics and Motivation of Self-Injurious Behavior

Elizabeth A. Osuch, M.D., Residency Training, Sheppard-Pratt, 6501 N Charles Street/Box 6815, Baltimore MD 21285; Frank W. Putnam, Jr., M.D.

Summary:

Objective: This study sought to develop a self-report scale (SIMS) to assess motivation for nonsuicidal, self-injurious behavior (SIB) in psychiatric patients, and to explore the relationships among motivation for SIB, characteristics of SIB, and psychopathology.

Method: A semistructured interview for presence and characteristics of SIB, and the SIMS, Dissociative Experiences Scale, Beck Depression Inventory, Davidson Trauma Scale, and Millon Clinical Multiaxial Inventory-II were given to 106 consecutively admitted inpatients. Factor analysis was performed on the SIMS.

Results: The SIMS had high Cronbach's alpha ($R = 0.96$, $N = 99$), and retest reliability ($R = 0.70$, $p < 0.001$, $N = 32$). SIMS score correlated with dissociation ($R = 0.70$, $p < 0.001$), and PTSD. High SIMS score suggested the presence of avoidant, passive-aggressive, and self-defeating personality styles, schizotypal and borderline personality pathology, and thought disorder and major depression. Six factors of the SIMS differentiated motivations for SIB. Some of these six groups differed in characteristics of SIB and psychopathology.

Conclusions: The SIMS is a self-report scale that takes seven to 15 minutes to complete, and appears to be reliable and valid. Patients with different SIMS profiles can have different characteristics of SIB and/or different psychopathology. Further studies may link SIMS total and subscale scores to responses to various treatment interventions and/or to biological factors.

NR81 Monday, May 19, 9:00 a.m.-10:30 a.m.

Mental Defense Mechanisms Predicting PTSD

Philippe J.R. Birmes, M.D., Department of Psychiatry, Chu Purpan, Place Du Docteur Baylac, Toulouse 31059, France; Pierre A. Delpla, M.D., Barbara A. Warner, M.D., Philippe Cadilhac, M.D., Laurent Schmitt, Ph.D.

Summary:

Objectives The aim of the study was to evaluate which mental defense mechanisms might predict the development of PTSD.

Methods. Victims of traumatic events were recruited from a general university hospital. Twenty-five participants were examined with a semistructured clinical interview, according DSM-IV PTSD criteria. All of them completed the Impact of Event Scale by Horowitz. All the subjects completed the Defense Style Questionnaire 40 (DSQ) in order to appreciate the different mechanisms, which were ranked in three levels: mature, neurotic, and immature. Finaly, we compared the defense styles between PTSD subjects and non-PTSD.

Results. Ten subjects were diagnosed as having PTSD and 15 were not. Among PTSD subjects only reaction formation, a neurotic defense, was employed significantly more often than in those without PTSD. Reaction formation average scores were 5.9 +/- 1.5 (PTSD) and 4.0 $\pm$ 1.4 (non-PTSD), $p \leq 0.01$.

Conclusions. These findings suggest that mental defense mechanisms may be indicative of a risk for the development of post-traumatic symptoms after event exposure. Using DSQ mature and immature defenses did not differ, although reaction formation played a role, particularly in regard to PTSD traumatic memories and perseverative thought.

NR82 Monday, May 19, 9:00 a.m.-10:30 a.m.

Dysfunctional Attitudes and Anger Attacks in Depression

Maya Spillmann, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, ACC 815, Boston MA 02114; Andrea R. Kolsky, B.A., Jane K. Burger, B.A., Joel A. Pava, Ph.D., Maurizio Fava, M.D.

Summary:

Anger attacks affect more than one third of depressed patients and they have been thought to be related to increased hopelessness and negative, dysfunctional attitudes.

Objective: We evaluated the relationship between the presence of anger attacks in depression and the degree of dysfunctional attitudes and negative cognitions.

Method: We studied 178 (53% women; mean age: 39.0 $\pm$ 10.4) outpatients meeting criteria for major depression. Patients were diagnosed with the Structured Clinical Interview for DSM-III-R-Patient Edition (SCID-P) and were administered the Anger Attacks Questionnaire (AAQ), the Dysfunctional Attitudes Scale (DAS), the Cognitions Questionnaire (CQ), and Beck's Hopelessness Scale (BHS).

Results: Anger attacks were reported by 40% of the 178 outpatients. The presence of anger attacks was associated with greater severity of depression ($p < .040$). In addition, depressed patients with anger attacks had significantly higher scores on the DAS ($p < .001$), and nonsignificantly higher scores on both the CQ ($p < .057$) and the BHS ($p < .060$), after adjusting for severity of depression.

Conclusion: The presence of anger attacks in depression is associated with increased levels of dysfunctional attitudes. Further studies should explore the nature of this relationship, in particular with regard to possible psychotherapeutic interventions.

NR83 Monday, May 19, 9:00 a.m.-10:30 a.m.

The Psychiatric Sequelae of Civilian Trauma: A Meta-Analysis

E. Sherwood Brown, M.D., Department of Psychiatry, UT Southwestern, 5323 Harry Hines Blvd/Box 9070, Dallas TX 75235; Mark Fulton, M.D., Frederick Petty, M.D., Aidela Wilkeson, M.D.

Summary:

Objective: The harmful physical and psychiatric effects of severe stress have long been recognized. Much of the literature on the psychiatric consequences of stress has focused on wartime combat trauma. However, by some estimates, 50% of the population experiences at least one traumatic event, and over 7% suffer from post-traumatic stress disorder (PTSD). This investigation reviews the literature on the psychiatric sequelae of civilian trauma and presents the results of a meta-analysis.

Method: A search of the MEDLINE data base from 1980 to the present for controlled studies on psychiatric disorders following civilian trauma was conducted. The data from the five studies meeting inclusion criteria were examined by meta-analysis.

Results: The meta-analysis revealed that generalized anxiety disorder (GAD), dysthymic disorder, PTSD, substance abuse, phobia, and major depressive disorder were significantly elevated compared with the pooled control group. In contrast, the rate of panic disorder was not significantly increased.

Conclusions: These data support that the psychiatric effects of civilian trauma include both anxiety and depressive disorders. The surprising increase in GAD is especially interesting and suggests further investigation on the role of stressors in anxiety disorders is needed.

NR84 Monday, May 19, 9:00 a.m.-10:30 a.m.

Interruption or Premature Termination of ECT

Kathryn M. Connor, M.D., Department of Psychiatry, Duke University, Box 3309/DUMC, Durham NC 27710; Andrew D. Krystal, M.D., Richard D. Weiner, M.D., Virginia H. Lindahl, B.A.

Summary:

Objectives: Interruption and premature termination of a course of electroconvulsive therapy (ECT) are important as they increase patient care expenditures and delay treatment response. One reason for such events is the development of cognitive dysfunction. Recognizing that these phenomena have not been investigated for present-day ECT, we studied factors associated with their occurrence.

Methods: A retrospective chart review of patients treated between 1991 and 1993 on a university-based hospital ECT service was performed including all inpatients at least 18 years old. In cases where the treatment course was interrupted or prematurely terminated, the medical chart was reviewed to determine the cause.

Results: Of 144 subjects identified, 40 (28%) experienced interrupted treatment and 22 (15%) premature termination of ECT for any reason. For 24 (17%) subjects, the cause was cognitive side effects (21 [15%] interruptions; 3 [2%] terminations). Significant predictors of these events ($p < 0.05$) were older age, generalized slowing on pre-ECT EEG, Parkinson's disease, and dementia.

Conclusions: Interruptions in the ECT course due to cognitive dysfunction occur in approximately one in six patients, particularly in the elderly and those with pre-existing cerebral disease. Practitioners should be aware of these relationships, which may affect the costs and duration of an ECT course.

NR85 Monday, May 19, 9:00 a.m.-10:30 a.m.

ECT Stimulus Intensity: How Much Is Enough?

Margaret D. Dean, M.D., Department of Psychiatry, Duke University, Box 3309/DUMC, Durham NC 27710; Andrew D. Krystal, M.D., Richard D. Weiner, M.D., Kathryn M. Connor, M.D., Virginia H. Lindahl, B.A., W. Ryan Massie

Summary:

Objectives: Uncertainty exists as to what should be the maximum amount of electrical charge necessary to produce an adequate ECT response. Little data exist to determine a reasonable charge maximum.

Methods: We retrospectively reviewed treatment records on 131 patients who received a clinical index ECT course at Duke University between 1991 and 1993. We determined how frequently patients required the maximum stimulus charge presently available in U.S. ECT devices (576 mC) and studied possible predictive factors.

Results: Twenty-three patients (18%) required a maximum stimulus at least once during their index ECT course. Of these, 8 (6% of total) had either a short EEG seizure (<25 seconds, 5 patients) or missed seizure (3 patients) at the maximum level. Only 38% of those with short or missed seizures were therapeutic responders vs. 64% for all other subjects. Older age was the strongest predictor of requiring the maximum *stimulus* level ($F = 5.6$, $p < 0.02$).

Conclusions: The maximum stimulus output is necessary in approximately 1/6 patients receiving moderately suprathreshold ECT. In 1/3 of these cases an even greater stimulus intensity would have been desirable had it been available. Increases in maximum stimulus output for ECT devices should be considered as a means to ensure adequate treatment response.

NR86 Monday, May 19, 9:00 a.m.-10:30 a.m.

Cost-Benefit of Accelerating the Effect of an Antidepressant

Maria B. Tome, M.D., Department of Psychiatry, Lewisham Hospital, Lewisham High Street, London SE136LH, England; Michael T. Isaac, M.D.

Summary:

Objective: To measure the cost and benefit of the rapid onset of antidepressant action of the SSRI antidepressant paroxetine by augmentation with 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. The economic analysis incorporates all direct costs involved. We applied decision analysis, cost effectiveness and cost benefit techniques, together with a sensitivity analysis.

Results: The direct cost of six weeks' treatment with the combination of pindolol and paroxetine was £174 ($278.40), compared with £234 ($374.40) for the antidepressant on its own. The index of improvement ranged from 21.39, ignoring the acceleration effect, to 85.37 or 125.26 incorporating the acceleration effect of the combination.

Conclusions: The direct costs of treatment are higher than those of previous pharmacoeconomic studies, but the rate of onset of antidepressant action must be taken into account. We present a generalizable and heuristically useful model by which this may be carried out.

NR87 Monday, May 19, 9:00 a.m.-10:30 a.m.

Psychiatrists' Perceptions of Religion and Its Association with Life Satisfaction

Sylvia Gheorghiu, M.D., Hazamir St. 24/4, P.O. Box 84095, Mevaseret, Jerusalem M 90805, Israel; Michael F. Godschalk, M.D., Thomas Mulligan, M.D.

Summary:

Objective: Considering the unique influence psychiatrists have on their patients, and that religion is important to most Americans (94% claim to be religious), a study about psychiatrists' perceptions of religion was warranted.

Methods: We randomly selected 100 psychiatrists from a list of all practicing Virginia psychiatrists. Subjects completed a survey containing questions derived from the Intrinsic/Extrinsic-religiosity I/E-R scale (I/E-R), the Life Satisfaction Index (LSI), and questions referring to the relationship between religion and medicine. We used descriptive statistics and Spearman's correlation coefficient to determine the association between I/E-R and LSI.

Results: Of 100 psychiatrists, 51 completed the survey, eight refused, and 41 didn't respond. Fifty-three percent of responders considered themselves religious. Only 2% felt that religion can hinder medical care; 86% thought that religion can complement medical care. Ninety percent were receptive to their patients' religious values. There was an inverse correlation between extrinsic religiosity and life satisfaction ($r = -0.257$, $p = 0.04$).

Conclusions: Although psychiatrists are less religious than their patients, they recognize the importance of religion to their patients. Life satisfaction of the surveyed psychiatrists was inversely correlated with their extrinsic religiosity.

NR88 Monday, May 19, 1:00 p.m.-2:30 p.m.

Cocaine Intoxication at Psychiatry Emergency Department Presentation, Hospital Admission and Length of Stay

Glenn W. Currier, M.D., Emergency, Bellevue/New York University, 2108 Lynngrove Drive, Manhattan Beach CA 90266; Michael H. Allen, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the relationship between cocaine intoxication at the time of emergency department presentation, hospital admission, and subsequent length of stay.

Summary:

Objective: This study examined the relationship between cocaine intoxication at time of emergency department presentation, hospital admissions, and subsequent length of stay.

Method: Semiquantitative cocaine urine toxicology screens (CUTS) were obtained for 393 subjects registered at the Bellevue Hospital Psychiatric Emergency Service in a two-month study period in 1995. Treatment course was compared for cocaine positive and negative patients.

Results: CUTS were performed for 24.9% of discharged patients and 50.2% of admitted patients. CUTS were positive in 62.4% of those tested, including 45.9% of discharged patients and 27.6% of admitted patients ($x^2 = 36.7$, df = 2, $p < .001$). While 45.0% of tested mood disordered subjects admitted to hospital were positive for cocaine, only 13.4% of patients admitted with a primary psychotic disorder were positive for cocaine. The odds ratio for admission fell from 0.73 for cocaine negative subjects to 0.50 for cocaine positive subjects (risk ratio 0.68, two-sided Fisher's Exact < .001, 95% C.I.). Patients who had positive CUTS at admission had a significantly briefer mean length of stay (23.3 days, SD 30.2) than did cocaine negative subjects (41.1 days, SD 37.2), (Mann-Whitley U = 5390, z = 3.69, p < .0001). CUTS positive mood disordered subjects had significantly briefer admissions (mean 25.3 days, SD 34.6) than did their negative counterparts (mean 53.2 days, SD 52.0), (Mann-Whitley U = 519, z = 2.11, p < .04). However, there was no significant differences in mean lengths of stay between cocaine positive (25.3 days, SD 34.6) and negative (37.7 days, SD 31.7) psychotic subjects. Life Table Analysis showed that survival curves for cocaine positive subjects were significantly lower than those of their cocaine negative counterparts, largely due to the effects of the mood disordered cohort.

Conclusions: In this population, positive CUTS results were predictive of direct discharge from the emergency department. Mood-disordered, but not psychotic, cocaine-positive subjects had briefer lengths of hospital stay. These results suggest that CUTS may be useful in emergency departments that serve cocaine-abusing psychiatric patients.

References:

Shaner A, Khalsa ME, Roberts L, et al: Unrecognized cocaine use among schizophrenic patients. *Am J Psychiatry* 150:758–762, 1993.

Sterling RC, Gottheil E, Weinstein S, Shannon D: Psychiatric symptomatology in crack cocaine abusers. *J Nerv Ment Dis* 182:564–569, 1994.

NR89 Monday, May 19, 1:00 p.m.-2:30 p.m.

Ten-Year Outcomes of Familial Male Alcoholics

Sunil Chhibber, M.D., Department of Psychiatry, Kansas University Medical Ctr, 3901 Rainbow Boulevard, Kansas City KS 66160; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.S., Barbara J. Powell, Ph.D., Barry I. Liskow, M.D., Jan L. Campbell, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how familial alcoholism, among males at least, appears to represent a distinct subtype of alcoholism with a fairly characteristic history and course.

Summary:

Objective: Retrospective studies comparing family-history-positive alcoholics (FH+) with family-history-negative alcoholics (FH–) 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 in their close biological relatives. Few long-term prospective studies of familial alcoholism exist.

Method: In this long-term, naturalistic, outcome 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. The patients were extensively examined at intake into the study and again one and 10 years later.

Results: At intake into the study we replicated previous investigations finding that, in comparison with the nonfamilial group, the familial alcoholics were younger, reported more unemployment, began drinking at an earlier age, had an earlier alcoholism onset, and suffered a greater number of drinking-related sequelae. The FH+ group also reported more psychiatric illness among their 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 follow-up (five had died). Surprisingly, we found no differences between the two groups for most of the outcome measures, although the total sample had improved significantly with respect to abusive drinking. The FH+ group received significantly more treatment during follow up and reported fewer drinking days in the six months prior to the one-year evaluation. Clinicians also rated the global drinking outcome of FH+ alcoholics more favorably. We wondered if the more intensive treatment served to offset the anticipated poorer prognosis of the familial alcoholic subgroup? Ten years later, 96 of the patients were dead (27%). Of the remaining 264 patients, 255 were reinterviewed a decade later; only 2% of the original sample were unaccounted for 10 years later. The one-year advantage found for the FH+ alcoholics *was not maintained* at the 10-year follow up, even though the FH+ patients continued to report more treatment for drinking than FH– patients. After 10 years, compared with the nonfamilial group, the FH+ patients were less likely to be abstinent (40% vs. 55%), reported higher alcoholism severity scores, and were rated as having a greater problem with other drugs during the previous year. They also acknowledged experiencing more stressors, described greater psychosocial dysfunction, and reported more medical problems over the entire 10-year period.

Conclusion: Familial alcoholism, among males at least, appears to represent a distinct subtype of alcoholism with a fairly characteristic history and course.

References:

1. Penick EC, Powell BJ, Bingham SF, et al: A comparative study of familial alcoholism. *Journal of Studies on Alcohol, 48*:136–146, 1987.

2. Schuckit MA, Smith TL: An 8-year follow up of 450 sons of alcoholics and control subjects. *Archives of General Psychiatry, 53*:202–210, 1996.

NR90 Monday, May 19, 1:00 p.m.-2:30 p.m.

Are Repeated Episodes of Sydenham's Chorea Associated with Increased Risk of OCD?

Fernando R. Asbahr, M.D., CNE Branch, NIMH-DIRP/Bldg 10, Room 2D46, 10 Center Drive/MSC 1284, Bethesda MD 20892; Andre B. Negrao, M.D., Jose A. daPaz, M.D., Maria J. Marques-Dias, M.D., Maria H.B. Kiss, M.D., Valentim Gentil, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe Sydenham's chorea and the relationship of streptococcal infections.

Summary:

Objective: Sydenham's chorea (SC) is a basal ganglia disorder associated with obsessive-compulsive symptoms (OCS). A literature review suggests that streptococcal infections may exacerbate cases of childhood-onset obsessive-compulsive disorders (OCD). The concomitant presence of OCS and chorea was studied during episodes of streptococcal infections in a pediatric sample.

Methods: Fifty outpatients with acute rheumatic fever (RF) were evaluated during their initial presentation and after three and six months. OCS were rated on the 44-item Leyton Obsessional Inventory and severity was rated on the 15-point NIMH Global Obsessive-Compulsive Scale.

Results: Thirty patients had SC and 20 had RF without chorea. OCS were observed only in patients with SC. Four out of the 30 SC patients had two episodes of chorea. During the first episode, two met DSM-IV criteria for OCD and two had no OCS. During the second episode, all four developed OCS along with chorea. Three out of four met criteria for OCD. In all cases the severity of OCS/OCD was greater in the second episode than in the first episode.

Conclusion: Recurrent episodes of SC seem to increase the severity of OCS. Our data reinforce the hypothesis that episodic worsening of OCD after streptococcal infections can have an autoimmune process analogous to Sydenham's chorea.

References:

Swedo SE, Leonard HL, Schapiro MB, et al: Sydenham's chorea: physical and psychological symptoms of St Vitus Dance. *Pediatrics* 91:706–713, 1993.

Swedo SE, Leonard HL, Kiessling LS: Speculation on antineuronal antibody-mediated neuropsychiatric disorders in childhood. *Pediatrics* 93:323–326, 1994.

NR91 Monday, May 19, 1:00 p.m.-2:30 p.m.

Volumetric Superior Temporal Gyrus Abnormality in Schizotypal Personality Disorder

Chandlee C. Dickey, M.D., Department of Psychiatry, Harvard Medical School, 221 Longwood Avenue, Boston MA 02115; Martha E. Shenton, Ph.D., Martina M. Voglmaier, Ph.D., Margaret Niznikiewicz, Ph.D., Larry J. Seidman, Ph.D., Robert W. McCarley, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe how schizotypal personality disorder compares with schizophrenia on MRI volume measures of temporal lobe structures.

Summary:

Kendler, in his Roscommon County Family Study, epidemiologically ascertained that schizotypal personality disorder (SPD) should be considered part of the schizophrenia spectrum disorders. In this study we sought to demonstrate anatomically the similarities between SPD and schizophrenia. Shenton had found schizophrenics to have reduced gray matter volumes of left superior temporal gyrus (STG), anterior hippocampus/amygdala, and parahippocampus. We acquired 1.5mm coronal images on 16 community-based, right-handed male subjects who met DSM-IV criteria for SPD. They were matched on age and did not differ significantly in terms of IQ or parental socioeconomic status from 14 normal controls. Following the procedure used by Shenton, regions of interest (ROI) were manually delineated on the brain images from this SPD population. SPD subjects were found to have statistically significantly smaller left STG gray matter volumes compared with normal controls ($p = .005$, Mann-Whitney U). Other temporal lobe ROI volumes did not differ. The relative volume of the left hippocampus did correlate negatively with degree of thought disorder on the TDI ($r = -.61$, $p < .02$). This is the first morphologic evidence of a temporal lobe abnormality in this population and strengthens the hypothesis that SPD should be considered part of the schizophrenia spectrum disorders.

References:

Kendler KS, McGuire M, Gruenberg AM, et al: The Roscommon family study I. methods diagnosis of probands, and risk of schizophrenia in relatives. *Archives of General Psychiatry.* 50:527–540, 1993.

Shenton ME, Kikinis R, Jolesz FA, et al: Abnormalities of the left temporal lobe and thought disorder in schizophrenia: a quantitative magnetic resonance imaging study. *New England Journal of Medicine.* 327:604–12, 1992.

NR92 Monday, May 19, 1:00 p.m.-2:30 p.m.

An Association Study of Neurotrophin-3 Gene's Polymorphism with Schizophrenia

Yu-Sang Lee, M.D., Department of Psychiatry, Yongin Mental Hospital, 4 Sangha-Ri Kusung-Myun, Yongsin-Si Kyungsi 449–910, South Korea; Jin-Hee Han, M.D., Young-Gyu Chai, Ph.D., Hyeong-Seob Kim, M.D., Jung-Sik Lee, M.D., Byung-Hwan Yang, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize Nt-3 gene, which plays an important role in the development of the brain, was not associated with schizophrenia in Korean male cohorts.

Summary:

Objective: We investigated the distribution of neurotrophin-3 (NT-3) gene's polymorphic markers of patients with schizophrenia and controls to find out evidence of neurodevelopmental characteristics of schizophrenia in Korea.

Method: The subjects were 88 male patients who met the DSM-III-R criteria for schizophrenia and 83 unaffected male controls. The age of patients ranged from 20 to 45 years, with a mean age of 31 years (SD = 7), while the controls' age ranged from 20 to 45 years with a mean age of 27 years (SD = 5). Patients and controls were unrelated and resided in the central part of Korea. Using polymerase chain reaction and polyacrylamide gel electrophoresis, dinucleotides repeat polymorphism ([CA]n repeat) in the promoter region of NT-3 gene was observed. For a comparison of NT-3 gene's allelic frequencies between patients and controls, chi-square tests were performed.

Results: The frequency of allele in schizophrenia was slightly increased in 147 base pair allele in comparison with that of controls ($X^2 = 1.884$, $df = 1$, $p < 0.170$), but there were no statistically significant differences in the distribution of NT-3 gene's polymorphic markers between schizophrenic and control groups.

Conclusion: Nt-3 gene, which plays an important role in the development of brain, was not associated with schizophrenia in Korean male cohorts.

References:

1. Nanko S, Hattori M, Kuwata S, et al: neurotrophin-3 gene polymorphism associated with schizophrenia. *Acta Psychiatrica Scand* 89:390–392, 1994.

2. Hattori M, Kuwata S, Fukuda R, et al: Dinucleotide repeat polymorphism in the promoter region of neurotrophin-3 gene. *Hum Molec Genet* 2:1511, 1993.

NR93 Monday, May 19, 1:00 p.m.-2:30 p.m.

Linkage Disequilibrium Between Bipolar Disorder and Markers on Chromosome 18p11.2

Alan R. Sanders, M.D., Clinical Neurogenetics, NIH/NIMH/Bldg 10, Rm 3N218, 9000 Rockville Pike, Bethesda MD 20892-1274; Takeo Yoshikawa, M.D., Judith A. Badner, M.D., Wade H. Berrettini, M.D., Elliott S. Gershon, M.D., Sevilla D. Detera-Wadleigh, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the finding of linkage disequilibrium to bipolar disorder.

Summary:

A replicated linkage to bipolar disorder (BP) spanned a large segment of the pericentromeric region of chromosome 18 (Berrettini et al. 1994; Stine et al. 1995). To narrow down the region of significance, we used linkage disequilibrium (LD) mapping within the interval, eventually focusing upon the 18p11.2 area. The transmission/disequilibrium test (TDT) was employed on marker data derived from the 22-pedigree Clinical Neurogenetics Branch (CNG) series. One of the markers, Clone 22, showed evidence of association with BP in the CNG series by the TDT ($P = 0.024$). The trinucleotide repeat of Clone 22, located in the 3′ untranslated region, was examined in each of these pedigrees for evidence of expansion, and none was found. Clone 22 was independently examined in the 96-pedigree NIMH collaborative series with the TDT showing an LD trend ($P = 0.2$). Combining the two series yielded stronger evidence of association by the TDT ($P = 0.015$). Clone 22 is a novel brain-expressed transcript isolated in our laboratory and may be considered as a positional candidate gene for BP. This represents an initial finding of linkage disequilibrium to BP, which may be examined in other series for evidence of replication.

References:

Berrettini WH, Ferraro TN, Goldin LR, et al: Chromosome 18 DNA markers and manic-depressive illness: evidence for a susceptibility gene. *Proc Natl Acad Sci U S A* 91:5918–5921, 1994.

Stine OC, Xu J, Koskela R, 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.

NR94 Monday, May 19, 1:00 p.m.-2:30 p.m.

Neuropsychological Functioning in Panic Disorder

Julie Akiko Gladsjo, Ph.D., Department of Psychiatry, University of CA/San Diego, 3350 La Jolla Village Drive, San Diego CA 92161; Mark H. Rapaport, M.D., Rebecca A. McKinney, B.A., Anthony Rabin, M.S., Michelle D. Auerbach, M.S., Lewis L. Judd, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how neuropsychological dysfunction was not associated with panic disorder.

Summary:

Background: Gray (1982) proposed that the septohippocampal system, which plays an important role in learning and memory, may mediate anxiety. Thus, patients with anxiety disorders may manifest neurocognitive performance deficits. Several researchers have examined the neuropsychological functioning of patients with panic disorder, but their results have been equivocal. We hypothesized that patients with panic disorder would demonstrate learning and memory deficits compared with normal comparison subjects.

Method: Sixty-nine patients who met DSM-IV criteria for panic disorder and 19 age- and education-comparable normal subjects were administered comprehensive neuropsychological test batteries. The battery assessed overall learning, visual memory, verbal memory, attention, visuospatial functioning, and psychomotor speed. Panic disorders subjects also completed anxiety ratings and panic-attack diaries. Multivariate analysis of covariance was employed to examine differences in neuropsychological test performance; hierarchical multiple regression was used to evaluate the contribution of clinical symptoms to neuropsychological impairment.

Results: There were no significant differences in neuropsychological test performance between patients with panic disorder and the normal volunteers. Anxiety severity and panic-attack frequency did not affect neuropsychological test performance.

Comment: This study is the largest and most comprehensive neuropsychological study of patients with panic disorder. Neuropsychological dysfunction was not associated with panic disorder.

References:

Admundson GJG, Stein MB, Larsen DK, Walker JR: (In press). Neurocognitive function in panic disorder and social phobia patients. *Anxiety.*

Lucas JA, Telch MJ, Bigler ED: Memory functioning in panic disorder: a neuropsychological perspective. *Journal of Anxiety Disorders, 5*:1–20, 1991.

NR95 Monday, May 19, 1:00 p.m.-2:30 p.m.

A Comparison of the Efficacy of Alprazolam-XR Plus Cognitive-Behavioral Therapy Versus Cognitive-Behavioral Therapy Plus Placebo for Acute Treatment at Three-month Follow-up

Michelle D. Auerbach, M.S., Department of Psychiatry, University of CA/San Diego, 8950 La Jolla Village Dr/2243, La Jolla CA 92037; Mark H. Rapaport, M.D., Julie Akiko Gladsjo, Ph.D., Rebecca A. McKinney, B.A., Todd Oliver, M.A., Lewis L. Judd, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the results, positive or negative, of combined treatment with benzodiazapines in cognitive behavioral therapy.

Summary:

Research indicates combined therapy of exposure and alprazolam is as effective as exposure alone during treatment for panic disorder with agoraphobia, but during taper and follow-up, there was an increased relapse rate in the combined-treatment group. The current study hypothesized that cognitive behavioral therapy (CBT) with alprazolam-xr would have identical efficacy during treatment and at three-month follow-up. Thirty-eight patients diagnosed with panic disorder were randomized to placebo or alprazo-

lam-xr (4mg a day) and 12 weeks of group CBT based on a modification of Telch's model. MANOVA was performed using number of panic attacks, PAI, ASI, and STAI, collected at baseline, eight weeks of treatment and at three-month follow-up. After eight weeks of treatment, both groups showed similar and significant reductions in panic attacks, panic symptoms, and measures of anxiety, relative to baseline. At three-month follow-up, both groups remained significantly better than at baseline, but the alprazolam-xr group had trends toward increased panic attacks (.33 ± .83 vs. .09 ± 27; $p < .07$) and panic symptoms (2.44 ± 6.29 vs. .94 ± 3.15; $p < .07$). The level of anxiety (2.17 ± 5.17 vs. .87 ± 2.47; $p < .03$) closely resembled baseline for the combined treatment group but this may have been driven by baseline differences (2.78 ± 2.44 vs. 8.6 ± 9.09). These results suggest combined treatment with benzodiazapines may not confer any added benefit to CBT in mild to moderately ill panic disorder patients.

References:

Marks MM, Swinson RP, Basoglu M, et al: Alprazolam and exposure alone and combined in panic disorder with agoraphobia: a controlled study in London and Toronto. *British J Psych,* 162:776–787, 1993.

Telch MJ, Lucas JA, Schmidt NB, et al: Group cognative-behavioral treatment of panic disorder. *Behav Res Ther,* 31(3): 279–287, 1993.

NR96 Monday, May 19, 1:00 p.m.-2:30 p.m.

Trauma Symptoms, Life Stress and Salivary Cortisol in Metastatic Breast Cancer Patients

Lisa Butler, Ph.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford CA 94305-5544; Cheryl Koopman, Ph.D., Sandra E. Sephton, M.S., Catherine Classen, Ph.D., David Spiegel, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe women diagnosed with metastatic breast cancer as being at risk for developing clinically significant levels of post-traumatic stress symptoms.

Summary:

Objective: This study was undertaken to examine the degree of trauma symptoms (intrusion, avoidance, anxiety) and their relationship to salivary cortisol, stressful life events, and aversive social support in women with metastatic breast cancer.

Methods: Subjects were 125 women diagnosed with metastatic breast cancer who were participating in an intervention trial to study the effect of group psychotherapy on adjustment and survival time. Self-reported IES, tension-anxiety POMS subscale, previous life events, and aversive social support data and salivary cortisol samples were gathered at baseline (prior to randomization).

Results: Trauma symptoms were moderately intercorrelated in this sample and IES subscale means were comparable to those reported for other traumatized populations. Exploratory multiple regression analyses revealed that neither overall mean salivary cortisol, nor the mean circadian amplitude for cortisol, were associated with any predictor variable. However, mean 9 p.m. cortisol levels were found to be positively associated with total IES scores but negatively associated with previous life stress.

Conclusions: The results of this study suggest that women diagnosed with metastatic breast cancer are at risk for developing clinically significant levels of post-traumatic stress symptoms. Furthermore, both current trauma symptoms and previous life stressors may affect endocrine functioning.

References:

Horowitz MJ, Field NP, Classen CC: Stress response syndromes and their treatment. In: Goldberger L & Breznitz S (eds.): *Handbook of Stress: Theoretical and Clinical Aspects* (pp. 757–773). New York: The Free Press, 1993.

Yehuda R, Giller EL, Levengood RA, et al: Hypothalamic-pituitary-adrenal functioning in post-traumatic stress disorder. In: Friedman M. J. Charney D. S. & Deutch A. Y (eds.): *Neurobiological and Clinical Consequences of Stress: From Normal Adaptation to PTSD* (pp. 351–365). Philadelphia: Lippincott-Raven, 1995.

NR97 Monday, May 19, 1:00 p.m.-2:30 p.m.

Effectiveness of Bupropion for Smoking Cessation for Smokers with a History of Major Depression

Kara E. Hayford, M.D., Department of Psychiatry, Mayo Clinic, 200 First Street, SW, Rochester MN 55905; Christi A. Patten, Ph.D., Teresa A. Rummans, M.D., Darrell R. Schroeder, M.S.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe how poor smoking treatment outcomes affect major depressive disorder.

Summary:

A history of major depression has been associated with poor smoking treatment outcomes. This study evaluated the efficacy of the antidepressant bupropion for smokers with a history of major depressive disorder (MDD). Data were gathered from a multicenter, double-blind, placebo-controlled trial. A total of 615 smokers (336 female, 279 male) were randomly assigned to placebo; 100 mg, 150 mg, or 300 mg of bupropion for a seven-week period. The SCID was used to assess MDD history; those with current MDD were excluded from the study. Self-reported smoking status was confirmed with carbon monoxide levels of ≤10 ppm. At baseline, smokers with a history of MDD ($N = 114$) were more likely than those without MDD history ($N = 501$) to be female (65.8% vs. 52.1%; $p = 0.008$), to have higher mean Beck Depression Inventory (BDI) scores (5.7 vs. 4.0; $p = 0.001$), higher mean Fagerstrom Tolerance Questionnaire scores (7.6 vs. 7.2; $p = 0.01$), and to have smoked more cigarettes per day (28.4 vs. 26.5; $p = 0.04$). Point prevalence smoking cessation rates did not differ significantly for those with and without a history of MDD at end of treatment (31.6% vs. 32.9%) or at week 52 (19.3% vs. 19.6%). A significant dose effect was detected at both time points ($p < 0.001$ and 0.04), but there was no significant effect of MDD history or dose by MDD history interaction. Changes in nicotine withdrawal symptoms, including BDI scores will be reported.

References:

Breslau N, Kilbey M, Andreski P: Nicotine dependence and major depression. *Archives of General Psychiatry,* 50:31–35, 1993.

Glassman AH, Helzer JE, Covey LS, et al: Smoking cessation and major depression. *Journal of the American Medical Association.* 264:1546–1549, 1990.

NR98 Monday, May 19, 1:00 p.m.-2:30 p.m.

Anemia and Macrocytosis in the Prediction of Serum Folate and B12, and Outcome in Major Depression

David Mischoulon, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 815, Boston MA 02114; Jane K. Burger, B.A., Andrew A. Nierenberg, M.D., John J. Worthington III, M.D., Maurizio Fava, M.D., Jonathan E. Alpert, M.D.

Educational Objectives:

Participants should come away from this presentation with a better understanding of the relationship between red blood cell count, hematocrit, mean corpuscular volume, and serum folate and between these indices and antidepressant response among adult outpatients with major depression.

Summary:

Objectives: Folate and B12 deficiency are common in major depressive disorder (MDD) and have been associated with poor response to serotonin reuptake inhibitors (SSRIs). Macrocytic anemia is also a manifestation of folate or B12 deficiency. We therefore examined whether red blood cell count (RBC), hematocrit (HCT), and mean corpuscular volume (MCV) are useful for detecting hypofolatemia or B12 deficiency, or predicting response to acute treatment (8 weeks) with fluoxetine (20 mg/day) among outpatients with MDD.

Methods: Our 213 subjects were adults (ages 18 to 65) with MDD by DSM-III-R criteria enrolled in a treatment study at the Massachusetts General Hospital. Exclusion criteria included alcohol abuse and unstable medical illness. Treatment outcome was assessed with the Hamilton Rating Scale for Depression. Serum folate, B12, and hematological indices were obtained prior to treatment.

Results: Neither macrocytosis (MCV > 100fl), nor anemia (RBC < 4.40 mill/mcl or HCT < 41%) were sensitive or specific predictors of folate or B12 deficiency or of antidepressant response.

Conclusions: Neither anemia nor macrocytosis should be relied upon to identify potential folate or B12 deficiency. Even among depressed outpatients who have normal red cell morphology and numbers, direct measurement of folate and B12 should be considered when evaluating refractoriness to standard treatment.

References:

Fava M, Borus JS, Alpert JE, et al: Folate, B12, and homocysteine in major depressive disorder. *Am J Psychiatry*, (in press)

Mischoulon D: The role of folate in major depression: mechanisms and clinical implications. *American Society of Clinical Psychopharmacology Progress Notes* 7(2):4–5, 1996.

NR99 Monday, May 19, 1:00 p.m.-2:30 p.m.

Predictors of Treatment Response in Pregnancy and Postpartum Disorders

James R. Strader, B.S., Department of Psychiatry, Emory University, 1639 Pierce Drive, Atlanta GA 30322; Alexis M. Llewellyn, B.A., Zachary N. Stowe, M.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to determine predictors of treatment response in postpartum onset major depression.

Summary:

Objective: To determine predictors of treatment response in postpartum onset major depression.

Method: Fifty-three (53) women presenting to the Emory University Pregnancy and Postpartum Mood Disorders Program were included in the present study. All met diagnostic criteria for major depression and were treated with SSRIs for at least eight weeks. Treatment response was defined by a 50% reduction in SIGH-D scores from baseline. Variables assessed to determine predictors of treatment response included time of onset, severity of illness, duration of illness, family and personal history of depression, and biological measures, including FSH, LH, estradiol, progesterone, prolactin, and cortisol.

Results: Of the 53 women in the study, 34 (64.2%) demonstrated a therapeutic response within four weeks, 13 (24.5%) responded from four to eight weeks, and six (11.3%) after eight weeks (Chi-square = 11.7, 2 d.f., p = 0.0028). Time of symptom onset after childbirth was observed to be significantly associated with response, with 64% of the early responders having an early onset of illness, 46% of the middle responders having early onset, and only 17% of the late responders having an early onset (Chi-square = 16.3, 2 d.f., p = 0.0003). No other variables were significantly associated with treatment response.

Conclusions: Most women suffering from postpartum major depression were effectively treated within eight weeks with only limited intervention. The time of onset of illness was the strongest predictor of treatment response. The biology of postpartum depression and treatment response is poorly understood, and further study is needed.

References:

Feiner NF: Predicting nonresponsiveness to depression treatments. *American Journal of Psychiatry* 153 (11): 1508–9, Nov 1996.

Schulberg HC, Block MR, Madonia MJ, et al: Treating major depression in primary care practice: eight month clinical outcomes. *Archives of General Psychiatry* 53 (101): 913–9, Oct. 1996.

NR100 Monday, May 19, 3:00 p.m.-5:00 p.m.

Prevalence of Polypharmacy in Patients on Antidepressants and Its Relation with Drugs and Drug Interaction

Mujeeb U. Shad, M.D., Psychiatric Research Unit, 1100 North St. Francis, Ste 200, Wichita KS 67214; Sheldon H. Preskorn, M.D., Cheryl A. Carmichael, B.B.A.

Summary:

The purpose of this study was to survey the frequency and nature of polypharmacy as practiced in two different treatment settings: a university outpatient psychiatric clinic (n = 237) and a VA Medical Center (n = 1075). The latter included in- and outpatients treated by either primary care physicians or various specialists. Only those patients on at least one antidepressant were included. Pharmaceutical products consisting of more than one drug were counted as separate chemical entities. Frequently-occurring drug combinations were examined for clinically significant drug-drug interactions. Two primary care sites will also be surveyed. Analysis of data showed:

	Univ. Psychiatric Clinic	*VAMC*
Patients on 1 drug	28%	7%
Patients on 2 drugs	24%	11%
Patients on 3 drugs	17%	12%
Patients on 4 or more	31%	70%
Mean # drugs prescribed	3	6

Polypharmacy during antidepressant treatment is the rule rather than the exception. Hence, a sizable percentage of patients are at potential risk for drug-drug interactions.

NR101 Monday, May 19, 3:00 p.m.-5:00 p.m.

Tramadol for Treatment-Refractory OCD

Nathan A. Shapira, M.D., Department of Psychiatry, University of Cincinnati, 231 Bethesda Avenue, Cincinnati OH 45267; Paul E. Keck, Jr., M.D., Toby D. Goldsmith, M.D., Brian J. McConville, M.D., Patrick J. Haggard, Susan L. McElroy, M.D.

Summary:

Objective: Serotonin reuptake inhibitors (SRIs) are often effective for obsessive-compulsive disorder (OCD); however, only 50% to 70% of patients have at least a partial response to SRIs. Tramadol has been reported effective in a patient with Tourette's syndrome and OCD, both refractory to standard therapy. Given that tramadol has not been systematically studied, we chose to examine its effectiveness in OCD.

Method: Seven patients with treatment-refractory OCD (mean ± SD of 2.9 ± 2.1 previously failed SRI trials) were treated with tramadol in a six-week, open-label trial using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the Hamilton Depression Rating Scale (HAM-D), and the Clinical Global Impression Scale (CGI) to assess response.

Results: Two patients did not complete the trial due to nausea (N = 1) and panic attack (N = 1). Mean ± SD tramadol dose for the six patients completing at least two weeks was 254 ± 119 mg/day. With intent-to-treat analysis for these patients, average baseline measurements for Y-BOCS, HAM-D, and CGI were 27.8 (SD = 4.6), 27.5(SD = 15.9), and 5.3/5.2 with endpoints of 20.7 (SD = 5.7), 28.8 (SD = 9.8), and 4.5/2.3, respectively. Using Wilcoxon signed-ranks test, changes in Y-BOCS scores were significant ($Z = 2, df = 1, p < .05$).

Conclusions: For treatment-refractory OCD, tramadol represents a possible alternative to SRIs. Long-term follow-up and controlled studies are required to demonstrate tramadol's effectiveness in OCD.

NR102 Monday, May 19, 3:00 p.m.-5:00 p.m.

Methylphenidate and Motor Organization in Children with ADHD

Johanne Renaud, M.D., Department of Psychiatry, Ste Justine Hospital, 3100 Ellendale 2, Montreal PQ H3J 1V4, Canada; Michelle Bourassa, M.Ps., Virginia I. Douglas, Ph.D., Gilles Pelletier, M.D., Guy Geoffroy, M.D., Philippe Robaey, M.D.

Summary:

Recent models emphasize a motor response organization deficit in ADHD. Motor response processes are studied through the analysis of lateralized readiness potentials (LRPs), a measure of the difference in electrical activity between the two hemispheres before the execution of a motor response. Brain activity of 12 6- to 9-year-old ADHD right-handed children was recorded over the motor cortices during a task in which they respond to arrows presented on a computer screen, with the compatible hand (i.e., same direction as arrow, 66% of trials) or the incompatible hand (opposite to arrow, 33% of trials) according to the stimulus color. Methylphenidate effects were investigated in a double-blind, crossover, placebo-controlled design. During two visits, behavioral and cerebral activity measures were taken one hour after administration of either placebo (lactose 100 mg) or methylphenidate (0.5 mg/kg) in a randomized order. Behavioral results showed a task effect, with longer reaction times and more errors for incompatible trials under both medication and placebo conditions ($p < .05$). Medication significantly decreased errors and reaction times for compatible and incompatible trials; however, this effect was stronger for the left hand ($p = .01$). Corresponding LRP analyses will be presented.

NR103 Monday, May 19, 3:00 p.m.-5:00 p.m.

Lamotrigine Treatment and Serotonin Receptor Function

I.S. Shiah, M.D., Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; L.N. Yatham, A.P. Zis, M.D., Raymond W. Lam, M.D.

Summary:

Objectives: To explore the role of 5-HT1A receptor function in the mechanisms of action of lamotrigine, we measured body temperature and plasma cortisol responses to a challenge with the selective 5-HT1A receptor agonist ipsapirone in humans.

Methods: We recruited ten healthy male subjects for the study. After obtaining a blood sample for baseline hormone levels and measuring body temperature, a single dose of 0.3 mg/kg of ipsapirone was given orally to all the subjects and further bloods and temperature readings were obtained at regular intervals for three hours. The ipsapirone challenge test was repeated after the subjects had been treated with lamotrigine (100 mg, p.o., daily) for one week.

Results: Neither the hypothermic nor the plasma cortisol responses induced by ipsapirone were significantly altered by the lamotrigine treatment.

Conclusions: Our findings provide no evidence to support that 5-HT1A receptor function is involved in the mechanisms of action of lamotrigine.

NR104 Monday, May 19 3:00 p.m.-5:00 p.m.

SSRIs Side Effects: Incidence and Management

Carlos Blanco-Jerez, M.D., Department of Psychiatry, Columbia University, 722 West 168th Street, Box 81, New York NY 10032; James J. Daly, M.D.

Summary:

Objective: The use of selective serotonin reuptake inhibitors has resulted in increased tolerability and safety of antidepressant therapy. However, their side effects can at times compromise the quality of life and compliance of the patients. We reviewed the incidence of those side effects, their postulated pathophysiologic mechanisms, and suggested approaches to their management.

Method: Computer-based literature review and information provided by the FDA and the manufacturers of the drugs.

Results: There is a significant variety in the type of SSRI-induced side effects, as well as in their reported incidence. Direct serotonin and serotonin-regulated dopamine mechanisms appear to be responsible for most of these adverse effects. Psychoeducation, dose schedule modification, adjuvant medication, and change to a different compound can be helpful in the management of SSRI-induced side effects.

Conclusion: Knowledge of the pathophysiology, incidence, and available management strategies of the SSRI-induced side effects can result in improved quality of life and adherence to treatment by patients.

NR105 Monday, May 19 3:00 p.m.-5:00 p.m.

Quantitative Assessment of Tremor in Depressed Patients Receiving Lithium Augmented by Paroxetine or Amitriptyline

Rocco M. Zaninelli, M.D., Clinical Research, Smithkline Beecham, Leopoldstrasse 175, 80804 Munich, Germany; Michael Bauer, M.D., Marc Jobert, Ph.D.

Summary:

Objective: Up to 40% of patients on stable lithium regimens experience tremor; this adverse event also occurs or is reinforced when lithium is combined with other medications. However, quantitative studies of lithium tremor and the factors affecting it are lacking. This double-blind study was carried out in order to quantitatively assess the possible tremor-enhancing effect of adding paroxetine (PAR) or amitriptyline (AMI) to ongoing lithium treatment.

Method: Patients having stable lithium levels (≥0.60 mmol/L) and suffering from a MDE according to DSM-III-R were randomly assigned to receive 20 mg/d PAR or 100 mg/d AMI. After 14 days the dosages could be electively increased to 30 or 150 mg/d, respectively. Tremor was assessed by axial accelerometry at baseline and weekly during the six-week treatment period. Accelerometric data were subjected to spectral analysis in order to determine the frequency bands containing greatest tremor activity.

Results: Analyzable data were obtained from 31 patients (14 PAR, 17 AMI). There was no significant difference between the groups with respect to changes in tremor activity relative to baseline. Peak frequencies were case-constant, but varied between patients. Both treatments increased tremor, with the most significant changes occurring after dosage increase. By the end of treatment, tremor activity returned to baseline levels in most patients. Increased tremor was not associated with decreased medication compliance.

Conclusion: Axial accelerometry appears to be a reliable method for quantitatively assessing psychopharmacologic tremor. This method may be of general use in establishing individual tremor profiles, which can be used to document changes in tremor during treatment.

NR106 Monday, May 19 3:00 p.m.-5:00 p.m.

Effect of Risperidone on Cognitive Function in Schizophrenic Patients: An Open-Label Study

Demetra Pappas, B.S., Taunton State, Harvard Medical School, 60 Hodges Avenue, Taunton MA 02780; Nina Leventhal, B.A., Joseph Langlois, M.A., David N. Osser, M.D., Howard H. Chang, M.D., Ileana Berman, M.D.

Summary:

There has been an increased interest in studying the effect of novel antipsychotics on cognitive function in chronically psychotic patients. Some studies have shown that clozapine may be superior to typical neuroleptics in improving cognitive function. The present data will illustrate the effect of risperidone on cognitive performance.

Method: A total of 35 treated patients were assessed psychiatrically and cognitively before and approximately six weeks after treatment with risperidone. All patients had a clinical diagnosis of schizophrenia or schizoaffective disorder. The patients' assessments included the Positive and Negative Syndrome Scale for schizophrenia (PANSS) and a battery of cognitive tests consisting of the Mini-Mental Status Examination (MMSE), tests of verbal fluency, Similarities, an abbreviated Boston Naming test, constructional praxis test, and tests of attention and memory, such as digit symbol, digit span, trail making, and word recall. We used paired t-tests to compare the baseline and the final psychiatric and cognitive assessments.

Results: On risperidone, the patients improved in all the PANSS scores, and in addition scored higher on the MMSE, Similarities, constructional praxis, and Boston Naming tests. The performance on tests of attention and memory did not change significantly during risperidone trial.

Conclusions: The present data support the hypothesis that like other novel antipsychotics, risperidone, in addition to improving schizophrenic symptoms, may have an effect on cognitive function as well. It remains uncertain whether the improvement of cognition is a result of the overall improvement in psychiatric symptoms or whether it is an effect of the drug itself. Further investigation under controlled conditions, which account for changes in psychiatric symptoms, are necessary to clarify this question.

NR107 Monday, May 19, 3:00 p.m.-5:00 p.m.

Sertraline Treatment of Diabetic Neuropathy

Isabel M. Jimenez, M.D., Department of Psychiatry, University of Miami Sch of Med, 1400 NW 10th Avenue, Ste 304A, Miami FL 33136; Paul J. Goodnick, M.D., Adarsh Kumar, Ph.D.

Summary:

Previous research has shown that antidepressants have been useful in treatment of pain, particularly diabetic neuropathy (Sindrup, 1994). Sertraline, an SSRI, has been found successful in treatment of both diabetes mellitus and depression (Goodnick, 1995, in press). The objective here was to apply sertraline (SRT) to treatment of diabetic neuropathy and apply these results to baseline platelet 5HT content (plt 5HT) and to final plasma SRT.

Method: Three males and five females with mean age 55.8 ± 7.6 yrs with diabetic neuropathy (without major depression) received SRT for eight wks with a maximal dose of 150 mg/day. Baseline and follow-up BDI, HDRS, VAS of pain, paresthesias, and three other Sx. Initial and final plt 5HT were obtained and end of study plasma SRT.

Results: Significant reductions in VAS, e.g., pain from 71.2 to 23.1 ($t = 3.74$, $p < .01$) and paresthesias from 53.8 to 15.0 ($t = 4.15$, $p < .01$). Low baseline HDRS (7.4) and BDI (8.1) did not change significantly. For 4 with baseline HDRS 4, plt 5HT content correlated with improvement ($r = 0.93$). Baseline 5HT content correlated with pain improvement ($r = 0.70$, $p = .05$). Platelet 5HT content fell significantly during the trial (206.8 to 8.2, $p < .001$). Plasma SRT correlated with reduction in paresthesia ($r = 0.70$).

Conclusions: Sertraline appears to be effective in diabetic neuropathy with relationship to both platelet 5HT content and plasma sertraline. A replication is in progress; double-blind follow-up is needed.

NR108 Monday, May 19, 3:00 p.m.-5:00 p.m.

Ethnicity, Red Blood Cell and Plasma Lithium Concentrations

Richard T. Kotomori, Jr., M.D., Department of Psychiatry, Harbor UCLA, 1124 W Carson Street, Torrance CA 90502-2004; Keh-Ming Lin, M.D., Paul Fu, M.D., Mike Smith, M.D.

Summary:

While several factors have been shown to influence the ability of a test dose of lithium (Li) to predict maintenance dosing, the role of ethnicity has not been explored. Recent research has shown that African Americans (AA) have increased RBC Li and increased side effects compared to Caucasians (Ca). The issue of whether these findings are directly related to plasma Li and whether RBC Li can be used to predict maintenance dosing has yet to be explored.

Objectives: 1) To determine whether the difference in RBC Li in Ca and AA is related to a difference in plasma Li; 2), to determine whether RBC Li can be used to predict maintenance dosing.

Methods: 27 AA and 29 Ca normal volunteers were given a single dose of Li carbonate 600 mg orally. Ten sequential blood samples were then drawn over the following 24 hours and analyzed for plasma Li and RBC Li.

Results: Our results confirmed previously noted higher RBC Li to plasma Li among AA. There were no significant differences in plasma Li between the two groups.

Conclusion: Data analysis regarding determination of predictive value of plasma Li at various times is still under study; however, initial analysis suggests that differences in RBC Li between AA and Ca do not play a significant role in the determination of plasma Li. Whether this is also true for the prediction of side effects remains unclear.

NR109 Monday, May 19, 3:00 p.m.-5:00 p.m.

Movement Disorder and Functional Impairment in the Middle-Aged and Elderly

John H. Eastham, Pharm.D., Department of Psychiatry, University of CA/San Diego, 3350 La Jolla Village Drive, San Diego CA 92161; Thomas L. Patterson, Ph.D., Enid Rockwell, M.D., Jovier D. Evans, Ph.D., Jonathan P. Lacro, Pharm.D., Dilip V. Jeste, M.D.

Summary:

Objective: We examined the impact of extrapyramidal symptoms (EPS) and tardive dyskinesia (TD) on activities of daily living (ADLs) in older schizophrenia outpatients.

Methods: 73 middle-aged and elderly subjects (range 45–79; mean 59 ± 9 yr.) with a DSM-IV diagnosis of schizophrenia were examined for the impact of EPS and TD on functional ability. Degree of EPS was assessed with the Simpson-Angus (S-A) scale. Severity of TD was measured with the Abnormal Involuntary Movement Scale (AIMS). We administered the Direct Assessment of Functional Status (DAFS) scale, an objective rating of simulated ADLs. Other assessments included standardized rating scales for negative symptoms, positive symptoms, general psychopathology, and global cognition. Regression analysis was used to determine the extent to which these variables predicted DAFS total.

Results: S-A scores significantly correlated with total DAFS scores (Pearson's $r = -.33$; $p < .005$) and on subscales of time orientation, communication, financial skills, and grooming skills (all r's < −.32; all p's < .008). AIMS did not correlate with DAFS items, although most subjects had mild or no TD (AIMS mean 4.1 ± 3.2). When subject's age, duration of illness, antipsychotic dose, S-A score, and degree of negative symptoms were entered into the regression analysis, S-A score was the most predictive of DAFS performance ($F = 5.39$; $p < 0.025$).

Conclusion: In older patients with schizophrenia, EPS affected ADL performance to a greater extent than did age, duration of illness, antipsychotic dose, and severity of negative symptoms.

NR110 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Safety and Efficacy of Paroxetine and Amitriptyline Augmentation of Lithium in the Treatment of Major Depression

Michael Bauer, M.D., Department of Psychiatry, Freie University, Eschenallee 3, 14050 Berlin, Germany; Rocco M. Zaninelli, M.D., Bernd Mueller-Oerlinghause, M.D., Wolfgang Meister, M.D.

Summary:

Objective: The use of lithium as prophylactic treatment for bipolar and unipolar disorders is widespread. However, there has been little prospective research regarding antidepressant augmentation in lithium-maintained patients who experience relapses of major depression. This study compares the safety and efficacy of paroxetine (PAR) and amitriptyline (AMI) when added to a stable lithium regimen.

Method: In this double-blind study, 44 patients having stable lithium levels (ℓ0.60 mmol/L) and suffering from a MDE according to DSM-III-R were randomly assigned to receive PAR (20–30 mg/d) or AMI (100–150 mg/d). During the six-week treatment period, efficacy was assessed weekly with the 17-item HAMD and the CGI, safety by the DOTES Scale and by quantitative measurement of tremor.

Results: 42 cases were eligible for analysis, 23 in the AMI and 19 in the PAR group. There was no significant difference between the groups with respect to the numbers of patients demonstrating emergent symptoms as recorded by the DOTES; the symptoms reported and their frequencies correspond to the known side-effect profiles of AMI and PAR. Tremor was increased in a dose-dependent manner by both treatments up to day 28, after which it subsided. The two groups did not differ significantly in the number of patients reaching a 50% reduction in baseline HAMD scores at week 6. In the CGI, the PAR group showed a greater decline in illness severity from day 21 onward.

Conclusion: Although PAR and AMI enhance lithium's tremorgenicity, the addition of these antidepressants to ongoing lithium therapy did not generally lead to increased frequencies of adverse events. Thus, this augmentation approach appears to be a relatively safe treatment option.

NR111 Monday, May 19, 3:00 p.m.-5:00 p.m.

Prescribing Trends of Antidepressants in Bipolar Depression: Phase II

Sunila Pandit, M.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Carlos A. Zarate, Jr., M.D., Mauricio Tohen, M.D., Rajesh Narendran, M.D., Alex Madrid, M.A., Eric Tomasini, B.A.

Summary:

Background: This study utilizing pharmacoepidemiologic methods was undertaken to determine the prescribing patterns of antidepressants, particularly in bipolar depression.

Method: From pharmacy records of the McLean Hospital, the number of patients receiving antidepressants from June 9, 1987, to December 14, 1995, was determined. We later linked these databases with patients who were diagnosed with DSM-III-R and DSM-IV bipolar depression during the same period of time.

Results: During the eight-year period, it was determined that out of 732 patients diagnosed with bipolar depression 667 received antidepressants. There was a decrease in the prescribing of tricyclic antidepressant (TCAs) from 68% in 1987 to 9% in 1995. Bupropion reached a peak of 22% in 1992–1993 and subsequently decreased to 14% in 1995. Monoamine oxidase inhibitors (MAOIs) went from 14% in 1987 to 2% in 1995. Prescribing trends for serotonin specific reuptake inhibitors (SSRIs) went from a low of 14% in 1988 to 46% in 1995.

Conclusion: At our center, prescribing of serotonin specific reuptake inhibitors (SSRIs), in bipolar depression has increased relative to other antidepressants.

NR112 Monday, May 19, 3:00 p.m.-5:00 p.m.

Olanzapine Crossover in Stable Outpatients

Laura J. Dalheim, M.D., Department of Psychiatry, St. Luke's/Roosevelt, 411 W 114th Street, Ste 3C, New York NY 10025; Peter J. Weiden, M.D., Ralph Aquila, M.D., Janet Standard, R.N., Marianne Emanuel, R.N., Annette Zygmunt

Summary:

Goals: There is little research on the risks vs. benefits of switching stable outpatients from one antipsychotic to another, and on specific crossover techniques. This study will present preliminary data on switching a consecutive series of stable, but symptomatic, outpatients to the new antipsychotic olanzapine.

Methods: Study participants are a cohort of stable but symptomatic outpatients with a SCID DSM-IV diagnosis of schizophrenia on conventional antipsychotics or risperidone. They are part of a larger random-assignment, outcome study comparing olanzapine with other therapies. Patients assigned to olanzapine have their previous antipsychotic abruptly discontinued and are started the next day on olanzapine 10mg qHS. The patients are seen weekly during a six-week stabilization period and receive symptom (BPSR) and side effect monitoring. Patients are allowed to remain on other adjuvant psychotropic medications (e.g. lithium, antidepressants). To date, there have been 10 patients crossed over to olanzapine who completed the six-week follow-up period. Most

(n = 7) were on other adjuvant psychotropics, and, before switching, most were either on haloperidol (n = 5) or risperidone (n = 3).

Results: The major finding is that no patient experienced a severe symptom exacerbation or serious adverse reaction after an abrupt crossover to olanzapine. Three cases had increased symptoms at post-crossover week 2, including generalized anxiety (n = 2) and increased auditory hallucinations (n = 1), all of which resolved by six weeks (olanzapine doses were usually increased to 15mg per day by week 3). Bothersome side effects included drowsiness (n = 2), dizziness (n = 2), and weight gain (n = 1); all of these were relatively mild.

Conclusions: Our preliminary data suggest that an abrupt crossover technique to olanzapine—discontinuing the previous antipsychotic and starting q10mg of olanzapine the next day—seems to be surprisingly well-tolerated. The reader needs to keep in mind limitations on generalizability of these observations. All of these patients had been relatively stable and compliant, were not on clozapine, were medically healthy, and were carefully monitored for any emerging crossover problems.

NR113 Monday, May 19, 3:00 p.m.-5:00 p.m.

Divalproex in Medication-Naive Bipolar II Depression

Mirene Winsberg, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford CA 94305-5543; Sally G. Degolia, M.D., Connie M. Strong, M.S., Terence A. Ketter, M.D.

Summary:

Objective: To assess the utility of divalproex (DVPX) in medication-naive bipolar II depression.

Method: We performed a 12-week open trial of DVPX monotherapy (mean dose 929 mg/d, mean level 80 mcg/mL) in seven (four women, three men, mean age 26.6) medication-naive bipolar II depressed outpatients.

Results: Mean illness and current episode durations were 12.3 years and 14.6 weeks, respectively. Five of seven patients had moderate to marked improvement. Mean Clinical Global Impression illness severity ratings decreased from 4.3 to 2.6 ($p = .001$), Hamilton Depression ratings decreased from 21.1 to 8.4 ($p < .02$), and Young Mania ratings decreased from 6.1 to 0.4 ($p < .02$). Adding two patients with prior trials of antidepressants (but not mood stabilizers) did not alter the pattern of these findings.

Conclusion: The high (71%) rate of antidepressant response to DVPX could be due to the mildness of illness and the lack of prior medication failures. This uncontrolled pilot study must be viewed with caution, and randomized double-blind, placebo-controlled studies of DVPX in medication-naive bipolar II patients are warranted to further evaluate the possibility that DVPX may be an effective, well tolerated, first-line monotherapy in this population.

NR114 Monday, May 19, 3:00 p.m.-5:00 p.m.

Open Multicenter Study with Zoplicone in Insomniac Patients

Guillermo Tortora, M.D., Hospital Borda, Ituzaingo 1250, 3A, Lanus Este-BS AS 1824, Argentina;

Summary:

Objective: To evaluate the efficacy and tolerance of zoplicone in insomnia patients.

Method: A multicenter open-label study was conducted to evaluate zoplicone for the treatment of insomnia outpatients; efficacy was evaluated with the Spiegel sleep questionnaire. The evaluations have been performed at days 0, 14, 28, 56. All cases were followed up according to good clinical practice rules.

Results: The study included 641 patients from 40 centers; females (66.4%) and males (33.6%). The mean age of subjects was 53.2 (range 16–92). More than half of the patients (46.9%) complained of insomnia for more than 90 days. The most commonly used dosage was 7.5 mg/day (85.9%). A total of 92.6% of the patients completed the study. Spiegel questionnarie scores improved during the study. Only 3.2% of the patients discontinued treatment due to adverse effects. The most frequent adverse reaction was bitter taste (2.9%).

Conclusion: This study confirms the international experience on efficacy and tolerance of zoplicone.

NR115 Monday, May 19, 3:00 p.m.-5:00 p.m.

Effects of Discontinuing Long-Term Antidepressant Treatment of Major Depression: A Meta-Analysis

Adele C. Viguera, M.D., Department of Psychiatry, Massachusetts General Hosp, Warren 605 Fruit Street, Boston MA 02114; Ross J. Baldessarini, M.D., Jonathan Friedberg, M.D.

Summary:

Discontinuation of maintenance treatment in bipolar disorders and schizophrenia is associated with a high risk of early relapse. Such risks are less well defined after stopping antidepressant medication.

Methods: A computerized literature search identified 27 follow-up studies involving a total of 3,037 patients, mainly with unipolar major depression, with continued vs. discontinued antidepressant treatment and suitable for comparisons of relapse rates or for survival analysis.

Results: Antidepressant treatment was discontinued after 5.78 ± 11.0 (0–48) months, with 16.6 ± 12.8 (5–66) months of follow-up in the 27 trials. Crude relapse rates (%/month) were 3.37-fold lower with treatment continued (1.85 ± 1.51 vs. 6.24 ± 5.34; $p < 0.0001$). Survival analysis of data pooled from 19 studies yielded a 3.37-fold later computed time-to-50% relapse ($p < 0.0001$), of 48.0 ± 4.7 months with antidepressant treatment maintained (N; eq 1,663) vs. 14.2 ± 0.5 months after stopping it (n = 952). Neither a longer period of stabilization on treatment nor gradual discontinuation (dose-tapering or discontinuing longer-acting antidepressants) was associated with lower relapse risk.

Conclusions: These findings differ appreciably from analyses for bipolar disorders and schizophrenia in that time-to-relapse was longer, not clearly related to the rapidity of drug discontinuation, and related inversely to the preceding length of stabilization. These differences are provocative and may suggest the diagnostic heterogeneity of major depressive disorders as compared with bipolar disorder and schizophrenia.

NR116 Monday, May 19, 3:00 p.m.-5:00 p.m.

Risks of Discontinuing Maintenance Treatment in Pregnant Women with Bipolar Disorder

Adele C. Viguera, M.D., Department of Psychiatry, Massachusetts General Hosp, Warren 605 Fruit Street, Boston MA 02114; Ruta M. Nonacs, M.D., Lee S. Cohen, M.D.

Summary:

Abrupt discontinuation of maintenance psychotropics can be followed by a high risk of early relapse. This risk is best quantified for the discontinuation of lithium therapy in bipolar disorder in which risk of mania, depression and suicidal behavior may rise. These data have been collected in nongravid cohorts. However, women planning pregnancy must weight the risks of continuing medications and prenatal exposure against risks of relapse in the setting of stopping their medications. For patients who choose to stop medications, the risks of gradual or rapid discontinuation on their course of bipolar disorder have not been quantified in this unique population.

This retrospective study describes the course of a cohort of 20 women with bipolar disorder during pregnancy and the postpartum whose maintenance medications were discontinued either abruptly or gradually. The rate of discontinuation of maintenance medications and its relationship to the time to relapse or subsyndromal worsening were recorded. Kaplan-Meier survival analysis will be presented that describes the time to relapse after abrupt versus gradual discontinuation of maintenance medications. The extent to which gradual discontinuation limits risk of relapse in this population will also be discussed. The implications of these findings for the management of this population will be reviewed.

NR117 Monday, May 19, 3:00 p.m.-5:00 p.m.

Risperidone Metabolism and Drug Interaction in Treatment-Refractory Patients

Jayme A. Bork, D.O., Department of Psychiatry, University of Kentucky, 206 Med Ctr Annex 4, Rm 213, Lexington KY 40536; Thea Rogers, Pharm D., Peter Wedlund, Ph.D., Wendy Chou, Pharm D., Jose de Leon, M.D.

Summary:

Background: Recent literature suggests that risperidone is primarily metabolized by the cytochrome P450 2D6 (CYP 2D6). This enzyme converts risperidone to 9-hydroxyrisperidone, an active metabolite. Approximately 7%–10% of the Caucasian population are poor CYP 2D6 metabolizers. It has been suggested that being a poor CYP 2D6 metabolizer does not have important implications since the total moiety (risperidone and 9-hydroxyrisperidone) is what is important.

Methods: Risperidone and 9-hydroxyrisperidone plasma concentrations were measured in 11 patients from a unit for treatment-refractory patients at Eastern State Hospital (Lexington, KY). Most patients were taking several medications. Plasma concentrations of risperidone and 9-hydroxyrisperidone were monitored as other medications were changed. The genotype for CYP 2D6 was also measured to establish the contributing effect of being a poor vs. an extensive metabolizer.

Results: As expected, the ratio risperidone/9-hydroxyrisperidone was disturbed by having a CYP 2D6 poor metabolizer genotype or taking drugs that inhibit or compete with CYP 2D6. Drugs inducing, competing with, or inhibiting the CYP 3A also appear to influence risperidone clearance, although this has not been previously described. The possible clinical implications of risperidone metabolism by CYP 2D6 and CYP 3A are discussed.

NR118 Monday, May 19, 3:00 p.m.-5:00 p.m.

SSRI Interactions with Warfarin

John Snuggs, M.D., Department of Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; William J. Meek, M.D., Cheryl Preece, M.S.

Summary:

Objective: Drug interactions involving the selective serotonin reuptake inhibitors (SSRIs) have been well documented. One potential interaction involves the use of SSRIs with warfarin or coumadin. Many scientific journals have published case reports in which the use of SSRIs with warfarin has resulted in significantly increased anticoagulation. The purpose of this study is to evaluate the possible occurrence and significance of a drug interaction between the SSRIs and warfarin among a large clinical sample.

Methods and Materials: Electronic medical records for Scott and White Clinic patients taking SSRIs in conjunction with warfarin during the period of September, 1993 to November, 1996 were considered eligible for review. A total of 133 patients were eligible and the records were reviewed by a physician.

Results: A preliminary review resulted in the identification of one case in which a dramatic increase in anticoagulation was directly correlated with the initiation of fluoxetine in a patient taking warfarin. More detailed information has been gathered on the entire group and is well documented in the final manuscript.

Conclusions: A potentially serious drug interaction may occur in a small group of patients who are started on an SSRI while taking warfarin for anticoagulation therapy. Future studies need to identify potential risk factors among this group of patients.

NR119 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Tolerability of Oral Loading of Divalproex Sodium in Acute Mania

James M. Martinez, B.A., Department of Psychiatry, UTMB at Galveston, 301 University Blvd/Graves Bld, Galveston TX 77555; James M. Russell, M.D., Robert M.A. Hirschfeld, M.D.

Summary:

Objective: In a recent study of valproate in acute mania, most of the clinical response appeared within one to four days of achieving serum valproate levels of 50 mg/L or greater. This study attempts to demonstrate that acutely manic patients can be safely loaded with 30 mg/kg/day of divalproex sodium in an attempt to achieve high-therapeutic serum levels (80–120 mg/L) quickly.

Method: Twelve acutely manic patients were loaded with divalproex sodium at 30 mg/kg/day for two days, and then maintained at 20 mg/kg/day thereafter. Serum valproate levels were drawn 48 to 72 hours after the initial loading dose, and Brief Psychiatric Rating Scale (BPRS) scores were recorded daily. We then retrospectively reviewed the charts for any adverse changes in daily vital signs, serum liver enzymes, and complete blood counts. We also reviewed daily nursing and physician notes for any observed or reported adverse effects.

Results: Two subjects withdrew from the study and one subject was noncompliant with medications; thus, these subjects are not included in this analysis. The remaining nine subjects were responders, with a mean decrease in BPRS scores of 33.3% (mean $\pm$ SD = 33.3 $\pm$ 15.2; range: 16–56%). Six of the nine responders had serum valproate levels drawn 48–72 hours after the initial loading dose, with a mean serum valproate level of greater than 90 mcg/ml (mean $\pm$ SD = 93.5 $\pm$ 23.2; range: 56–124 mcg/ml). All of the responders tolerated the loading doses well, with only two reports of sedation and one report of nausea and emesis. A decrease in white blood cell count and low granulocyte count (count prior to load unknown) was also noted in one subject.

Conclusion: Acutely manic patients can tolerate oral loading of divalproex sodium well with minimal side effects. Further study is needed to determine if oral loading can consistently achieve high-therapeutic serum valproate levels quickly and what effect it will have on response time.

NR120 Monday, May 19, 3:00 p.m.-5:00 p.m.

Survival Analysis of Olanzapine Treatment

Svetlana L.J. Milenkovic, M.D., 341 Bloor St. West Apt 1307, Toronto ON M5S 1W8, Canada; Neil Conacher, M.D.

Summary:

All participants previously diagnosed with treatment-resistant schizophrenia and/or bipolar affective disorder, aged 18 to 55, will be included in the study. All study subjects will be admitted to the inpatient service of the Kingston Psychiatric Hospital. Prior to initiation of olanzapine treatment, baseline evaluations will be conducted using the following assessments: the Schedule for Affective Disorders and Schizophrenia Change and Psychosis and Disorganization Scale (SADS-C & PD); the Scales for the Assessment of Negative Symptoms (SANS); the Clinical Global Impres-

sions (CGI) Scale; the Simpson-Angus Neurologic Rating Scale (S-ANRS); and the Simpson Dyskinesia Scale (SDS). In addition, baseline bloodwork, EKG, and physical examination will be done on each subject. After withdrawal from all previous antipsychotic medications, study subjects will be treated openly with olanzapine according to a standardized titration and dosage schedule. During the acute treatment phase, study subjects will be evaluated for behavioral response and side effects biweekly with the SADS-C & PD, SANS, CGI, S-ANRS, and SDS. Improvement will be defined if there is a decrease of psychopathologic features for eight weeks (four consecutive biweekly ratings). Study subjects will also be rated on their level of remission at 16 weeks. Survival analysis will be used to estimate time to remission in study subjects.

NR121 Monday, May 19, 3:00 p.m.-5:00 p.m.

Serotonin Transporter Blocking Properties of Nefazodone Assessed by Measurement of Platelet Serotonin

Meena Narayan, M.D., Department of Psychiatry, Yale University, 20 York Street, New Haven CT 06510; George Anderson, Ph.D., J. Craig Nelson, M.D.

Summary:

Objective: Serotonin (5-HT) transporter blocking properties of the newly introduced 5-HT_2 antagonist nefazodone have been questioned. This study aims to determine whether nefazodone has 5-HT transporter blocking properties at clinical doses in depressed patients.

Methods: Platelet 5-HT was measured before and during treatment with nefazodone (n = 7) or a selective serotonin reuptake inhibitor (SSRI) (n = 10) in patients with major depressive disorder. Change in platelet 5-HT at 2 and ≥6 weeks was used as an index of the cumulative peripheral 5-HT uptake blockade produced by nefazodone and SSRIs. Corresponding Hamilton depression rating scale (HDRS) scores were also obtained over the course of the study.

Results: The decrease from mean baseline platelet 5-HT after SSRI treatment was significantly greater than the change after nefazodone treatment (–88% vs –3%, Mann Whitney U test, p = 0.00006). Pre-treatment platelet 5-HT, post-treatment platelet 5-HT, or percent decrease in platelet 5-HT did not correlate with percent change in HDRS scores in either treatment group.

Conclusion: It appears unlikely that therapeutic doses of nefazodone cause sustained 5-HT uptake inhibition at the platelet 5-HT transporter. The contradictory findings of previous studies will be reviewed.

NR122 Monday, May 19, 3:00 p.m.-5:00 p.m.

Divalproex Treatment of Mania in Elderly Patients

Meena Narayan, M.D., Department of Psychiatry, Yale University, 20 York Street, New Haven CT 06510; Simona Noaghiul, M.D., J. Craig Nelson, M.D.

Summary:

Introduction: Treatment of elderly manic patients remains a challenge, in part because of the problems with the use of lithium and carbamazepine in this group. Divalproex appears to be an effective alternative in younger patients, but its use has not been well studied in the elderly. This retrospective study evaluates the efficacy of divalproex in elderly hospitalized patients with mania.

Methods: Charts of consecutive patients with a diagnosis of DSM-IV bipolar I disorder, manic episode, treated with divalproex were reviewed. Response to treatment was measured using the Clinical Global Impression (CGI) Scale.

Results: Twenty-one patients with a mean age of 70.5 years (range 60 to 82 years) were identified. Thirteen of the 21 patients had a history of lithium treatment. Twenty patients with psychotic symptoms received neuroleptics during the index episode. The mean final dose of divalproex was 1405 mg/day (range 500 to 3000 mg/day) and the mean serum level was 72 ug/ml (range 31 to 106 ug/ml). Overall, 19 of the 21 patients (90%) had much or very much improvement on the CGI and were considered responders. The only remarkable side effect was sedation, which occurred in two patients and improved with reduction in divalproex dose.

Conclusions: This retrospective study suggests that divalproex is an effective treatment for mania in elderly patients and that it is well tolerated even with fairly aggressive dosing.

NR123 Monday, May 19, 3:00 p.m.-5:00 p.m.

Maladaptive Schemas and Axis II Personality Traits in Survivors of Sexual Abuse with PTSD

Naureen Atiullah, M.D., Department of Psychiatry, Brown University, 345 Blackstone Blvd/Butler Hos, Providence RI 02906; Caron Zlotnick, Ph.D., M. Tracie Shea, Ph.D., Katy Amory, B.A.

Summary:

Objective: Recently, Beck (1990) proposed that maladaptive cognitive schemas play a key role in personality dysfunctioning. The present study attempted to test Beck's predictions that each Axis II personality disorder is characterized by a subset of schemas, using a sample of female survivors of sexual abuse with post-traumatic stress disorder (PTSD).

Method: 73 patients with histories of sexual abuse and PTSD were administered the Personality Diagnostic Questionnaire-Revised and the Schema Questionnaire to provide measures of personality impairment and 13 maladaptive schemas, respectively.

Results: Correlations showed that various personality traits were significantly related to specific schemas, as proposed by Beck. These were: borderline personality and insufficient control (r = 0.65), fear of abandonment (r = 0.58), and mistrust (r = 0.42); paranoid personality disorder and mistrust (r = 0.53); dependent personality and dependence (r = 0.58); fear of abandonment (r = 0.43) and incompetence (r = 0.37); avoidant personality and defectiveness (r = 0.67) and incompetence (r = 0.52); obsessive-compulsive personality and unrelenting standards (r = 0.45) and insufficient control (r = 0.30); schizoid personality and defectiveness (r = 0.52); schizoid personality was unrelated to enmeshment (r = 0.07); schizotypal personality and mistrust (r = 0.57); antisocial personality and insufficient control (r = 0.56) and mistrust (r = 0.43); histrionic personality and insufficient control (r = 0.50), and dependence (r = 0.45).

Conclusion: Our results were generally consistent with Beck's cognitive theory of personality disorders. Future research needs to examine the generalizibility of our findings.

NR124 Monday, May 19, 3:00 p.m.-5:00 p.m.

Deficits of Recall in Depressed Patients: Evidence for a Subcortical Dysfunction in Major Depression

P.H. Fossati, M.D., Department of Psychiatry, Pitie Salpetriere, Boulevard De L'Hopital, Paris 13, France; Be Deweer, Ph.D., Na Raoux, Ph.D., J.F. Allilaire, M.D.

Summary:

Objective: To assess encoding and retrievial processes and to define the nature of memory failure associated with depression.

Methods: Ten inpatients with depression and ten normal controls were assessed with a neuropsychological battery including: explicit memory tasks (California Verbal Learning Test and Grober & Buschke's procedure); implicit memory tasks (Word

Completion and Word Completion with new-association); frontal tasks (verbal fluency, cognitive estimate, Nelson's test).

Results: Although there was no difference between patients and controls on implicit memory tasks and frontal tasks, patients exhibited a deficit in explicit verbal learning. Depressive subjects performed poorly in free recall and demonstrated poor consistency. Patients show normal free recall improvement across trials. Despite a control of encoding processes, free recall measure revealed significant differences. Patients recalled almost all items when semantic cues were provided. Recognition results showed a ceiling effect.

Discussion: Depressive subjects exhibited a deficit in free recall and poor consistency, while cued recall and recognition were normal. Patients' results are characterized by difficulties in maintaining retrieval strategies. Memory failure in depression could reflect an impairment in processes depending on executive functions controlled by the subcortical structures.

NR125 Monday, May 19, 3:00 p.m.-5:00 p.m.

Preliminary Analysis of a Self-Report Questionnaire of Affective Temperament

Rustin R. Berlow, M.D., Department of Psychiatry, University of CA/San Diego, PO Box 721047, San Diego CA 92172-1047; Mauro V. Mendlowicz, M.D., Jose Montes, M.D., Mark H. Rapaport, M.D., John R. Kelsoe, Jr., M.D., Hagop S. Akiskal, M.D.

Summary:

Objective: We report preliminary data supporting the development of a self-report questionnaire to evaluate temperament.

Method: Akiskal has operationalized four temperaments, hyperthymic, dysthymic, cyclothymic, and irritable in a set of 56 questions, 14 for each temperament. These true-false questions define aspects of each temperament which an individual might endorse. A sample of 197 subjects-inpatients, outpatients, and controls-completed a prototype self-report instrument. Data were analyzed using (unrotated) Principal Components Analysis. Secondary analysis used Varimax Rotation.

Results: Of 14 possible, the mean number (and std dev) of endorsed items for each scale was: dysthymic 5.4 (3.2), cyclothymic 4.2 (3.2), hyperthymic 4.7 (3.7), and irritable 3.3 (3.2). Four factors were identified (corresponding to the four temperaments), with Eigenvalues of: 11.7, 7.4, 2.8, and 2.6. Examination of the questions using Varimax Rotation showed strong loading, consistent with theoretical and clinical expectations. Factor loadings greater than 0.4 were obtained for 10/14 dysthymic (71.4%), 11/14 cyclothymic (78.6%), 11/14 hyperthymic (78.6%), and 9/14 irritable (64.3%), questions.

Conclusion: Our data, combined with prior studies, suggest that it is possible to develop and validate a self-report measure to assess affective temperament.

NR126 Monday, May 19, 3:00 p.m.-5:00 p.m.

Psychotic Depression as a Separate Entity

Marcelo F. Mello, Ph.D., Department of Psychiatry, Universidade S Paul, Teodoro Sampaio 352 c101, Sa Paulo SP 05406-000, Brazil; Helio Elkis, Ph.D., Vania Baggio, M.D., Monica G. Cereser, M.D.

Summary:

Psychotic depression is considered by many as a separate entity. We compare retrospectively psychotic depressive patients with those with schizophrenic disorder and nonpsychotic depression. A randomized sample of 150 records of outpatients with a diagnosis of depressive episode and schizophrenia were analyzed from a total of 1,895 outpatient (Santa Casa-SP Brazil), during 1996. The bipolars were excluded. Complete demographic and psychopathological measures, and treatment information of present and past episodes were collected. The diagnoses were confirmed using DSM-IV. The sample was subdivided into three groups: MDD with psychotic symptoms, MDD without psychotic symptoms, and schizophrenic disorder. Using factor analyses and T tests, we found significant differences between MDD without psychotic symptoms and the schizophrenics in measures of outcome and demographic data, but there were no differences between the psychotic depression group and the schizophrenic group of patients. These results reinforce the thesis from some authors that psychotic depression is a separate entity that shares characteristics of both groups and has its own peculiarities. More prospectives studies with structured diagnostic interviews must be done to answer some questions of the validity of this concept.

NR127 Monday, May 19, 3:00 p.m.-5:00 p.m.

Kindling Effect in Bipolar Disorder

Diego J. Palao, M.D., Department of Psychiatry, Mollet Hospital, Cristobal Colon; 1, Mollet Barcelona 08100, Spain; Myriam Cavero, M.D., Inma Jodar, Ph.D., Manuel M. Marquez, M.D., Carlos Lopez, M.D.

Summary:

Introduction: The kindling model applied to bipolar disorder (BD) is based on neuroelectric phenomena and the effect of some psychotropic drugs. The only evidence supporting this model arises from retrospective studies in which fewer life events (LE) are associated with recurrent affective episodes than to first episodes.

Objective: We sought to study the kindling effect in BD, emphasizing some methodological problems of previous reports.

Methods: Twenty-six randomly selected bipolar outpatients (DSM-IV) were administered the Scale of Assessment of LE and Social Support of the Department of Mental Health of California (1981). We analyzed the relationship between independent LE associated with first episode and with two following ones.

Results: We did not find a greater frequency of LE previous to the first episode in relationship to following ones; a negative association was found ($p < .02$). There were no differences in LE according to kind of first episode (hypomanic, manic, or depressive). We did not find differences in social support during the first episode and at the present ($p > .05$).

Conclusions: The existence of kindling effect in BD was not replicated. No differences were found in LE between manic/hypomanic episodes and depressive episodes. Social support did not decrease over the course of illness.

NR128 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Recognition and Diagnosis of Bipolar II Disorder

Phillip W. Antunes, M.D., Department of Psychiatry, Scott and White Hospital, 2401 South 31st Street, Temple TX 76508; Jack D. Burke, Jr., M.D., Kimberly C. Burke, M.S., Cheryl Preece, M.S., Sheree Atkinson

Summary:

Objective: The purpose of this study is to examine how frequently bipolar II disorder is considered and diagnosed in a large psychiatric outpatient setting.

Methods and Materials: Medical records for outpatients seen in the Department of Psychiatry at Scott and White Clinic in Temple, Texas from July 1, 1994 to July 1, 1996 were reviewed by trained staff. Data were collected on demographics, psychiatric and medical diagnoses, symptoms of hypomania and mania, as well as illicit drug and alcohol use.

Results: Initial analyses of 1,000 patients newly diagnosed with major depressive disorder during the time frame indicate that

inquiry regarding symptoms of hypomania were documented in only 38% of the cases. Bipolar II disorder was initially diagnosed in 114 patients.

Conclusions: Although the diagnostic entity of bipolar II disorder has been included in the DSM-IV, it is often not considered and may be underdiagnosed at initial presentation by depressed patients.

NR129 Monday, May 19, 3:00 p.m.-5:00 p.m.

Frontal Cognitive Deficit and Psychomotor Retardation

Paul Jacques, M.D., Department of Psychiatry, Hop. Enfant-Jesus, 1401 18eme Rue, Quebec PQ G1J 1Z4, Canada; Philippe Baruch, M.D., Sophie Lemlin, Ph.D.

Summary:

Psychomotor retardation has always been considered a clinical component allowing the categorization of depressed patients and constitution of more homogeneous groups. Recent works in functional imaging (Dolan and Bench, 1993) support the hypothesis that retarded patients present a frontal hypometabolism independent of the affective illness severity.

Objective: To compare, in a group of patients with major depressive disorder with and without clinical psychomotor retardation, the performance of cognitive tasks that classically assess the frontal lobe functions.

Method: Twenty-seven untreated patients (men = 13, women = 14, age = 42.6 ± 6.1) with major depressive episode (DSM-IV) were evaluated clinically with global depressive scales (Hamilton-21 items, Montgomery-Asberg), anxiety scale (Covi), and with the Depressive Retardation Rating Scale (DRRS). Neuropsychological battery consisted of the following tests: Wisconsin Card Sorting Test, Trail Making Test, Verbal Fluency, Motor Sequence, and the Wechsler vocabulary test. The results were categorically (retarded vs. nonretarded) and dimensionally (correlation computed on the whole group) analyzed.

Results: Patients with (n = 13) and without (n = 14) psychomotor retardation were comparable for age, education level, score on the Wechsler Vocabulary Test, anxiety level (Covi), and the global intensity of the depression according to HDRS. However, patients with psychomotor retardation were more impaired on several neuropsychological tasks (WCST-category and perseverative errors, Trail Making Test A and B, Motor Sequence). When the whole group of patients were considered, significant correlations were found between these cognitives parameters and DRRS (correlation from 0,452 to 0,629), but nor HDRS neither MADRS.

Conclusion: This study shows that compared to the nonretarded depressive, the patients with psychomotor retardation exhibit a more severe impairement on frontal-type cognitive tasks.

NR130 Monday, May 19, 3:00 p.m.-5:00 p.m.

Gabapentin for Mood Instability Associated with Migraine

Turai S. Kumaran, M.D., Department of Psychiatry, St. Francis Medical Center, 410-B Glen Malcolm Drive, Glenshaw PA 15116; Manohar K. Shetty, M.D., David J. Lynn, M.D.

Summary:

Introduction: Two anticonvulsants, valproate and carbamazepine, have been used for mood stabilization. We looked at the effects of a new anticonvulsant, gabapentin, on mood stabilization on specific groups of patients.

Method: The characteristics of the patients chosen were: females aged 29 to 40 with symptoms of irritability and dysphoria with premenstrual exacerbation: incomplete response to antidepressants; migraine headaches with poor compliance with sumatriptan. Excluded from the study were patients taking approved mood stabilizers; showing mania, hypomania, or suicidal ideation; or current or past use of gabapentin. After using specific parameters for affective disorder, we started patients on gabapentin. Patients have been followed for five months as of 12/1/96.

Results: Patients reported a decrease in their irritability, dysphoria, and premenstrual exacerbation. Compliance with psychotherapy and social functioning improved. Sumatriptan was discontinued at the end of one month because of marked reductions in migraine attacks.

Discussion: This is a nonconventional use of gabapentin in a specific group of patients who do not have classical bipolar disorder. Gabapentin seemed to have mood-stabilizing effects in this group with premenstrual exacerbation of irritability. It also prevented migraine symptoms. This is a preliminary study; its limitations are small number of cases, open design, and lack of a control group. Our findings suggest that a larger and more elaborate study be done.

NR131 Monday, May 19, 3:00 p.m.-5:00 p.m.

Affective Symptoms from Corticosteroids: A Hypothesis for Bipolar Disorder

E. Sherwood Brown, M.D., Department of Psychiatry, UT Southwestern, 5323 Harry Hines Blvd/Box 9070, Dallas TX 75235; Trisha Suppes, M.D., David A. Khan

Summary:

Objective: Corticosteroids, such as prednisone, are commonly prescribed medications given for a variety of illnesses mediated by the immune system. The literature on mood symptoms during corticosteroid therapy is reviewed.

Method: A search of the MEDLINE data base was conducted to obtain papers addressing mood symptoms during corticosteroid therapy.

Result: A total of 28 papers are included in the review. The limited data available suggest that psychiatric symptoms are common and include mania, depression, mood lability, and psychosis. The symptoms appear to be dose-dependent, but other risk factors and the effects of multiple courses are not known. Some data suggest that the mood symptoms during corticosteroid therapy respond to lithium and sometimes worsen with the use of tricyclic antidepressants.

Conclusions: The data are surprisingly limited. However, the symptoms reported and treatment responses are strikingly similar to those observed in persons with bipolar disorder. Thus these symptoms may provide a model for bipolar disorder and suggest further investigation of the role of endogenous steroids in mood regulation is needed. Previously presented, in part, at the 1996 ACNP meeting. The basis of an ongoing project supported, in part, by NARSAD (ESB) and NIMH fellowship 1-F32-MH11580-01 (ESB).

NR132 Monday, May 19, 3:00 p.m.-5:00 p.m.

Catecholamine Depletion in Euthymic Subjects with a History of Major Depression

Robert M. Berman, M.D., Department of Psychiatry, West Haven VAMC, 950 Campbell Avenue/116A, West Haven CT 06516; Helen L. Miller, M.D., Angela C. Cappiello, M.D., Amit Anand, M.D., Dan A. Oren, M.D., Dennis S. Charney, M.D.

Summary:

*Objective:*This study explores the role of catecholamine function in euthymic unmedicated subjects with a remote history of major depression, employing a methodology to deplete brain catecholamines via administration of alpha-methyl-para-tyrosine (AMPT), a potent inhibitor of the rate-limiting step in catecholamine synthesis.

Method: Subjects underwent two sets of studies days in a double-blind, random-ordered, crossover design. They received either active catecholamine depletion (via administration of 5 mg of AMPT) or sedation-controlled, sham catecholamine depletion (via administration of 250 mg of diphenhydramine), over a two-day observation period. Behavioral ratings included the 25-item Hamilton Depression Rating Scale (HDRS).

Results: To date, seven subjects have completed the protocol and one terminated early. When undergoing active depletion, subjects commonly experienced marked increases in HDRS scores (mean ΔHDRS = 15.6, SD = 10.6); whereas during control depletion, subjects did not experience significant HDRS increases from baseline (mean ΔHDRS = 2.5, SD = 3.7; paired t-test $p = 0.03$). Four of eight subjects undergoing active depletion experienced greater than a 20-point increase in HDRS scores.

Conclusion: Depressive reaction to catecholamine depletion may represent a reliable marker for a history of depression. Further work is needed to clarify the significance of this finding.

NR133 Monday, May 19, 3:00 p.m.-5:00 p.m.

Analysis of Psychomotor Function Using Q-Sort Methodology

Shragit Glassman, M.D., Department of Psychiatry, University of Toronto, 2075 Bayview Avenue, North York ON M4N 3M5, Canada; Neil Westrich, M.D., Michael Bagby, Ph.D., Kathryn Parker, Anthony J. Levitt, M.D.

Summary:

Objective: This study evaluates agreement between experts on the description of the four possible components of psychomotor function; namely motor agitation (MA), motor retardation (MR), psychic agitation (PA), and psychic retardation (PR).

Method: Eighty statements were generated from existing interviews and questionaires to reflect patients' experience of the psychomotor function, 20 for each of component. Twenty experts in the phenomenology of psychiatric illness were asked to rank the items using a q-sort method. Each clinical performed a q-sort for each component, separating the 20 statements into a forced five-category distribution; that is 1 = least characteristic to 5 = most characteristic. Each category was permitted only four items. Overall sum score for each statement were calculated and the statements were then re-sorted into a "prototype" ranking for each component.

Results: Using Spearman coefficients, the correlations between raters and the prototype ranged from .43 to .77 ($p < .0001$) with a mean ($\pm$SD) of .60 ($\pm$.1). Spearman Brown split-half coefficient, used to test the reliability (internal consistency), was as follows: MA = .94, MR = .93, PA = .85, and PR = .92.

Conclusions: Therefore, each of the four components of psychomotor function can be described with a high degree of reliability and consistency by expert clinicians. Definition of these four components has diagnostic and, possibly, prognostic value in psychiatric illness.

NR134 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Anticonvulsant Lamotrigine in Treatment-Resistant Manic-Depressive Illness

Jonathan Sporn, M.D., Department of Psychiatry, Mass General Hospital, 815 WACC/15 Parkman Street, Boston MA 02114; Gary S. Sachs, M.D.

Summary:

Objectives: Anticonvulsants are used extensively in the treatment of bipolar disorder. Treating depression in bipolar disorder can be difficult due to the limited antidepressant effects of the standard mood stabilizers and the tendency of antidepressants to induce mania or decrease cycle length. Lamotrigine is a new anticonvulsant with few side effects that may have mood stabilizing and elevating effects. Its mechanism of action probably involves the inhibition of excessive release of excitatory amino acids such as glutamate. Decreasing glutamate activity may be antidepressant and mood stabilizing.

Methods: A case series of 16 patients treated with lamotrigine (dose range 50 mg–250 mg, mean dose of good responders = 141mg.) is presented along with two case reports. All patients were considered treatment-resistant bipolar type I or II. Patients were rated on average five weeks after starting lamotrigine using a semistructured follow-up form that includes symptom rating, CGI, and GAF scores.

Results: Eight of the 16 patients were rated as "good responders" (CGI#2) and had a mean increase in their GAF of 16.

Conclusion: Lamotrigine appears to have antidepressant and mood stabilizing effects but this requires confirmation in randomized controlled trials.

NR135 Monday, May 19, 3:00 p.m.-5:00 p.m.

Suicidal Ideation During Pregnancy

Cassandra P. Morabito, M.Ed., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WAC 815, Boston MA 02114; Lee S. Cohen, M.D., Jennie W. Bailey, B.A., Mary H. Collins, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Introduction: Studies of suicide during pregnancy suggest that pregnant women are less likely to commit suicide than nonpregnant women. However, suicidal ideation during pregnancy has not been studied. This report describes the frequency of suicidal ideation in a cohort of women with a history of major depression who were prospectively followed during pregnancy.

Methods: Women with a history of a major depression were accessioned into a naturalistic longitudinal study of the course and treatment of psychiatric illness during pregnancy and the postpartum period. These women were evaluated at each trimester for presence or absence of mood symptoms using the depression module of the Structured Clinical Interview for the DSM-IV, Hamilton Depression Rating Scale, and Beck Depression Inventory. The relationship between suicidal ideation and variables including (1) severity of illness prior to pregnancy, (2) severity of affective disorder at time of assessment, (3) suicidal ideation during past worst episode of depression, and (4) treatment status (pharmacologic and nonpharmacologic) was investigated.

Results: Of 30 women, eight had suicidal ideation during at least one trimester of their pregnancy as measured by at least one of the three rating scales. No suicide attempts were made.

Conclusion: While completed suicide may be uncommon during pregnancy, suicidal ideation may be more frequent. The implications of this finding for assessment of pregnant women with a history of mood disorder are discussed.

NR136 Monday, May 19, 3:00 p.m.-5:00 p.m.

A Comparison of Obstetrical Complication Rates Among Bipolar Subgroups

Claudia F. Baldassano, M.D., Department of Psychiatry, Massachusetts General Hospital, WACC 815/15 Parkman Street, Boston MA 02114; Una Jain, B.A., Amy E. Shriver, B.A., Gary S. Sachs, M.D.

Summary:

Objective: Obstetrical complications have been associated with several psychiatric illnesses including bipolar mood disorder. This poster compares obstetrical complication rates in subgroups of

bipolar patients (e.g., early onset versus late onset type, bipolar I vs. bipolar II and male vs female).

Methods: Birth history questionnaires (personal and birth history of children) sent to all patients participating in the MGH bipolar clinic were harvested along with demographic and clinical data from standardized evaluation forms. All patients meeting DSM-IV criteria for bipolar disorder who completed a personal birth history questionnaire were included. Diagnosis and age of onset were established using SCID mood modules modified to determine age of first depression, hypomania, mania, or mixed episode. Subjects were classified as early onset probands if their first episode occurred prior to age 19.

Results: Preliminary results for 36 bipolar patients (26 type I and 10 type II) yield a complication rate of 8%. The observed complication rate in the analyzed subgroups did not differ significantly. However, the observed trends suggest a larger sample (n = 100 subjects) may yield significant results.

Conclusion: Examining obstetrical complication rates may be useful in understanding the differences between bipolar subgroups, but large samples are necessary to obtain statistical power.

NR137 Monday, May 19, 3:00 p.m.-5:00 p.m.

Chronic Choline Administration Does Not Increase Brain Choline:Creatine

Christina M. Demopulos, M.D., Department of Psychiatry, Mass General Hospital, ACC 815/15 Parkman Street, Boston MA 02114; Perry F. Renshaw, M.D., Gary S. Sachs, M.D., Una Jain, B.A., Andrew L. Stoll, M.D., Amy E. Shriver, B.A.

Summary:

Objective: Magnetic resonance spectroscopy (MRS) demonstrates increases in brain choline:creatine following acute administration of exogenous choline. This study sought to determine the effect of chronic choline administration.

Methods: MRS was used to measure brain choline in rapid-cycling bipolar patients during a double-blind study of choline versus placebo. Investigators blind to treatment used MRS to determine basal ganglia Cho:Cr at baseline, after two weeks placebo administration, and after three, five, eight, and 12 weeks of treatment.

Results: Preliminary analysis of seven subjects for whom longitudinal data are available reveals no significant differences at baseline in Cho:Cr. During the double-blind phase, one of four placebo-treated patients and two of three choline-treated patients experienced increases of 0.075 or greater in Cho:Cr. In no subject did this increase persist beyond the fifth week of treatment. Mean change from baseline Cho:Cr was not significant at any point in the study.

Conclusion: This preliminary analysis raises concern. Acute changes in Cho:Cr produced by exogenous choline may not persist. Should this result be confirmed, studies of the clinical efficacy of choline must determine if efficacy is correlated with acute or chronic change in Cho:Cr.

NR138 Monday, May 19, 3:00 p.m.-5:00 p.m.

Antidepressant Withdrawal-Induced Mania

Amy E. Shriver, B.A., Department of Psychiatry, Massachusetts General Hospital, ACC 815/15 Parkman Street, Boston MA 02114; Claudia F. Baldassano, M.D., Christina M. Demopulos, M.D., Una Jain, B.A., Gary S. Sachs, M.D.

Summary:

Objective: To investigate the prevalence of antidepressant-withdrawal-induced mood elevation in bipolar patients.

Method: Patients at the Massachusetts General Hospital Bipolar Mood Disorder Clinic meeting DSM-IV criteria for bipolar illness were followed using a systematic follow-up procedure. At each visit, the SCID mood disorder modules were completed, a clinical status was assigned, and all treatments were recorded. Data harvested from the charts were used to determine mood-elevation episodes for each patient. Treatments used during the two-week interval prior to onset of each mood-elevation episode were recorded to determine if the episode was "spontaneous," associated with "antidepressant use," or was associated with "antidepressant dosage decrease or discontinuation."

Results: Chart review identified 93 episodes of mood elevation (hypomania, mania, or mixed) in 37 patients over a five-year period. Of these, 9% met our criteria for being associated with a decrease or discontinuation of antidepressant therapy. Two of these patients had repeated episodes of mood elevation associated with a decrease or discontinuation of antidepressants.

Conclusions: Our results demonstrate that a small but clinically important percentage of mood elevation observed in our clinic is associated with withdrawal of antidepressant medication. This observation suggests caution is necessary when discontinuing antidepressant therapy in bipolar patients.

NR139 Monday, May 19, 3:00 p.m.-5:00 p.m.

Anger Attacks in Bipolar Depression Versus Unipolar Depression

Una Jain, B.A., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 815, Boston MA 02114; Vinita C. Leslie, M.A., Bronwyn R. Keefe, B.A., Gary S. Sachs, M.D., Maurizio Fava, M.D.

Summary:

Objective: Anger attacks are reported commonly among depressed patients. The relationship of anger attacks to bipolar or unipolar depression is unclear. We hypothesized a higher frequency of anger attacks in bipolar than in unipolar depression patients.

Methods: Patients entering the Bipolar Clinic and the Depression Clinic at Massachusetts General Hospital complete a packet of self-rated forms including an Anger Attacks Questionnaire (designed by Maurizio Fava, M.D.). Evaluations including SCID mood disorder modules were performed by trained research psychiatrists.

Results: A preliminary analysis compared the prevalence of anger attacks in the month before study entry in 100 depressed patients (unipolar = 50, bipolar = 50). While 17 (34%) of the 50 unipolar depressed patients reported anger attacks, none (0%) of the bipolar depressed patients experienced these attacks. This difference is statistically significant ($p < 0.001$).

Conclusion: These results are contrary to our hypothesis. The absence of anger attacks in depressed bipolar patients may simply reflect the high frequency of angergic depression in these patients (mixed episodes were excluded); however, anger attacks have been associated with nonmelancholic ("atypical") forms of unipolar depression. If confirmed by a larger study these results suggest the absence of anger attacks during depression may be more characteristic of bipolar than unipolar patients.

NR140 Monday, May 19, 3:00 p.m.-5:00 p.m.

SAD Treatment: Light Box Versus Dawn Simulator, A.M. Versus P.M.

Paul Desan, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 815, Boston MA 02114-2438; Christine J. Truman, B.A., Una Jain, B.A., Claudia F. Baldassano, M.D., Dina R. Hirshfeld, Ph.D., Gary S. Sachs, M.D.

Summary:

Objective: To evaluate the comparative efficacy of four treatment regimes for seasonal affective disorder: light box or dawn simulator in the early morning or the late afternoon. It was anticipated that afternoon treatment with the dawn simulator would be an inactive placebo.

Method: Patients meeting the DSM-IV criteria for depression with seasonal pattern, with Hamilton-31 score greater than 19 were randomly assigned to either 10,000 lux light box treatment for one hour or to dawn simulation with a 50 watt halogen desk lamp and randomly assigned to treatment at either 6–8 a.m. or 4–6 p.m. Patients were rated by interviewers blind to treatment condition at 1, 2, 4, or 6 weeks. Ratings were analyzed by ANOVA (Fisher's correction) with last observation carried forward (LOCF).

Results: Results collected for 34 patients in 1994–95 and 1995–96 found no significant differences among the groups, with mean ± s.e. Ham-31 ratings of 27.9 ± 0.8 at baseline, 16.0 ± 1.6 at 2 weeks and 9.2 ± 1.6 at 6 weeks, with a trend towards highest ratings in the afternoon dawn simulation at 2 weeks. Additional subjects studied during this year will be presented.

Conclusion: Results from this preliminary study are consistent with the original hypothesis, but do not reach significance.

NR141 Monday, May 19, 3:00 p.m.-5:00 p.m.

Comorbidity of Social Phobia and Personality Disorders

Antonio E. Nardi, M.D., Department of Psychiatry, Federal University Rio, R. Visconde de Piraja, 407/702, Rio De Janeiro RJ 22410-003, Brazil; Ivan Figueira, M.D., Marcio V. Versiani, M.D.

Summary:

Objective: Social phobia is frequently associated with other disorders. We decided to investigate the personality disorders (PD) in a group of social phobics before drug treatment.

Method: 57 social phobics (DSM-IV) selected for drug treatment in the Anxiety and Depression Research Program - Federal University of Rio de Janeiro, were examined for PD. They had four interviews with two investigators based on the DSM-IV axis II criteria. A family member was also interviewed.

Results: Generalized social phobia was observed in 40 (70.2%) patients; in 36 (90%) of them the diagnosis of avoidant PD was also identified. None of the circumscribed patients (17, 29.8%) met the criteria for avoidant PD. Dependent PD was observed in 33 (57.9%) and obsessive-compulsive PD in 14 (24.6%). Paranoid PD was noted in 6 (10.5%) patients. Only 9 (15.8%) patients had no PD. Two PD were identified in 32 (56.1%) patients: avoidant + dependent in 22 (38.6%) and avoidant + obsessive-compulsive in 10 (17.5%).

Conclusion: PD is very frequent in social phobia, especially in the generalized subtype. Comorbid disorders may increase the personal distress and impairment and may be a predictor of poor therapeutic response.

NR142 Monday, May 19, 3:00 p.m.-5:00 p.m.

Discontinuation of Long-Term Benzodiazepine Use: Predictive Model of Success in a Double-Blind, Controlled-Study

Elie G. Hantouche, M.D., SHU, St Anne Hospital, 29 Av Georges Bernanos, Paris 75005, France; Luc Jacob, M.D., Denis Comet, M.D., Professor Julien-Dan Guelfi

Summary:

Objective: To evaluate the efficacy of α-β L-aspartate magnesium (Asp Mg) in discontinuation of long-term benzodiazepine use and to search for a predictive model of success for BZD cessation.

Method: Using a double-blind procedure, 144 patients selected as chronic users of one of three BZD (lorazepam, alprazolam, or bromazepam; duration of use > 6 months; regular dose ≥ 3 mg lorazepam equivalent) and with clinical remission (HAM-Anxiety <14; Raskin-Depression <6) had entered a controlled study (versus placebo) and were randomized in two parallel groups. The trial was conducted on three consecutive phases: co-administration of Asp Mg or placebo with BZD during one month; gradual taper of BZD during one month; follow-up during a third month after complete BZD discontinuation, with urinary BZD control on d75 and d90.

Results: The intent-to-treat analysis showed at the endpoint an overall rate of 80% of "BZD discontinuation" and of 35.4% of "BZD cessation without withdrawal" in the total population (no intergroup differences were observed on these rates). However, there were positive differences between Asp Mg versus placebo on the following: 1) prolonged delay of BZD use if reuptake (30 days vs 20 days, p [log-rank] = 0.5); 2) reduction of withdrawal intensity assessed by: 11% of important difficulties during BZD cessation versus 23% with placebo (p = 0,2) and on Tyrer Withdrawal Questionnaire (BWSQ) (final score 4.0 vs 4.8, p = 0.10); 3) lower modification of anxiety during BZD tapering and discontinuation (Δ HAM-A between d30-d90 of 6% vs 23% in placebo group, p = 0.10). Moreover, three predictive factors of "success" (BZD cessation without withdrawal phenomenon) were identified by uni and multivariate analysis (with logistic regression): chronicity of anxiety disorder (p = 0.04); initial score of STAI-Trait (p = 0.002) and amplitude of change BWSQ during tapering phase (p < 0.0001). This last parameter was the most important predictive factor: a change of 2 points on BWSQ was equivalent to 22 years of anxiety duration, on success probability. The quality of this model is quite satisfactory (r^2 = 39% and concordance = 83%).

NR143 Monday, May 19, 3:00 p.m.-5:00 p.m.

Prevalence of Psychopathology in Families of Patients with OCD

Kurt K. Hubbard, B.A., Department of Psychiatry, North Shore Hospital, 400 Community Drive, Manhasset NY 11030; Andrew Shack, M.A., Juliana R. Lachenmeyer, Ph.D., Regina Ucello, B.A., Kevin B. Handley, M.A.

Summary:

Research on the relationship between obsessive-compulsive disorder (OCD) and psychopathology in family members does not indicate a clear relationship. Paulis (1995) suggests that the reason for the mixed findings is because OCD is a heterogeneous disorder. Rausmussen (1993) states that most studies report a relationship between OCD and family psychopathology, but the question of what specific disorders or symptomatology "predisposes" an individual for OCD has not been thoroughly addressed. The present study asked OCD patients (N = 45) about psychiatric history of family members. OCD was assessed using SCID-IV and the Yale-Brown Obsessive Compulsive Scale. The Global Assessment of Functioning (GAF) was also administered. Data indicate that there is a significant relationship between family psychopathology and OCD, with 82% reporting psychopathology in the family (of these, 86% were parents). Fifty-five percent of the OCD patients reported having a family member with OCD. Depression was reported in 42% of family members. GAF scores for those individuals who reported family psychopathology were significantly lower (p > .05) than those who reported no psychopathology. Clinical issues involving the role of family psychopathology in the development, maintenance, and treatment of OCD will be addressed.

NR144 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Effect of CCK-4 in Social Phobia and OCD

Martin A. Katzman, M.D., Department of Psychiatry, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Jacques Bradwejn, M.D., Diana Koszycki, Ph.D., F. Vaccarino, Ph.D., Margaret A. Richter, M.D.

Summary:

Objective: The CCK receptor agonist, CCK-4, produces robust panicogenic effects in panic disorder (PD) patients, presumably via a CCKergic mechanism. The aim of this study was to investigate the effects of CCK-4 in other diagnostic groups. We present herein preliminary data on the effects of CCK-4 in social phobia (SP) (n = 4) and obsessive-compulsive disorder (OCD) (n = 6).

Method: A single (subject)-blind, placebo-controlled design was used. Acceptable subjects received a single i.v. injection of placebo followed by CCK-4 (20 μg) on the same day. Behavioral response was assessed with a DSM-IV Panic Symptom Scale (PSS) and a visual analog scale measuring anxiety and core symptoms of OCD and SP. Cardiovascular and hormonal responses were also measured. Between-group comparisons were done with Mann-Whitney and Fisher's exact tests and within-group comparisons with Wilcoxon and McNemar's tests.

Results: There were no significant between-group differences in the number and sum intensity of PSS symptoms, panic rate, and change from baseline in anxiety, heart rate, and blood pressure during CCK-4 or placebo injections. CCK-4 induced a panic attack in 1/4 SP (25%) and 2/6 (33%) OCD patients. In the OCD group, the number and sum intensity of PSS symptoms and the maximum increase from baseline in heart rate and systolic BP were greater with CCK-4 than placebo (all ps < 0.05). In the SP group, the number of PSS symptoms tended to be greater with CCK-4 (p = 0.068). CCK-4 had no effect on SP or OCD symptoms.

Conclusion: These data indicate that sensitivity to CCK-4 is comparable in SP and OCD patients. The panic rate in these patients is considerably lower than that reported in PD patients (75% to 88%), suggesting a lower sensitivity to CCK-4 in SP and OCD as compared to PD.

This study was funded by the Medical Research Council of Canada.

NR145 Monday, May 19, 3:00 p.m.-5:00 p.m.

Effects of Citalopram Treatment on Behavioral, Cardiovascular and Neuroendocrine Response to CCK Tetrapeptide Challenge in Panic Disorder Pts

Jakov Shlik, M.D., Department Psychobiology, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Anu Aluoja, M.A., Veiko Vasar, M.D., Eero Vasar, M.D., Toomas Podar, M.D., Jacques Bradwejn, M.D.

Summary:

Recent studies have shown that treatment with antipanic drugs may decrease panic response induced with cholecystokinin tetrapeptide (CCK-4) in patients with panic disorder (PD). The present study was intended to further explore the effects of treatment with a selective serotonin reuptake inhibitor (SSRI) on multidimensional sensitivity to the panicogenic effects of CCK-4 in PD. Nine PD patients were challenged with CCK-4 (20 μg) before and eight of them after eight weeks of treatment with the SSRI citalopram. All patients responded to treatment by showing a significant general improvement and reaching a panic-free state for two weeks. At the rechallenge with CCK-4, patients displayed a marked reduction in the intensity and number of panic symptoms. The frequency of panic attacks induced with CCK-4 decreased from 100% before treatment to 50%. Citalopram treatment had no substantial effects on cardiovascular (heart rate and blood pressure) or hormonal (cortisol, prolactin, growth hormone) responses to CCK-4. Patients who still panicked after the treatment demonstrated a blunted growth hormone response to CCK-4 that was not seen in non-panickers. This study suggests that successful treatment with a SSRI can reduce an enhanced sensitivity to CCK-4 without modifying cardiovascular and neuroendocrine responses to CCK-4 in panic disorder patients.

NR146 Monday, May 19, 3:00 p.m.-5:00 p.m.

Psychiatric Diagnoses of Veterans Seeking Treatment in a Trauma Recovery Unit

Cenk Tek, M.D., Department of Psychiatry, University of Maryland AB, 22 South Greene Street, Baltimore MD 21201; Stephen F. Bono, Ph.D., Pedro E. Martinez, M.D.

Summary:

Objective: This study examines the differences in psychiatric assessments of veterans with and without current PTSD who applied for treatment at a VA Trauma Recovery Unit.

Method: All veterans who applied for initial treatment at the Baltimore VA Trauma Recovery Unit between February 1996 and September 1996 were assessed via Structured Interview for DSM-III-R and Clinician Administered PTSD Scale (CAPS). Veterans also completed the Mississippi Scale for Combat-related PTSD, Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI) self-report scales; sociodemographic data were also compiled. Subjects were divided into Current PTSD vs. Non-PTSD groups based upon the CAPS results. Of the 74 first-time applicants, 54 completed the study. Serial Chi-square or T-tests were computed on the two groups.

Results: Twenty-seven (49.1%) of the subjects had current diagnoses of PTSD. There were no significant differences between groups in type of trauma, sociodemographic variables, past psychiatric treatment. Of the PTSD group, 26 (96.3%) had at least one other current psychiatric disorder, versus only 18 (65%) of the non-PTSD group. On a comparison of current and lifetime psychiatric disorders, statistically significant differences were found only with current major depression and current panic disorder. Both were more frequent in the PTSD group. No significant difference could be found between the two groups' Mississippi, BDI, or BAI scores.

Conclusion: As previously demonstrated, PTSD patients have high rates of comorbid psychiatric disorders. However, outside of major depression and panic disorder, no differences could be discerned between the two groups. These findings may be limited by the small sample size. Also, self-report scales such as the Mississippi may not be reliable in treatment-seeking populations.

NR147 Monday, May 19, 3:00 p.m.-5:00 p.m.

Dissociative Symptomatology in Patients with OCD and PTSD

Munazzah Khawaja, M.D., Department of Psychiatry, UTMB at Galveston, 301 University Boulevard, Galveston TX 77555; Teresa A. Pigott, M.D., James M. Martinez, B.A., Dennis L. Murphy, M.D., Sheila M. Seay, M.A., Jean P. Goodwin, M.D.

Summary:

Obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD) are classified as anxiety disorders in DSM-IV. Recurrent, anxiety-provoking, intrusive thoughts and/or images are common core symptoms in OCD and PTSD. The 28-item Dissociative Experiences Scale (DES) was developed to assess dissociative psychopathology. The DES has demonstrated reliability and validity as a measure of dissociative symptomatology in various psychiatric disorders. Total DES scores ≤30 are consistent with significant dissociative symptoms. Factor analysis of the DES has also identified three subscales with construct validity:

psychogenic amnesia (AM), depersonalization/derealization (D), and absorption (AB). PTSD has been associated with elevated total DES scores (mean ± SEM, 30.0 ± 1.5). With these issues in mind, the DES was administered to 51 subjects meeting DSM-IV criteria for OCD in the current study (mean age ± SEM, 38.0 ± 1.6 yr.; 30 males, 21 females). In contrast to PTSD subjects, the total DES score in the OCD patients (mean ± SEM, 12.8 ± 1.9) was similar to that reported in control subjects. DES subscale scores in the OCD patients were also similar to those reported for controls (mean ± SEM, AB, 19.9 ± 2.6; D, 9.4 ± 2.0; AM, 3.9 ± 1.2). Only five of the OCD patients (9.8%) had total DES scores greater than 30. Further analysis revealed that the OCD patients with elevated DES scores also met DSM-IV criteria for chronic PTSD. These results suggest that: a) most patients with OCD do not endorse substantial levels of dissociative symptomatology as measured by the DES; and b) a significantly elevated DES score (>30) in an OCD patient may suggest the presence of comorbid PTSD.

NR148 Monday, May 19, 3:00 p.m.-5:00 p.m.

Sensory Phenomena in Sydenham's Chorea

M. Yanki Yazgan, M.D., Department of Psychiatry, Marmara University Hospital, Altunizade, Istanbul 81, Turkey; Ayse Arman, M.D., Sennur Zaimogl, M.D., Mefkure Eraksoy, M.D.

Summary:

Sydenham's chorea (SC) has been proposed as a model to understand the role of immunologic mechanisms in TS and OCD. Sensory phenomena associated with repetitive movements in TS and OCD are thought to be central to the pathophysiology of these disorders.

Objective: To determine in SC (in contrast to TS) the presence and characteristics of the sensory phenomena associated with repetitive behaviors.

Methods: Ten SC patients (mean age: 8.7 ± 4.0) and their gender-matched TS controls without a history of streptococcal infection (mean age: 8.9 ± 3.5) participated. Diagnostic criteria: Revised Jones criteria (SC), DSM-IV. Behavioral ratings: Choreiform Movements Rating Scale, Yale Global Tic Severity Scale (YGTSS), Y-BOCS, and Children's Behavior Checklist, Sensory Phenomena Assesment Schedule (based on Leckman 1993).

Results: All but one SC patient reported experiencing sensory phenomena associated with their repetitive movements. These were mostly physical in nature (80% in SC vs 30% in TS, $p < .05$), perceived as voluntary (70% vs 80%, n.s.), relieved with the repetitive movement, and experienced in similar locations in both groups (extremities and trunk/midline). The sites of sensory phenomena and repetitive movements were different in both groups.

Conclusion: Sensory phenomena associated with repetitive movements are present in SC. Their distribution and association with the movements appear to be comparable between SC and TS. These phenomenological similarities between TS and SC deserve further research.

NR149 Monday, May 19, 3:00 p.m.-5:00 p.m.

Age of Onset of OCD as a Predictive Factor of Response to Clomipramine

Roseli Gedanke Shavitt, M.D., Department of Psychiatry, Sao Paulo University, Rua Ovidio Pires de Campos S/N, Sao Paulo 05403-010, Brazil; M. Conceicao do Rosar Campos, M.D., Euripedes C. Miguel, M.D.

Summary:

Background: Obsessive-compulsive disorder (OCD) is a chronic condition, that can bring considerable impairment to a patient's life. Recent studies suggest that OCD is a heterogeneous disorder. Pauls et al. (1995) demonstrated a genetic relationship between OCD and Tourette's Syndrome (TS). Miguel et al. (1995) observed phenomenological differences between patients with only OCD and those with OCD and TS. Recent studies suggest that early- and late-onset OCD may have different clinical profiles. The identification of OCD subgroups may lead to more specific therapeutic regimens. This study investigates the age of onset of OCD as a predictive factor of response to clomipramine.

Method: Ten consecutive, drug-free outpatients (5 men, age-range = 17–50 years) have been studied. The Structural Clinical Interview for the DSM-IV, TS-OC Questionnaire, Yale Global Tic Severity Scale, USP-Harvard Repetitive Behaviors Interview, Yale-Brown Obsessive-Compulsive Scale-YBOCS, Global Clinical Impression, Beck Depression, and Beck Anxiety Inventories were used in the first 12 weeks of exclusive clomipramine treatment (75–300 mg daily).

Results: 33% of patients with early-onset and 67% with late-onset OCD had a 40% or greater reduction in YBOCS scores by the 12th week.

Conclusions: Despite the limited number of patients studied so far, there seems to be a trend toward a better response to clomipramine for the late-onset OCD patients.

NR150 Monday, May 19, 3:00 p.m.-5:00 p.m.

Early-Onset OCD: A Different Subtype

M. Conceicao do Rosar Campos, M.D., Inst. de Psiquiatria, Rua Ovidio Pires de Campos S/N, Sao Paulo, SP Brasil; Roseli Gedanke Shavitt, M.D., Marcos Tomanik Mercadante, M.D., Euripedes C. Miguel, M.D.

Summary:

Background: Recent studies suggest that some forms of OCD may represent a variant expression of Tourette Syndrome (TS) and that patients with OCD associated with TS present more frequently "tic-like" compulsions (such as touching, rubbing, and tapping) than the OCD patients without TS. The purpose of this study is to determine whether the age of onset is another important factor in subtyping OCD and to identify possible sociodemographic, phenomenological, and comorbidity differences between OCD patients with the onset of their symptoms before the age of 10 (early onset) and after the age of 18 (late onset).

Method: We evaluated seven early-onset and nine late-onset adult OCD patients diagnosed according to the DSM-IV criteria. The Structured Clinical Interview for DSM-IV (SCID), Yale-Brown Obsessive Compulsive Scale, Yale Global Tic Severity Scale, the Beck Depression Inventory, the Beck Anxiety, and the USP-Harvard Repetitive Behavior Interview were administered to all patients.

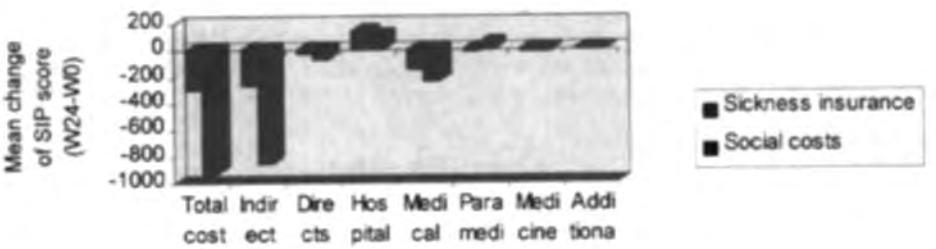
Results: "Tic-like" compulsions were present in 38% of the early-onset group compared to 13% in the late-onset one ($p < 0.05$). Thirty-one percent of the early-onset patients had a family history of OCD compared to none in the other group ($p < 0.01$).

Conclusions: These preliminary results, despite the small number of patients, suggest that the age of onset may be useful in subtyping OCD.

NR151 Monday, May 19, 3:00 p.m.-5:00 p.m.

Implicit and Explicit Memory for Threatening Stimuli in Panic Disorder Patients

Rebecca A. McKinney, B.A., Department of Psychiatry, University of CA/San Diego, 8950 La Jolla Village Dr, 2243, La Jolla CA 92037; Julie Akiko Gladsjo, Ph.D., Mark H. Rapaport, M.D., Michelle D. Auerbach, M.S., Anthony Rabin, M.S., John Lucas, Ph.D.



* p<0,05

Summary:

Background: One key premise of cognitive therapy is that mood states are established and maintained by negative schemas. Memory research with depressed patients finds a statistically significant increase in overall recall for negative words when compared with controls. Mathews et al. (1989) studied generalized anxiety disorder (GAD) patients and found an implicit negative recall bias only for threatening words. We hypothesized that an implicit negative recall bias would be present in patients with panic disorder compared with controls.

Method: Sixty-eight DSM-IV diagnosed panic disorder patients and 19 healthy control subjects matched for age, gender, and education were presented with both threat-related and nonthreatening words in an imagination task. Recall was measured under both implicit (word stem completion) and explicit (cued recall) conditions. A subject group x recall type x word content factorial ANOVA was performed, followed by tests of simple effects.

Results: Panic disorder patients and healthy control subjects had similar performances across the two recall conditions as well as in their recall of threatening vs. nonthreatening words. Most importantly, panic disorder patients did not demonstrate a facilitation of threat word recall in the implicit recall condition.

Comments: The data suggest that panic disorder patients do not pay special attention to physically or socially threatening stimuli. This may reflect an inherent psychological difference between GAD and panic disorder.

NR152 Monday, May 19, 3:00 p.m.-5:00 p.m.

Comparison of Sertraline and Fluoxetine on Quality of Life in Depressed Outpatients

Daniel Sechter, Department of Psychiatry, Chu Saint Jacques, Besangon 25030, France; Sylvie Troy

Summary:

This double-blind, six-month, comparative study evaluated the quality of life of 238 depressed outpatients assessed with the SIP (Sickness Impact Profile).

Methods: Efficacy and safety were evaluated after two, four, six, eight, 12, 18 and 24 weeks. Quality of life was evaluated after three and six months of treatment.

Results: This six-month comparative study supported efficacy and good tolerance for both drugs in the treatment of depressive episode. Globally there was a more favorable and statistically significant outcome in sertraline-treated patients on four items, a trend for five others (mobility p = 0,08; ambulation p = 0,09; SIP C p = 0,08; recreation and pastimes p = 0,07 and SIP E p = 0,07).

Conclusion: This six-month study supports the efficacy of sertraline in the treatment of depressive patients and suggests a superiority over fluoxetine with a better effect on quality of life.

NR153 Monday, May 19, 3:00 p.m.-5:00 p.m.

Evaluation of Dreams in Combat-Related PTSD

Karin F. Esposito, M.D., Department of Psychiatry, VA Medical Center, 1201 NW 16th Street, Miami FL 33125; Amparo B. Benitez, D.O., Thomas A. Mellman, M.D.

Summary:

Background: Nightmares that replicate traumatic events have been found to be specific to post-traumatic stress disorder (PTSD) and frequent among combat veteran patients. However, there has been limited systematic assessment of the content of dreams in PTSD subjects.

Methods: A PTSD dream-rating instrument was developed reflecting dimensions derived from the dream content analysis and PTSD literatures. "PTSD-like" dreams were hypothesized to feature settings, characters, and objects similar to traumatic experiences along with high threat, low contemporaneity, and low distortion. Subjects were recruited from an outpatient PTSD clinic or a PTSD unit for combat-related PTSD. A sleep/dream diary was used to stimulate dream recall. In addition, patients received other diagnostic and severity assessments.

Results: High interrater reliability was achieved (ICC = 0.99). One-third of the dreams reported contained settings, characters, or objects characteristic of combat, one-third were rated as highly threatening, and an additional 50% were rated as moderately threatening. Sixty percent were set at least partially in the present and two-thirds did not replicate actual events. To date we have not found significant relationships between dream ratings and measures of overall PTSD severity (CAPS) and psychosocial functioning (LIFE). There was, however, an effect of setting, with lower "PTSD-like" ratings from patients participating in the more intensive milieu and dream workshop ($p < 0.05$).

Conclusions: Dreams reported by patients with PTSD vary with regard to the hypothesized "PTSD-like" features, yet are often moderately to highly threatening. Reports may be affected by setting.

NR154 Monday, May 19, 3:00 p.m.-5:00 p.m.

Impact of Alprazolam on Neuropsychological Functioning in Panic Disorder

Julie Akiko Gladsjo, Ph.D., Department of Psychiatry, University of CA/San Diego, 3350 La Jolla Village Drive, San Diego CA 92161; Mark H. Rapaport, M.D., Rebecca A. McKinney, B.A., Anthony Rabin, M.S., Michelle D. Auerbach, M.S., Lewis L. Judd, M.D.

Summary:

Background: Acute benzodiazepine use in normal volunteers is associated with neuropsychological deficits, including anterograde amnesia and psychomotor impairments. It is unclear whether benzodiazepines exert similar effects on chronically

treated anxiety patients. Two of three previous studies investigating the effects of chronic benzodiazepines in anxiety patients did not find any neuropsychological effect. We hypothesized that panic disorder patients treated with alprazolam would not differ from placebo-treated subjects on neuropsychological performance.

Method: Fifty-five DSM-IV-diagnosed panic disorder patients were administered comprehensive neuropsychological batteries at baseline and eight weeks later. Patients were randomized to alprazolam-XR 2 mg BID or placebo. Patients were medication-free for at least two weeks prior to testing. The battery assessed learning, visual and verbal memory, attention, visuospatial functioning, and psychomotor speed. Repeated-measures MANOVA was used to examine group differences in neuropsychological test performance.

Results: There were no significant group differences in neuropsychological performance, except for visual memory, where patients on placebo performed slightly better at both assessments. There was a significant practice effect for psychomotor and attention abilities. Most importantly, there were no significant group X time interactions.

Comment: This study demonstrates that subjects with panic disorder did not show neuropsychological dysfunction in conjunction with chronic benzodiazepine administration.

NR155 Monday, May 19, 3:00 p.m.-5:00 p.m.

A Study of the Sampoong Disaster Survivors in Korea

Byung-Joo Ham, M.D., Department of Psychiatry, Korea University, 126-1, Anamdong, Sungbuk-Ku, Seoul, Korea; Min Soo Lee, M.D., Dong-Il Kwak, M.D., Joon-Sang Lee, M.D.

Summary:

Objective: The purpose of this study was to assess the clinical manifestations of psychiatric symptoms and MMPI profile, and to examine factors affecting the severity of symptoms among survivors of a devastating disaster, which was caused by a human being. The major affecting factors of interest were age, sex, marital status, educational level, loss of consciousness, witness of death, death of related person, duration until rescue, duration of hospital days, and duration of psychiatric treatment.

Method: The survivors of the Sampoong department store collapse were evaluated in October, 1995, five months after the disaster. Among the original 681 subjects, 624 were evaluated with the Psychiatric Evaluation Form, the Impact of Event Scale, and the MMPI.

Results: The most common complaint was sleep disturbance (54.2%), followed by headache (31.8%), irritability/anger (23.3%), and intense distress over reminders (24.2%). Common somatic complaints were headache, backache, extremity pain, chest discomfort, and gastrointestinal discomfort. Most of the subjects showed various psychiatric symptoms. Some factors affected the severity of psychiatric symptoms. The older and the lower educational level the patient was, the more severe their symptoms. The divorced and the widowed survivors had more severe symptoms than others. The subjects who experienced loss of consciousness, longer duration until the rescue, more hospital days, and psychiatric treatment had more severe symptoms. On MMPI, the survivors had clinical elevations on scale F, 1, 2, 3, 6, and 7. The discrimination analysis showed that L, F, K, Hs, D, Hy, Pt, Sc, and Ma scales had significantly high discrimination function coefficients between survivors and normal controls.

Conclusion: On the basis of our results, it is suggested that evaluation of specific psychiatric symptoms after this type of traumatic disaster is possible. And these findings indicate that a substantial proportion of the adult population may experience post-traumatic stress symptoms after the disaster, which was caused by a human being. The factors affecting the severity of symptoms identified in this study may prove useful in screening exposed individuals for appropriate evaluation and treatment. Although our study has some limitations, we hope that the more controlled studies of this area in the future would support our results.

NR156 Monday, May 19, 3:00 p.m.-5:00 p.m.

Hypochondriasis as an Obsessive-Compulsive Spectrum Disorder

Martin Aigner, M.D., Waehringer Guertel 18–20, Vienna 1090, Austria; Ulrike Demal, Ph.D., Werner Zitterl, M.D., Michael Bach, M.D.

Summary:

Hypochondriac fears are a symptom of many mental disorders. Some authors even question the existence of hypochondriasis as a distinct disorder. With the concept of the obsessive-compulsive related disorders (Hollander, 1993), hypochondriasis is seen as a variant of obsessive-compulsive disorder (OCD).

The fear-inducing obsessions of being ill and the fear-reducing compulsions of "doctor shopping" may be conceptualized as an obsessive-compulsive behavior. Disease conviction can be conceptualized as an OCD form with poor insight.

A sample of OCD patients and patients with hypochondriasis ($n = 37$, 20 males, 17 females, mean age = 35 ± 10) was included in the study. Obsessive-compulsive symptoms were assessed by the Y-BOCS, hypochondriasis by the Whiteley Index, and somatoform symptoms by the SOMS (Rief et al., 1992).

In the Y-BOCS there was no significant difference between "pure" OCD and hypochondriasis cases (24.7 ± 6.7 vs 26.7 ± 5.3; $p = 0.41$). However, compared with OCD patients, patients with hypochondriasis showed significantly higher scores on the Whiteley Index (4.3 ± 2.8 vs 10.8 ± 2.0, $p < 0.001$), especially on the bodily preoccupation subscore (0.5 ± 0.7 vs 2.1 ± 1.0, $p < 0.001$), as well as on the SOMS (7.9 ± 7.2 vs 18.3 ± 9.0, $p = 0.006$).

Taken together, these data suggest that there is a cognitive spectrum including "pure" obsessions and hypochondriacal concerns as it is formulated in the obsessive-compulsive spectrum disorders. In contrast, both diagnostic groups are considered clearly distinct entities with regard to somatic and somatoform symptoms.

NR157 Monday, May 19, 3:00 p.m.-5:00 p.m.

Temporal Relationship Between Alexithymia and Somatization During Inpatient Treatment

Michael Bach, M.D., Department of Psychiatry, University of Vienna, Waehringer Guertel 18–20, A-1090 Vienna A, Austria; Ulrike Lupke, Ph.D., Ralph Schaible, Ph.D., Detlev O. Nutzinger, M.D.

Summary:

In this prospective treatment study, the temporal relationship between alexithymia and somatization was investigated in 59 psychosomatic inpatients (41 females, 18 males, mean age = 39.07 [SD = 9.47]). Patients were asked to complete the following instruments at admittance and after six weeks of integrative behavior therapy: 20-item Toronto-Alexithymia Scale (TAS-20), Whiteley Index (WI), Checklist for Somatoform Symptoms (SOMS), and the SCL-90-R. After treatment, a significant decrease ($p < 0.003$, Bonferroni correction) was observed for most psychometric variables (WI, SOMS, SCL-90-R subscales for somatization, obsessive-compulsiveness, interpersonal sensitivity, depression, anxiety, phobic anxiety, paranoid ideation, psychoticism, and the SCL-90-R general symptomatic index). However, the degree of alexithymia remained consistent (mean TAS-20 score: pre-treatment

51.68, post-treatment 49.00, t = 2.68, p = n.s.). This finding underlines the conceptualization of alexithymia as a state-independent personality trait. In addition, as a result of linear logistic regression analyses, high pretreatment alexithymia scores emerged as significant predictors of persistent symptomatology (as indicated by a symptom decrease of less than 50% on the SCL-90-R general symptomatic index), independent of other measures of psychopathology and illness severity (Beta value: 9.11, $p < 0.002$). These data contrast with previous observations from longitudinal studies in patients with eating disorders, alcohol dependence, or anxiety disorders, giving evidence of the potential role of alexithymia in predicting an unfavorable treatment outcome, particularly in somatizing patients.

NR158 Monday, May 19, 3:00 p.m.-5:00 p.m.

Screening for DSM-IV Somatoform Disorders in Chronic Pain Patients

Michael Bach, M.D., Department of Psychiatry, University of Vienna, Waehringer Guertel 18–20, A-1090 Vienna A, Austria; Martin Aigner, M.D., Sandra Krones, Anna Spacek, M.D., Hans-Georg Kress, M.D.

Summary:

At present, screening instruments for accurately identifying somatoform disorders in chronic pain patients are still needed. In this study, we investigated the clinical utility of the Screening Instrument for Somatoform Symptoms (SOMS, Rief et al., 1995), a self-rating scale of 31 medically unexplained somatic symptoms according to DSM-IV somatoform disorders. The SOMS was administered to 105 chronic pain patients (71 females, 34 males, mean age = 50.86 yrs. [SD = 12.35]). In addition, psychiatric diagnoses were determined according to DSM-IV. Fifty-two patients (49.5%) met criteria for a DSM-IV somatoform disorder. These patients showed significantly higher SOMS item scores compared with subjects without somatoform disorders (mean scores: 6.69 vs. 4.67, $p < 0.02$). Different SOMS cut-off item scores were evaluated by comparing their sensitivity, specificity, and predictive value for confirming a diagnosis of DSM-IV somatoform disorders. With respect to the Somatic Symptom Index (SSI-4,6)-concept, a cut-off score of ≥4 somatoform items appeared useful for classifying overall caseness of a somatoform disorder. However, for adequately identifying particular DSM-IV somatoform disorders, efficient cut-off scores largely differed across a range from ≤3 items (for pain disorder) to ≥7 items (for somatization disorder). Therefore, the efficiency of self-rating screening instruments for the identification of somatoform disorders substantially depends on the intended application and purpose.

NR159 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Gene Encoding Tryptophan Hydroxylase Is Intact in SAD, OCD, Anorexia Nervosa

Ling Han, c/o Dr. Goldman, NIH/NIAAA lab of Neurogen., 12420 Parklawn Drive, Rockville MD 20851; Norman E. Rosenthal, M.D., David Nielsen, Ph.D., Markku I. Linnoila, M.D., David S. Goldman, M.D., Kimberly Jefferson, B.S., Walter H. Kaye, M.D., Dennis L. Murphy, M.D., Anil K. Malhotra, M.D., Julie Humphries, M.D., David Picker, M.D., Matti Virkkunen, M.D., Alexandro Rotondo, M.D., Giovouuc Cosseuo, M.D., Marty Altemus, M.D.

Summary:

Objective: The goal of this study was to evaluate the potential role of genetic variation in the TPH gene coding sequence in the pathogenesis of several psychiatric diseases in which altered serotonin function has been implicated: Bipolar affective disorder (BP), obsessive-compulsive disorder (OCD), anorexia nervosa (AN), seasonal affective disorder (SAD), panic disorder (PD) and alcoholism.

Methods: 93% of the TPH coding sequence was screened for sequence variation by PCR SSCP methods in 72 SAD, 88 OCD, 128 AN, 36 BP, 45 PD and 142 normal volunteers. Also included were 61 alcoholism randomly selected from a Finnish alcoholic population in which an association of a TPH intron 7 polymorphism with suicidality was observed. Polymorphisms detected by SSCP were characterized by sequencing method and by allele-specific restriction enzyme digestion. Genotyping was further made in 8 Finnish alcoholic suicidal attemptives.

Results: A rare silent mutation was identified in exon 10 and is designated as T1095C. C1095 was found in 1 individual with OCD and in 2 individuals with AN, each of these three individuals was heterozygous [C1095/T1095]. No association was observed between this TPH T1095C variant with either OCD, AN or suicidality.

Conclusion: These results suggest that the coding sequence of the TPH gene may be intact in several diseases in which disturbed serotonin turnover has been implicated.

NR160 Monday, May 19, 3:00 p.m.-5:00 p.m.

Stimulant Effects on Acoustic Startle in ADD

Arthi Parwani, M.D., Department of Psychiatry, New York VAMC, 423 East 23rd Street, New York NY 10010; Michal Kunz, M.D., Lenard A. Adler, M.D., Elsa Bartlett, Ed.D., Erica J. Duncan, M.D., Rajiv Rajan, M.D.

Summary:

Objective: Deficits in sensorimotor gating as measured by prepulse inhibition of acoustic startle (PPI) have been associated with dopaminergic dysfunction. Dysfunction of dopaminergic tracts has also been implicated in ADD, a syndrome characterized by distractibility and inattention. Therefore, we studied the effects of the dopaminergic agents methylphenidate and dextroamphetamine on the acoustic startle response in adult ADD patients.

Method: Acoustic startle stimuli were presented alone and at 30,60, and 120 msec after a brief prepulse to seven ADD patients both off stimulants and after being stabilized to maximal clinical effect on dextroamphetamine or methylphenidate.

Results: As compared to baseline, patients on stimulants showed (1) decreased amplitudes in the pulse alone ($F = 5.59$, $p = .06$) as well as in the 30 and 120 msec prepulse conditions ($F = 3.84$, $p = .10$), and (2) longer onset latencies in the 60 and 120 msec conditions ($F = 5.09$, $p = .07$). Data on additional patients and correlations between startle response and Wender Utah rating scales (WURS) and auditory and visual continuous performance tasks (CPT) will be reported.

Conclusion: These data suggest that psychostimulants diminish stimulus reactivity and reflex excitability across several parameters of the acoustic startle response in ADD patients.

NR161 Monday, May 19, 3:00 p.m.-5:00 p.m.

Relationships Among Psychopathology, Gender and Monoamine Metabolism in Chronic Schizophrenia

Dae-Yeob Kang, M.D., Department of Psychiatry, VA Medical Center, 4150 Clement Street, San Francisco CA 94121; John Poole, Ph.D., Sophia Vinogradov, M.D., Jason Willis-Shore, B.A., Faith Corwin, Ph.D., Margeaux Lieberman, B.A., Elysa Marco, B.A.

Summary:

Objective: The dopamine (DA) hypothesis of schizophrenia has been found to have its limitations, and there is increasing evidence for the role of other neurotransmitters in the pathophysiology of the disorder. Principal candidates in recent years have included serotonin (5-hydroxytryptamine, 5-HT) and norepinephrine (NE).

In this study, we examined the relationship among psychopathology, gender, and monoamine metabolites.

Method: Thirty-seven clinically stable, medicated, chronically ill schizophrenic outpatients (22 males, 15 females) were evaluated using an extended version of the Positive and Negative Syndrome Scale (PANSS-E). To determine levels of plasma monoamines (DA, NE, 5-HT) and their metabolites (homovanillic acid [HVA], 3-methoxyhydroxyphenyglycol [MHPG], 5-hydroxyindoleacetic acid [5-HIAA]), blood samples were taken by venipuncture and analyzed by high performance liquid chromatography (HPLC).

Results: Plasma MHPG was significantly correlated with total score on the PANSS-E (Pearson's $r = 0.31$, $p = 0.03$) and with positive symptoms subscores (Pearson's $r = 0.32$, $p = 0.03$) in all patients, but HVA and 5-HIAA showed no such relationship. Female schizophrenics had more severe depression-anxiety subscores than males ($t = -3.28$, $p = 0.002$), and there was a significant correlation between depression-anxiety subscores and MHPG levels in female but not male schizophrenics (Pearson's $r = 0.453$, $p = 0.045$).

Conclusions: These results implicate an alteration in NE metabolism in at least some schizophrenics, especially in female schizophrenics who have depression-anxiety symptoms.

NR162 Monday, May 19, 3:00 p.m.-5:00 p.m.

Responses to Clonidine and Pre- and Post-Menopausal Women

Ann M. Woo-Ming, M.D., Department of Psychiatry, Mt. Sinai Medical Center, One Gustave Levy Place, New York NY 10029; Robert L. Trestman, M.D., Antonia S. New, M.D., Larry J. Siever, M.D.

Summary:

Background: While a blunted growth hormone (GH) response to the clonidine (CLON) challenge test has been shown to distinguish males with major depression (MDD) from normal controls (Siever, et al 1992; Checkley, et al 1984), this finding is not consistent in female subjects (Shittecatte 1989, Charney 1982). Menopausal (MEN) MDD and normal control (NC) subjects appear to have a more blunted GH response to CLON than comparable premenopausal (PRE) subjects (Shittecatte, et al 1994; Matussek, et al 1980). Furthermore, baseline GH secretion and GH response to CLON may be higher in the luteal phase of the menstrual cycle (Liebenluft 1994). We attempted to investigate the relationship among diagnosis, phase of menstrual cycle, menopausal status, age, and GH response to intravenous CLON, an index of postsynaptic alpha-adrenergic function.

Results: GH response to IV clonidine, an index of postsynaptic alpha-adrenergic function, was measured in 53 subjects with the following diagnoses: lifetime history of MDD (MDD +, $n = 37$), those with no lifetime history of MDD (MDD–, $n = 8$), and healthy controls ($n = 8$). There was a significant inverse correlation between age and GH response ($r = -.38$, $n = 53$, $p < .01$), but there were no differences in GH response among the three groups (NC: 3.1 ± 3.6, MDD +: 5.8 ± 5.4, MDD–: 6.0 ± 8.0; p = ns). A large number of subjects ($n = 26$, 49% of the sample) showed a GH response of less than 4ng/dl (considered a blunted response). There were no differences in blunting status among the three groups (NC: 5/8 or 62%; MDD +: 16/21 or 43%; MDD–: 5/8 or 62%; $X^2 = 1.6$, df2, p = ns). A total of 47 of the subjects were PRE (NC, $n = 7$; MDD+, $n = 33$; MDD–, $n = 7$). There were no group differences in their GH responses (NC:3.5 ± 3.6; MDD+: 6.5 ± 5.3, MDD–: 6.8 ± 8.2). There was no correlation between day of the menstrual cycle and GH response ($r = .11$, p = ns). However, women who were menopausal ($n = 6$) demonstrated significantly reduced GH responses (0.1 ± 0.1) compared to premenopausal women (6.1 ± 5.6, $n = 47$; $t = 7.0$, $p < .001$).

Conclusion: Thus, in our sample, the GH response to clonidine failed to differentiate among diagnostic groups, regardless of phase or status of menstruation. As in previous studies, there was a significant effect of age and MEN status on GH response, regardless of diagnosis. The GH response to clonidine may not be a useful way to differentiate among female MDD +, MDD–, and NC groups.

NR163 Monday, May 19, 3:00 p.m.-5:00 p.m.

Low Cholesterol and Violence

Rizwan M. Mufti, M.D., Department of Psychiatry, Wayne State University, 2751 East Jefferson, Detroit MI 48207; Richard Balon, M.D., Cynthia Arfken, Ph.D.

Summary:

Objective: During clinical trials of lipid-lowering drugs it was observed that relative mortality from cardiac disease had decreased while the total mortality remained the same. However, there were more deaths from violence, aggression, suicide, and accidents. We decided to test if there is any link between low cholesterol and violent behavior in long-term psychiatric inpatients.

Method: Retrospective chart review of two groups of 20 patients each. Controls were comprised of patients with no exhibition of violent or aggressive behavior, while cases were comprised of patients who showed violent and aggressive behavior judged by the use of seclusion and restraints during a two-month period. The two groups were compared for cholesterol and triglycerides.

Results: Both groups were comparable for sex, race, diagnosis, and distribution. Cases were younger (31.9 ± 7.8 years vs 41.7 ± 7.4 years). Cases had lower cholesterol levels 152.3 ± 24.1 mg/dl as compared with controls 200.2 ± 43.4 mg/dl $p < .001$; there was no significant difference in triglyceride levels $p = 0.158$, N.S. Logistics regression $p = .003$ and analysis of covariance $p = .013$ showed an independent association between violence and low cholesterol levels, which was nonlinear.

Conclusion: It appears that the patients who have incidences of violence tend to have lower cholesterol levels than nonviolent patients.

NR164 Monday, May 19, 3:00 p.m.-5:00 p.m.

Prolactin Levels of Premenopausal Women Treated with Risperidone and Conventional Neuroleptics

Renuka Ananthamoorthy, M.D., Department of Psychiatry, Cabrini Medical, 227 East 19th Street, New York NY 10003; Giovanni Caracci, M.D.

Summary:

Although there have been some reports of high prolactin levels in risperidone-treated patients, they either do not include premenopausal women or have found no significant differences between risperidone and conventional neuroleptic treatment.

Method: We compared prolactin level in 20 premenopausal women treated with risperidone with 20 premenopausal women treated with conventional neuroleptics.

Results: The mean age was 41 for the risperidone-treated group and 37 for the conventional-treatment group ($p = .046$). The two groups differed for dose: $\bar{X} = 3.1$ in the risperidone group vs. 46.8 in the conventional neuroleptic group ($p = .007$), but did not differ for a number of days on medications (126 vs. 128). Risperidone-treated patients had significantly higher prolactin levels than patients treated with neuroleptics ($\bar{X} = 102$ micro grams/1 vs 48 micro grams/1, SD = 50 vs 27) ($F = 17.64$; $p = .00001$). Eight (40%) of the risperidone-treated patients were symptomatic (six with amenorrhea and two with galactorrhea).

Conclusions: This study found a higher increase than previously reported in risperidone-treated premenopausal women. The clinical implications of our findings will be discussed.

NR165 Monday, May 19, 3:00 p.m.-5:00 p.m.

Behavioral and Biological Effects of Acute Depletion of Plasma Tryptophan in Patients with Alcoholism and in Normal Volunteers

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Summary:

The rate of brain serotonin turnover may depend on plasma levels of the essential amino acid tryptophan. We investigated the biochemical, behavioral, cognitive, and electrophysiological effects of rapid plasma tryptophan depletion in normal volunteers undergoing a 36-hour cerebrospinal fluid (CSF) collection via lumbar drain. Ten subjects who were diagnostically normal by SCID interview received a 48-hour, 160-mg/d, low-tryptophan diet followed the next morning by a tryptophan-depleting 16-amino acid drink, in a double blind, placebo-controlled (acute tryptophan depletion and control testing), crossover fashion. Total plasma tryptophan and free plasma tryptophan levels decreased 85.7% and 87.6% (n = 4), respectively, during the acute phase of tryptophan depletion. Two of 12 subjects who experienced mild nausea accompanied by one episode of emesis were eliminated from the study. CSF will be analyzed for 5-HIAA concentration using gas chromatography-mass spectrometry (GC-MS). In the future, we will examine the effect of reduced serotonin turnover rate on impulsivity and alcohol-seeking behavior (craving) in patients with alcohol dependence.

NR166 Monday, May 19, 3:00 p.m.-5:00 p.m.

Differences of Eye Tracking Pattern in Schizophrenia, Affective and Schizoaffective Disorders: A Lab Investigation Using Electrooculography

Ingo Gerdsen, M.D., Department of Psychiatry, Heidel Bergi University, Lessingstr 12, 69115 Heidelberg 69115, Germany;

Summary:

Background: Smooth pursuit performance varies considerably among individuals and is affected by many factors such as the properties of the stimulus, attention, age, and neuropsychiatric disorders. In schizophrenia and affective disorders, increased rates of saccadic intrusions have been observed during smooth pursuit. The aim of our ongoing study was to compare various dynamic measures of smooth pursuit and saccadic eye movement between depressive schizophrenic and schizoaffective disorders to evaluate a possible diagnosis related specifity.

Methods: 15 schizophrenic, 14 depressive, and 10 schizophrenic patients with superimposed mood disturbance were diagnosed according to DSM-IV criteria; 14 normal controls were also included. Psychopathological symptoms were assessed on the BPRS, SANS, SAPS, and Hamilton Depression Rating Scale. Pursuit was measured during tracking of a predictable, sinusoidal target motion using the Nicolet Nystar oculomotor standard testing protocol.

Results: Compared to normal controls, all patients showed an elevated rate of inappropriate saccades, which was clearly higher for schizophrenic subjects. Also differences in performance of patients peak velocity to peak stimulus was observed. Mean gain values were 0.64 for depressive patients, including patients with schizoaffective disorder, and 0.78 for schizophrenics ($p < 0.0118$). Other measures, including delay and accuracy ($p < 0.055$), failed to reach significance.

Conclusion: Our preliminary data show that by oculomotor testing, significant diagnosis-related differences in eye-tracking pattern between all groups can be identified. Of particular significance could be that impaired gain performance is similar for both affective and schizoaffective subjects in contrast to schizophrenic subjects. This might suggest more involvement of frontal lobe structures for schizophrenics with superimposed mood disturbance.

NR167 Monday, May 19, 3:00 p.m.-5:00 p.m.

Hemispheric Asymmetry of Benzodiazepine Receptor Binding Sites in Schizophrenia: A Study with I-Iomazenil SPECT

Ingo Gerdsen, M.D., Department of Psychiatry, Heidel Bergi University, Lessingstr 12, 69115 Heidelberg 69115, Germany; Joerg Pinkert, M.D., Liane Oehme, M.A., Bettina Ripke, M.A., Klaus Zoephel, M.D., U.Neumann, M.D.

Summary:

Background: GABA is the major inhibitory transmitter in the brain and has also been implicated in the pathophysiology of schizophrenia. Benzodiazepines enhance the inhibitory effects of GABA on special receptor sites. The aim of this study was to investigate the regional benzodiazepine receptor binding and correlation with psychometric measures in schizophrenic subjects.

Methods: 12 schizophrenic patients were diagnosed according to DSM-IV criteria. Psychopathological symptoms were assessed on the BPRS, SANS, and Strauss Carpenter Scale. Two SPECT scans were performed for each patient 10 min. and 120 min. after intravenous injection of 150MBqs ^{123}I-Iomazenil using a dual head camera. ROI's were defined on frontal, temporal, parietal, and occipital regions, on GABA receptor free white matter areas, and the cerebellum. Specific ^{123}I-Iomazenil binding was calculated by a semiquantitative approach.

Results: The highest Iomazenil uptake was detected in the occipital cortex. Reduced specific ^{123}I-Iomazenil binding (15–20%) was found for the left cortical hemisphere. The differences were significant for both the left frontal ($p < 0.0023$) and temporal ($p < 0.01$) region compared to the right frontal and temporal region. A significant correlation was also found for specific receptor binding of the anterior cingulate cortex and left temporal lobe ($p < 0.021$) with severity of the disease.

Conclusion: Our data could suggest a prominent unilateral loss of GABAergic interneurons or alterations of benzodiazepine receptor binding sites during the course of the disease. Alternatively, early regional developmental abnormalities could be responsible for these asymmetric neurochemical changes in brains of schizophrenics, affecting mainly the left dominant hemisphere. In addition, our results indicate that chronic schizophrenia may involve more substantial alterations of intrinsic circuits within the anterior cingulate cortex.

NR168 Monday, May 19, 3:00 p.m.-5:00 p.m.

New Windows into Bipolar Illness: Serial Perfusion MRI Scanning in Rapid-Cycling Bipolar Patients

Andrew M. Speer, M.D., Dept of Psych, Medical U of South Carolina, 171 Ashley Ave, Charleston SC 29425-0001; Vidya H. Upadhyaya, M.D., Daryl E. Bohning, Ph.D., S. Craig Risch, M.D., Diana J. Vincent, Ph.D., Mark S. George, M.D.

Summary:

Background: Functional imaging studies of bipolar affective disorder (BPAD) have suggested that mania may be associated with

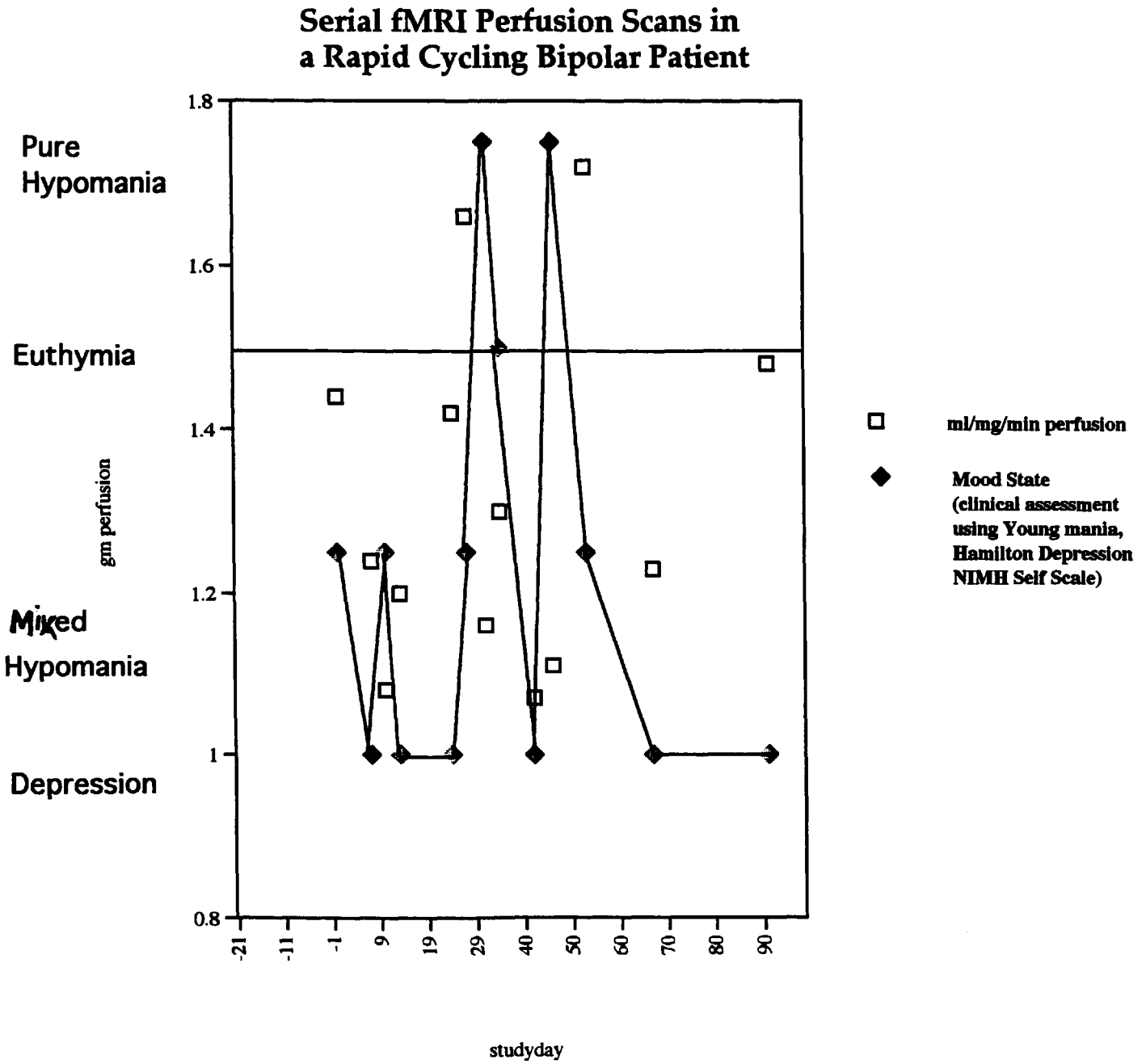
increased global brain metabolism. We have recently implemented a non-contrast-based perfusion MRI (pfMRI) technique (spin-labeling and inversion recovery), which magnetically tags hydrogen atoms in the bloodstream, yielding absolute and relative global and regional perfusion rates. Because there is no radiation, this MRI technique allows unlimited serial imaging in the same patient.

Methods: In initial pilot work, we have serially scanned a 43-year-old male patient with rapid cycling BPAD (average cycle length of 7 days) using pfMRI 13 times over three months. During the same time of day, images were acquired at a consistent brain level (anterior cingulate and prefrontal cortex).

Results: In this pilot patient we found that *global* gray matter perfusion correlated with varying mood states, although the relationship is complex. Regional analysis is in progress.

Conclusion: It appears that there may not be a one-to-one relationship between clinical state on the day of the scan and global gray matter perfusion, that is, global perfusion may precede or lag behind clinical course. However, this initial pilot study demonstrates the feasibility of performing serial imaging using pfMRI. This new imaging tool will likely aid in capturing dynamic global and regional changes in neuropsychiatric disorders.

Acknowledgment: Stanley Foundation, Picker International



NR169 Monday, May 19, 3:00 p.m.-5:00 p.m.

Neuroimaging in Geriatric Psychiatry: A Review

Srinivasan S. Pillay, M.D., 32 Whites Avenue #3305, Watertown MA 02172-4305; Scott L. Rauch, M.D., Perry F. Renshaw, M.D., Stephanie L. Rose, B.A.

Summary:

Objective: To review neuroimaging studies in geriatric patients.

Method: The authors reviewed 155 articles on contemporary neuroimaging modalities. Tables describing advantages and disadvantages of computerized tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single photon emission computed tomography (SPECT) in the clinical evaluation of geriatric patients are presented. The authors present summary tables of CT, MRI, PET, and SPECT findings in patients with dementia of the Alzheimer's type (DAT). In addition, they present summary tables of CT, MRI, and PET studies in elderly depressed patients.

Results: Studies show that patients with DAT have increased ventricular volume, increased frequency of white matter lesions (WMLs), and atrophy of fronto-temporal areas. In addition, they have smaller hippocampal and amygdala volumes, and glucose hypometabolism and hypoperfusion of the temporo-parietal regions of the cerebral cortex. In elderly depressed patients, studies show an increased ventricular volume, increased frequency of WMLs, and decreased regional cerebral blood flow in the anterior cingulate and prefrontal cortex.

Conclusion: Studies to date show that neuroimaging is potentially useful in differentiating geriatric depression from dementia. To date, no findings appear to be pathognomonic. Further research in neuroimaging in elderly patients may be useful for improving syndromal definitions.

NR170 Monday, May 19, 3:00 p.m.-5:00 p.m.

MRI/Event-Related Potential Abnormalities in First-Episode Psychosis

Yoshio Hirayasu, M.D., Psychiatry 116A, Harvard Medical School, 940 Belmont Street, Brockton MA 02401; Martha E. Shenton, Ph.D., Dean F. Salisbury, Ph.D., Chandlee C. Dickey, M.D., Iris A. Fischer, B.A., Robert W. McCarley, M.D.

Summary:

Objective: Recent studies using MRI on chronic schizophrenics have shown reduced left posterior superior temporal gyrus (STG) gray matter. This finding is associated with reduced left temporal voltage of the P300 event-related potential (ERP). However, the roles of chronic morbidity or long-term neuroleptic treatment in these abnormalities remains unclear.

Method: To test if temporal lobe MR and P300 abnormalities were present at schizophrenia onset, MRIs and auditory ERPs were acquired from first-episode patients with schizophrenia (n = 15), affective psychosis (n = 16), and from age-matched normal controls (n = 18).

Results: First-episode schizophrenics showed smaller P300 amplitude over the left temporal region than either first-episode affective psychotics or controls. Schizophrenics showed significantly smaller gray matter in whole left STG than either first-episode affective psychotics or controls. First-episode schizophrenics also showed a smaller posterior left STG and left hippocampus than either first-episode affective psychotics or controls. Correlational analyses showed a positive correlation between left temporal P300 amplitude and left posterior STG volume only in first-episode schizophrenics.

Conclusions: These data suggest that the MR and ERP left temporal abnormalities reported in chronic schizophrenia are present at disease onset in schizophrenia but not in affective disorder.

NR171 Monday, May 19, 3:00 p.m.-5:00 p.m.

Relationships Between Corpus Callosum Size, Cingulate Gyrus Metabolic Rate and Symptoms of Schizophrenia

Jack E. Downhill, Jr., M.D., Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy P1/Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., M. Mehmet Haznedar, M.D., Tse Chung Wei, Ph.D., Jacqueline Spiegel-Cohen, M.S.

Summary:

Cingulate gyrus activation has been associated with hallucinations in imaging studies of schizophrenic patients. Primate data suggest that cingulate connections between the right and left hemisphere pass through the body of the corpus callosum. This study examines the hypotheses that differences in size of the body of the corpus callosum and that asymmetry in metabolic activity will be related to the symptoms of schizophrenia. Subjects comprised 27 patients with schizophrenia: seven females, 20 males, mean age = 38.3, SD = 14.3) Patients were evaluated with the Comprehensive Assessment of Symptoms and History structured interview and met DSM-III-R diagnostic criteria for schizophrenia and the BPRS. MRI slices were acquired with a SPGR sequence in the axial plane at 1.2 mm intervals and resectioned to the coronal plane perpendicular to the anterior-posterior commissure line. A realigned mid-sagittal MRI slice was used for tracing the corpus callosum and axial slices for tracing the cingulate gyrus. FDG-PET data were coregistered with MRI. Correlation coefficients were obtained between 30 anteroposterior sectors of the corpus callosum, cingulate metabolic rates, and BPRS symptom subscales and smoothed with a moving average. As predicted on an anatomical basis, sectors in the middle (body) of the corpus callosum were significantly correlated with the positive symptom subscale of the BPRS (sectors #14–16, $r = .41, .42, .42$, respectively, all $p < 0.05$). Cingulate gyrus metabolic asymmetry (absolute value of left minus right anterior cingulate glucose use) was negatively correlated with corpus callosum area #15–17, $r = 0.33, 0.34, 0.33$ $p < 0.05$ (one tailed). Left minus right posterior cingulate glucose was negatively correlated in area 17–21, $r = 0.36, 0.37, .50, .36$ $p < .05$ (one tailed).

The data suggest that symptoms of schizophrenia increase with increased corpus callosum body area, Left-right assymetry in the cingulate is greater with smaller corpus callosum body areas. The changes, therefore, are suggestive of greater interhemispheric communication between left and right cingulate being related to increased symptoms.

NR172 Monday, May 19, 3:00 p.m.-5:00 p.m.

Temporal Lobe Volume in Schizotypal Personality Disorder and Schizophrenia

Jack E. Downhill, Jr., M.D., Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy P1/Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Stacey Barth, M.S., Sonia Lees-Roitman, M.S., Melissa Nunn, B.S., Larry J. Siever, M.D.

Summary:

We obtained magnetic resonance images on seven patients with schizotypal personality disorder (SPD), 12 patients with chronic schizophrenia, and 11 age- and sex-matched normal controls. MRI slices were acquired with a SPGR sequence in the axial plane at 1.2 mm intervals and resectioned to the coronal plane perpendicular to the anterior-posterior commissure line. The superior temporal gyrus (STG) and the entire temporal lobe were outlined on approximately 40 consecutive slices (from the anterior appearance of temporal stem to the last appearance of fibers in the crux of the fornix). The STG and the remainder of the temporal volume gray matter following segmentation were entered into a

three-way ANOVA. The reduced size of the left superior temporal gyrus in patients with schizophrenia found by Shenton and others was statistically confirmed ($F = 6.45$, $df = 2,27$, $p = 0.005$). Patients with schizotypy and schizophrenia had similar reductions of the entire temporal lobe bilaterally (main effect of diagnosis, $F = 7.44$, $df = 2,27$, $p = 0.003$), and this effect was greater for the inferior and medial parts of the temporal lobe (−19.3% in schizophrenia and −15.7% in schizotypals) than for the superior temporal gyrus (−12% in schizophrenics and −10.7% in schizotypals; group × region interaction, $F = 8.44$, $df = 2,27$, $p = 0.0014$). No group interaction with hemisphere was significant.

These data are consistent with the data from family and adoption studies that schizotypy is part of the schizophrenia spectrum. They suggest that atrophy in temporal regions cannot fully be attributed to chronic effects of neuroleptics or institutionalization as only 50% of our schizotypals have taken neuroleptics and none are institutionalized.

NR173 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Clonidine Challenge Test in Depression: A PET Study in Women

Cynthia H. Fu, M.D., Department of Psychiatry, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Gregory M. Brown, M.D., Shitij Kapur, M.D., Alan Wilson, Ph.D., Sylvain Houle, M.D.

Summary:

Objective: Clonidine, an α2-adrenergic agonist, produces a well documented growth hormone response, which has been used as an index of central noradrenergic function. In depression, there is a consistently blunted response. This study examines the central noradrenergic system in depression in women, using the clonidine challenge test as a probe, as measured by PET.

Method: Six women with a DSM-IV diagnosis of major depression by SCID, clinical interview and a HAM-D score > 17, not taking any medications, received 1.4 μg/kg of clonidine intravenously. Regional cerebral blood flow was measured at baseline and at two periods following the clonidine infusion with ^{15}O-H_2O using PET. The PET images were co-registered with MRI. The control group consisted of an age- and menstrual cycle-matched group of six women.

Results: Previous work involving six healthy males showed increased rCBF in the left anterior cingulate and inferior frontal gyri and decreased rCBF in the right precuneus, cuneus, and cerebellum. The results from this study are pending, although we may predict differences in the areas of brain activation with respect to gender and depression.

Conclusions: This study may provide further evidence of the involvement of the noradrenergic system in depression and may postulate some specific regions of interest.

NR174 Monday, May 19, 3:00 p.m.-5:00 p.m.

Goal-Oriented Cognitive-Behavior Therapy in a Group Setting for Treatment of Late-Life Depression

Ellen J. Klausner, Ph.D., Department of Psychiatry, NY Hosp/ Cornell Univ Med Ctr, 21 Bloomingdale Road, White Plains NY 10605; John F. Clarkin, Ph.D., Lisa Speilman, Ph.D., George S. Alexopoulos, M.D., Christopher Pupo, B.A., Robert C. Abrams, M.D.

Summary:

This study compares the effectiveness of two different group psychotherapies on depression and disability in late life. One group utilized an expanded version of cognitive-behavioral therapy (CBT), which focused on patient-identified goals. Therapeutic components of this manualized treatment included psychoeducation, cognitive restructuring, and the development of hope. The other group utilized reminiscence therapy, which encouraged individuals to review their lives to gain perspective on their accomplishments. Both groups met for one hour, weekly, for 11 weeks.

Fourteen subjects, over age 55, who met criteria for DSM-IV major depressive disorder were randomly assigned to one of the two therapy groups. Ninety percent of the subjects were receiving pharmacological treatment, and all had failed to achieve remission of symptoms. All individuals were evaluated at entry to the study, and at study completion. Depressive symptoms were assessed with observer-based and self-report measures.

Results indicated that although depressed mood, disability, and suicidal ideation improved in both groups, the CBT group exhibited greater improvement. Moreover, while hopelessness was significantly reduced in the CBT group, the reminiscence group demonstrated a slight increase in level of hopelessness. Larger studies are necessary to identify the specific elements instrumental to the treatment of depression.

NR175 Monday, May 19, 3:00 p.m.-5:00 p.m.

Acute Dystonia in Two Demented Patients

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Summary:

Objective: Evidence from previous studies has shown that acute dystonic reactions are rare in elderly patients, with reported rates less than 2%. Few of these articles addressed dystonias in demented patients. We present two cases of acute dystonias in demented patients following the initiation of antipsychotic medication.

Method: Chart review of two dystonic patients from a geriatric psychiatry inpatient unit.

Results: Our first patient, a 62-year-old white male with a seven-year history of dementia, developed torticollis six days after starting loxapine. Multiple medications were tried to relieve the dystonia. The dystonia slowly improved but had not totally resolved two months later. In addition, a palmar flexion reaction of the right hand was transiently present, as well as a one-day presentation of total body myoclonus. The second patient, a 53-year-old white male with a three-year history of dementia, experienced an acute dystonia six days after initiating routine risperidone. His torticollis remained unresolved weeks later using only diphenhydramine. Both men had been exposed to haloperidol for one month before their hospitalization. The prolonged course of the dystonias proved impressive.

Conclusion: These cases illustrate the need for further identification and investigation of acute dystonic reactions in demented patients.

NR176 Monday, May 19, 3:00 p.m.-5:00 p.m.

Use of Mood Agents in Bipolar Geriatric Patients

Diana R. Sanderson, M.D., Department of Psychiatry, Erie County Medical Center, 462 Grider Street, Buffalo NY 14215; Sudeep Chakravorty, M.D., Michele T. Pato, M.D.

Summary:

Introduction: This three-year retrospective study of inpatient geriatric bipolar patients compared the efficacy of the mood stabilizers lithium, carbamazepine, and valproate using measures of length of treatment (LOT) and changes in GAF. Prevalence of bipolar disorder in this sample was also compared to previous data (Post, et al).

Methods: Chart review of all bipolars admitted to a county hospital was done from 1993 through 1995. A total of 82 geriatric charts (age ≥ 60 y/o) were selected from a total 486 bipolar patients. Demographics, laboratory values, LOT, GAF change, and improvement measures were collected.

Results: The prevalence of geriatric bipolar illness (16.8%) was similar to that previously reported (5–19%) (Post, et al). Only 52 of the 82 charts met criteria for further analysis. Other charts were excluded because of multiple medications or protracted LOT due to medical comorbidity. Mean LOT for the three drugs were: Li (n = 41) $\bar{\chi}$ = 24.05 ± 17.64, carbamazepine (n = 9) $\bar{\chi}$ = 26.75 ± 16.8, and valproate (n = 8) $\bar{\chi}$ = 20.33 ± 8.39. Mean GAF changes were: Li + $\bar{\chi}$ = 28.4 ± 15.9, carbamazepine $\bar{\chi}$ = 27.7 ± 8.73, and depakote $\bar{\chi}$ = 27.875 ± 10.78. However, results are confounded by a tendency to start patients on lithium before other medications and by uneven sample size.

Conclusions: Significance testing will be presented as it is expounded to five years to increase sample. We will then see if the trend in LOT for valproate over lithium and carbamazepine is borne out.

NR177 Monday, May 19, 3:00 p.m.-5:00 p.m.

White Matter Lesions in Elderly Depressed Subjects

Eric J. Lenze, M.D., Department of Psychiatry, Washington University Med Sch, 4940 Childrens Place, St Louis MO 63110; Yvette I. Sheline, M.D., Dewitte Cross, M.D., Daniel Lin, B.S., Michael Vannier, M.D.

Summary:

Introduction: Hyperintensities in the subcortical white matter have been described in many conditions including normal aging. A widely reported finding has been an increase in white matter hyperintensities in depressed elderly individuals compared to controls; however, the majority of studies did not control for degree of cerebrovascular risk factors. This study attempted to look at this issue more closely.

Methods: Ten elderly female subjects with a history of recurrent major depression and ten matched case controls underwent MRI. All subjects were screened to exclude cerebrovascular risk factors, serious medical illness, or problems potentially affecting the CNS. The scans were examined by two raters for presence of white matter hyperintensities; any disagreements were resolved by a neuroradiologist. The raters independently measured volumes of all hyperintensities using an automated ANALYZE sequence, using a threshold of two standard deviations above the white matter peak on T2 scans. Each rater measured all scans twice—inter-rater and intra-rater reliability were both 0.99.

Results: There were no differences between depressed subjects and controls in total volume (p = 0.97) or number (p = 0.10) of hyperintensities.

Conclusion: The results support the hypothesis that differences in white matter hyperintensities in elderly depressed subjects are a function of cerebrovascular disease.

NR178 Monday, May 19, 3:00 p.m.-5:00 p.m.

A Survey of Depression Knowledge/Understanding in Nursing Home Aides

Luis G. Allen, M.D., Department of Psychiatry, Hillside Hospital, 75-59 263rd St/Lowenstein Res, Glen Oaks NY 11004; Blaine S. Greenwald, M.D., Anjan Chatterjee, M.D., Donald H. Gemson, M.D.

Summary:

Depression occurs in 10% to 40% of nursing home residents, yet is often underrecognized. Ninety percent of direct care is provided by aides.

Objective: To evaluate aides' knowledge/understanding of depression.

Methods: A 27-item survey was administered face-to-face to 33 nurse's aides at three facilities in New York and Pennsylvania that addressed aide characteristics and knowledge about depression.

Results: 91% percent of interviewees were women; 56% were white, 42% black, and 6% Hispanic. 64% were American and 36% Caribbean. Mean years (±SD) of education were 12.7 ± 1.3; years at current facility 6.3 ± 5.3; and years as an aide 10.5 ± 8.0. Average number of residents/aide was 14.2 ± 6.0. 27% considered depression to be a psychiatric condition, 30% a "feeling," 18% a medical condition, 6% a memory problem, and 18% normal aging. Also, 77–100% recognized conventional features of major depression, but 36% to 69% also identified unrelated phenomena. Aides estimated 36% of residents in their care were depressed, and 97% felt doctors could probably help with medications and talk therapy. 73% felt that Alzheimer's disease/dementia patients could also be depressed.

Continuing education about depression occurred primarily in the larger teaching nursing home in NY (91% of aides), but not the smaller facilities located in semi-rural settings (33% of aides).

Influence of personal characteristics of aides (history of depression, family with depression) was also analyzed.

Conclusions: Most aides recognized typical depression symptoms, sophisticated concepts (agitation as depression, depression complicating dementia), an expected depression frequency, and treatment potential. However, many considered depression not a psychiatric condition and identified inappropriate items (e.g. hair loss) as part of depression. Continuing education is needed about depression as a psychiatric syndrome with characteristic features, especially in smaller, nonacademic facilities.

NR179 Monday, May 19, 3:00 p.m.-5:00 p.m.

T2 Signal Intensities in Alzheimer's Disease

Ramin V. Parsey, M.D., Department of Psychiatry, Duke University, Box 3812/DUMC, Durham NC 27710; K. Ranga Krishnan, M.D.

Summary:

Certain brain regions are represented as hypointensities on T2 weighted magnetic resonance images. These hypointensities are thought to be related to iron. Iron has been implicated in the pathophysiology of Alzheimer's disease (AD). In hopes of establishing a biological marker or noninvasive diagnostic tool for AD, we did a quantitative analysis of the T2 signal intensities in 13 AD patients and 16 age- and sex-matched controls. Whole-slice T2 signal intensities were lower but nonsignificantly in AD patients. T2 intensities were significantly lower in the red nuclei and putamena. There were no differences in left frontal lobe intensities. While there do not appear to be global differences in T2 signal intensities, there are regional variations that justify further investigation.

NR180 Monday, May 19, 3:00 p.m.-5:00 p.m.

Clinical Implications of Comorbid Antisocial BPD in Older Patients with Substance Use Disorders

Trevia F. Hayden, M.D., Department of Psychiatry, University of Maryland, 645 W Redwood Street, Baltimore MD 21201-1542; Joseph G. Liberto, M.D., Edward Shearin, Ph.D., Paul E. Ruskin, M.D.

Summary:

Little is known about older addicted patients with comorbid personality disorders. The purpose of the study is to compare a cohort of older addicted patients with and without antisocial personality

disorder (ASPD) and/or borderline personality disorder (BPD). Fifty patients in an older (age 50–75) adult outpatient substance abuse program at the VA Maryland Healthcare System, Baltimore Division, were screened for ASPD and/or BPD. Substance-use-disordered patients with and without ASPD/BPD were compared on measures of sociodemographic variables, frequency and types of substance used, treatment history, and preexisting psychopathology. The primary outcome measures examined were retention in treatment, group attendance, and abstinence in the first three months of treatment. Of the substance use disorder patients, 47% (24/50) met screening criteria for ASPD and/or BPD. Of the patients with comorbid ASPD/BPD, 25% abused cocaine compared with 11% of those without comorbid PD ($p < 0.01$). In addition, 43% of the ASPD/BPD patients required psychiatric treatment for mood disorders compared with 17% of the non-PD group ($p < 0.01$). There was no statistically significant difference in the rate of retention between the two groups at three months. In both cases the rate of abstinence was high.

NR181 Monday, May 19, 3:00 p.m.-5:00 p.m.

Temperament and Treatment Response in Major Depressive Disorder

Julie R. Newman, Department of Psychiatry, Massachusetts General Hospital, 15 Parkman/ACC 815, Boston MA 02114; Scott E. Ewing, D.O., Rachel D. McColl, B.A., Joseph S. Borus, B.A., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Maurizio Fava, M.D.

Summary:

Objective: Recent studies have found temperament types as defined by Cloninger to be a good predictor of antidepressant treatment response in depressed patients. We sought to replicate these findings using a large sample of depressed outpatients.

Methods: We treated 199 outpatients (89 males and 110 females, mean age 40.0 ± 10.7) with major depressive disorder, as assessed with the Structured Clinical Interview for DSM-III-R, - Patient Edition (SCID-P), in an eight-week open trial with fluoxetine 20 mg/day. The Tridimensional Personality Questionnaire (TPQ) was administered to all patients before and after treatment.

Results: There was a significant relationship between pretreatment scores on the TPQ subscale of harm avoidance and severity of depression at baseline as determined by Hamilton Depression Rating Scale-17-item (HAM-D-17) scores. When corrected for baseline HAM-D-17 scores, no significant relationship was found between response to fluoxetine and either temperament type or any TPQ subscale, including harm avoidance.

Conclusions: In contrast to previous studies, we failed to find a relationship between temperament type as defined by the TPQ and antidepressant response.

NR182 Monday, May 19, 3:00 p.m.-5:00 p.m.

Effect of Crisis Treatment on Functional Improvement

Douglas R. Dolnak, D.O., Department of Psychiatry, University of CA/San Diego, 8950 Vill LaJolla Dr, Ste 2243, La Jolla CA 92037; Mark H. Rapaport, M.D., William B. Hawthorne, M.D.

Summary:

Residential crisis treatment programs are alternatives to inpatient hospital treatment that employ psychosocial and psychopharmacologic management in a less restrictive setting. There are few data evaluating the effectiveness of these programs, especially their utility in acutely altering psychosocial functioning. The objective of this pilot study is to gather data investigating the utility of the Scale of Functioning (SOF) and the Global Assessment of Functioning (GAF) with the chronic mentally ill in a crisis program. We hypothesize that the short-term residential rehabilitation will offer patients a 20% or greater improvement in daily functioning as measured by the SOF and GAF. The SOF is a well-validated, 15-item, multidimensional scale designed to assess functioning with inpatients and outpatients. Forty (40) medically stable subjects between 18 and 65 years of age will be assessed by a physician rater with a formal structured interview for DSM-IV, the SOF, and GAF at intake and at discharge from the facility. The first 12 subjects have completed this pilot study: 42% had major depression, 30% had schizophrenia, and 28% had bipolar disorder. Mean baseline SOF and GAF scores were 32.5 ± 3.89 (SD) and 31.6 ± 4.07, respectively. Mean SOF and GAF scores at discharge were 41.4 ± 5.21 (a 27% improvement) and 50.6 ± 6.78 (a 60% improvement), respectively. Preliminary analysis is limited by a small sample size, short treatment duration, and lack of a control group—therefore inferential statistics were not employed—but suggests that residential treatment causes a rapid increase in psychosocial functioning.

NR183 Monday, May 19, 3:00 p.m.-5:00 p.m.

Effectiveness of a Psychiatric Pain Clinic

John V. Anooshian, M.D., Department of Psychiatry, University of Hawaii, 1356 Lusitana Street, 4th Flr, Honolulu HI 96813; Jon M. Streltzer, M.D., Deborah Goebert, M.S.

Summary:

Objective: To determine the efficacy of a unidisciplinary (psychiatric) pain consultation clinic in a primary care setting.

Method: Ninety-eight outpatients were referred over a three-and-one-half-year period to the pain clinic from a primary care clinic serving a multiethnic, indigent population. Criteria for referral included suspicion of psychological factors or difficulty in medication management. Patient characteristics and outcomes were abstracted by chart review.

Results: Referring physicians were 4.85 times more likely to identify unresponsive, intractable pain as the reason for referral, whereas pain clinic psychiatrists were 1.9 times more likely to diagnose medication dependency as the primary problem. More than 40% had comorbid conditions—26% with depression and 17% with substance abuse. Using DSM-IV criteria, 84% of patients were diagnosed with pain disorder with psychological factors. Interventions included detoxification, substitution, and reduction of medication as well as nonpharmaceutical methods. Many patients (59%) followed recommendations. However, 10% never returned for follow-up visits at the primary care clinic, often because narcotics were no longer prescribed. Patients had significantly fewer medical visits and tests six months after attending the pain clinic compared to six months before (2.6 vs. 4.7, $p < 0.0001$; 0.5 vs. 1.7, $p < 0.0001$, respectively). Additionally, 62% had improved functioning and 54% had less pain overall.

Conclusion: Psychiatric pain clinics can provide effective treatment, particularly for difficult patients.

NR184 Monday, May 19, 3:00 p.m.-5:00 p.m.

The Arizona Sexual Experience Scale: Validity and Reliability

Cynthia A. McGahuey, A.A., Department of Psychiatry, University of Arizona, 1501 N Campbell/AHSC 7402, Tucson AZ 85724; Alan J. Gelenberg, M.D., Cindi A. Laukes, M.F.A., Rachel Manber, Ph.D., Kathy M. McKnight, B.S., Francisco A. Moreno, M.D., Pedro L. Delgado, M.D.

Summary:

While sexual dysfunction is common in patients with anxiety and mood disorders, many newer psychotropic agents can also induce sexual dysfunction. Unfortunately, quantification of sexual

dysfunction in these patients has been limited because the available validated rating scales for this purpose are too lengthy and intrusive (include many questions regarding specific sexual activities and preferences). In order to measure psychotropic drug-induced sexual dysfunction, the authors have developed the Arizona Sexual Experiences Scale (ASEX). This presentation will provide preliminary data on the validity of the ASEX, an easy-to-use, five-item rating scale that quantifies sex drive arousal, vaginal lubrication/penile erection, ability to reach orgasm, and satisfaction from orgasm.

In order to assess the validity of the ASEX, it was administered to a sample of hospital employees (N = 100) and patients with major depression or panic disorder (N = 100). All subjects also fill out the Brief Index of Sexual Functioning (BISF), a validated 21-item scale for assessment of sexual dysfunction; the Beck Depression Inventory; and the Inventory of Depressive Symptomatology. Patients are additionally assessed with the Hamilton Depression and Anxiety Rating Scales. Convergent validity is determined by correlating responses on the ASEX with those on the BISF, and divergent validity is determined by correlating responses to individual items on the ASEX with depression and anxiety ratings. Preliminary analyses from the first 50 subjects suggest that individual items of the ASEX are highly significantly correlated with related items on the BISF, but not with depression or anxiety score. The ASEX was much easier to administer (5-10 minutes) and was perceived as being relatively unintrusive by subjects. Detailed data on the reliability and validity of the ASEX will be presented. The ASEX is an important new tool with which to rapidly identify and assess medication-induced sexual dysfunction in routine clinical settings and clinical trials.

NR185 Monday, May 19, 3:00 p.m.-5:00 p.m.

ECT Outcome of Dually Diagnosed Patients

Judy S. Uy, M.D., Department of Psychiatry, Bronx Lebanon Hospital, 1276 Fulton Avenue, 4 South, Bronx NY 10486; Ramanbhai C. Patel, M.D., Ali Khadivi, Ph.D.

Summary:

Objective: Considering the vast literature on electroconvulsive therapy (ECT) it is remarkable how little is known about the effectiveness of ECT on dually diagnosed patients. This study was undertaken to compare the length of stay and rehospitalization rate of dually diagnosed patients who received ECT treatment with non-dually diagnosed subjects who received ECT treatment.

Method: The data was collected from a retrospective review of the records of all nonoverlapping mixed-aged adult patients (N = 51) who had inpatient bilateral ECT treatment from 1992 to 1996 at a major inner city hospital. Based on the discharge diagnosis the sample was divided in two groups; dual diagnosed patients (n = 29) and non-dual diagnosed patients (n = 22). Dual diagnosis was defined as having major Axis I diagnosis with comorbid substance abuse.

Results: The sample was 53% male, 47% female and predominately Hispanic (63%) and Afro-American (29%). The Mean age was 44. The two groups were not significantly different on the demographic variables, diagnosis, number of ECT treatments and mean seizure time. 48% of the sample was readmitted within one year and 22% of the readmitted subjects had relapsed within 30 days of discharge. Surprisingly the two groups were not significantly different on length of stay, readmission within a year, or readmission within the 30 days of discharge.

Conclusion: ECT outcome of dually diagnosis patients is similar to outcome for non-dual diagnosis patients. However, given the high relapse rate, the study underscores the need for maintenance ECT.

NR186 Monday, May 19, 3:00 p.m.-5:00 p.m.

Aminophylline Lengthens Short Seizures During ECT

Liat Stern, M.D., Department of Psychiatry, Sheba Medical Center, Tel-Hshomer, Ramat Gan 52621, Israel; Pinhas N. Dannon, M.D., Shmuel Hirschmann, M.D., Daniela Amytal, M.D., Leon J. Grunhaus, M.D.

Summary:

Background: ECT is considered to be one of the most effective treatments for patients with major depression and persistent psychosis. During most ECT courses, seizure threshold increases and seizure duration decreases. Short seizures are accepted as one of the factors of poor outcome. Methylxanthine preparations, caffeine, and theophylline have been used to prolong seizure duration. Most of the studies on this subject have utilized caffeine. The use of aminophylline, more readily available than caffeine, has not been well documented.

Objective: To test the capability of aminophylline to increase seizure length in patients with short seizures.

Methods: Patients were considered for this protocol whenever during the course of ECT seizure length was shorter than 25 seconds and the energy level administered had reached 70% of maximal machine output, without evidence of clinical improvement. Intravenous aminophylline, 3–5 mg per kg, was administered to 14 drug-free patients, 10 minutes before the ECT session. Seizure length was assessed clinically and per EEG. Patients were used as their own controls. Statistical comparisons were done using paired t-tests, comparing seizure length before and after administration of aminophylline.

Results: A significant increase ($P < 0.03$) in seizure length was achieved and maintained on three subsequent treatments with aminophylline. No adverse events were noted from the addition of aminophylline.

Conclusions: Aminophylline can be safely used to increase seizure length in patients with short seizures.

NR187 Monday, May 19, 3:00 p.m.-5:00 p.m.

Anxiogenic Effects of Naloxone Hydrochloride and Sodium Lactate in Normal Volunteers

Smit S. Sinha, M.D., c/o Dr. Gorman/Psych., Columbia University, 722 W 168th Street, New York NY 10032; Donald F. Klein, M.D.

Summary:

Objective: The endogenous brain opioid system has been implicated in the regulation of anxiety and panic. The present study attempted to determine if blockade of endogenous opioids by naloxone, an opioid receptor antagonist, followed by administration of sodium lactate, a known panicogen in panic disorder patients, has anxiogenic effects in normal controls.

Methods: Subjects were 10 male normal volunteers. Subjects were given an infusion of naloxone (1 mg/kg) followed by administration of 0.5m sodium lactate infusion. HR, BP, and RR were monitored continuously. Subjective symptoms were evaluated by the Acute Panic Inventory (API), Brief Psychiatric Rating Scale, a 10-point anxiety scale, and breathlessness scale (BORG).

Results: 1.) Preliminary results show that normal controls have significant increases in tidal volume following naloxone and lactate infusion compared with naloxone infusion alone. 2.) Normal controls exhibit significant increases in scores on the API, Anxiety Scale, and BORG scale following the infusion of naloxone and lactate compared with naloxone alone.

Conclusions: 1.) The endogenous opioid system has a role in the regulation of anxiety in a normal individual. 2.) Endogenous opioids may inhibit the anxiogenic effects of sodium lactate in a normal individual. Opiate receptor blockade may antagonize this inhibitory effect.

NR188 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

SSRI Dose Interruption Study: Interim Data

Sharon L. Blomgren, M.D., DC 1046, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; William Krebs, Ph.D., Michael Wilson, M.S., Richard Ascroft, R.Ph., Maurizio Fave, M.D., Jerrold Rosenbaum, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize significant differences in the clinical consequences of missed doses of fluoxetine, sertraline, and paroxetine in the treatment of depression.

Summary:

Objective: Sudden discontinuation or missed doses of antidepressants have been associated with acute discomfort. This may relate to the half-life of the parent drug or metabolite. We conducted a controlled study to characterize symptoms that are likely to occur upon interruption of fluoxetine, sertraline, or paroxetine therapy and estimate their frequencies of occurrence.

Method: This multisite study used an open-label, controlled, parallel design with a double-blinded interruption period to compare mean incidence of discontinuation-emergent signs and symptoms (DESS) in patients clinically stable on maintenance doses (4–24 months) of fluoxetine (20–60 mg/d), sertraline (50–200 mg/d), or paroxetine (20–60 mg/day). For a five-to-eight-day blinded period, placebo was substituted for active drug. DESS events were assessed by questionnaire: depressive symptoms were measured using the MADRS and HAM-D.

Results: Groups were demographically comparable. After interruption of therapy these results were observed:

Drug Treatment	*n*	*Number of DESS events (Mean ± SD)*	*Increase in MADRS Score (Mean ± SD)*
Fluoxetine	23	3 ± 4.25	0.6 ± 4.53
Paroxetine	21	10‡± 8	6.5* ± 6.85
Sertraline	21	10.1 ‡± 7.16	8.2 †± 11.76

p-value vs. fluoxetine = .033*, .009†, <.001‡

Conclusions: Brief interruptions of sertraline and paroxetine therapy produced significantly more adverse events than interruption of fluoxetine therapy. Additionally, fluoxetine offered consistent antidepressant action during interruptions; sertraline and paroxetine did not.

References:

1. Lazowick AL, Levin GM: Potential withdrawal syndrome associated with SSRI discontinuation. *Annals of Pharmacotherapy.* 29(12): 1284–85, 1995.

2. Coupland NJ, Bell CJ, Potokar JP: Serotonin reuptake inhibitor withdrawal. *J Clin Psychopharmacol:* 16:356–362, 1996.

NR189 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Optimal Length of Continuation Therapy: A Prospective Assessment During Fluoxetine Long-Term Treatment of MDD

David Michelson, M.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Frederick W. Reimherr, M.D., Charles M. Beasley, Jr., M.D., Michael Wilson, M.S.

Summary:

Objective: To determine prospectively optimal length of fluoxetine continuation therapy following successful acute treatment of major depressive disorder.

Method: Outpatients were treated for 12 to 14 weeks with fluoxetine (20 mg/day). Patients meeting response criteria were randomized to 50 weeks of double-blind continuation therapy consisting of placebo crossover periods as follows:

- immediate placebo crossover for 50 weeks (crossover group-1);
- fluoxetine for 14 weeks followed by placebo crossover for 36 weeks (crossover group-2);
- fluoxetine for 38 weeks followed by placebo crossover for 12 weeks (crossover group-3);
- fluoxetine for 50 weeks (no crossover).

Actual relapse rates and Kaplan-Meier estimates were determined during three fixed 12-week time intervals following each placebo crossover.

Results: Relapse rates were statistically significantly higher in patients initiating placebo in crossover group-1 (48.6% vs. 26.4% $p < 0.001$) and crossover group-2 (23.2% vs. 9.0% $p = 0.027$) than in patients remaining on fluoxetine. Relapse rates were numerically, but not statistically significantly, higher in patients initiating placebo in crossover group-3 than in patients remaining on fluoxetine (16.2% vs. 10.7% $p = 0.717$), possibly because sample size decreased as the study progressed.

Conclusions: These data suggest that following a successful 12-week course of acute therapy, additional protection against relapse is associated with continuation therapy of at least 14 weeks.

References:

1. Keller MB, Klerman GL, Lavori PW, et al: Long-term outcome of episodes of major depression: clinical and public health significance. *JAMA*; 252:788–792, 1984.

2. Prien RF, Kupfer DJ: Continuation drug therapy for major depressive episodes: how long should it be maintained: *Am J Psychiatry*; 143:18–23, 1986.

NR190 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Olanzapine Versus Risperidone in the Treatment of Schizophrenia and Other Psychotic Disorders

Pierre V. Tran, M.D., MC 541, Eli Lilly and Company, Lilly Corporate Center DC 0538, Indianapolis IN 46121; Gary D. Tollefson, M.D., Susan Hamilton, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the major differences and similarities between the two newest antipsychotics, olanzapine and risperidone, with respect to their pharmacology, efficacy, and safety features as well as the key defining criteria of an atypical antipsychotic.

Summary:

This double-blind, randomized study, which enrolled 297 patients meeting DSM-IV criteria for schizophrenia, schizophreniform disorder, and schizoaffective disorder, was designed to allow a head-to-head comparison of olanzapine (10–20 mg) (mean modal dose 16.9 mg/day) and risperidone (4–12 mg) (mean modal dose 7.3 mg/day). Across various efficacy measures, both olanzapine and risperidone demonstrated efficacy on overall positive and negative symptomatology. However, after 28 weeks of treatment, olanzapine showed statistically significant superiority in reducing mood symptoms (PANSS mood), improving clinical response (defined as at least 30% reduction in PANSS total score), and prevention of relapse (defined as at least 20% or more worsening in PANSS total and CGI ≥3 after an initial period of stabilization). Safety measures, both objective and subjective, show that olanzapine was statistically significantly superior to risperidone in regard to adverse events, especially rate of extrapyramidal symptoms (EPS) and sexual dysfunction, as well as prolactin

elevation. In conclusion, when compared against the three criteria for defining an atypical antipsychotic (i.e., low EPS potential, broad efficacy profile, and minimal prolactin elevation), olanzapine significantly outperforms risperidone.

References:

1. Beasley Jr CM, Tollefson GD, Tran P, et al: The Olanzapine HGAD Study Group: olanzapine versus placebo and haloperidol: acute phase results of the North American double-blind olanzapine trial. *Neuropsychopharmacol* 14(2):105–118, 1996.

2. Marder SR, Meibach RC: Risperidone in the treatment of schizophrenia. *Am J Psychiatry* 151(6):825–835, 1994.

NR191 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Effects of First Trimester Fluoxetine Exposure on the Newborn

David J. Goldstein, M.D., DC 0532, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Lois A. Corbin, R.N., Karen L. Sundell, B.S.

Summary:

Objective: To determine whether first trimester exposure to fluoxetine, a selective serotonin reuptake inhibitor, is associated with increased frequency of fetal malformation.

Method: Using data from the Eli Lilly and Company worldwide fluoxetine pregnancy database, we compared outcomes of all confirmed, prospectively identified, first trimester exposures with the results of several historic assessments. Outcomes were available for 796 pregnancies (37 from clinical trials and 759 from spontaneous reports), six times the number of pregnancy outcomes previously reported in any single study of fluoxetine. Maternal dosage ranged from 10 to 80 mg per day.

Results: Spontaneous abortions were reported in 110 (13.8%) of the 796 pregnancies. Malformations, deformations, and disruptions (including those identified after the prenatal period) were reported in 34 (5.0%). These rates are consistent with those found in historic assessments. No consistent or recurring pattern of abnormalities was observed, another indication that fluoxetine is not teratongenic. Of the 586 normal infants, 33 (5.6%) had newborn complications unrelated to malformations, and four (0.7%) had prolonged hospitalization or intensive care nursery admission, similar to reference samples.

Conclusions: This evaluation suggests that first trimester exposure to fluoxetine does not increase the risk for fetal malformations.

References:

1. Pastuszak A, Schick-Boschetto B, Zuber C, et al: Pregnancy outcome following first trimester exposure to fluoxetine. *JAMA*; 269:2246–8, 1993.

2. Goldstein D: Effects of third trimester fluoxetine exposure on the newborn. *J Clin Psych*; 15:417–420, 1995.

NR192 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Placental Passage of Antidepressants

Zachary N. Stowe, M.D., Department of Psychiatry, Emory University, 1639 Pierce Drive, Ste 4003, Atlanta GA 30322; Alexis M. Llewellyn, B.A., James R. Strader, B.S., C.D. Kilts, Ph.D., James C. Ritchie, Ph.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate significant differences in the degree of placental passage for medications within the class (sertraline vs. fluoxetine).

Summary:

Objective: The purpose of this study was to determine the magnitude of placental passage for various antidepressants in women treated during pregnancy by measuring the maternal serum and umbilical cord concentrations at delivery.

Method: A total of 29 maternal serum and umbilical cord paired samples were taken at delivery. Analysis for the parent compound and primary metabolite has been completed on 17 of these pairs for maternal medication concentration.

Results: All antidepressants and their metabolites were found in umbilical cord blood, with the majority of antidepressants demonstrating incomplete placental passage with an [umbilical cord] to [maternal serum] ratio of <1.0. Specifically, the U/M ratio for fluoxetine = 0.94 ± 0.37 (n = 9), norfluoxetine = 0.79 ± 0.28 (n = 9), sertraline = 0.43 ± 0.15 (n = 7), with single sample pairs for paroxetine (0.67) and venlafaxine (29.6).

Conclusion: These preliminary data suggest that there is no evidence of accumulation in the fetal circulation of fluoxetine, paroxetine, or sertraline. These data also demonstrate significant differences in the degree of placental passage for medications within the class (sertraline vs. fluoxetine, $p < 0.05$). Such novel data could provide a scientific contribution to treatment guidelines and a basis for determining fetal exposure.

References:

1. Altshuler LL, Cohen L, Szuba MP, et al: Pharmacologic management of psychiatric illness during pregnancy. *Am J Psychiatry.* 153(5):592–606, 1996.

2. Miller LJ: Clinical strategies for the use of psychotropic drugs during pregnancy. *Psychiatric Medicine.* 9(2):275–98, 1991.

NR193 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Naltrexone in the Treatment of Nicotine Dependence: A Preliminary Study

Stephanie S. O'Malley, Ph.D., Department of Psychiatry, Yale University Medical School, One Long Wharf Drive, Box 18, New Haven CT 06511; Suchitra Krishnan-Sarin, Ph.D., Borislav Meandzija, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that naltrexone may be useful in augmenting the efficacy of transdermal nicotine replacement therapy.

Summary:

The opioid antagonist naltrexone is approved for use in the treatment of alcohol dependence and has been shown to reduce the risk of continued drinking following a lapse. Given that nicotine, like alcohol, activates the endogenous opioid system, we examined the effect of naltrexone with and without transdermal nicotine replacement therapy in subjects attempting to stop smoking. Sixty smokers who were not alcohol dependent were randomized to receive naltrexone 50 mg qd or matching placebo for four weeks. In addition, subjects received one of three nicotine patch conditions: 21 mg for four weeks; 21 mg qd for two weeks followed by 14 mg and then 7 mg for one week each; or no patch. Subjects were provided with information from the American Lung Association's pamphlet "A Lifetime of Freedom from Smoking" and participated in weekly research assessments.

Naltrexone without patch produced the lowest rate of abstinence from cigarettes. In addition, naltrexone was associated with increased levels of nicotine withdrawal. However, among subjects receiving nicotine replacement therapy, naltrexone reduced the number of cigarettes smoked compared with placebo. The results of this study suggest that naltrexone may be useful in augmenting the efficacy of transdermal nicotine replacement therapy. (Supported by NIH grants P50-DA04060, KO2-AA00171).

References:

1. O'Malley SS, Croop RS, Wroblewski JM, et al: Naltrexone in the treatment of alcohol dependence: a combined analysis of two trials. *Psychiatric Annals, 25*:681–688, 1995.

2. Pomerleaur OF, Fertig JB, Seyler LE, Jaffe J: Neuroendocrine reactivity to nicotine in smokers. *Psychopharmacology, 83*:61–67, 1983.

NR194 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Prospective Assessment of Mood Disorders in HIV Infection

Paula Bird, M.S.N., Department of Psychiatry, University of NC-Chapel Hill, CB#7160/Neurosciences Hospital, Chapel Hill NC 27599; Jane Leserman, Ph.D., Diana O. Perkins, M.D., Susan G. Silva, Ph.D., Dwight L. Evans, M.D., Robert N. Golden, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be more familiar with the rates of major depression over the course of several years among HIV seropositive and HIV seronegative gay men who have been recruited for study from a low prevalence area.

Summary:

Objective: It is uncertain if a relationship between HIV infection and psychiatric morbidity exists, particularly for mood disorders. We studied prospectively the incidence of DSM-III-R Axis I disorders in HIV-infected gay men.

Method: We studied 85 HIV-infected and 61 uninfected gay men every six months for up to four years; HIV-infected men were asymptomatic at study entry. Psychiatric diagnosis was determined by review of a modified SCID. Mood symptom severity was measured with the Hamilton Depression Rating Scale and the Profile of Mood States, and HIV disease was assessed by physical exam.

Results: We found no differences in the incidence of any DSM-III-R Axis I disorders in HIV-infected compared with uninfected men. For major depressive disorder, incidence per six-month follow-up period is:

Month	*06*	*12*	*18*	*24*	*30*	*36*	*42*	*48*
HIV+	9%	9%	12%	4%	6%	6%	7%	2%
HIV–	8%	6%	7%	12%	3%	11%	0%	4%

In addition, there were no significant differences between the HIV-infected (26%) and uninfected (33%) men for developing one or more major depressions during the follow-up. Severity of depressed or tense mood, or depressive symptoms did not significantly differ at any visit. Although 33% of the HIV-infected men developed clinical symptoms of HIV disease progression during the follow-up, incidence of depression remained similar to those of HIV-uninfected subjects. Consistent with our previous findings, a history of major depression predicted development of this disorder during follow-up ($p = .0001$).

Conclusions: In our cohort, HIV-infected gay men are not more likely to develop a psychiatric disorder than uninfected men. Major depression should not be considered an "expected" reaction to HIV disease progression.

References:

1. Perkins DO, Stern RA, Golden RN, et al: Mood disorders in HIV infection: prevalence and risk factors in a non-epicenter of the AIDS epidemic. *Am J Psychiatry* 151:233–236, 1994.

2. Perkins DO, Leserman J, Stern RA, et al: Somatic symptoms and HIV infection: relationship to depressive symptoms and indicators of HIV disease. *Am J Psychiatry* 152(12):1776–1781, 1995.

NR195 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Prevalence of Dysthymia in Primary Care

Meir Steiner, M.D., Department of Psychiatry, McMaster University, 50 Charlton Ave E/St. Joseph's, Hamilton ON L8N 4A6, Canada; Gina Browne, Ph.D., Jacqueline Roberts, M.Sc., Edward J. Dunn, Ph.D., Barbara A. Bell, M.D., Ellen Jamieson, M.Ed.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that primary care populations have a higher concentration of dysthymia, major depression, and panic disorder and fewer persons who endorse alcohol and drug dependence when compared with data from community surveys.

Summary:

The prevalence of psychiatric disorders is higher in primary care than in population surveys, although little distinction has been made about which disorders and comorbidities are over- and under-represented in primary care.

Objective: The purposes of this study were to ascertain the 12-month prevalence of current Axis I psychiatric disorders in primary care compared with the prevalences reported in a population survey, and to identify the most frequent comorbid psychiatric disorders.

Methods: 4327 (69%) of 6280 eligible consenting adults enrolled in an Ontario Health Service Organization were screened using the University of Michigan CIDI revised short form for nine psychiatric disorders, as part of a larger ongoing study of the effectiveness, benefits, and comparative costs of sertraline vs. IPT in dysthymia.

Results: Dysthymia, major depression, panic disorder, and simple phobia were 1.4 to 2.4 times more prevalent, whereas social phobia, generalized anxiety, and alcohol and drug dependence were 1.7 to 4.5 times less prevalent in primary care versus community populations. Of the 30% (1279 of 4327) of persons identified with a psychiatric disorder, 39% had comorbid disorders. There was a pattern of fewer persons having more comorbid disorders.

Conclusion: Our data confirm that primary care populations have a higher concentration of dysthymia (5.1%), major depression (14.4%), and panic disorder (5.6%) and fewer persons who endorse alcohol and drug dependence when compared with data from community surveys.

[Supported by a grant from the Medical Research Council of Canada - Pharmaceutical Manufacturers Association of Canada and Pfizer Canada Inc.]

References:

1. Kessler RC, McGonagle KA, Zhao S, et al: Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. *Arch Gen Psychiatry* 51:8–19, 1994.

2. Miranda J, Hohmann AA, Sttkisson CC, Larson DB: *Mental Disorders in Primary Care.* San Francisco, Jossey-Bass, 1994.

NR196 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Treatment Response in Dysthymic Patients With and Without a History of MDD

Maurizio Fava, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, ACC 815, Boston MA 02114; A. John Rush, M.D., Richard C. Shelton, M.D., Michael E. Thase, M.D., Lorrin M. Koran, M.D.

Educational Objectives:

At the conclusion of this presentation the participant will become familiar with the differences between dysthymic patients with and without a history of MDD.

Summary:

Very little research has been conducted to assess whether there are differences between patients with pure dysthymia (i.e., without a history of major depression) and those with dysthymia who have a history of major depression.

Objective: We compare demographic and diagnostic characteristics and response to antidepressant drug treatment among dysthymic outpatients with and without a history of major depression.

Methods: A total of 410 outpatients (266 females and 146 males; mean age: 41.7 ± 9.1 years) participating in a double-blind, multicenter study were randomized into one of three treatment groups: sertraline with doses up to 200 mg/day (n = 134), imipramine with doses up to 300 mg/day (n = 136), or placebo (n = 140). In this 12-week study, remission was defined as no longer meeting DSM-III-R criteria for dysthymia and having a score of 0 on item # 1 (depressed mood) of the Hamilton Depression Rating Scale.

Results: The rates of remission in dysthymic patients with a history of major depression were 48% for sertraline, 50% for imipramine, and 29% for placebo, with both active treatments significantly superior to placebo. Remission rates among dysthymic patients without a history of major depression were 50% for sertraline, 36% for imipramine, and 30% for placebo, with sertraline, but not imipramine, achieving a statistically significant difference compared with placebo.

Conclusion: Among outpatients with current dysthymia, the absence of a history of major depression may be associated with greater response to treatment with the selective serotonin reuptake inhibitor sertraline than with the tricylic antidepressant imipramine.

References:

1. Thase ME, Fava M, Halbreich U, et al: A placebo-controlled randomized clinical trial comparing sertraline and imipramine for the treatment of dysthymia. *Archives of General Psychiatry* 53:777–784, 1996.

2. Keller MB, Shapiro RW: Double depression: superimposition of acute depressive episodes on chronic depressive disorders. *Am J Psychiatry* 139:438–442, 1982.

NR197 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Ten-Year Cumulative Probability of Recurrence After Recovery from an Index Episode of MDD

Timothy I. Mueller, M.D., Department of Psychiatry, Brown University/Butler Hosp, 345 Blackstone Blvd., Providence RI 02906 0; Andrew C. Leon, Ph.D., Martin B. Keller, M.D., David A. Solomon, M.D., Jean Endicott, Ph.D., Meredith Warshaw, M.S.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the majority of CDS probands who presented for treatment of MDD recovered, and the majority of those who recovered experienced a recurrence. Female gender and clinical measures suggesting a more severe index episode predicted recurrence.

Summary:

Objective: For many people with MDD, recovery is not permanent. We present data on the cumulative probability of recovery after recurrence from MDD for up to 10 years of prospective follow-up.

Methods: Between 1978 and 1981, the NIMH Collaborative Depression Study (CDS) recruited 955 probands with a mood disorder who were prospectively followed with biannual (first five years) or annual (subsequently) systematic interviews. During the 10 years of naturalistic follow-up reported herein, 378 of the 431 probands with MDD only at intake recovered from the index episode. Time to recurrence was calculated using survival analysis.

Results: Following recovery, 258 experienced a recurrence and 120 remained well. Those with a recurrence were more likely to be female and have longer durations and a greater number of episodes of MDD prior to intake. At 10 years of follow-up, the median length of the well interval in those with a recurrence was 124 weeks. The Kaplan-Meier cumulative probability of recurrence was 78%.

Conclusion: The majority of CDS probands who presented for treatment of MDD recovered. The majority of those who recovered experienced a recurrence. Female gender and clinical measures suggesting a more severe index episode predicted recurrence.

References:

1. Keller MB, Lavori PW, Rice J: The persistent risk of chronicity in recurrent episodes of nonbipolar major depressive disorder: a prospective follow-up. *Am J Psychiatry* 143:24–28, 1986.

2. Maj M, Veltro F, Pirozzi R, et al: Pattern of recurrence of illness after recovery from an episode of major depression: a prospective study. *Am J Psychiatry* 149:795–800, 1992.

NR198 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

Treatment of Premenstrual Dysphoric Disorder with Sertraline During the Luteal Phase: A Randomized, Double-Blind Placebo-Controlled Crossover Trial

Steven A. Young, M.D., 1254 Holly Cove Drive, Jupiter FL 33458; Peyton H. Hurt, M.D., David M. Benedek, M.D., Robin S. Howard, M.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate an understanding of recent findings concerning the etiology of premenstrual dysphoric disorder and the usefulness of sertraline in treating this disorder, particularly when used only during the luteal phase.

Summary:

Objective: The authors designed a randomized, double-blind, crossover study to assess the efficacy of sertraline in the treatment of premenstrual dysphoric disorder (PMDD) when given only during the luteal phase of the menstrual cycle.

Methods: 31 subjects were selected for a seven-month study period that included an initial two months of screening, two months of treatment with placebo or sertraline, a washout month, and two months crossed over to either placebo or sertraline. Eleven subjects completed the study. Symptoms were monitored with daily reports using the Calendar of Premenstrual Experience (COPE). For each study phase, premenstrual COPE scores (seven days prior to menses) were examined using repeated measures analysis of variance.

Results: When comparing COPE results during the treatment periods of the luteal phase, there was significant treatment effect, with higher scores during the placebo cycles compared with the sertraline-treated cycles (P = 0.0052 behavioral, P = 0.014 physical).

Conclusions: This study is the first to demonstrate a significant response to an SSRI when used only during the luteal phase.

References:

1. Wood SH, Mortola JF: Treatment of premenstrual syndrome with fluoxetine: a double-blind, placebo-controlled, crossover study. *Obstetrics and Gynecology* 80:339–44, 1992.

2. Halbreich U, Tworek H: Altered serotonergic activity in women with dysphoric premenstrual syndrome. *Int J Psychiatry Med* 23:1–27, 1993.

NR199 Tuesday, May 20, 9:00 a.m.-10:30 a.m.

A Controlled Study of Light Therapy in Premenstrual Dysphoric Disorder

Raymond W. Lam, M.D., Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Diana Carter, M.B., Shaila Misri, M.B., Annie Kuan, B.A., Lakshmi N. Yatham, Athanasios P. Zis, M.D.

Educational Objectives:

To describe new findings about the clinical use of bright light therapy in the treatment of late luteal phase dysphoric disorder (equivalent to DSM-IV premenstrual dysphoric disorder).

Summary:

Objective: We report preliminary results from a placebo-controlled study of dim versus bright light therapy in late luteal phase dysphoric disorder (LLPDD).

Methods: 14 female patients meeting DSM-III-R criteria for LLPDD underwent a six-cycle randomized, counter-balanced, crossover study. After two cycles of prospective symptom monitoring, patients were randomized to either 10,000 lux white light (active condition), or 500 lux red light (placebo condition), administered by a cool-white fluorescent light box for 30 minutes/day during the last two weeks of each cycle. After two treatment cycles, patients were crossed over to the other condition for another two cycles. Patients were assessed each cycle at the end of the follicular and luteal phases by blinded raters using standardized depression rating scales and the Premenstrual Tension Syndrome Scale (PMTS). Differences between luteal phase and follicular phase scores within each cycle were summed across the two cycles.

Results: The bright white light condition significantly reduced depression and PMS scores (29-item Ham-D, BDI, CGI, PMTS) during the symptomatic luteal phase compared with baseline ($p < 0.05$), while the dim red light condition did not. During the bright white light treatment, patients were rated as much or very much improved on the CGI in 89% of the cycles, compared with 65% of the cycles in the dim red light condition ($p < 0.03$).

Conclusions: These results suggest that bright light therapy is an effective, well-tolerated, nonpharmacologic treatment for LLPDD.

References:

1. Parry BL, Mahan AM, Mostofi N, et al: Light therapy of late luteal phase dysphoric disorder: an extended study. *Am J Psychiatry* 150:1417-1419, 1993.

2. Maskall DD, Lam RW, Carter D, et al: Seasonality of symptoms in premenstrual dysphoric disorder. Submitted for publication.

NR200 Tuesday, May 20, 12 noon-2:00 p.m.

Abrupt Discontinuation of Fluoxetine: A Randomized, Placebo-Controlled Study

David Michelson, M.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Roland Onawala, Ph.D., Charles M. Beasley, Jr. M.D.

Summary:

Objective: Shorter acting SSRIs are associated with more treatment interruption-related symptoms than fluoxetine. To rule out the possibility that fluoxetine's longer half-life is associated with late occurring events, we studied adverse events over six weeks following abrupt discontinuation of fluoxetine.

Method: 395 fluoxetine-treated (20mg/day for 12 weeks) patients in a double-blind, placebo controlled study of maintenance treatment of depression were randomized in a double-blind fashion to continued fluoxetine (N = 99) or abrupt substitution of placebo (N = 96). Patients were seen one, two, four and six weeks following randomization and reports of adverse events (AEs) were systematically collected.

Results: Overall new or worsened AEs and patient discontinuations related to AEs were similar for both groups at each visit before and after randomization. Several mild common events were slightly more frequent at individual visits.

Conclusion: Abrupt discontinuation of fluoxetine is not associated with increased number of AEs over a six-week period. Several mild, common symptoms occurring only in small numbers of patients were slightly more frequent at individual visits, but were not clinically significant and may overstate statistical significance since a conservative approach not correcting for multiple comparisons was employed. These data suggest fluoxetine discontinuation is not associated with the emergence of clinically significant symptoms over a six-week period.

NR201 Tuesday, May 20, 12 noon-2:00 p.m.

Fluoxetine Versus Desipramine in Depressed Females with Advanced Cancers

Steven J. Romano, M.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Rosalinda Tepner, R.Ph., Michael Wilson, M.S.

Summary:

Objective: Depression frequently coexists in patients with cancer. However, to date only one study has tested an SSRI, fluoxetine, in this population.

Method: In a prospective six-week, double-blind, placebo trial, we compared fluoxetine to desipramine in treating depressive symptoms in 40 female cancer patients. Scales used to compare fluoxetine and desipramine therapies in patients with comorbid cancer were: Hamilton Rating Scale for Depression (HAMD), the Hamilton Rating Scale for Anxiety (HAMA), the Clinical Global Impressions (CGI), the Patient's Global Improvement (PGI), the Functional Living Index for Cancer (FLIC), the Memorial Pain Assessment Card (MPAC), and the SF-36 Health Survey.

Results:

- Both drugs improved symptoms of depression and anxiety as evidenced by the HAMD, the HAMA, the CGI, and PGI scales, and showed a trend toward significance in improvement in the FLIC.
- Both drugs showed significant improvement in the SF-36 quality of life scores of Role Emotional, Social Functioning, Mental Health, and Vitality.
- Fluoxetine, alone, was associated with significant improvement in the MPAC Mood Scale scores.

Conclusion: Because fluoxetine improved certain cancer-related measures more than desipramine, we conclude that fluoxetine may offer enhanced benefit to patients with comorbid cancer and depressive illness. Our results, while meaningful, require a larger sample size to substantiate.

NR202 Tuesday, May 20, 12 noon-2:00 p.m.

Effectiveness of Fluoxetine Therapy in Bulimia Nervosa Regardless of Baseline Depression

David J. Goldstein, M.D., DC 0532, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Michael Wilson, M.S., Richard Ascroft, B.S.

Summary:

Objective: To evaluate the efficacy of fluoxetine in the treatment of bulimia nervosa with or without comorbid depression.

Methods: Two multicenter, double-blind, parallel, randomized, placebo-controlled trials of fluoxetine in the treatment of bulimia were analyzed to determine the influence of comorbid depression on efficacy. Change in median number of binge-eating and vomiting episodes was used to assess efficacy. Data were stratified by Hamilton Rating Scale for Depression (HAMD) scores and by presence or absence of reported historical or current depression. ANCOVA was used to assess both the influence of the severity of depression and the presence or absence of comorbid depression on efficacy.

Results: Fluoxetine (60 mg) was associated with a statistically significant reduction ($p < .01$) in median number of both binge-eating and vomiting episodes. Improvements were independent of the patients' baseline HAMD score and of reported historical or current comorbid depression.

Conclusion: Fluoxetine (60 mg) was effective in the treatment of bulimia, regardless of the presence or absence of comorbid depression. Our results suggest that fluoxetine's efficacy in the treatment of bulimia nervosa is not simply a secondary effect of its antidepressant properties.

NR203 Tuesday, May 20, 12 noon-2:00 p.m.

Effect of Fluoxetine Therapy on Weight in Depressed Geriatric Patients

David J. Goldstein, M.D., DC 0532, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Charles M. Beasley, Jr., M.D., Michael Wilson, M.S.

Summary:

Objective: Fluoxetine and other selective serotonin reuptake inhibitors (SSRIs) have been recommended for antidepressant therapy in the elderly because they are safer in overdose and have far fewer cardiac and anticholinergic effects than tricyclic antidepressants.

Method: A report of fluoxetine-associated weight loss in the elderly prompted us to perform a retrospective evaluation of a multicenter, randomized, double-blind study of 671 patients, 60 years or older with major depression treated with 20 mg fluoxetine or placebo. We categorized patients into two groups according to adiposity: low/normal body mass index, and high body mass index, and we evaluated weekly weights.

Results:

- Fluoxetine-treated patients had a mean weight loss of 1.01 ± 2.05% from baseline, while there was little change in the placebo-treated patients' weights.
- The high body mass index group (but not the low/normal group) had a statistically greater proportion of patients who lost at least 5% of their baseline weight.
- Only one patient treated with fluoxetine and in the low body mass index group discontinued due to weight loss (2.7 kg).

Conclusions: Medically relevant weight loss in elderly patients treated with fluoxetine for depression is uncommon.

NR204 Tuesday, May 20, 12 noon-2:00 p.m.

Olanzapine Versus Haloperidol in the Treatment of First-Episode Psychosis

Todd Sanger, Ph.D., Lilly Research Lab, Eli Lilly and Company, Lilly Corporate Center, DC 0538, Indianapolis IN 46285; Gary D. Tollefson, M.D., Jeffrey A. Lieberman, M.D., Mauricio Tohen, M.D.

Summary:

These analyses explore the effect of olanzapine versus haloperidol in the treatment of first-episode psychosis in an international, multicenter, double-blind, parallel trial. This trial compared the efficacy and safety of a single dose range of olanzapine, 5–20 mg/day, to a single dose range of haloperidol, 5–20 mg/day, in the treatment of 1,996 inpatients and outpatients with a DSM-III-R diagnosis of schizophrenia, schizophreniform disorder, or schizoaffective disorder. Patients were assigned by random allocation to double-blind therapy in the ratio of two olanzapine to one haloperidol assignment. The acute phase of the trial was six weeks in length, which was followed by a double-blind responder extension and a open-label nonresponder extension. Of the 1,996 patients enrolled in the trial, 83 (59 olanzapine, 24 haloperidol) were in their first episode of psychosis with an episode duration of ≤ 5 years and age at onset of ≤ 45 years. In this subgroup of first-episode patients, olanzapine was statistically significantly superior to haloperidol in the reduction of BPRS total score, BPRS negative score, PANSS total score, and PANSS positive score from baseline to endpoint of the acute phase (last-observation-carried-forward). Also, haloperidol first-episode patients suffered statistically significantly more EPS and akathisia than olanzapine first-episode patients as measured by changes in Simpson-Angus total and Barnes global item from baseline to endpoint of the acute therapy. Additional results will be presented to investigate the difference in response between first-episode and multi-episode patients as well as explore factors which may influence response in first-episode patients.

NR205 Tuesday, May 20, 12 noon-2:00 p.m.

Gender Differences in the Response of Olanzapine Versus Haloperidol in the Treatment of First-Episode Psychosis

Mauricio Tohen, M.D., Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Todd Sanger, Ph.D., Gary D. Tollefson, M.D.

Summary:

In a subsample of a large multisite, double-blind, parallel trial comparing olanzapine versus haloperidol, 82 first-episode patients were recruited, 25 female and 57 male. Twelve of the 18 (66.7%) female patients randomized to olanzapine were classified as responders (40% reduction in the Brief Psychiatric Rating Scale [BPRS] total score) compared with 0 of 7 with haloperidol ($p = 0.005$). Males also had a better response to olanzapine compared to haloperidol (67.5% versus 41.2%) ($p = 0.082$). Specific response to negative symptoms was also assessed with the BPRS. Female patients had a significantly better response to olanzapine compared to haloperidol ($p = 0.005$). There was no difference in male patients. In terms of BPRS positive symptoms, males had a significantly better response to olanzapine compared to haloperidol ($p = 0.036$). When the first-episode group was compared with the multiple-episode group, there was a statistically significant better response in the first-episode compared with the multiple-episode group in the BPRS total score. (Mean change 16.59 versus 10.62. $p = <.001$.). There was no difference between the first -and the multiple-episode patients when treated with haloperidol. Olanzapine appears to be more effective than haloperidol in the case of first-episode female patients. Further studies need to be completed to replicate these findings.

NR206 Tuesday, May 20, 12 noon-2:00 p.m.

Olanzapine Versus Haloperidol in the Treatment of Schizoaffective Bipolar Patients

Mauricio Tohen, M.D., Research, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Todd Sanger, Ph.D., Gary D. Tollefson, M.D., Susan L. McElroy, M.D.

Summary:

Olanzapine is a new atypical antipsychotic agent that has affinity to both 5-HT2A and D2 receptors but binds more potently to the 5HT2A receptor by a factor of 3:1. In a subsample of a large multisite, blind parallel study comparing olanzapine with haloperidol, 73 patients with schizoaffective disorder including currently bipolar (N = 28), currently mixed (N = 43), currently depressed (N = 52), and euthymic (N = 48) were assessed with the Brief Psychiatric Rating Scale (BPRS) and the Montgomery-Asberg Depression Rating Scale (MADRS) at baseline and at week 6. Five items of the BPRS scale for conceptual disorganization, with tension, grandiosity, hostility, excitement, disorientation) were utilized to assess "manic" symptoms. Patients with schizoaffective bipolar disorder, currently manic, who were randomized to olanzapine had a mean change of 6.06 compared with 3.36 for the haloperidol group (p = .251). Patients with schizoaffective bipolar disorder, mixed, had a mean change of 1.47 for the olanzapine group and 2.82 for the haloperidol group (p = .439). With the MADRS rating scale, patients with schizoaffective bipolar disorder, currently depressed, had a mean change of 8.57 in the olanzapine group and a worsening change of 6.63 in the haloperidol group (p = 0.002). Olanzapine appears to have mood stabilizing properties in patients with schizoaffective disorder. Further studies need to be completed to replicate these findings.

NR207 Tuesday, May 20, 12 noon-2:00 p.m.

Fluoxetine Plus Pindolol in Unipolar Major Depression

Victor Perez, M.D., Department of Psychiatry, Hospital Sant Pau, Antoni M. Calret, #167, Barcelona 08025, Spain; Inmaculada Gilaberte, M.D., Douglas Faries, Dolors Puigdemont, M.D., Enric Alvarez, M.D., Francesc Artigas, Ph.D.

Summary:

Introduction: Current antidepressant treatments have a slow onset of action and are efficacious in less than two-thirds of patients. Experimental data indicate that biochemical effects of antidepressants inhibiting serotonin (5-HT) uptake are self-limited due to the activation of autoreceptors in serotonergic neurones. Pindolol is an antagonist of 5-HT autoreceptors in rat and human brain. Open-label studies with SSRIs plus pindolol suggest a faster antidepressant action.

Methods: Using a double-blind parallel design, 111 patients with major depression were randomly assigned to treatment with fluoxetine (20 mg/day) + placebo (tid) or fluoxetine (20 mg/day) + pindolol (2.5 mg tid).

Results: At endpoint, 75% of the patients treated with fluoxetine + pindolol and 59% of those treated with fluoxetine + placebo responded to treatment (p = 0.04). Number of days to reach a sustained response was lower in the combination group (19 vs. 29 days, medians; p = 0.01). There were no differences in the side-effect profile between treatment groups. Pharmacokinetic data indicate that the enhanced response rate of fluoxetine + pindolol was not due to increased plasma fluoxetine levels in their group.

Interpretation: The present study confirms in a controlled manner the usefulness of pindolol in enhancing the antidepressant efficacy of SSRIs.

NR208 Tuesday, May 20, 12 noon-2:00 p.m.

A Randomized, Double-Blind Comparison of Mirtazapine and Fluoxetine in Patients with Major Depression

David Wheatley, M.D., Psychological Medicine, Royal Masonic Hospital, Ravens Court Park, London W60TN, United Kingdom; Charlotte Kremer, M.D.

Summary:

Objective: To compare the efficacy and tolerability of mirtazapine and fluoxetine in depressed inpatients and outpatients.

Methods: Patients with a major depressive episode (DSM-III-R), a baseline score of ≥21 on the 17-item HAMD, and ≥2 on depressed mood item, were randomized to a six-week treatment with either mirtazapine (n = 66) or fluoxetine (n = 67). Efficacy was evaluated by the HAMD, CGI, and the Visual Analogue Mood Rating Scale (VAMRS), and the effects on sleep by the Leeds Sleep Evaluation Questionnaire. The efficacy analyses were performed on the Intent-To-Treat Group using the Last Observation Carried Forward method.

Results: Mean total 17-item HAM-D scores at baseline were 26.0 for the mirtazapine and 26.1 for the fluoxetine-treated group. The decrease from baseline on the HAMD was larger in the mirtazapine than in the fluoxetine group throughout the treatment period (endpoind change −14.2 and −10.3, respectively), reaching statistical significance at weeks 3 and 4. Similar numbers of patients dropped out due to adverse events (AEs); tolerability profiles were comparable.

Conclusion: The results demonstrate that mirtazapine is more effective than fluoxetine in depressed patients with high HAM-D baseline scores, whereas the tolerability profiles are similar.

NR209 Tuesday, May 20, 12 noon-2:00 p.m.

Fluoxetine Safety in Patients with Heart Disease

Steven P. Roose, M.D., Clin. Psychopharmacology, NY State Psychiatric Institute, 722 West 168th Street, Pl 98, New York NY 10032; Alexander H. Glassman, M.D., Evelyn Attia, M.D., Sally Woodring, R.N., Elsa Giardina, M.D., J. Thomas Bigger, Jr., M.D.

Summary:

TCAs are effective in patients with heart disease, but the rate of adverse events limits their utility. Are the SSRIs an alternative to the TCAs in depressed patients with cardiac disease? We studied the cardiovascular effects of an SSRI, fluoxetine, in the treatment of 27 depressed patients with pre-existing cardiac disease. The cardiovascular effects of fluoxetine are compared with the effects previously established for the tricyclic, nortriptyline.

Cardiovascular measures were recorded at baseline, week 2, and week 7 of treatment. Fluoxetine induced a statistically significant 6% decrease in mean heart rate and an 8% increase in ejection fraction. Fluoxetine had no effect on cardiac conduction or ventricular arrhythmia. There were no significant findings that emerged at week 7 that were not evident at week 2 despite the fact that mean plasma level of fluoxetine increased from 169 ± 69 at week 2 to 654 ± 287 at week 7. In a historical comparison group of 60 patients nortriptyline induced a significant increase in orthostatic drop and a 9% increase in heart rate. Nortriptyline had a 20% (12 of 60) rate of adverse cardiac events compared with a 4% (1 of 27) rate for fluoxetine (chi square = 2.71 p < .07).

Fluoxetine appears to be a benign treatment in depressed patients with cardiac disease and has fewer adverse cardiovascular effects than nortriptyline. However, it is premature to consider fluoxetine a "safe" medication in patients with cardiovascular disease because the study included a relatively small number of patients, N = 27, and a limited number of cardiac conditions.

NR210 Tuesday, May 20, 12 noon-2:00 p.m.

Early Morning, Short-Acting Beta-Blockers as Treatment for Winter Depression

Christina C. Norman, M.A., Department of Psychology, SUNY Stony Brook, Stony Brook NY 11794-2500; David S. Schlager, M.D.

Summary:

Objective: Preliminary findings suggest that beta-adrenergic antagonists may be effective in treating winter depression, an effect theoretically mediated by suppression of nocturnal melatonin. This study attempted to replicate an earlier finding that early morning administration of a short acting beta-adrenergic blocker, propranolol, is an effective treatment for winter SAD.

Method: 19 subjects were studied with DSM-III-R recurrent major depression with seasonal pattern (SAD). To enter, subjects scored at least 12 on the 21-item Hamilton Rating Scale for Depression (HRSD) or at least 9 on the HRSD, and at least 18 on the 29-item Structured Interview Guide for the Hamilton-SAD version (SIGH-SAD). Subjects were randomized to receive either placebo or 30 mg of propranolol at 6:00 A.M. for five days, after which subjects feeling no better or worse doubled their dose to two pills (placebo or 60 mg of propranolol). Final assessment was after 14 days of treatment.

Results: Significant differences between drug and placebo were observed in decreases of depression severity scores on both the SIGH-SAD (mean decrease = 16.4 and 8.0, respectively; repeated measures ANOVA $F = 4.4$, $df = 1,17$; $p < .05$) and HRSD (mean decrease = 8.5 and 2.5, $F = 6.3$, $p < .05$). Mean propranolol dose was 48 mg. None of the subjects randomized to active medication reported significant adverse effects.

Conclusions: The findings provide additional support for the efficacy of such a treatment in winter depression. Melatonin suppression by timed beta blockade may play a role in such effects.

NR211 Tuesday, May 20, 12 noon-2:00 p.m.

Olanzapine Response in Acute Schizophrenia, Schizoaffective Disorder and Psychotic Mood Disorders

Carlos A. Zarate, M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Rajesh Narendran, M.D., Alex Madrid, M.A., Arielle Berman, B.Sc., James Greaney, Pharm.D., Max Sederer, B.A.

Summary:

Background: In controlled studies of patients with schizophrenia, the atypical antipsychotic olanzapine has been shown to be superior in efficacy to haloperidol at doses of 10 mg/day. However, little is known about the efficacy of olanzapine in patients with treatment refractory schizophrenia, schizoaffective disorder (SA), and psychotic mood disorders. The purpose of this study was to assess the efficacy and safety of olanzapine in the treatment of these disorders and to identify clinical factors associated with olanzapine response.

Method: In a naturalistic setting, medical records of 74 hospitalized patients treated with olanzapine were reviewed and scored for indications, doses, and effects of this novel antipsychotic agent.

Results: Subjects (44 women, 30 men), aged 45 ± 16 years, were given olanzapine for bipolar disorder (30%), SA (25%), major depression (15%), schizophrenia (15%), and atypical psychosis (5%). Daily doses of olanzapine average 10 ± 3 (3–25) mg. Olanzapine was discontinued in only 11% due to inefficacy (7%) or intolerability (4%). Forty-eight (67%) patients had a moderate to marked response to olanzapine. Adverse events occurred in 38% (7% of those discontinued). Most common adverse events included sedation (18%), agitation (3%), and headaches (3%). Benefits were associated with bipolar, manic or mixed diagnosis, and shorter length of stay prior to olanzapine treatment. None of the other variables examined predicted olanzapine response.

Conclusion: Olanzapine appeared to be effective and safe for patients with refractory schizophrenia, SA, and psychotic mood disorders. Olanzapine may be a useful alternative or adjunctive treatment for patients with bipolar manic disorder when used in combination with mood stabilizers.

NR212 Tuesday, May 20, 12 noon-2:00 p.m.

Perinatal Outcome Following Fluoxetine Exposure: A Preliminary Report

Lee S. Cohen, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC 815, Boston MA 02114; Lynn R. Grush, M.D., Jennie W. Bailey, B.A., Jerrold F. Rosenbaum, M.D.

Summary:

Introduction: Recent findings suggest that some women who suffer from psychiatric disorders including mood disorder may experience new-onset, persistence, or exacerbation of underlying illness during pregnancy. These patients may be treated with antidepressants during pregnancy and during labor and delivery. Data are available regarding the safety of fluoxetine with respect to risk for major organ malformation. Less is known about acute and long-term perinatal outcome following fetal exposure to fluoxetine. This preliminary report describes the perinatal outcome of 35 children whose mothers used fluoxetine at or around the time of labor and delivery.

Methods: Subjects (N = 35) included children whose mothers had been followed through the Perinatal and Reproductive Psychiatry Program at the Massachusetts General Hospital. Mothers of these children suffered from mood and anxiety disorders and had been treated with fluoxetine for various portions of pregnancy but all used the drug proximate to labor and delivery. Obstetrical and neonatal records were obtained for mother-infant pairs and were evaluated in an effort to ascertain the frequency of obstetrical complications, course of labor and delivery, and neonatal complications (if any).

Results: An absence of clinically significant neonatal complications was noted following prenatal exposure to fluoxetine. In addition, clinically significant obstetrical complications were not observed following prenatal exposure to this drug.

Conclusion: While the safety of fluoxetine has been supported in many studies with respect to risk for major congenital malformations, less consistent have been reports of its safety when used during the latter trimesters of pregnancy and during labor and delivery. This preliminary report supports the low frequency of perinatal complications when fluoxetine is used during pregnancy and particularly during labor and delivery.

NR213 Tuesday, May 20, 12 noon-2:00 p.m.

Pindolol Acceleration of SSRI Antidepressants: A Six-Month Study

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: For the first time to describe the longer-term follow-up of augmentation of the antidepressant paroxetine with pindolol, a $5HT_{1A}$ autoreceptor blocker, in a double-blind, randomized, placebo-controlled trial.

Method: Eighty outpatients (mean age 36 [range 19 to 65], 48 female, 32 male) were recruited, each patient receiving paroxetine (20 mg *o.d.*) plus, randomly, either pindolol (2.5 mg *t.d.s.*) or placebo for six weeks. Paroxetine (open label) was offered to all patients for a further 18 weeks. Follow-up assessments of 69 patients, using the Global Impression, Montgomery-Asberg Depression Rating Scale, and the Beck Depression Inventory, took place at weeks 8, 16, and 24.

Results: Patients originally treated with pindolol ($n = 32$) showed significantly better clinical outcome at week 24 when compared with patients originally taking paroxetine alone, whether they complied fully with follow-up treatment or not. Compliance with follow-up treatment had a significant positive effect on outcome at weeks

16 and 24 in those patients originally treated with paroxetine alone (n = 37).

Conclusions: The acceleration of the antidepressant effects of paroxetine observed with administration of pindolol for six weeks is sustained in the longer term. The clinical and economic potential are considerable, and further large scale studies are warranted.

NR214 Tuesday, May 20, 12 noon-2:00 p.m.

Treatment-Resistant Schizophrenia: Efficacy of Risperidone Versus Haloperidol

Donna Ames, M.D., Department of Psychiatry, WLA VA Medical Center/Bldg 210, 11301 Wilshire Blvd/Rm 15, Los Angeles CA 90073; William C. Wirshing, M.D., Barringer D. Marshall, Jr., M.D., Michael F. Green, Ph.D., Susan R. McGurk, Ph.D., Jim Mintz, Ph.D., Stephen R. Marder, M.D.

Summary:

Objective: To examine the safety and efficacy of risperidone (RIS) compared with haloperidol (HAL) in treatment refractory patients with schizophrenia.

Method: 67 subjects with a history of nonresponse to conventional antipsychotics participated in a double-blind, three-phase study (one week placebo wash-in; four weeks fixed dose [6 mg RIS vs 15 mg HAL]; and four weeks, clinician-choice flexible dose [3–15 mg RIS vs 5–30 mg HAL]). Patients were evaluated weekly using measures of psychopathology, neurotoxicity, mood, OCD, and subjective response.

Results: RIS was associated with a greater improvement than HAL from baseline on measures of overall psychopathology (24% vs 10%, ANCOVA, F = 4.67, df = 1, 62, p = 0.03). HAL demonstrated a slight advantage over RIS for OCD and depressive symptom efficacy. A greater percentage (61%) of the HAL group required side effect medication than the RIS treated group (21%) (χ^2 = 10.1, df = 1, p = 0.001). Subjective response to RIS was largely positive, while it was predominantly dysphoric for HAL treated patients (F = 7.0, df = 1, p = 0.01).

Conclusions: These results suggest that RIS is more efficacious than HAL in the treatment refractory patient. They also demonstrate that RIS causes less EPS, requires less adjunctive side effect medication, and results in substantially less subjective dysphoria than HAL in this refractory population.

NR215 Tuesday, May 20, 12 noon-2:00 p.m.

Loss of Initial Response to Risperidone Treatment

Jennifer L. Francis, B.S., Clinical Unit, Western State Hospital, PO Box 2500, Staunton VA 24402; Michael S. Shutty, Ph.D., Robert A. Leadbetter, M.D.

Summary:

Objective: A report describing risperidone therapy for chronically psychotic patients suggests a subgroup experience an "awakenings" phenomenon, i.e. significant reduction of symptoms are followed by gradual return to pretreatment levels. We examined the prevalence of this phenomenon in 69 consecutive patients started on risperidone in a state hospital.

Methods: Using a standardized survey method, we assessed psychiatrist judgments of risperidone efficacy in 47 (68%) schizophrenic and 22 (32%) schizoaffective inpatients. A 60-day test-retest reliability check revealed 95% chance-corrected agreement. The relationships between treatment outcome and diagnosis, response to standard antipsychotic treatment, length of hospitalization, and age were also examined.

Results: Thirty-one (45%) patients improved, five (7%) patients were intolerant, 19 (28%) experienced no change or worsened, and 14 (20%) evidenced the awakenings phenomenon during risperidone treatment. More patients with schizophrenia (25%) versus schizoaffective disorder (9%) tended to lose an initial response. Nontreatment-resistant patients showed greater improvement rates (57%) than resistant patients (32%), whereas treatment-resistant patients (30%) were more likely to lose an initial response than nonresistant patients (8%), though diagnosis confounds the latter finding.

Conclusions: We found one-fifth of patients lost initial risperidone treatment gains after six to ten months; this subgroup is characterized primarily by treatment-resistant schizophrenic patients.

NR216 Tuesday, May 20, 12 noon-2:00 p.m.

[3H]RY-80, A Selective Radioligand for GABA-alpha Receptors with Alpha-5 Subunits

Rona J. Hu, M.D., Neuroscience, National Institutes of Health, 10/4N212, 10 Center Drive, Bethesda MD 20892; Christine Cook, B.S., Stephen Hurt, Ph.D., Ruiyan Liu, Ph.D., James M. Cook, Ph.D., Phil Skolnick, Ph.D.

Summary:

Objective: Currently used $GABA_A$ agonists (e.g. benzodiazepines) have multiple clinical effects: anxiolytic, anticonvulsant, sedative, amnestic, ataxic, etc. Designing drugs with fewer side effects is an obviously desirable goal, made possible with our developing understanding of $GABA_A$ receptor subunits and their potential for pharmacologically selective agents.

Method: The α_5 subunit was targeted because of its narrow distribution (enriched in hippocampus) in adult brain. We previously reported on a series of novel imidazobenzodiazepines with high affinity and selectivity for α_5-containing receptors. One of these, RY-80, was tritiated and tested in native (rat hippocampal) and recombinant ($\alpha_5\beta_3\gamma_2$) receptors.

Results: [^{3}H]RY-80 bound with high affinity and as predicted for an α_5-selective ligand. Affinities of known $GABA_A$ receptor ligands determined with [^{3}H]RY-80 confirmed its α_5-selectivity. The new ligand was also used to predict the pharmacological actions of a novel α_5-selective agent, and to quantitate α_5-bearing receptors in neonatal rat cortex.

Conclusions: Until now, development of selective drugs based on $GABA_A$ receptor heterogeneity was hampered by the lack of subunit-selective agents. [^{3}H]RY-80 is a useful tool for drug evaluation studies and to define the neuropharmacological roles of α_5 $GABA_A$ receptors.

NR217 Tuesday, May 20, 12 noon-2:00 p.m.

Personality and SSRI Treatment

Lee A. Kelley, M.D., Department of Psychiatry, University of Missouri, 1 Hospital Drive, Columbia MO 65212; Marian Hjelmfelt, Ph.D., Arthur Goodwin, M.S.

Summary:

Introduction: A growing body of evidence suggests some patients report personality changes following treatment with psychotropic medications. Previous studies have not addressed treatment with selective serotonin re-uptake inhibitors (SSRIs).

Purpose: To determine the kinds of personality changes that may occur with SSRI treatment.

Hypothesis: Patients receiving SSRIs would show decreases on personality disorder scales, and would exhibit increased extroversion and change-oriented personality characteristics.

Method: 31 students receiving SSRI treatment for various mental health problems at a university student clinic completed the Milion Clinical Multiaxial Inventory-III (MCMI-III) and the Personality Styles Inventory (PSI) prior to SSRI treatment, and again after two months and four months of treatment. A comparison group of

23 student volunteers completed the same inventories at baseline, two months, and four months.

Results: As compared with the volunteers, the SSRI group showed statistically significant decreases on a number of MCMI-III personality scales, and significant increases on histrionic and narcissistic scales. On the PSI, the SSRI group showed a trend toward increased extroversion but did not become more change-oriented over time.

Conclusions: The benefits of SSRIs may extend beyond treatment of Axis I disorders, possibly changing our view of personality and treatment approaches.

NR218 Tuesday, May 20, 12 noon-2:00 p.m.

Continuity of Medication in a Mental Health System

Daniel J. Luchins, M.D., Department of Psychiatry, University of Chicago, 5841 S. Maryland Ave., MC-3077, Chicago IL 60637-2602; Randy Malan, R.Ph., Patricia Hanrahan, Ph.D., John Harris, M.A.

Summary:

To document the continuity (or lack of continuity) of pharmacotherapy provided for patients discharged from state operated facilities in Illinois, we examined all 627 patients discharged during the first year of risperidone's availability (2/20/94–2/22/95) on whom Medicaid billing data were available for a minimum of one year (through 2/22/96). There was a striking lack of continuity of pharmacotherapy. In 279 (44.5%) cases, risperidone was not continued in the 16 days following discharge. Since our patients receive only a two-week supply of medications on discharge, this suggests a disruption in their medication immediately following discharge. An additional 272 (43.4%) patients failed to receive risperidone later during the follow-up period. In fact, only 76 (12.1%) patients remained on risperidone throughout the study period.

Using Medicaid billing data we also noted a striking difference in average daily medical costs between groups of patients who did or did not have continuity of pharmacotherapy. For those who did not receive risperidone in the 16 days following discharges, the average daily cost was $90.29; for those who discontinued at a later date it was $80.69; and for those who stayed on risperidone throughout the study period it was $47.52. The significance of these findings and factors that underlie them will be discussed.

NR219 Tuesday, May 20, 12 noon-2:00 p.m.

A Meta-Analysis of Anxiety/Agitation in Double-Blind Clinical Trials of Mirtazapine

Jan A. Fawcett, M.D., Department of Psychiatry, Rush-Presbyterian Medical Cntr, 1725 West Harrison, Suite 955, Chicago IL 60612

Summary:

Introduction: The prognosis for recovery from major depression is worse in patients with symptoms of significant anxiety. Prospective studies indicate that the risk of suicide is greater in patients with symptoms of severe anxiety, panic attacks, and agitation. Mirtazapine is a new antidepressant structurally unrelated to SSRI, TCA, or MAOI. Mirtazapine is a centrally acting presynatic α_2 antagonist and a potent antagonist of 5-HT_2 and 5-HT_3 serotonin receptors, with no significant affinity for 5-HT_1 receptors.

Objective: To evaluate the efficacy of mirtazapine for the relief of agitation/anxiety (sum of HAM-D items 9,10,11) or anxiety/somatization (sum of HAM-D items 10,11,12,13,15, and 17).

Methods: A meta-analysis of eight randomized, double-blind, placebo-controlled clinical trials was conducted for 161 mirtazapine-treated and 132 placebo-treated patients with major depression and a total baseline HAM-D score ≥ 18 and a baseline score of 6 or more for the sum of agitation/anxiety. Four of the clinical trials included an amitriptyline control group.

Results: The mirtazapine patients showed a significantly ($p \leq .02$) greater reduction in agitation/anxiety compared with placebo at weeks 1, 2, 4, 6, and at the endpoint. The meta-analysis of the amitriptyline-controlled clinical trials showed no significant difference between mirtazapine and amitriptyline at weeks 1, 3, 4, 5, 6, and at the endpoint. Similar results were noted for the analysis of anxiety/somatization. Mirtazapine showed a significantly ($p \leq .03$) greater reduction in anxiety/somatization at weeks 1–6 compared with placebo and no significant difference compared with amitriptyline at weeks 1–6.

Conclusion: Mirtazapine is superior to placebo and comparable to amitriptyline for the treatment of patients with major depression and symptoms of agitation/anxiety or anxiety/somatization.

NR220 Tuesday, May 20, 12 noon-2:00 p.m.

An Open-Label Study of Nefazodone in General Psychiatric Practices: Treatment of Depression with a Focus on Anxiety, Sleep and Sexual Function

Jan A. Fawcett, M.D., Department of Psychiatry, Rush-Presbyterian Medical Cntr, 1725 West Harrison, Suite 955, Chicago IL 60612; John M. Zajecka, M.D., Frederick W. Reimherr, M.D., Susan G. Kornstein, M.D., Frances E. Borian, R.N., John R. Ieni, Ph.D., Darlene N. Jody, M.D.

Summary:

Introduction: Nefazodone is an antidepressant with a unique pharmacology: potent 5-HT2 receptor antagonism combined with reuptake inhibition of 5-HT and norepinephrine. Clinical studies have demonstrated nefazodone and the selective serotonin reuptake inhibitors (SSRIs) to have similar antidepressant response rates. Nefazodone treatment has favorable effects on anxiety and sleep symptoms in depressed patients and does not compromise sexual function. We report here data from a large, prospective, open-label study of nefazodone in the general psychiatric practice setting.

Methods: This 12-week, open-label study was conducted at 150 sites in the United States. Men and women 18 to 75 years old with depressive symptoms of sufficient severity to require antidepressant treatment were entered. Nefazodone, given BID, was dosed flexibly within the therapeutic dose range (300–600 mg/day) according to subject response and tolerability. Efficacy assessments included the CGI, the Patient Global Assessment, and patient self-evaluations of anxiety, sleep quality, and sexual function.

Results: A total of 1,151 patients were enrolled; 985 were suitable for efficacy analysis. About 60% were considered responders to nefazodone treatment based on the CGI (i.e., rated "much" or "very much" improved by the clinician). Significant improvement from baseline in anxiety, sleep, and sexual function were found on the patient self-evaluations, beginning at week 1 and continuing to endpoint. Nefazodone treatment was safe and well tolerated.

Conclusions: Nefazodone is a safe and well-tolerated treatment for depression that has favorable effects on anxiety and sleep, and does not compromise sexual function.

NR221 Tuesday, May 20, 12 noon-2:00 p.m.

Steroselective Excretion of Fluoxetine and Norfluoxetine in Breast Milk and Neonatal Exposure

John Kim, M.S., Pharmaceutical Science, University of BC, 2146 East Hill, Vancouver BC V6T 1Z3, Canada; Shaila Misri, M.D., K. Wayne Riggs, Ph.D., Deirdre M. Ryan, M.B., Diana Carter, M.B., Dan W. Rurak, D.Phil.

Summary:

Objective: To determine the excretion of fluoxetine and norfluoxetine in breast milk and infant drug exposure via breast feeding.

Methods: Six nursing mothers (31 ± 5.5 years, infant 3.6 ± 2.3 months) receiving fluoxetine for major depression were studied, and were taking 10–60 mg Prozac daily for at least three to four weeks. Maternal and infant serum, and breast milk were simultaneously collected. Samples were analyzed by a stereoselective gas chromatographic/mass spectrometry assay.

Results: Maternal serum fluoxetine and norfluoxetine concentrations were within the therapeutic range (mean 29.2, 87.7, 28.4, and 91.7 ng/ml for [R]-fluoxetine, [S]-fluoxetine, [R]-norfluoxetine and [S]-norfluoxetine, respectively). Fluoxetine and norfluoxetine were present in all breast milk samples, with milk/serum ratios of 0.74 ± 0.29 and 0.59 ± 0.27, respectively. There were no detectable levels (<0.5 ng/ml) of either compound in four (age = 2.5–4.5 months) out of six infant serum samples. In the other two infants, norfluoxetine, but not fluoxetine, was detected at levels that were 36% (13.6 ng/ml, age = 6d) and 3% (7.4 ng/ml, age = 7 months) of maternal levels.

Conclusions: The accumulation of norfluoxetine in the one six-day-old infant may be due to low neonatal elimination. The reported perinatal complications in fluoxetine-exposed neonates may be related to this accumulation.

NR222 Tuesday, May 20, 12 noon-2:00 p.m.

An Open Trial of Once Versus Twice Daily Nefazodone

Paul J. Markovitz, M.D., Mood & Anxiety Treatment Ctr, 2101 Richmond Rd, Suite 1030, Beachwood OH 44122; Susan C. Wagner, M.A.

Summary:

Objective: Nefazodone is routinely administered twice daily (BID). An open trial was conducted to assess the efficacy and dosing requirements of BID versus once daily (QD) nefazodone administration.

Method: Outpatients (112 F/97 M) meeting DSM-IV criteria for major depression were studied. A total of 61 patients were treated with BID nefazodone when the medication was initially released. One hundred forty-eight patients gave informed consent, and took nefazodone at bedtime. Dropouts in both groups are included in the data analysis. Outcome was assessed by a CGI scale where 1 is no depression, 2 is >50% but <100% symptomatic improvement, and 3 is <50% improvement.

Results: Total nefazodone dosage was similar in both groups (468.8 + 130.1 mg in BID group, and 495.1 + 146 mg in QD group, p = .204, NS). Final CGI scores indicated improvement in 75% of patients in both the BID group (1 = 43%, 2 = 32%) and the QD group (1 = 51%, 2 = 26%), and no statistical difference between groups. Both trial lengths were comparable (BID = 36.1 + 28.6 weeks, QD = 28.8 + 21.7 weeks, NS).

Conclusions: The data suggest nefazodone is equally effective at the same total dosage whether administered BID or QD. Controlled studies are indicated.

NR223 Tuesday, May 20, 12 noon-2:00 p.m.

Effects of Fluoxetine on Interpersonal Sensitivity in Depressed Outpatients

Brian Baker, M.B., Department of Psychiatry, Toronto Hospital, 3D-ECW 399 Bathurst Street, Toronto Ontario M5T 2S8, Canada; Paul Sandor, M.D., David Newman, M.D., Miney Paquette, P. Dorian, M.D., C. Shapiro, M.D., M.J. Irvine, D.Phil.

Summary:

Objective: Fluoxetine is the most widely prescribed antidepressant. There has been speculation that it could affect personality, but except for aggression and impulsivity, this has not been systematically evaluated.

Method: In a randomized, double-blind, parallel group six-week study, patients diagnosed with major depressive disorder (MDD) by independent SCID, after one week placebo, received fluoxetine or doxepin; they were psychiatrically reassessed every two weeks (in a reported cardiac study) by HAM-D, Montgomery Asberg, Beck Depression Inventory, and Symptoms Checklist 90R[SCL90R].

Results: A total of 39 patients were available for analysis, 36 having complete data. Patients on fluoxetine (N = 20) (mean daily dose 37 + 18 mg) were similar to those on doxepin (N = 19) (169 + 42mg) on demographic variables and all scales and SCL90R subscales. The only difference in drug effect was in the Interpersonal Sensitivity subscale of the SCL90R. A group by time effect of fluoxetine over doxepin was revealed (p < .04). Internal consistency measures of the subscale revealed Cronbach's alpha values ranging from 0.73 to 0.81.

Conclusion: The effect on the interpersonal sensitivity may be more positively affected by fluoxetine than doxepin in outpatients with MDD, but more extensive investigation is required.

NR224 Tuesday, May 20, 12 noon-2:00 p.m.

Once-Daily Dosing of Nefazodone for the Treatment of Depression in Patients Previously Stabilized on Twice-Daily Dosing

Sheldon H. Preskorn, M.D., Psychiatric Research Institute, 1100 North St. Francis, Ste 200, Wichita KS 67214; Ryan D. Magnus, M.D., Paul J. Markovitz, M.D., Stephen M. Stahl, M.D., Frances E. Borian, R.N., Suha Hamid, Pharm.D., John R. Ieni, Ph.D., Darlene N. Jody, M.D.

Summary:

Objective: This 12-week continuation trial assessed whether the safety, tolerability, and efficacy of nefazodone in depressed patients obtained in 12 weeks of twice daily (BID) dosing could be sustained with once-daily (QD) dosing at the same total daily dose.

Method: Depressed patients requiring antidepressant treatment were prescribed nefazodone BID for 12 weeks at their optimally tolerated dose (300–600 mg/day). Responders were switched to nefazodone QD in two steps. In step 1, the morning dose was reduced by 1/2 and the evening dose was increased by 1/2. In step 2, after seven days, the morning dose was eliminated and added to the evening dose. Efficacy was assessed using the HAM-D, CGI, and PGA scales. Self-evaluations of anxiety, sleep, and sexual function were obtained. Safety and tolerability were monitored at weekly, then biweekly intervals by the clinician and through spontaneous reports of adverse events by the patient.

Results: QD dosing was well tolerated across the nefazodone therapeutic dose range. Of 47 patients enrolled, four patients (8.5%) discontinued due to adverse events. Of 41 evaluable patients, continued maintenance of antidepressant response or further improvement in depressive symptoms were observed in 39 (95%) patients by CGI and 40 (98%) by PGA. Mean HAM-D scores were 3.3 at the beginning of QD treatment and 2.9 at endpoint. Improvements in anxiety and sleep achieved during BID dosing were also maintained. QD treatment of nefazodone did not compromise sexual function.

Conclusions: These preliminary data suggest that patients previously stabilized on BID nefazodone can be safely switched to QD nefazodone without compromising efficacy or tolerability.

NR225 Tuesday, May 20, 12 noon-2:00 p.m.

Sertraline Does Not Inhibit Cytochrome P450 (CYP) 3A-Mediated Drug Metabolism in Vivo

Sheldon H. Preskorn, M.D., Psychiatric Research Institute, 1100 North St. Francis, Ste 200, Wichita KS 67214; Jeffrey A. Alderman, Ph.D., David J. Greenblatt, M.D., Dale W. Horst, Ph.D.

Summary:

Given its weak in-vitro potency for CYP 3A inhibition (about 3 orders of magnitude less than ketoconazole), three separate studies have been performed in healthy volunteers to determine whether sertraline (SRT) inhibits the CYP 3A-mediated metabolism of three drugs: alprazolam (APZ), carbamazepine (CBZ), and terfenadine (TFD). In the APZ study, 12 volunteers received a single 1 mg dose of alprazolam on day 1 followed by 14 days of 50 mg q.d. sertraline. A second 1 mg alprazolam dose was given on day 15. Alprazolam pharmacokinetic parameters (mean ± SD) on days 1 and 15, respectively, were 12.3 ± 0.4 and 11.7 ± 0.5 ng/ml for Cmax, 234 ± 14 and 215 ± 12 ng/h-ml for AUC ∞ 14.4 ± 0.8 and 13.8 ± 1.0 h for $T_{1/2}$ and 1.8 ± 0.2 and 2.0 ± 0.2 h for Tmax. No parameter was significantly different on day 15 compared with day 1. Two separate placebo-controlled studies examined the effect of sertraline (200 mg/day for at least two weeks) or of placebo on chronically administered CBZ, 200 mg b.i.d., or TFD, 60 mg b.i.d (n = 13 and 20, respectively). In both studies, there were no significant differences between CBZ and TFD pharmacokinetic parameters for sertraline vs placebo-treated groups. Thus, sertraline administered across the recommended dosage range of 50 to 200 mg/day was not found to inhibit the metabolism of CYP 3A metabolized drugs.

NR226 Tuesday, May 20, 12 noon-2:00 p.m.

Immediate Crossover from Fluoxetine to Mirtazapine

Ryan D. Magnus, M.D., Psychiatric Research Institute, 1100 North St. Francis, Ste 200, Wichita KS 67214; Kelli Omo, R.N., Mujeeb U. Shad, M.D., Sheldon H. Preskorn, M.D.

Summary:

A common question about a new medication is: Can it be safely started immediately after stopping a previous treatment? The issue is whether a clinically significant adverse drug-drug interaction might occur. That is particularly relevant when switching from fluoxetine due to the extended half-life of its active metabolite, norfluoxetine, and its effects on multiple cytochrome P450 (CYP) enzymes.

Method: Patients (n = 35) who were not responding optimally to fluoxetine were switched immediately to the new antidepressant, mirtazapine. The patients were evaluated on at least three baseline visits prior to the switch and then seen at weekly visits after the switch. The following assessments were made at each visit: a Hamilton Depression Rating Scale, Clinical Global Impression, vital signs, assessment of emergent adverse effects, and plasma samples to measure attainment of steady-state with mirtazapine and washout of fluoxetine/norfluoxetine.

Result: There were not immediate or unexpected adverse effects to suggest an untoward pharmacodynamic interaction. Plasma levels are being analyzed to determine whether the levels of mirtazapine are altered by the persistence of fluoxetine and norfluoxetine levels using each patient as their own control and doing a group comparison.

NR227 Tuesday, May 20, 12 noon-2:00 p.m.

Genetics of Impulsivity and Novelty Seeking

Christopher Reist, M.D., Department of Psychiatry, VA Medical Center, 5901 East 7th Street, Long Beach CA 90822; Daiga M. Helmeste, Ph.D., Ryan Vu, Dominic Tran, Siu Wa Tang, M.D.

Summary:

Investigations into the biological basis of personality have suggested a prominent role for the serotonin and dopamine neurotransmitter system. The D4 seven repeat polymorphism has been reported (Ebstein, 1996) to be associated with increased measures of novelty seeking. Previous work by our group has suggested a correlation between impulsivity and second messenger (Ca^{++}) coupling of the $5HT_{2A}$ receptor (Reist, 1996). A mutation of the $5HT_{2A}$ receptor (Tyr452) has been identified that is associated with reduced Ca^{++} signal transduction. It is therefore of interest to examine personality traits in subjects with this mutation. To explore this hypothesis we determined the genotype of the D4 receptor and the serotonin $5HT_{2A}$ receptor and related these findings to measures of novelty seeking and impulsivity. In our group of 75 subjects the expected distribution of D4 polymorphisms were found (4,4 [31%]; 4,7 [25%]; 2,4 [11%]; 7,7 [7%]). When the sample was divided based on the presence or absence of the 7 repeat allele, no differences in novelty-seeking scores were observed. In the subset of subjects for which $5HT_{2A}$ receptor genotyping and platelet calcium response was also measured, four subjects with the Tyr452 mutation exhibited blunted Ca^{++} response and lower impulsivity scores. (Supported by NARSAD.)

NR228 Tuesday, May 20, 12 noon-2:00 p.m.

Neurodevelopment of Children Exposed in Utero to Antidepressant Drugs

Donna E. Stewart, M.D., Women's Health, Toronto Hospital, 200 Elizabeth Street, EN 1-222, Toronto ON M5G 2C4, Canada; Irena Nulman, M.D., Gideon Koren, M.D., Joanne Rouet, Ph.D., Jacob Wolpin, Ph.D., H. Alan Gardner, M.D.,Jochen Theis, M.D., Nathalie Kulin, B.Sc.

Summary:

Background: The purpose of this study was to determine if preschool children whose mothers took tricyclic or SSRI antidepressants during pregnancy showed IQ, language, or behavioral changes compared with control children.

Methods: We studied 80 children of mothers who had received a tricyclic antidepressant, 55 children whose mothers had received fluoxetine, and 84 children whose mothers had received known nonteratogenic drugs during their pregnancies. All children were preschool age and their global IQ and language development were assessed after at least 16 months of postnatal age by the Bayley and McCarthy tests (for IQ) and Reynell test (for language).

Results: The mean (± SD) global IQ scores were 118 ± 17 in the children of mothers who received a tricyclic antidepressant, 117 ± 17 in those whose mothers received fluoxetine, and 115 ± 14 in those whose mothers received a nonteratogenic drug. The language scores were similar in all three groups. The results were similar in those children exposed to a tricyclic or fluoxetine in the first trimester or throughout pregnancy. Similarly, children in the three groups did not differ in their scores on temperament, mood, arousal, activity, distractibility, or behavioral problems.

Conclusion: In utero exposure to tricyclic antidepressants or fluoxetine does not appear to affect global IQ, language, and behavioral development measured in preschool children.

NR229 Tuesday, May 20, 12 noon-2:00 p.m.

Incidence of Sexual Dysfunction in Normal Volunteers on Fluvoxamine Therapy

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Summary:

Published literature suggests that sexual dysfunction (SD) occurring as a consequence of fluvoxamine (FLU) therapy is uncommon (<1%), although rates up to 92% have been reported for other selective serotonin reuptake inhibitors.

Objective: This study evaluated self-reported SD in 20 healthy normal volunteers (10 males [M]; 10 premenopausal females [F]) aged 19 to 43 years, enrolled in a phenotyping study using FLU as a hepatic metabolism inhibitor.

Methods: Subjects had eight visits at two week intervals over a 16-week period. A one-page, standardized, self-report questionnaire assessed adverse events (AE) at visits 1-6 (off FLU) and 7-8 (on FLU 150 mg QD). A comprehensive form was completed for each AE.

Results: Using Student's *t*-test, no sex difference was seen for age or total body weight for the group. No subject reported SD off FLU. Twenty percent of subjects (2 M, 2 F) and 35 percent of subjects (3 M, 4 F) reported SD at 2 weeks and 4 weeks of FLU therapy, respectively. Types of SD included decreased ability to achieve orgasm, decreased libido, and impaired erection. There were no reports of increased libido.

Conclusion: M & F have a 35% self-reported incidence of SD on moderate doses of FLU. True incidence rates may be higher as normal volunteers may be reluctant to report SD. Physicians should be alert to the high incidence of SD in patients on FLU therapy, and note that onset may not occur immediately, but may be present within one month of initiation of therapy.

NR230 Tuesday, May 20, 12 noon-2:00 p.m.

The Long-Term Efficacy and Safety of Quetiapine

Lisa A. Arvanitis, M.D., CMA, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850; Ihor W. Rak, M.D.

Summary:

Quetiapine, (ICI 204,636) is a promising new atypical dibenzothiazepine antipsychotic agent with a clozapine-like pharmacologic profile. Like clozapine, quetiapine is limbic-selective and causes minimal dystonic liability in haloperidol-sensitized and drug-naive monkeys, which predicts minimal extrapyramidal symptom (EPS) liability in man. Further, quetiapine, like clozapine, does not cause sustained elevations of plasma prolactin concentrations after short-term administration in rats. Short-term (≤ 6 weeks) Phase II and III clinical trials confirmed that quetiapine is effective in the treatment of the positive and negative symptoms associated with acute exacerbation of schizophrenia. Quetiapine is well tolerated and is not associated with dose-related safety or tolerability issues. Specifically, quetiapine, across the dose range, did not differ from placebo in the incidence of extrapyramidal symptoms or in plasma prolactin concentrations. We present here data on the long-term efficacy, safety, and tolerability of quetiapine in subjects with chronic or subchronic schizophrenia (n = 1085) enrolled in ongoing, open-label extensions to 11 international Phase III clinical and clinical pharmacology trials. Subjects received from 50 to 800 mg/day of quetiapine, dosed according to clinical response and tolerability, for up to two years. In these trials, efficacy was assessed using the Brief Psychiatric Rating Scale (BPRS), Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression (CGI), and the Modified Scale for the Assessment of Negative Symptoms (SANS). Safety was assessed using the Simpson-Angus Scale (SAS) and Abnormal Involuntary Movement Scale (AIMS) in addition to physical examinations, vital signs, weights, clinical laboratories, electrocardiograms, and the assessment of adverse events. In these trials, quetiapine was well tolerated with no additional safety issues arising after long-term treatment. Efficacy and safety results will be presented and discussed.

NR231 Tuesday, May 20, 12 noon-2:00 p.m.

Efficacy, Safety and Tolerability of Quetiapine in Elderly Subjects with Psychotic Disorders

Marc Cantillon, M.D., CMA, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850; Lisa A. Arvanitis, M.D.

Summary:

Because elderly patients with psychotic disorders are less able to tolerate the parkinsonism, anticholinergic, and cardiovascular side effects of standard antipsychotic medications, an effective antipsychotic with a low incidence of these effects, and minimal extrapyramidal symptom (EPS) liability, would represent a major advance in the treatment of psychotic disorders in the elderly. Quetiapine (ICI 204,636) is a promising new atypical antipsychotic. Phase II and III clinical trials in younger subjects have confirmed that quetiapine is effective in the treatment of the positive and negative symptoms associated with acute exacerbation of schizophrenia. Quetiapine was also well tolerated across the dose range and did not differ from placebo in the incidence of EPS or plasma prolactin concentrations. Presented here are data on the efficacy, safety, and tolerability of quetiapine from an ongoing U.S., multicenter, open-label trial (n = 152) in men and women at least 65 years of age with idiopathic (ie, schizophrenia, bipolar disorder) and organic (ie, psychoses associated with Alzheimer's disease and vascular dementia) psychoses. Subjects received from 25 to 800 mg/day of quetiapine, dosed according to clinical response and tolerability, for up to one year. Efficacy was assessed using the BPRS and the CGI. Safety was assessed using the Simpson-Angus Scale (SAS) and AIMS in addition to physical examinations, vital signs, weights, clinical laboratories, ECGs, and the assessment of adverse events. Quetiapine was well tolerated by the elderly subjects in this trial, with no major safety concerns arising. Twelve subjects were withdrawn because of adverse events. The most frequently reported adverse events were somnolence, dizziness, and postural hypotension. Low incidences of anticholinergic and EPS adverse events were seen. Mean SAS total score decreased at end point, with little change in AIMS total score. Quetiapine had no clinically important effects on hematology or clinical chemistry values, ECGs, or vital signs. The results from this trial, together with results from trials conducted in younger subjects that have confirmed the antipsychotic efficacy of quetiapine and its favorable safety and tolerability profile across the dose range, support the use of quetiapine as an attractive alternative to standard antipsychotic agents in the elderly.

NR232 Tuesday, May 20, 12 noon-2:00 p.m.

The Atypical Profile of Quetiapine Is Supported by Its Lack of Sustained Elevation of Plasma Prolactin Concentrations

Lisa A. Arvanitis, M.D., CMA, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850; Jeffrey M. Goldstein, Ph.D.

Summary:

Many patients with schizophrenia are noncompliant with standard antipsychotic treatments because of the side effects they cause, such as extrapyramidal symptoms (EPS) and the gynecomastia, galactorrhea, amenorrhea, and impotence caused by chronic elevation of plasma prolactin (PRL). Quetiapine (ICI

204,636) is an atypical dibenzothiazepine antipsychotic agent with a clozapine-like pharmacological profile that may improve compliance and outcome in patients with schizophrenia. Like clozapine, quetiapine is limbic selective and causes minimal dystonic liability in haloperidol-sensitized and drug-naive monkeys, which may translate to lack of EPS in man. In addition, quetiapine like clozapine, does not cause sustained elevations of PRL after short-term administration to rats. The efficacy of quetiapine in the treatment of the positive and negative symptoms of schizophrenia was demonstrated in a number of short-term (≤ 6 weeks) placebo- and comparator-controlled clinical trials. In these trials, quetiapine was well tolerated and the incidence of EPS, as assessed by the Simpson Scale, use of EPS medication, and EPS adverse events, was no different than with placebo. These promising findings of efficacy, safety, and an atypical profile were further supported by the PRL data presented here from five short-term (six week), randomized, controlled, double-blind clinical trials in 1,405 hospitalized subjects with acute exacerbation of chronic or subchronic schizophrenia. Three trials were placebo controlled (including one trial with a haloperidol group), one was haloperidol controlled, and one was chlorpromazine controlled. In the placebo-controlled trials, there were no statistically significant differences between quetiapine and placebo with regard to effects on PRL. In the trials with haloperidol, quetiapine produced decreases in PRL, while increases in PRL were seen with haloperidol. In the chlorpromazine-controlled trial, the decrease from baseline with quetiapine was significantly greater than that with chlorpromazine ($p = 0.004$). In conclusion, the finding that quetiapine's effects on PRL were no different than that of placebo across clinically effective dose ranges adds further support for the atypical profile of quetiapine and distinguishes it from standard antipsychotic agents. By avoiding the unwanted side effects associated with increased PRL levels, quetiapine therapy is likely to improve compliance and, ultimately, clinical outcome.

NR233 Tuesday, May 20, 12 noon-2:00 p.m.

Quetiapine, a Promising New Antipsychotic Agent: Overview of Safety and Tolerability

Jeffrey M. Goldstein, Ph.D., CMA, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850; Lisa A. Arvanitis, M.D.

Summary:

Quetiapine (ICI 204,636) is a new atypical antipsychotic agent. Short-term (≤6 weeks) clinical trials demonstrated that quetiapine was consistently superior to placebo and comparable to haloperidol and chlorpromazine in improving the symptoms of acute psychotic exacerbation of schizophrenia. Presented here is an overview of quetiapine safety and tolerability with data from seven short-term (≤6 weeks), controlled clinical trials in 1,417 hospitalized subjects with schizophrenia. Four trials were placebo-controlled, including one trial with a haloperidol group. Two trials were six-week, chlorpromazine- or haloperidol-controlled ($n = 201$ and 448, respectively) trials in subjects with schizophrenia. Safety was assessed using the Simpson-Angus Scale (SAS), Abnormal Involuntary Movement Scale (AIMS), physical examinations, vital signs, weights, clinical laboratories, electrocardiograms (ECG), and the assessment of adverse events.

Overall, quetiapine was well tolerated. No deaths were reported with quetiapine and the incidence of serious adverse events and withdrawals for adverse events was similar between the quetiapine and placebo groups and less than seen in the haloperidol group. In the placebo-controlled trials, adverse events that had a significantly higher incidence with quetiapine were: somnolence, dizziness, dry mouth, SGPT and SGOT increased, abdominal pain, and weight gain. There was no difference between quetiapine, across the dose range, and placebo with regard to plasma prolactin levels and EPS, as assessed by the incidence of EPS adverse events, SAS total scores, and use of anticholinergic medications. Quetiapine had no clinically important effects on hematology, ECG, or vital sign variables. Quetiapine treatment was associated with asymptomatic, reversible elevations in ALT; small decreases in thyroid hormone levels without increases in TSH; and a 1.5-2.5 kg weight gain.

A favorable safety and tolerability profile across the dose range, combined with data supporting efficacy in the treatment of the positive and negative symptoms of schizophrenia, suggest that quetiapine may represent an important advance in the treatment of schizophrenia.

NR234 Tuesday, May 20, 12 noon-2:00 p.m.

Low-Dose Venlafaxine Treatment in Panic Disorder

Laszlo A. Papp, M.D., Department of Psychiatry, Columbia University, 722 West 168th Street, Unit 24, New York NY 10032; Smit S. Sinha, M.D.,Jeremy D. Coplan, M.D., Jack M. Gorman, M.D.

Summary:

Objective: To assess the efficacy of venlafaxine in panic disorder (PD).

Method: Thirteen patients with DSM-IV PD with agoraphobia enrolled in 10 weeks of open flexible dose venlafaxine treatment. Two patients dropped out after the first dose complaining of nausea, and two at week 4 and 5 due to problems unrelated to venlafaxine. The completer sample consisted of seven women and two men (mean age:37.7) with an average of 2.22 panic attacks/week with an average duration of illness of 7.9 years. The dose was to increase from 25 mg/day by 50 mg/week to a maximum of 250 mg/day.

Results: As several patients experienced nausea, insomnia, and jitteriness at initiation, the starting dose of venlafaxine was subsequently lowered to 12.5 mg/day and in two patients to 6.25 mg/day. Due to the re-emergence of side effects in four patients the dose could not be increased beyond 50 mg/day. The mean dose at week 1 was 16.26 mg/day, reached 78.01 mg/day by week 7, and remained essentially unchanged through the trial. By week 7 all nine patients were panic free and the rating scales (CGI, HAM-A) showed significant and sustained improvement.

Conclusion: Venlafaxine appears to be an effective antipanic agent even when administered at substantially lower than usual antidepressant dose levels.

NR235 Tuesday, May 20, 12 noon-2:00 p.m.

Finding and Treating Depression in Alzheimer's Patients: A Study of the Effects on Patients and Caregivers

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Summary:

Rationale: Depression occurs frequently in patients with Alzheimer's disease, compounding the burden on patients and family caregivers. Too often it goes unrecognized and untreated.

Hypothesis: We postulated that Alzheimer's patients with depression would respond to antidepressant drug therapy, as well as improve in the quality of their social interaction. We postulated that their cognitive status would be unchanged, and that the caregiver's perceived burden would decrease, and their social interactions would increase.

Methodology: In this study Alzheimer's patients were screened for depression, using the Hamilton Depression Scale and the Cornell Scale for Depression in Dementia. Twelve patients with

depression and dementia due to Alzheimer's disease were selected for this open study. Patients were treated with venlafaxine, 37.5 mgm bid for 16 weeks, with research observations carried out at 0, 4, and 16 weeks.

Results: Depression decreased significantly (p = .01) However, contrary to our expectations, functional capacity continued to decline, while cognition remained unchanged over the study period. Also contrary to expectation, caregiver burden, depressive symptomatology, and social interactions remained unchanged.

Conclusion: Depression in Alzheimer's patients can and should be treated. Longer term studies are needed to determine the impact on functional capacity of the patient and burden and other psychopathology in caregivers.

NR236 Tuesday, May 20, 12 noon-2:00 p.m.

Clozapine-Induced Gastrointestinal Symptoms

Maria D. D. Llorente, M.D., Department of Psychiatry, University of Miami, 1201 NW 16th Street, Miami FL 33125; Mercedes Gonzalez-Blanco, M.D., Brandon Boswell, B.A.

Summary:

Introduction: Nausea and vomiting as side effects of clozapine are puzzling in view of its antidopaminergic properties which should produce antiemetic effects. We hypothesize that those patients who develop gastrointestinal(GI) side effects have preexisting gastroesophageal pathology that is exacerbated by the properties of clozapine.

Methods: All patients followed in the university clozapine clinic were monitored for side effects known to occur with clozapine. Any patient who developed significant GI complaints (heartburn, nausea, vomiting) or recurrent respiratory infections were referred for upper GI series.

Results: A total of 15 (9 men; 6 women; mean age 43.1 years) of 83 patients started on clozapine developed GI symptoms as follows: 13 hypersalivation, 8 nausea, 5 vomiting, 9 epigastric discomfort, 4 recurrent respiratory infections. The 14 UGI series revealed: 12 hiatal hernias, 1 gastroesophageal reflux, 1 distal esophagus with tertiary contractions. The patient without a UGI had ingested bleach two years before and had sustained a diffuse grade I burn, esophagus to duodenum. Mean clozapine dose when symptoms developed was 320 mg/d (150-650mg/d).

Conclusions: Patients with preexisting GI pathology, particularly hiatal hernias, are at risk for developing GI side effects from clozapine. No patient had similar symptoms resulting from other neuroleptics and the effect from clozapine appears to be dose dependent. Concomitant medications may worsen this effect and should be used cautiously.

NR237 Tuesday, May 20, 12 noon-2:00 p.m.

ECT Pulsewidth 0.5 Millisecond is More Efficient than 1.0 Millisecond Stimuli

Conrad M. Swartz, M.D., Department of Psychiatry, VA Medical Center, Psychiatry Service-116A, Mountain Home TN 37684; David T. Manly, M.D.

Summary:

Objective: To describe the efficiency of ECT stimulus characteristics.

Background: Greater efficiency enables lower electrical dosage and might diminish side effects.

Method: Physiological measurements were made of 24 patients. In study 1, after the first ECT each patient received four sessions with asymmetric bilateral stimuli of charge 2.5× age but differing combinations of pulsewidth (1/2, 1 msec) and frequency (30, 60 Hz). In study 2, measurements after 1 msec 30 Hz and a stronger stimulus were compared.

Results: The stronger stimulus induced higher peak heart rate ($p < .01$) and less seizure failure ($p < .01$) but no differences in EEG. Similar results occurred when comparing 1/2 and 1 msec stimuli. Of the seven subjects with at least one failed motor seizure, 71% failed with both 1 msec but not 1/2 msec stimuli ($p = 0.005$). Repeated measures ANOVA on differential peak heart rate was significant ($p = 0.03$), as were differences between 1/2 and 1 msec pulsewidths ($p = 0.022$ to $p = 0.048$) but not differences between 30 and 60 Hz frequencies.

Conclusions: 0.5 msec stimuli are more efficient than 1.0 msec stimuli. Peak heart rate shows sensitivity to ECT seizure quality.

NR238 Tuesday, May 20, 12 noon-2:00 p.m.

Betaxolol Is Effective for Anxiety Disorders

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Summary:

Objective: To determine if betaxolol, a long-acting beta blocker that penetrates the CNS, mitigates anxiety symptoms in open studies of inpatients and outpatients with generalized anxiety disorder, adjustment disorder with anxiety, or panic disorder. Prior studies examined beta blockers that were short acting so presumably predisposed to anxiety rebound.

Method: Betaxolol was clinically administered to 11 outpatients with generalized anxiety disorder (GAD) and two with adjustment disorder with anxiety, 10 females and 3 males aged 24–73. Five GAD patients had concurrent panic disorder. It was also given to 16 inpatients with GAD and two with adjustment disorder with anxiety, 11 females and 7 males aged 22–78. Doses were increased until the patient responded or declined further dosage. Severity was rated by a four-point global scale.

Results: All five panic patients became asymptomatic within two days and remained so, including two severe cases ($p < .001$). Eleven outpatients (85%, $p < .0001$) and all inpatients ($p < .0001$) improved to no more than marginally ill within two days; the two outpatients who discontinued betaxolol later improved on other beta blockers. Doses were usually 5 mg qd-BID; four inpatients took 20–40 mg/day.

Conclusions: In this open study betaxolol administration was followed by rapid and strong improvements; patients appeared dramatically different. The efficacy of betaxolol appeared compelling.

NR239 Tuesday, May 20, 12 noon-2:00 p.m.

The Relative Efficacy of New and Atypical Neuroleptics in Chronic Psychiatric Inpatients

Cheryl K. Cantrell, M.D., Delaware Psychiatric Center, 1901 N Dupont Highway, New Castle DE 19720; Eric S. Cole, Ph.D.

Summary:

Objective: Clinical use of new and atypical neuroleptics has proliferated in recent years. Comparative efficacy research is needed. The present investigation compares response rates in chronic psychiatric inpatients to clinical trials of three new neuroleptics.

Method: From 1991 through 1996, 250 chronic psychiatric inpatients with refractory psychosis were given 330 naturalistic clinical trials of clozapine (N = 102, average duration 9.1 months, average dose 505 mg/day), risperidone (N = 178, average duration 4.9 months, average dose 7.1 mg/day), or olanzapine (N = 53, average duration 1.8 months, average dose 11.5 mg/day). Positive response rates were assessed retrospectively with both subjective (physician report) and objective (discharge from hospital) measures.

Results: Patients showed "good to excellent" subjective response rates of 55% on clozapine, 34% on risperidone, and 40% on olanzapine. Discharge rates were 22% on clozapine, 14% on risperidone, and 6% on olanzapine with another 9% awaiting discharge. A subset of geriatric patients on risperidone showed a 48% "good to excellent" response rate and a 19% discharge rate.

Conclusions: Clozapine has been very effective in this treatment-resistant population. Risperidone, while less impressive in the general population, was more effective in geriatric psychiatric patients. Olanzapine's overall efficacy rate is good and expected to improve with longer trials.

NR240 Tuesday, May 20, 12 noon-2:00 p.m.

Method to Assess a Fast Antidepressant Action

Inmaculada Gilaberte, M.D., Medical, Eli Lilly and Company, Avda Industrial, #30, Alcobendas 28100, Spain; Victor Perez-Sola, M.D., Douglas Faries, Domenec Serrano, M.D., Francesc Artigas, Ph.D., Enric Alvarez, M.D.

Summary:

Introduction: There is considerable debate about the onset of antidepressant action and the design of trials addressing this issue. We report on the methodology used in a clinical trial specifically designed to examine whether fluoxetine + pindolol had a shorter time to onset than fluoxetine + placebo.

Method: A six-week, double-blind, parallel study with two treatment arms was conducted. A total of 111 major depressive patients (DSM-IV) were randomized in the study. HAMD and MADRS scales were used to detect symptomatological changes. One-week, single-blind, placebo phase was used to discard placebo responders. A "sustained response" criterion (maintained 50% reduction of symptom severity) was defined to assess the timing of clinically relevant responses. Clinical ratings were made twice a week during the first three weeks of active treatment.

Results: No differences were observed regarding sensitivity in detecting symptomatology changes between HAMD and MADRS scales. Survival analysis on all randomized patients suggested that the fluoxetine + pindolol treatment group had a faster onset of action than fluoxetine + placebo. However, treatment differences became negligible when survival analysis was conducted conditional of patients who achieved a sustained response.

Conclusions: Increased response rate was clearly related to a shorter time to achieve a sustained response. It appears difficult to discern between both clinical variables with the existing methodology.

NR241 Tuesday, May 20, 12 noon-2:00 p.m.

Cost-Effectiveness of Clozapine: A Retrospective Study

Prabir K. Mullick, M.D., Department of Psychiatry, St. Francis Medical Center, 4608 Penn Ave, PC Mullick Asso, Pittsburgh PA 15201; Raj Sarma, M.D., Manohar K. Shetty, M.D., Koushik Mukherjee, M.D., David J. Lynn, M.D., Jack Merchant, R.N.

Summary:

Introduction: Clozapine is a novel antipsychotic. In this study we looked at the cost-effectiveness of clozapine therapy on chronic patients with schizophrenia who in addition to meeting the criteria for clozapine therapy, also had extrapyramidal symptoms, aggressive behavior,or comorbid psychopathology.

Methods: Fifty patients were selected who have been on treatment with antipsychotics from 1988 to date. The period from 1988 to 1992, with patients on classical antipsychotics acted as control period and the period 1992 to 1996 with patients on clozapine acted as test period. The charts were reviewed retrospectively for the number of hospitalizations between 1988 and 1992 and between 1992 to 1996. The cost for the hospitalization was computed for the periods mentioned.

Results: Prior to 1992 the average hospitalization for this group was four year, which dropped to 1.5/year showing a 60% decrease. The cost, including the cost of clozapine and weekly blood work, was 40% less for the period from 1992 to 1996. There was a substantial improvement in work functioning and relationships.

Conclusion: We showed a significant savings after starting clozapine. Patients showed improvement in EPS, relationships and social function. A few patients dropped out of therapy because of inconvenience of getting blood work done. As most of the patients are on Medicaid there was a substantial saving to the county.

NR242 Tuesday, May 20, 12 noon-2:00 p.m.

Tolerability of Mirtazapine Used in High or Low Initial Dose

Stephen M. Stahl, M.D., Department of Psychiatry, University of CA, San Diego, 8899 University Cntr Lane #130, San Diego CA 92122; Charlotte Kremer, M.D., Roger Pinder, Ph.D.

Summary:

Objective: Sleep studies in rats have demonstrated that low-dose mirtazapine (≤ 2.2 mg/kg i.p or s.c. or 22 mg/kg p.o.) had only sleep-promoting effects, enhancing the deeper stages of sleep in the rat. Higher doses of mirtazapine (> 2.2 mg/kg i.p or s.c. or 22 mg/kg p.o.) produced the REM sleep suppression characteristic for antidepressants; they were not hypnotic, and even caused a mild increase in active waking. We therefore compared adverse events with mirtazapine used in recommended (≥ 15 mg/day) or low, subtherapeutic (5–10 mg/day) initial doses in short-term treatment of depression, as results of animal studies suggested differences in tolerability.

Method: Pooled incidences of reported adverse events (AEs) were calculated for all placebo-controlled studies using low, subtherapeutic (mirtazapine, n = 580; placebo, n = 361) or recommended (mirtazapine, n = 244; placebo, n = 174) initial doses of mirtazapine. The results are presented using placebo-adjusted rates (% AEs with mirtazapine minus % AEs with placebo). A positive rate indicates a higher incidence in the mirtazapine group; a negative rate a higher incidence in the placebo group.

Results: In general, reported incidences of adverse events, and adjusted placebo rates were similar in both study sets. However, there were a few striking differences in antihistaminergic AEs, all of them favoring high initial doses. Placebo-adjusted rates of somnolence with high dose were +4.6%, and with low dose +36.5%. Respective values for weight gain were +1.2% and +13.3%, and for increased appetite +7.5% and +14.1%.

Conclusion: Initial doses of mirtazapine ≥15 mg/day seem to be linked with substantially lower incidences of antihistaminergic AEs, and further support the notion that the intrinsic noradrenergic activity of mirtazapine used in initial doses within the recommended dose range (15–45 mg/day) counteracts its antihistaminergic effects.

NR243 Tuesday, May 20, 12 noon-2:00 p.m.

Meta-Analysis of Randomized, Double-Blind Placebo Controlled Studies of Mirtazapine Versus Amitriptyline

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Summary:

Objective: A meta-analysis was performed on efficacy and safety data from four randomized, double-blind, six-week, single-center studies comparing mirtazapine (n = 194; 5–35 mg/day)

with amitriptyline, (n = 193, 40–280 mg/day) and placebo (n = 193) in outpatients with a DSM-III diagnosis of major depressive episode.

Methods: The statistical analysis was performed on an intent-to-treat basis, using the appropriate statistical methodology for meta-analytical approach, and the "last observation carried forward" method for efficacy analyses.

Results: On all the main efficacy variables both active drugs produced significantly greater improvements and significantly greater percentages of responders or remitters than placebo. Tolerability of mirtazapine was equivalent to placebo, except for sedation-related symptoms, appetite increase, and weight gain. There were no differences between mirtazapine and placebo regarding the incidence of serotonergic adverse events. Tolerability of mirtazapine was superior to amitriptyline, with respect to anticholinergic and cardiac adverse events, tremor, and postural symptoms.

Conclusion: The results demonstrate that mirtazapine is as effective as amitriptyline but with significantly better tolerability profile.

NR244 Tuesday, May 20, 12 noon-2:00 p.m.

Sertraline Treatment of Panic Disorder: Combined Results from Two Placebo-Controlled Trials

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Summary:

Two randomized, 10-week, multicenter studies comparing sertraline (dose 50–200 mg) with placebo were conducted in outpatients with panic disorder with or without agoraphobia (DSM-III-R). Patients were required to have had four panic attacks in the four weeks prior to baseline and at least three panic attacks in the two-week, single-blind placebo lead-in. Both studies (N = 342) had identical designs, and there were no significant between-study differences in key clinical and demographic variables, so the results are combined for this presentation. There was a significant treatment advantage for sertraline vs. placebo in all of the primary efficacy measures. Frequency of major panic attacks was significantly reduced for the sertraline group relative to the placebo group by week 2 ($p < .005$), and this advantage was sustained through the end of the study. Patient global ratings of improvement also achieved significance for sertraline by week 3 ($p < .005$). Treatment with sertraline was well tolerated, with only 8% attrition for adverse events. The results of these combined studies are consistent with the individual results of each study, and suggest that sertraline is safe and effective in the treatment of panic disorder.

NR245 Tuesday, May 20, 12 noon-2:00 p.m.

Bioavailability and Pharmacokinetics of an Extended Release (ER) Formulation of Venlafaxine

Clifford Dilea, Pharm.D., Wyeth-Ayerst, 145 King of Prussia Road, Radnor PA 19087; Steven Troy, M.S., Cathie Leister, M.S., Patrick D. Martin, M.D.

Summary:

Objective: Assess the relative bioavailability and pharmacokinetics of three extended release (ER) formulations of venlafaxine and the reference venlafaxine immediate release (IR) formulation.

Methods: This was a multiple dose, randomized, four-period, crossover study. Twenty-four healthy volunteers (12 male, 12 female) received in random order venlafaxine ER (NY) 2 x 75 mg q24h, venlafaxine ER (PR) 2 x 75 mg q24h, venlafaxine ER (PR) 1 x 150 mg q24h, and venlafaxine IR 75 mg q12h. Plasma samples were assayed for venlafaxine and O-desmethylvenlafaxine (ODV) by HPLC, and the plasma concentrations were analyzed by model-independent pharmacokinetic methods.

Results: All three venlafaxine ER formulations had similar mean venlafaxine and ODV pharmacokinetic parameters. There were no apparent gender differences in the pharmacokinetic parameters. All formulations were safe and well tolerated.

Conclusion: The three venlafaxine ER formulations were bioequivalent to each other, and they all provided similar exposure (AUC24h) to the reference IR formulation with respect to both venlafaxine and ODV.

NR246 Tuesday, May 20, 12 noon-2:00 p.m.

Charleston, SC: Drug Interactions Surveillance Program

C. Lindsay DeVane, Pharm.D., Department of Psychiatry, Medical University of SC, 171 Ashley Avenue, Charleston SC 29425-0742; John S. Markowitz, M.D., Harry S. Gill, Ph.D., S. Craig Risch, M.D.

Summary:

The Charleston Area Drug Interactions Surveillance Program (CADISP) was initiated in July 1995 to screen patients receiving one of the newer antidepressants along with other metabolized drugs for the presence of pharmacokinetic and/or pharmacodynamic interactions. We hypothesized that many pharmacokinetic interactions occur but go unnoticed because either drug plasma concentrations are not monitored or the consequences of the interaction are clinically insignificant. We sought to enroll as many patients as possible into a surveillance program whereby plasma concentrations were determined for co-administered drugs in the presence and absence of a newer antidepressant (SSRI, nefazodone, venlafaxine). Informed consent was obtained in a prospective manner. Over 120 sets of patient data have been collected in this ongoing program involving a variety of drugs, which are substrates for the major cytochrome (CYP) P-450 enzymes. Novel interactions were documented with probable mechanisms related to inhibition of CYP1A2, 2D6, 2C, and 3A4, although in most all situations the consequences were of limited clinical significance. The results provide confirmation of predictions made from in vitro-determined cytochrome enzyme affinities for the various antidepressants, in vivo pharmacokinetic studies conducted in healthy volunteers, and previously published case reports. This is the first comprehensive, prospective, post-marketing drug surveillance program to document the prevalence and significance of drug interactions involving antidepressant inhibition of cytochrome enzymes.

NR247 Tuesday, May 20, 12 noon-2:00 p.m.

Serum Cholesterol in Patients with OCD During Treatment with Behavior Therapy and Fluvoxamine Versus Placebo

Helmut Peter, M.D., Hospital, Psychiatric University, Martinistr 52, Hamburg 20246, Germany; Susanne Tabrizian, Iver E. Hand, M.D.

Summary:

Patients with panic disorder are reported to have elevated cholesterol levels, which could explain their increased cardiovascular morbidity. Recently, some studies suggest that several phobic disorders, anxious depression, and obsessive-compulsive disorder are also associated with increased serum cholesterol. Further investigation is needed to clarify whether this lipid alteration is a state or trait factor.

Method: A total of 29 patients with obsessive-compulsive disorder participated in the study. Serum cholesterol was measured at pretreatment and at the end of the ten-week treatment period.

All patients received multimodal behavior therapy (BT), and additionally, in a double-blind fashion, fluvoxamine or placebo. Severity of OCD was assessed by the YBOCS.

Results: (1) Patients with obsessive-compulsive disorder have elevated cholesterol levels comparable to those in patients with panic disorder. (2) Cholesterol levels decrease significantly from pre- to post-treatment (3) Comparison of responders (>35% reduction in Y-BOCS ratings) and nonresponders reveals an almost significant ($p < 0.08$) difference.

Discussion: Our data support the assumption that not only anxiety disorders but also other psychiatric disorders associated with higher levels of anxiety (e.g. obsessive-compulsive disorder) are connected with serum cholesterol elevation. Effective treatment (BT and/or SSRI) seems to decrease cholesterol levels significantly. Further studies are required to verify these results.

NR248 Tuesday, May 20, 12 noon-2:00 p.m.

Studies on Positive and Negative Mirtazapine at Some Human Brain Receptors

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Summary:

Mirtazapine is an antidepressant newly marketed in the United States. It is unique among antidepressants because its actions involve blockade of several different neurotransmitter receptors, without effects on monoamine oxidase or monoamine uptake systems. The drug is marketed as the racemic mixture. Therefore, we studied the two stereoisomers of this drug at several human neurotransmitter receptors. Normal human brain tissue was the source of receptors in established radioligand binding assays for the following: α_1- and α_2-adrenergic, $5HT_{1A}$, $5HT_{1D}$, $5HT_{2A}$, $5HT_{2C}$, muscarinic, histamine H_1 and dopamine D_2 receptors. Mirtazapine and its stereoisomers most potently blocked the histamine H_1 receptor (K_d's 0.2 – 0.4 nM). Interestingly, although (–)-mirtazapine was about two-old and 20-fold more potent than (+)-mirtazapine at the histamine H_1 ($K_d \approx 0.2$ nM) and muscarinic ($K_d \approx 300$ nM) receptors, respectively, (+)-mirtazapine was about 20-fold more potent than (–)-mirtazapine at the α_2-adrenergic receptor ($K_d \approx 70$ nM). All compounds were weakest at the $5HT_{2A}$ and dopamine D_2 receptors. If α_2-adrenergic receptor blockade is involved with the therapeutic effects of this drug, then the (+)-form of mirtazapine might provide a more potent drug (mg/kg), with fewer side effects associated with histamine H_1 receptor blockade (sedation, weight gain). (Supported by Mayo Foundation.)

NR249 Tuesday, May 20, 12 noon-2:00 p.m.

Overview of the Efficacy of Quetiapine

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Summary:

Quetiapine (ICI 204,636) is a promising new atypical antipsychotic agent. Presented here is an overview of quetiapine efficacy data from four short-term (≤6 weeks), randomized, placebo-controlled, double-blind clinical trials in 768 hospitalized subjects with acute exacerbation of chronic or subchronic schizophrenia. One of these trials used five fixed doses of quetiapine (75, 150, 300, 600, and 750 mg/day) and three trials were dose-titrated. The fixed dose trial also included a haloperidol group (12 mg/day). A fifth trial (n = 201) was a six-week, randomized, chlorpromazine-controlled, double-blind, dose-titrated, safety, and efficacy trial in subjects with acute exacerbation of schizophrenia. Efficacy in all trials was assessed weekly using the BPRS, CGI, and SANS.

Quetiapine was consistently superior to placebo in improving the symptoms of acute psychotic exacerbation of schizophrenia as measured by the BPRS total score and CGI Severity of Illness score, and was consistently superior to placebo in improving both positive and negative symptoms associated with schizophrenia. In addition, efficacy was demonstrated over a dose range of 150 to 750 mg/day. Quetiapine was also comparable to haloperidol and chlorpromazine in measures of overall efficacy.

These favorable efficacy results, coupled with quetiapine's minimal potential for inducing EPS or elevations in plasma prolactin concentrations, favor quetiapine as first-line treatment for schizophrenia.

NR250 Tuesday, May 20, 12 noon-2:00 p.m.

The Effect of Phenytoin and Cimetidine on the Pharmacokinetics of Quetiapine

James Y.W. Wong, Ph.D., CMA, Zeneca Pharm, 1800 Concord Pike, Wilmington DE 19850; Barbara J. Ewing, Ph.D., Per T. Thyrum, M.D., Chiao Yeh, Ph.D.

Summary:

Quetiapine (ICI 204,636) is a dibenzothiazepine derivative currently in phase III clinical development as an antipsychotic agent. A comprehensive Phase II and III clinical trial program has shown quetiapine to be effective in treating the positive and negative symptoms of schizophrenia. In vitro studies have shown that quetiapine is metabolized primarily by CYP3A4. Clinical trials were conducted to investigate the effect of phenytoin, a specific CYP3A4 inducer (Trial 1) and cimetidine, a nonspecific CYP inhibitor (Trial 2), on the multiple-dose pharmacokinetics of quetiapine. Ten psychotic men completed Trial 1 and the effect of phenytoin (100 mg) was determined following 10-day coadministration with quetiapine (250 mg TID). Seven psychotic men completed Trial 2 and the effect of cimetidine (400 mg) was investigated following four-day coadministration with quetiapine (150 mg TID). Phenytoin produced a five-fold increase in the mean oral clearance (CL/f) of quetiapine but cimetidine did not significantly affect the pharmacokinetics of quetiapine. The results from these trials indicate that dose adjustment may be necessary when quetiapine is to be administered with CYP3A4 inducers. Dose adjustment is not necessary when quetiapine is coadministered with cimetidine.

NR251 Tuesday, May 20, 12 noon-2:00 p.m.

In Vitro Prediction of Potential Metabolic Drug Interactions for Quetiapine

Scott W. Grimm, Ph.D., DDM, Zeneca Pharmaceuticals, 1800 Concord Pike, Wilmington DE 19850; Karen R. Stams, B.S., Khanh Bui, Ph.D.

Summary:

Quetiapine (ICI 204,636) is a dibenzothiazepine derivative in clinical development as an antipsychotic agent. A comprehensive clinical trial program has confirmed that quetiapine is effective in the treatment of the positive and negative symptoms of schizophrenia and that, across the dose range, it does not differ from placebo in the incidence of extrapyramidal symptoms. Quetiapine is metabolized extensively in man by sulfoxidation, hydroxylation, N- and O-dealkylation, and oxidation of the parent alcohol to a carboxylic acid. In order to predict potential drug interactions, in vitro studies were conducted 1) to determine the CYP enzymes involved in major metabolism pathways for quetiapine in man and 2) to investigate whether quetiapine or nine of its metabolites could inhibit marker activities for CYP1A2, CYP2C8/9, CYP2C19, CYP2D6, and CYP3A. Similar to quetiapine metabolism in vivo, human liver microsomes demonstrated sulfoxidation was the major metabolic pathway, and lesser pathways including N- and O-

dealkylation and 7-hydroxylation. Using a combination of specific inhibitors for the human CYP enzymes and heterologously expressed CYPs, CYP3A4 was demonstrated to be responsible for sulfoxidation, the N- and O-dealkylation of quetiapine, and partially responsible for 7-hydroxylation. CYP2D6 may also play a role in the 7-hydroxylation pathway. These results suggest that quetiapine may exhibit a higher potential for drug interactions with inhibitors or inducers of CYP3A4 than with drugs that modify the levels or activities of other CYP enzymes in man. Quetiapine and nine of its metabolites were found to inhibit the metabolism of substrate probes for human CYP enzymes although the CYP inhibition was observed at concentrations that were several times higher than plasma concentrations that had been determined following high doses of quetiapine. The lack of potent CYP inhibition in vitro suggests that quetiapine and its metabolites will have little inhibitory effect on in vivo drug metabolism mediated by CYP1A2, 2C9, 2C19, 2D6, or 3A4.

NR252 Tuesday, May 20, 12 noon-2:00 p.m.

Sertraline Efficacy in Elderly Patients Suffering from Major Depression

Carlo Berti, Dr., Medical Department, Pfizer, Ltd., Sandwich Kent CTJ39NJ, England; K. Wilson, A. Whitehead

Summary:

We report initial findings from a large study evaluating sertraline in the prevention of relapse of depression in elderly patients. A total of 254 patients (mean age: 77.6 ± 6.9 years) with major depression (DSM-III-R) were treated with sertraline (50-200mg/day). After Phase I, acute treatment (8 weeks titration) and Phase II (8 weeks maintenance), 77% of the responders received 50 mg/day and 19% received 100mg/day. The remaining 4% of subjects required doses of 150 mg or 200 mg/day to benefit. Patients significantly ($p > 0.001$) improved on both HAM-D (62% reduction from baseline) and MADRS (62% reduction). Responders (three consecutive HAM-D assessments of ≤ 10) were randomized to continue on sertraline or placebo for an additional two years (Phases III and IV).

The preliminary analysis of Phases I and II suggests that sertraline 50 mg/day is a suitable regimen to produce significant improvement in depressed elderly patients. The improvement in sleep paralleled the overall improvement in HAM-D scores. Anxiety scores followed a similar pattern but at a slightly slower rate of improvement.

The investigators concluded that sertraline is effective and well tolerated in the acute treatment and maintenance therapy of major depression in an elderly population.

NR253 Tuesday, May 20, 12 noon-2:00 p.m.

Clozapine in Schizophrenia with Comorbid OCD

Michael Poyurovsky, M.D., Department of Research, Tirat Carmel, PO Box 9, Tirat Carmel 30200, Israel; Abraham Weizman, M.D.

Summary:

Schizophrenia with comorbid obsessive-compulsive disorder (OCD) is seen in up to 25% of schizophrenic patients and characterized by treatment resistance. We report preliminary data on seven schizophrenic patients (4 male, 3 female; age range 19-40 years) with comorbid OCD enrolled in a 12-week open trial with clozapine. Diagnosis of schizophrenia and OCD was established by the Structural Clinical Interview for DSM-IV Disorders, the Brief Psychiatric Rating Scale (BPRS), and the Yale Brown Obsessive-Compulsive Scale (Y-BOCS). Prior neuroleptic medication was gradually terminated and after a one-week wash-out period clozapine was initiated (12.5-25 mg/d) and gradually titrated. BPRS and Y-BOCS ratings were repeated every two weeks during treatment. All seven patients completed the trial. Maximum clozapine dose was 100-125 mg/d. Y-BOCS scores decreased on an average of 41.6% ($p < 0.01$). BPRS scores decreased on an average of 37.1% ($p < 0.05$). Hypersalivation and sedation were the most distressful clozapine-induced side effects. In conclusion though lack of efficacy of clozapine monotherapy in refractory OCD has been recently reported, the beneficial effect of low-dose clozapine in our schizophrenic patients with comorbid OCD may provide evidence of heterogeneity of OCD with subtypes involving various neurotransmitter regulations.

NR254 Tuesday, May 20, 12 noon-2:00 p.m.

Mirtazapine Versus Amitriptyline in Relapse Prevention

Norman Sussman, M.D., Department of Psychiatry, NYU School of Medicine, 201 East 68th St., Suite 204, New York NY 10016; Charlotte Kremer, M.D.

Summary:

Aim: To compare rates and time to first relapse (17-HAMD score ≥ 16) during long-term treatment with either mirtazapine or amitriptyline in a placebo-controlled study.

Method: Responders to short-term treatment with either mirtazapine (n = 70, 5-35 mg/day), amitriptyline (n = 83, 40–280 mg/day), or placebo (n = 51) continued long-term treatment up to one year under double-blind conditions. A survival analysis (Kaplan-Mayer) was performed using the day number as the time variable. Pair-wise comparisons between the groups were performed using the Log-rank test and Breslow's method in case of a tie.

Results: In the mirtazapine group 8.6% of patients had a relapse, which was statistically significantly less compared to the amitriptyline (21.5%, $p = 0.04$), or placebo group (35.5%, $p < 0.0001$). Significantly less amitriptyline- compared to placebo-treated patients had a relapse ($p = 0.02$). Time to first relapse was significantly shorter in the placebo group compared to active control groups.

Conclusion: Mirtazapine is superior to amitriptyline and placebo in relapse prevention during long-term treatment.

NR255 Tuesday, May 20, 12 noon-2:00 p.m.

The Emergence of Adverse Events Following Venlafaxine Extended Release (ER) Discontinuation

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Summary:

Objective: The prevalence of discontinuation-emergent symptoms among patients discontinuing antidepressants is unknown. We participated in a multicenter study and compared the rate of emergence of adverse events following the discontinuation of the extended release venlafaxine (venlafaxine-ER) with that occurring after placebo discontinuation.

Method: Twenty outpatients met DSM-IV criteria for major depressive disorder and had a 21-item Hamilton Rating Scale for Depression (HAM-D-21) score ≥ 20 at screen and no greater than 20% decrease in HAM-D at the baseline visit. Patients were studied over an eight-week period and then tapered for one to two weeks, except for those receiving the lowest dose (75 mg/day).

Results: During the three days after study drug discontinuation, 7 out of 9 (78%; 95% C.I. = .46-.93) venlafaxine-treated subjects and 2 out of 9 (22%; 95% C.I. = .06-.55) placebo-treated patients reported the emergence of adverse events, a statistically significant difference (Fisher's exact test; $p = .03$).

Conclusions: Our results suggest that discontinuation-emergent adverse events were fairly common among venlafaxine-treated patients and consequently clinicians should consider tapering venlafaxine gradually, consistent with recommendations included in the physician's package insert and with recommendations for selective serotonin reuptake inhibitors.

NR256 Tuesday, May 20, 12 noon-2:00 p.m.

The Effects of Risperidone Versus Haloperidol on Frontal Lobe Functioning in Treatment-Resistant Schizophrenia

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Summary:

The Trail Making Test is a measure of visuoscanning and tracking ability. This test is particularly sensitive to brain injury, and is also impaired in psychiatric populations including schizophrenics. In the present study, a battery of neuropsychological tests was administered to 60 treatment-resistant schizophrenia patients who participated in a randomized, double-blind, prospective, parallel group comparison of haloperidol vs. risperidone. Patients were tested during a maximum 7-day medication-free period and again following four weeks of fixed-dose medications of either 6 mg of risperidone or 15 mg of haloperidol.

A treatment X time repeated measures ANCOVA controlling for performance on Trail Making A demonstrated an improvement in Trail Making B relative to drug-free performance for patients receiving risperidone (N = 29) but not haloperidol (N = 31). This finding was not altered by controlling for effects of benztropine, which was differentially administered to the two treatment groups at the fixed-dose phase testing. Additionally, performance on Trail Making B was significantly correlated at baseline and fixed-dose phases with Wisconsin Card Sort categories and number of correct responses, spatial working memory, and verbal fluency. These results suggest that performance on Trail Making B is an index of cognitive functioning that is not adversely affected by benztropine and is positively influenced by treatment with risperidone.

NR257 Tuesday, May 20, 12 noon-2:00 p.m.

Risperidone and Glucose Tolerance

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Summary:

Case reports suggest that atypical antipsychotic drugs such as clozapine may exacerbate existing diabetes mellitus (DM) or elicit DM in predisposed individuals. It is not known whether the atypical antipsychotic drug, risperidone, also affects glucose tolerance. To evaluate this, we monitored glycosylated hemoglobin (HbA1c) in all patients referred to a specialized atypical antipsychotic clinic in a Veterans Administration Medical Center setting. HbA1c was measured prior to the first administration of risperidone and again after six to nine months of treatment. Comparisons of pre and post values were made using a paired t-test. In our sample (n = 30), there were no significant changes in HbA1c associated with risperidone treatment overall. However, in the patients with preexisting DM (n = 4), there was a significant increase in HbA1c. In addition, in some of these DM patients, the doses of hypoglycemic drugs had to be increased. Our data suggest that in patients with DM, attention must be paid to glucose tolerance during treatment with risperidone. Our future studies will examine the influence of family history, race, weight, and risperidone dose on glucose tolerance.

NR258 Tuesday, May 20, 12 noon-2:00 p.m.

Buspirone Augmentation of Nefazodone in Depression

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Summary:

Objectives: This six-week, open-label clinical trial assessed the safety and clinical effects of adding buspirone to augment the antidepressant response of nefazodone in depressed patients with partial or no response to nefazodone.

Method: This was a multicenter, open-label study of buspirone (30–60 mg/day) added to nefazodone partial/nonresponders (300–600 mg/day for at least eight weeks). Buspirone was initiated at 5 mg t.i.d. and titrated to a minimum target dose of 10 mg t.i.d. by day 7. Antidepressant response was evaluated using the CGI and PGA scales. A responder was defined as having CGI of 1 (very much improved) or 2 (much improved).

Results: Forty-three patients entered the study; 18 patients completed the study and 16 patients discontinued due to adverse events (dizziness, headache, nausea). Of the 23 patients who were considered evaluable (at least four weeks of augmentation), 10 patients (43%) responded to the addition of buspirone therapy.

Conclusion: These preliminary findings suggest that buspirone may provide clinical benefits as an augmenting agent in depressed patients with partial/no response to nefazodone. The high discontinuation rates due to adverse events may be related to the use of too high a starting dose (buspirone 5 mg t.i.d.). There is a pharmacokinetic interaction between nefazodone, which inhibits the cytochrome P_{450} enzyme $3A_{3/4}$, and buspirone, which is metabolized by this enzyme, that may have resulted in higher than expected plasma levels of buspirone. A lower initial dose of buspirone (2.5 mg b.i.d.) should be considered when used in combination with nefazodone.

NR259 Tuesday, May 20, 12 noon-2:00 p.m.

Ginkgo Biloba Extract in Schizophrenic Patients

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Summary:

Cognitive impairment, found in virtually all schizophrenic patients and seen as a major predictor of poor outcome, remains practically unaffected by the available treatment of schizophrenia. Current treatments in schizophrenia address psychotic symptoms, but none of them effectively and specifically target cognitive deficits. Unfortunately, tacrine, the only FDA-approved agent for the treatment of cognitive impairment, has a severe side effect profile. In Europe, however, another agent, ginkgo biloba extract (GBE), with practically no side effects, is frequently used for the treatment of cognitive deficits. We conducted a clinical trial of adjunctive GBE in a group of schizophrenic patients and we assessed the cognitive and psychiatric condition of the patients before and during GBE treatment.

Method: We propose to present the data obtained from assessing a group of 10 schizophrenic patients, stabilized on their current medication, who received 80–200 mg/day of GBE in divided doses. Patients had psychiatric and cognitive assessments

before and at least six weeks after GBE initiation. The cognitive battery included tests of attention, such as digit symbol and digit span; tests of visual and auditory memory; executive function; and measures of verbal fluency. Paired t-test analysis with one-tail degree of significance was performed to compare the final and baseline assessments.

Results: Patients received from 80–160 mg/day of GBE. Our preliminary findings suggest that, although patients did not improve in psychiatric symptoms, they scored better on some tests of attention such as digit symbol ($p = 0.01$) and on tests of delayed memory (delayed visual recall: $p = 0.002$; delayed word recall: $p = 0.07$).

Conclusion: These preliminary findings suggest that GBE may have a beneficial effect on cognitive function in schizophrenia, but should be considered with caution due to the lack of controlled conditions of the trial and the small sample size. Nevertheless, this clinical trial encourages further investigation of adjunctive GBE treatment in chronically psychotic patients.

NR260 Tuesday, May 20, 12 noon-2:00 p.m.

Trends in the Use of SSRIs at Nine Department of Veterans Affairs Facilities

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Summary:

Purpose: This study was designed to answer the questions: At what average dose are fluoxetine, paroxetine, and sertraline administered in the outpatient setting? Is there dose escalation with any of the selective serotonin reuptake inhibitors?

Methods: Information was collected on more than 63,000 outpatient SSRI prescriptions from nine Veterans Affairs hospitals in three adjoining states. Data (average daily dose, cost, and number of prescriptions for each drug) were divided into two consecutive six-month groups.

Results: For fluoxetine and sertraline, the second six-month cost/day average remained the same, while paroxetine decreased slightly. Average dose/day decreased 8.1% for fluoxetine, was unchanged for paroxetine, and increased 2.3% for sertraline. The proportion of specific dosage strengths changed for each drug. Fluoxetine's modest decrease in daily dose correlated with an increase in the use of the 10 mg capsule. Paroxetine's cost decreased two cents/day with no decrease in dose/day. Sertraline was prescribed the most and its cost/day remained stable. The average daily dose increased from 87.8 mg to 89.8 mg/day. The minor increase in dose was offset by the increased use of split 100 mg tablets.

Conclusion: This study shows that dose escalation is not a significant issue.

NR261 Tuesday, May 20, 12 noon-2:00 p.m.

Gabapentin: An Effective Therapy for Patients with Bipolar Affective Disorder

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Summary:

Purpose: An open study was performed to determine if the use of gabapentin, monotherapy or in addition to other psychiatric medications, could be effective in improving concentration, mood, sleep disorder, and appetite in patients with bipolar affective disorder.

Methods: Retrospective analysis of medical records of 47 patients diagnosed with bipolar affective disorder, with or without concomitant diagnosis of OCD or panic disorder was accomplished. Patients had been on gabapentin therapy for at least six months. Patients were asked during monthly medication checks to comment whether concentration, mood, sleep, appetite, or irritability had improved, worsened, or stayed the same over the preceding month. Gabapentin therapy was titrated to an effective dose range from 600 to 4800 mg/day with a mean of 1500 mg/day.

Results: The majority of patients reported improvement. We were able to eliminate one or more concomitant medications for a number of patients. The majority of patients reported no side effects and there were no reports of serious adverse events.

Conclusion: Gabapentin is a safe, effective therapy when used alone or in combination to treat patients with bipolar affective disorder. The need for double-blind, placebo-controlled trials exists.

NR262 Tuesday, May 20, 12 noon-2:00 p.m.

A Controlled Study of Bromocriptine and Placebo in Treating Neuroleptic-Induced Amenorrhea

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Summary:

Objective: The purpose of this study was to determine the effect of bromocriptine on amenorrhea induced by neuroleptics.

Method: A total of 30 female patients with amenorrhea induced by neuroleptics, who suffered from schizophrenia and had been taking neuroleptics. Their psychiatric status was stable at least one month, and no physical disorders were found to explain their amonorrhea. The patients were randomized to receive bromocriptine (with increasing to 7.5/day) and placebo for six weeks. During trial, their neuroleptics weren't changed.

Results: In the trial group, three patients dropped out, including one who could not tolerate the side effects (nausea and vomiting); two had to stop because of worsening psychiatric symptoms. Nine of 12 (75%) patients who completed the trial returned their menses, though four of the nine only had slight bleeding; the average response time was 23 days (13–38 days); all the 15 patients in the control group completed the trial, not only one patient returned to their menses. There was significant difference between the two groups ($p < 0.001$).

Conclusion: Bromocriptine had a satisfactory effect on neuroleptic-induced amonorrhea, but it should be used cautiously because of its side effects, especially worsening psychiatric symptoms.

NR263 Tuesday, May 20, 12 noon-2:00 p.m.

Effect of Penfluridol on Positive and Negative Symptoms of Schizophrenia

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Summary:

Objective: The purpose of this study was to assess the response of positive and negative schizophrenia symptoms to penfluridol.

Method: A total of 93 schizophrenic inpatients, treated with only one kind of neuroleptic, penfluridol, at least 12 weeks. Psychiatric symptoms and side effect were rated with SANS/SAPS and TESS, respectively.

Results: The patients were classified into positive ($N = 35$), negative ($N = 37$), and mixed ($N = 21$) groups, according to the Andreasen's typological model (1982), and then 27 "pure" negative schizophrenia (the global rating of negative symptom ≤ 2) were picked out. All the symptoms of SANS/SAPS in all the three groups were significantly improved except the formal thought disorder symptom in the negative group. The positive group improved more than the other two groups, and the "pure" group also signifi-

cantly improved: There were no significant differences between the three groups in the improvements of total SAPS, but the positive group improved better than the negative and the mixed groups in the improvements of total SANS; there were no differences in side effects between the three groups. The highest incidence of side effect was EPS, and the patients could tolerate it by combining anticholergics. No severe side effects were found.

Conclusion: This respective study showed that penfluridol could markedly improve positive symptoms of schizophrenia and it could reduce negative symptoms also. Its high incidence of side effects could be reduced to a tolerable degree when combining anticholergic agents.

NR264 Tuesday, May 20, 12 noon-2:00 p.m.

Risperidone in Adolescents with Psychosis and Mood Disorders

Herman A. Tolbert, M.D., Department of Psychiatry, Ohio State University, 1670 Upham Drive, Suite 460, Columbus OH 43210-1250; Henry A. Nasrallah, M.D., Nicholas Votolato, R.P.H., Noelle K. Gehm, B.S.

Summary:

In a retrospective study of the use of the atypical antipsychotic risperidone in younger age groups, the medical records of all adolescents admitted to our department's inpatient unit who received risperidone over a two-year period were reviewed.

Twenty-four adolescents were identified to have received risperidone as part of their inpatient treatment. Thirteen were female and 11 were male. Seventeen were Caucasian and seven were African American. The mean age of the sample was 15.8 years, with a range of 13–18 years. The mean dose received was 4.02 mg/day with a range of 0.5–10 mgs/day. A total of 16/24 adolescents had mood disorders (five bipolar and 11 major depression), 7/24 had psychotic disorders, and one had OCD.

Seventy-one percent of the sample (17.24) improved partially or significantly according to the records; 13% (3/24) showed no response. Risperidone was discontinued in 5/24 (21%) due to side effects, but one of these five patients had shown a good response. The side effects included 4/24 with sedation, 3/24 with EPS, and 2/24 with orthostatic hypotension. Symptoms that improved included paranoia, thought disorder, manic symptoms, and depressive symptoms. In several patients, improvement in negative symptoms such as interactiveness, appropriateness, insight, or social withdrawal, were documented. These results indicate the usefulness of the novel antipsychotic risperidone in the management of psychiatrically hospitalized adolescents.

NR265 Tuesday, May 20, 12 noon-2:00 p.m.

Acute Effect of Paroxetine and Amitriptyline on the Psychomotor Performance in Healthy Volunteers

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Summary:

Paroxetine, a selective serotonin reuptake blocker, is known to have fewer cognitive side effects than older antidepressants such as amitriptyline. To confirm these previous findings objectively, we compared the effects of paroxetine on the psychomotor performance with those of amitriptyline, using objective psychomotor performance tests in a double-blind, two-way, single dose, crossover study employing 10 healthy volunteers.

Assessments of psychomotor performances were carried out before and six hours after administration of a single dose of paroxetine (40 mg) or amitriptyline (50 mg) at 10:00 A.M. Each treatment day was separated by one week of washout.

The psychomotor performances were measured using Vienna Determination Unit, Vienna Reaction Unit, Vienna Signal Detection, Purdue Pegboard Test, and Finger Tapping Test.

The data were analyzed using two-way with two repeated measure ANOVA on a crossover model.

Paroxetine 40 mg produced no significant performance decrements on nearly every test of psychomotor performances, whereas amitriptyline 50 mg produced markedly impaired performance on most of the psychomotor tests.

In conclusion, this study confirmed pervious findings that paroxetine is generally devoid of adverse side effects on psychomotor performance.

NR266 Tuesday, May 20, 12 noon-2:00 p.m.

Mirtazapine Versus Amitriptyline and Placebo in the Treatment of Severely Depressed Patients

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Summary:

Objective: To compare efficacy and safety of mirtazapine (n = 79, 5–35 mg/day), amitriptyline (n = 89, 40–280 mg/day), and placebo (n = 82) in a six-week treatment of severely depressed patients (baseline 17-HAMD score ≥25).

Method: Efficacy and safety data from severely depressed patients participating in four three-arm studies of mirtazapine were pooled and analyzed using appropriate meta-analytical methodology.

Results: On all main efficacy variables both active drugs were statistically and clinically superior to placebo. On the 17-HAMD scale, reduction from baseline at the endpoint was −13.0 points for mirtazapine, -13.5 for amitriptyline, and −8.7 for placebo. Using the CGI criterion, 53.2% of the mirtazapine-, 53.9% of the amitriptyline-, and 34.1% of the placebo-treated patients were classified as responders. Tolerability of mirtazapine was comparable to placebo (6.2% and 3.6% of patients respectively dropped out due to adverse events), and superior to amitriptyline (15.6% of drop outs due to adverse events, significantly more compared to the other two groups).

Conclusion: The results demonstrate that mirtazapine and amitriptyline are of equivalent efficacy in the treatment of severely depressed patients, but mirtazapine is significantly better tolerated.

NR267 Tuesday, May 20, 12 noon-2:00 p.m.

Cross-Over Comparison of CYP2D6 Inhibition: Insignificant Effect of Venlafaxine Compared to Sertraline, Paroxetine and Fluoxetine

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Summary:

We evaluated the CYP2D6 inhibition of four antidepressants (AD) using the dextromethorphan/dextrorphan (DM/DP) ratio as a noninvasive probe. Oral administration of 30 mg DM, followed by an eight hour urine collection to quantitate DM and DP conc., phenotypes individuals as poor (PM, DM/DP ≥ 0.3) or extensive metabolizers (EM, DM/DP < 0.3) for CYP2D6 enzyme activity. In this crossover study, 12 EMs received eight days of treatment of each AD, with a two-week washout between each treatment phase. All subjects were healthy and not taking any drug, caffeine,

or tobacco products during the entire study period. The order of AD treatment for each subject was randomized except for fluoxetine (due to the long t1/2 of parent drug and metabolite), which was always the last drug administered. Doses administered were venlafaxine (V) (37.5 mg BID x 3 days, 75 mg BID x 5 days), sertraline (S) 100 mg QD, paroxetine (P) 20 mg QD, and fluoxetine (F) 60 mg OD (loading dose to simulate conc. achieved for 20 mg/day at true steady-state). DM administration and eight-hour urine collections were done the day prior to the first dose of each AD (baseline) and one hour after the last dose of each AD. Interim data for six (25 ± 2.3 yrs., 81.6 ± 11.2 kg., 6 males) of 12 completing subjects is reported here. Percent change (mean ± SD and range) between each subject's DM/DP at baseline and post AD treatment, and the proportion of subjects who shifted phenotype (EM to PM) were determined.

Drug	Mean ± SD Δ in DM/DP(%)	Range of Δ DM/DP(%)	EM->PM
Venlafaxine	-13 ± 33	-37 to 38	0/6
Sertraline	92 ± 104	-40 to 220	0/6
Paroxetine	10245 ± 11802	1132 to 32150	4/6
Fluoxetine	4682 ± 5824	581 to 16233	3/6

Fisher's PLSD statistic showed significant differences in post AD treatment DM/DP ratios between V and P ($p = 0.008$), V and F ($p = 0.0013$), S and P ($p = 0.0009$), and S and F ($p = 0.0014$). Most subjects exhibited a small, nonsignificant decrease in DM/DP ratio with venlafaxine treatment. Sertraline exhibited mild CYP2D6 inhibition in most subjects. The large increases in DM/DP with fluoxetine and paroxetine demonstrate their potent inhibitory effect at CYP2D6. Fluoxetine was the most potent CYP2D6 inhibitor for 2/6 subjects, paroxetine for 4/6 subjects. This difference in CYP2D6 inhibition potency may be a function of AD drug concentrations achieved (samples currently being assayed). These data document the lack of significant CYP2D6 inhibition with venlafaxine compared to sertraline, fluoxetine, and paroxetine.

NR268 Tuesday, May 20, 12 noon-2:00 p.m.

Outcome of Risperdone Treatment in Alzheimer's Disease Patients with Psychotic Symptoms and Behavioral Disturbances

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Summary:

Objectives: To evaluate the clinical outcome of Alzheimer's disease (AD) patients treated with risperidone for the control of psychotic symptoms and behavioral disturbances.

Methods: We evaluated 41 patients treated with risperidone at the dementia management clinic. Subjects were clinically diagnosed as probable AD by NINCDS-ADRDA with significant secondary psychotic symptoms and behavioral disturbances. A battery of tests was administered at baseline and was repeated after three months of treatment. This battery included the Positive and Negative Symptoms Scale (PANSS), Scale for the Assessment of Negative Symptoms in AD (SANS-AD), Hamilton Depression Scale (Ham-D), Clinical Dementia Rating (CDR), Mini-Mental State Exam (MMSE), Behavioral Pathology in AD Rating Scale (BEHAVE-AD), Abnormal Involuntary Movement Scale (AIMS), and Simpson-Angus Extrapyramidal Symptoms Scale (SAS)

Results: The subjects' age was 76 ± 12 years, 60% were female, chronicity of 6 ± 4 years, education of 12.5 ± 3 years and a mean dose of risperidone of 1.5 mg per day. At baseline, the PANSS score was 67.5 ± 14, MMSE was 10 ± 5, CDR was 2 ± 0.6, and BEHAVE-AD was 11 ± 4. There was significant improvement in PANSS total score and BEHA-AD scores at the three-month period, with no significant change in the MMSE.

Conclusions: Treatment with risperidone appears to help control secondary psychotic symptoms and behavioral disturbances in patients with AD.

NR269 Tuesday, May 20, 12 noon-2:00 p.m.

Low-Growth Hormone After Clonidine in Adversely Reared Primates

Jeremy D. Coplan, M.D., Department of Psychiatry, Columbia University/Physicians, 722 West 168th Street, Unit 24, New York NY 10032; Eric Smith, Ph.D., Ronald Trost, M.D., David E. Scharff, M. D., Jack M. Gorman, M.D., Leonard Rosenblum, M.D.

Summary:

Reduced human growth hormone (HGH) response to the α_{-2} agonist clonidine is among the most consistent neuroendocrine abnormalities observed in patients with PD, major depression, generalized anxiety disorder, and social phobia. The reduced HGH response to clonidine may bear generalized relevance to a hypothetical vulnerability diathesis for anxiety and affective disorders. In nonhuman primate studies, we have shown that adversely reared subjects exhibit persistent elevations of CSF CRF, somatostatin, HVA, and 5-HIAA, each of which may exert an inhibitory influence on GH secretion. Eleven bonnet macaques, nine of whom had been adversely reared, and on whom previously drawn CSF CRF values were available, served as subjects for clonidine infusions while under ketamine anesthesia. Maximal GH response to clonidine correlated inversely with CSF CRF (Pearson's $r = -.72$; $df = 10$; $p = .01$). "High" CRF subjects showed lower GH secretion in comparison to the "low" CRF subjects (group by time interaction: $F = 2.9$; df

NR270 Tuesday, May 20, 12 noon-2:00 p.m.

Clozapine to Olanzapine Conversion: Preliminary Results

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Summary:

Objective: Clozapine presents a remarkable treatment breakthrough for the severely mentally ill. Olanzapine availability has generated enthusiasm that clozapine patients can be safely switched without loss of therapeutic efficacy. This study reports our experience in a state hospital setting.

Methods: Physicians rated clozapine patients on 11 functional areas, then were free to switch patients to olanzapine. After eight weeks, drug dosages and clinical responses were analyzed.

Results: Of 99 patients on clozapine, 23 were started on olanzapine. Patients switched were twice as likely to have had no improvement in ADL's, social functioning, performance in therapeutic activities, or polydipsia/hyponatremia. Average clozapine dose decreased from 536.9mg/d to 218.5mg/d. Only seven of 23 patients tolerated complete clozapine discontinuance. Mean olanzapine dose was 13.48 mg/d; however, improved patients' dose was 16.67 mg/d, while the dose for patients the "same" or "worse" was 11.43 mg/d. Neither days on olanzapine nor change in clozapine dose predicted improvement. Clozapine daily cost pre-olanzapine was $15.62; at the end of the study period, daily cost for olanzapine plus clozapine was $15.07.

Conclusions: One-third of clozapine inpatients switched to olanzapine showed clinical improvement at eight weeks. Improvement

correlated with olanzapine dose. Although clozapine dose decreased 59%, daily drug costs did *not* change.

NR271 Tuesday, May 20, 12 noon-2:00 p.m.

Venlafaxine Treatment of Trichotillomania: An Open Series of Ten Cases

Richard L. O'Sullivan, M.D., Department of Psychiatry, Harvard Medical School, MGH-East, Building 149, 13 St Charlestown MA 02129; Nancy J. Keuthen, Ph.D., Dayami Rodriguez, B.A., Paige Goodchild, B.A., Gary A. Christenson, M.D., Scott L. Rauch, M.D.

Summary:

Background: Trichotillomania (TTM) is manifested by chronic severe hair pulling. Effective treatments include both behavioral and pharmacological ones, but efficacy of all treatments has been limited. To explore other treatment options we openly treated 10 TTM patients with venlafaxine. We report here a retrospective review of these cases.

Method: A chart review was conducted on 10 consecutive TTM patients treated with venlafaxine. Mean treatment duration was 15.1 ± 5.8 weeks, with a mean venlafaxine dose of 274 ± 61 mgs. Clinical rating scales were used at routine visits.

Results: Using an intention-to-treat analysis, significant improvement in TTM symptoms was noted from baseline to last clinical visit on both behavioral (MGH Hair Pulling Scale, $p = .02$, Psychiatric Institute Trichotillomania Scale, $p = .02$) and psychosocial measures (MGH Trichotillomania Impact Scale, $p = .009$) of TTM. Clinical Global Improvement score ranged from slight to much improvement (mean 2.38). There were no significant differences from baseline to end-point scores on the Beck Depression and Beck Anxiety Inventories.

Conclusion: Results from this open treatment review indicate venlafaxine improved TTM symptoms with short-term treatment. Longer controlled trials with extended baseline periods are needed to optimally assess pharmacological treatments of TTM.

NR272 Tuesday, May 20, 12 noon-2:00 p.m.

A Double-Blind, Placebo-Controlled Trial of Once-Daily Venlafaxine Extended Release (ER) in Outpatients with Major Depression

Michael E. Thase, M.D., Department of Psychiatry, Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh PA 15210

Summary:

Objective: To compare the efficacy and safety of once-daily venlafaxine extended release (ER) with those of placebo in outpatients with major depression.

Methods: This was a randomized, double-blind, placebo-controlled evaluation of venlafaxine ER in outpatients with major depression. Outpatients with DSM-III-R major depression were randomly assigned to venlafaxine ER 75 mg or placebo once daily for up to eight weeks. If the response was inadequate after two weeks, the dosage of venlafaxine ER could be increased to 150 mg daily and to 225 mg daily after another two weeks. Data from 191 patients were evaluated for efficacy—91 venlafaxine ER-treated patients and 100 placebo-treated patients.

Results: Venlafaxine ER was superior ($p < 0.05$) to placebo beginning at week 4 on the HAM-D and MADRS, week 2 on the CGI severity scale, and at week 3 on the HAM-D depressed mood item and continuing through week 8. The most common adverse events with venlafaxine ER were nausea, insomnia, and somnolence. The incidence of nausea with venlafaxine was highest during the first week, decreased by 50% during the second week, and was comparable to that of placebo from week 3 onward.

Conclusions: Venlafaxine ER administered in once daily doses of 75 to 225 mg is effective and well tolerated for the treatment of major depression.

NR273 Tuesday, May 20, 12 noon-2:00 p.m.

Characterization and Inhibition of Human Cytochrome P450 Enzymes Involved in the In Vitro Metabolism of Mirtazapine

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Summary:

Objective: For the characterization of the human cytochrome P450 enzymes involved in the in vitro metabolism of mirtazapine, [^{3}H]-mirtazapine was incubated at two concentrations (low and high) with the cytochrome P450 enzymes CYP1A1, CYP1A2, CYP2A6, CYP2C9, CYP2D6, CYP2E1, CYP3A4, and a series of 10 human liver microsomes, and the rates of formation of possible metabolites 8-OH mirtazapine, N-demethyl mirtazapine and N-oxide mirtazapine were investigated. In addition, the inhibition of CYP1A2, CYP2D6, and CYP3A by mirtazapine was investigated using a pool of human liver microsomes (seven individuals). The K_i of mirtazapine and the types of inhibition were determined. Fluvoxamine (CYP1A2), fluoxetine (CYP2D6), and ketoconazole (CYP3A) were used as positive controls.

Results: CYP3A is the most important P450 subfamily with respect to the formation of both N-demethyl and N-oxide mirtazapine, whereas CYP2D6 was responsible for the formation of 8-OH mirtazapine. CYP1A2 was the second major enzyme involved in the formation of 8-OH mirtazapine. Mirtazapine was found to be a competitive inhibitor of CYP1A2 (k_i = 159 μM), CYP2D6 (K_i = 41 μM), and CYP3A (K_i = 210 μM). Mirtazapine was approximately 900- and 10-fold less potent than the cytochrome P450 inhibitors fluvoxamine (K_i = 0.18 μM) and fluoxetine (K_i = 4.1 μM), respectively. Ketoconazole displayed a type of inhibition other than noncompetitive or competitive interaction. The calculated K_i values for the noncompetitive model were 0.07 and 0.15 μM for 0.1 and 0.4 μM ketoconazole, respectively. In addition, the obtained data show that 0.1 μM ketoconazole had a larger effect than 25 μM mirtazapine, thus indicating at least 250-fold potency difference. At steady state, the mirtazapine plasma concentrations at the dose levels recommended for clinical use are far below the observed k_i values in the present study.

Conclusion: Based on in vitro modeling, mirtazapine is unlikely to cause a potentially clinically meaningful inhibition of any of these CYP enzymes under clinically relevant dosing conditions. Nevertheless, confirmatory in vivo studies are underway.

NR274 Tuesday, May 20, 12 noon-2:00 p.m.

Remission Rates During Short-Term Treatment with Mirtazapine

Milana V. Zivkov, M.D., Medical Services, NV Organon, Molenstraat 110, Oss 5340BH, Netherlands; Charlotte Kremer, M.D.

Summary:

Objective: To analyze the remission rates (percentages of patients with 17-HAMD score ≤ 7), the most stringent outcome criterion of antidepressant treatment, in the double-blind, randomized, short-term, active-control studies of mirtazapine.

Method: Percentages of patients who completed the full study period were calculated for all amitriptyline-controlled studies ($n = 7$), as well as for other active-controlled studies (clomipramine, $n = 1$; doxepin, $n = 1$; and trazodone, $n = 1$). Amitriptyline-controlled studies were further divided into subset where mirtazapine was

used in dosages between 5 and 35 mg/day (n = 4) and subset with dosages 20-60 mg/day (n = 3). In the other active-controlled studies mirtazapine was used in doses between 20 and 80 mg/day.

Results: Remission rates for mirtazapine were between 33% and 50% in the studies using the lower doses of mirtazapine. In the studies using the higher doses, remission rates obtained during the mirtazapine treatment were between 48% and 58%.

Conclusion: In general, remission rates obtained with mirtazapine are high (33-58%), and in the majority of the studies are higher than those obtained with the active comparator. High initial doses of mirtazapine appear to be related to increased remission rates.

NR275 Tuesday, May 20, 12 noon-2:00 p.m.

The Pharmaco-Economic Profile of Fluvoxamine in Recurrent Depression

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Summary:

Depressive illness is a common psychiatric disorder in the community and represents a large economic burden on society in terms of the indirect costs associated with loss of productivity, direct costs of treatment, and intangible costs of suffering and stress. An important part of these costs results from the recurrent nature of depression. Expectations are that 50% to 85% of patients with a major depressive episode will experience at least one recurrence. With each additional episode, risks of chronicity, psychosocial impairment, and suicide are increased.

In a recent French, 18-month, double-blind, placebo-controlled trial comparing the efficacy of fluvoxamine and placebo in preventing recurrence of depression, results indicated that the incidence of recurrence was significantly lower (12.7% vs 35.1%, $p < .001$) and the time to first recurrence was significantly longer (11.1% vs 37.2%, $p < .001$) with fluvoxamine than with placebo. Intuitively, these clinical endpoints lead to economic advantages for fluvoxamine. However, to quantify these in a real-life setting, a cost-effectiveness analysis was carried out to compare the maintenance treatment of fluvoxamine with that of "usual care," comprising other SSRIs and TCAs according to current practice in France. The key elements in the pharmaco-economic profile of fluvoxamine, as derived from the model, are presented.

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Effects of Divalproex on 5-HT1A Receptor Function

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Summary:

Objectives: The authors examined the effects of divalproex sodium on the 5-HT1A receptor function in humans by measuring body temperature, ACTH/cortisol and behavioral responses to ipsapirone, a selective 5-HT1A receptor agonist.

Methods: Ten healthy male volunteers were recruited for the study. Each subject received 0.3 mg/kg ipsapirone hydrochloride tablets at time "0". Blood samples for hormone levels and measurements of body temperature were obtained at 0, 30, 60, 90, 120, 150, and 180 minutes. The ipsapirone challenge tests were repeated after one week treatment with 1000 mg/day divalproex sodium.

Results: The hypothermia induced by ipsapirone was significantly attenuated by the divalproex sodium treatment, whereas the ACTH/cortisol release and the behavioral responses following ipsapirone challenges were not altered.

Conclusions: Our findings suggest that divalproex sodium may enhance 5-HT neurotransmission in humans via a subsensitization of 5-HT1A autoreceptors, but does not appear to have an effect on postsynaptic 5-HT1A receptors.

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Olanzapine in Treatment-Refractory Schizophrenia

Juan-Carlos Gomez, M.D., Medical, Eli Lilly and Company, Avenida De La Industria 30, Alcobendas Madrid 28100, Spain; Joaquin Martin, M.D., Enrique Garcia Bernardo, M.D., Victor Peralta, M.D., Enrique Alvarez, M.D., Manuel Gurpegui, M.D.

Summary:

Clozapine is currently the treatment of choice for neuroleptic-resistant schizophrenia (between 30% and 50% of these patients respond to clozapine). Olanzapine is a new antipsychotic drug that has shown efficacy against positive and negative symptoms of schizophrenia, with minimum extrapyramidal side effects. Olanzapine has not yet been tested in treatment-refractory schizophrenic patients.

A total of 21 schizophrenic patients (DSM-IV criteria) with documented lack of response to two conventional antipsychotic drugs entered this six-week prospective, open-label, clinical trial. All patients were treated for six weeks with olanzapine 15 to 25 mg/day.

As a group, patients showed improvement in positive and negative symptoms and at the end of six weeks of therapy, 38% of the patients met criteria for treatment response (≥ 35% decrease in BPRS total score, plus post-treatment CGI-severity ≤ 3 or BPRS total ≤ 18).

There were no treatment discontinuations during the six-week treatment trial and there were no clinical reports of extrapyramidal side effects and no patients required anticholinergic medication while taking olanzapine.

In conclusion, this uncontrolled study suggests that olanzapine may be effective in a significant number of neuroleptic-resistant schizophrenic patients, but blinded controlled trials are needed to confirm our results.

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Cognitive Profile and Soft Signs in Clozapine Versus Risperidone Treatment

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Summary:

Twenty-eight DSM-IV schizophrenic inpatients (mean age 39.71 years; mean duration of illness 17.95 years) with a history of neuroleptic nonresponse were treated in a prospective, 12-week, open trial with either clozapine or risperidone (clozapine mean dose 445 mg; risperidone mean dose 11.6 mg). Response was assessed biweekly with PANSS, CGI, and Simpson-Angus Scale. In order to explore the specific effect on neuropsychological functioning by each drug and the relationship of baseline neurological soft signs (NSS) with response, patients received a battery of neuropsychological tests measuring attention, memory, and executive functions at baseline and week 12 together with baseline measures of NSS.

Overall, the cognitive effects of clozapine and risperidone were modest over the course of this trial. Risperidone improved some attention measures (Symbol Digit Test; p .021), while patients on clozapine showed a decline in short-term memory (Hopkins Verbal Learning Test; p .038). Total NSS score was associated at baseline with concurrent negative symptom score for the total group,

while total NSS score and Sequencing score predicted poorer response on negative symptoms for clozapine only (p .05). Possible implications of these results for the long-term rehabilitation of these patients will be discussed.

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Buspirone Treatment of Aggressive Child Inpatients

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Summary:

Objectives: An open-label study with buspirone was conducted in prepubertal psychiatric inpatients to evaluate safety, tolerability, and effects of buspirone on symptom clusters of anxiety, impulsivity, and aggressivity.

Method: This was a single-site, open-label study of buspirone in psychiatric inpatients. The study consisted of three phases: Phase 1-Screening (two weeks), Phase 2-Titration (three weeks), and Phase 3-Maintenance (six weeks). The initial dose of buspirone was 5 mg/day, titrated to maximum dose of 50 mg/day (BID) based on clinical response and tolerability. Efficacy was assessed using CDI (Child Depression Inventory), MAVRIC (Measure of Aggression, Violence, and Rage In Children), and RCMAS (Revised Children Manifest Anxiety Scales) scales.

Results: Of the 25 patients enrolled (mean age 8, range 5–11), 19 patients completed the study and six (24%) discontinued due to adverse events. Average dose of buspirone was 28 mg/day. There were significant reductions in the following: 50% ($p < 0.0001$) decrease in symptoms of depression on CDI, 29% ($p < 0.02$) decrease in aggressivity on MAVRIC, 16% ($p < 0.04$) decrease in social anxiety on RCMAS, and 89% ($p < 0.01$) decrease in number of episodes per day, and 86% ($p < 0.02$) decrease in number of hours per day that children spent in seclusion/restraint. None of the 19 children reported severe side effects.

Conclusion: These data suggest that buspirone may be beneficial in reducing depressive, anxious, and impulsive-aggressive symptom clusters in child psychiatric inpatients and that it is safe and well tolerated in children.

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Naltrexone as a Treatment for Repetitive Self-Injurious Behavior: Efficacy Over One Year

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Summary:

Objective: Repetitive self-injurious behavior (SIB) is a dangerous and often treatment-refractory syndrome. The authors sought to determine if naltrexone could decrease SIB in a sample of adult psychiatric patients, and if a decrease persisted for more than one year.

Method: Seven female patients with SIB accompanied by analgesia and dysphoria reduction were administered oral naltrexone, 50 mg per day, in an open-label trial. Mean follow-up for an initial evaluation period was 10.7 weeks. Long-term follow-up was for one year.

Results: SIB ceased entirely in six of seven patients during the initial period of naltrexone treatment. One patient had superficial cutting on two occasions over the first seven weeks, which reflected a significant reduction in frequency of SIB. Two of the patients who briefly discontinued naltrexone had a rapid resumption of SIB, which resolved upon restarting naltrexone. A similar pattern of reduction in rates of SIB was found at one year.

Conclusion: The initial and long-term follow-up observations are consistent with the hypothesis that the endogenous opioid system is involved in cases of SIB that are characterized by analgesia and dysphoria reduction. Further placebo-controlled studies to explore the effectiveness of naltrexone for treating patients with this syndrome are warranted.

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Pharmacokinetic Effects of Venlafaxine on Imipramine Metabolism

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Summary:

Significant efforts have been made to understand the interactions of the new antidepressants with the cytochrome P450 isoenzymes. This research has shown many such interactions with relevant clinical implications. Venlafaxine (VF) is an antidepressant that works by blocking the reuptake of both serotonin and norepinephrine. In vitro inhibition studies with human microsomes indicate minimal effects on CYP2D6, CYP1A2, CYP3A4, and CYP2C9 isoenzyme function. To evaluate these findings in vivo, the metabolism of a single 100 mg dose of imipramine was studied in seven healthy volunteers before and after three days of treatment with 150 mg per day of VF. Serial blood samples were collected and assayed by HPLC for imipramine (IMI), desipramine (DMI), OH-IMI, and OH-DMI levels to determine any pharmacokinetic changes in metabolism. For IMI, venlafaxine had no significant effect on AUC or Cmax. For DMI, venlafaxine resulted in an increased AUC (849 to 1343; $p = 0.04$) and Cmax (18.6 hours to 23.9 hours; $p = 0.03$; one tailed). CYP2D6 phenotype (dextromethorphan) was completed and will be discussed. In addition, effects on hydroxymetabolites of IMI and DMI will be presented.

NR282 Tuesday, May 20, 12 noon-2:00 p.m.

Selegiline-Citalopram Combination for Patients with Parkinson's Disease and Depression

Zoltan Rihmer, M.D., Department of Psychiatry, National Institute, Hu Vosvolgyi Ut 116, Budapest 1021, Hungary; Maria Satori, M.D.

Summary:

Objective: The authors evaluated the efficacy and safety of the selegiline-citalopram combination in the treatment of major depression in patients with Parkinson's disease.

Method: Eight consecutive outpatients whose mild to moderate Parkinson's disease responded well to selegiline monotherapy (5–10 mg/day) were treated with 20 mg citalopram daily. The response to the antidepressant medication was evaluated on the 17-item Hamilton Depression Rating Scale (HDRS) at baseline and at week 8, and on the Clinical Global Improvement Scale (CGIS: 0 = no change or worsening, 1 = minimal improvement, 2 = marked improvement, 3 = complete remission) at the end of weeks 4 and 8.

Results: The majority of the patients (six out of eight) responded well to the citalopram treatment (more than 50 percent reduction in the total HDRS score, and CGIS score 2 or 3). No adverse events occured during the study or at the end of the four-to-five-month follow-up.

Conclusions: The results suggest that combination of low dose of selegiline (a selective, irreversible MAO-B inhibitor) and citalopram (an SSRI antidepressant) may be an effective and safe method in the treatment of major depression in patients with Parkinson's disease.

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Nonverbal Learning Improvement in Schizophrenia After Eight Weeks of Risperidone: Preliminary Evidence for Right Hemisphere Changes from the WMS-R

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Summary:

Objective: To assess cognitive change with the Wechsler Memory Scale-Revised (WMS-R) after eight weeks of risperidone in 10 patients with schizophrenia. The hypothesis was that risperidone may elicit circumscribed improvement of nonverbal learning. The rationale was based on the sensitivity of nonverbal learning tests to the integrity of right anterior cerebral structures, which have been implicated in the affective disorders associated with psychosis by Flor-Henry. Clinical reports of increased efficacy of risperidone among schizoaffective patients, as well as the Czobor and Volavak spectral EEG and Gallhofer maze data, converge on the relevance of this cortical region.

Results: There was significant improvement on nonverbal materials (Visual Index Baseline $M = 83.40$, $SD = 16.98$, Post-Tx $M = 96.20$, $SD = 19.10$), $t(9) = 2.56$, $p = .03$ not apparent for verbal materials (Verbal Index Baseline $M = 71.50$, $SD = 13.21$; Post-Tx = $M = 75.20$, $SD = 14.95$), $t(9) = .79$, $p = .45$. The improvement was specific to new learning (Visual Reproduction Baseline $M = 28.80$, $SD = 6.25$; Post-Tx = $M = 32.90$, $SD = 5.60$), $t(9) = 2.18$, $p = .05$, and not delayed recall (VR Savings Baseline $M = 79\%$, $SD = 23\%$; Post-Tx$M = 82\%$, $SD = 17\%$), $t(9) = .39$, $p = .71$. A discussion of these preliminary data could suggest that a selective improvement of nonverbal learning with risperidone may implicate a right anterior cerebral focus with implications to pathogenesis that may prove useful in choosing among alternative treatments.

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Weight Change During Mirtazapine Therapy

Paul J. Goodnick, M.D., Department of Psychiatry, University of Miami, D79, 1400 NW 10th Avenue, Ste 304, Miami FL 33136; Charlotte Kremer, M.D., Peggy Wingard, M.D.

Summary:

Mirtazapine is a unique antidepressant recently released for use in the U.S. It acts by antagonism of presynaptic alpha2 receptors to increase release of both NE and 5HT, while its blockade of 5HT2 and 5HT3 postsynaptic receptors prevents insomnia, sexual dysfunction, and nausea. It has, however, been reported in the U.S. to produce a mean rate of weight gain of 2.2 kg vs 1.2 kg on PBO. It has been hypothesized that this weight gain, not found in European studies in the U.K. or Finland, might be related to doses used, i.e., the U.S. doses of 5–35 mg/day may be more likely to produce weight gain than the range of 15–60 mg/day used in Europe.

To investigate this possibility, a meta-analysis was done of randomized patients from four different U.S. studies including 194 on mirtazapine (MTZ), 193 on amitriptyline (AMI), and 191 on PBO. Baseline MTZ weight was 74.19 SD 15.01 kg, which increased to 75.98 SD 17.06 by end of week 4. Over the next two weeks, change was minimal with a final of 76.02 SD 17.05. This is in contrast to PBO of 75.43 SD 17.86, 75.60 SD 17.81, and 75.16 SD 17.73. Further, in contrast to AMI, which led to weight gain even at highest degree of severe obesity (> 40), MTZ weight gain fell with increased weight: (< 19), underweight; 2.00 SD 1.29; (19–25) normal:1.79 SD 1.75; (26–29), overweight: 2.00 SD 1.82; (30–39) obesity: 1.44 SD 2.66; & (> 40)severe obesity: 0.60.

Conclusion: The activation of NE activity at higher doses of MTZ appears to offset weight gain effect, which seems to be related to higher antihistamine impact found at lower doses. The degree of weight gain also appears to be inversely proportional to BWI in contrast to amitriptyline.

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Lack of Typical SSRI Adverse Effects and Sexual Dysfunction with Mirtazapine Is Related to Specific Blockade of 5HT2 and 5HT3 Receptors

Paul J. Goodnick, M.D., Department of Psychiatry, University of Miami, D79, 1400 NW 10th Avenue, Ste 304, Miami FL 33136; Milana V. Zivkov, M.D.

Summary:

Introduction: Mirtazapine, a noradrenergic and specific serotonergic antidepressant, potentiates noradrenergic neurotransmission directly via blockade of α_2-autoreceptors, and indirectly enhances 5-HT_1-mediated serotonergic neurotransmission. Mirtazapine directly blocks the 5-HT_2 and 5-HT_3 receptors held responsible for development of typical SSRI-related side effects such as nausea, vomiting, diarrhea, insomnia, agitation, and symptoms of sexual dysfunction. This novel pharmacological profile was expected to result in improved tolerability of the drug.

Objective: The tolerability data of patients (mirtazapine n = 359; placebo n = 328) who took at least one dose of study medication while participating in placebo-controlled studies of mirtazapine were analyzed. Side effects were coded according to the WHO terminology.

Results: The data show that there are no statistically significant or clinically relevant differences between mirtazapine and placebo regarding incidences of typical SSRI-related side effects. Only libido decreases (male), with incidence lower than in the placebo group (4% vs 7%), and libido decreases (female) with incidence equal to placebo group (4% vs 4%) were registered during the use of mirtazapine.

Conclusion: Our analysis demonstrates that in vitro and in vivo data regarding mirtazapine's receptor binding profile can explain clinical data obtained during treatment of depressed patients. It may be concluded that the "designed" receptor binding profile of mirtazapine results in improved tolerability with respect to typical SSRI-related side effects, including sexual dysfunction.

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Hemodynamic Control During ECT Treatments

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Summary:

ECT is associated with acute hemodynamic changes during treatment. We designed a randomized, double-blind IRB study to compare the hemodynamic effects of nicardipine and labetalol alone and in combination during ECT procedures.

Methods: Twenty-four patients undergoing ECT participated in this study. Fifteen patients received labetalol 10 mg, alone or in combination with nicardipine, 1.25 mg, 2.5 mg, or 5 mg, iv bolus. Nine patients received nicardipine, 2.5 mg or 5 mg iv bolus, alone or in combination with labetalol 10 mg iv. The systolic, diastolic and mean arterial pressure (MAP) and heart rate (HR) were recorded noninvasively at one-minute intervals. Four minutes after the labetalol/nicardipine bolus anaesthesia was induced with methohexital, 1 mg.kg, and succinylcholine, 1.2–1.5 mg.kg. was administered for muscle relaxation. A bilateral electrical stimulus was delivered (MECTA-SR1) to induce generalized seizures. The EEG was continuously recorded and the duration of the EEG and motor (isolated foot) seizure activity was noted. Data were analyzed by ANOVA followed by pairwise comparisons.

Results: The median age of patients was 67 (range 44–86). Nicardipine, 1.25–5 mg, produced a significant reduction in baseline MAP within one to two minutes of the bolus injection. This was accompanied by a significant increase in HR after the highest nicardipine dose (5 mg). With the 2.5 and 5 mg nicardipine doses, the MAP reduction was maintained during the treatment and recovery periods. The seizure duration (mean motor: 34–47 s and EEG: 54–78 s) was not significantly decreased by the use of nicardipine ($P < 0.05$ vs baseline).

Conclusion: Bolus administration of nicardipine, 1.25–5 mg, produced a rapid onset of its clinical effects without exacerbating the cardiovascular depressant effects of methohexital; however, when used alone, nicardipine was not effective in blocking the HR response to ECT. These results would suggest that labetalol, 10 mg iv, followed by nicardipine, 1.25–2.5 mg iv bolus, is the optimal drug combination for providing protection against the acute hemodynamic response to ECT.

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EEG-Monitoring of ECT: First Results with the Fast-Fourier Frequency Analysis

Here W. Folkerts, M.D., Clinic Muenster, Psychiatric University, Albert-Schweitzer Str 11, Muenser 48149, Germany; G. Wagner, M.D., S. Theysohn

Summary:

Objective: The question of how to define a therapeutically adequate electroconvulsive therapy (ECT) has been under discussion since the early days of ECT. Although convention has asserted a demand for a minimum seizure time, the complex conditions involved in developing a generalized seizure make it problematic for therapeutic efficacy of ECT only to be linked with seizure duration.

Methods: In a prospective study we analyzed the ictal EEG of 50 subjects during ECT with the analogous EEG and a computerized EEG-frequency analysis calculating a spectral edge frequency (SEF 90) and the frequency bands using the pEEG-monitor (Draeger AG, Luebeck, Germany).

Results: We found no significant differences of seizure length between analogous EEG and the computerized EEG, which was −2.6 +/− 23.2 (sign rank 633,2 p = 0.20). In addition to the analogous EEG, the computerized EEG provides detailed information about the depth of the narcosis and the postictal suppression.

Conclusions: The frequency analysis of the ictal EEG during ECT could possibly give more detailed answers to the question of how to define therapeutically adequate ECT using EEG parameters.

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The Effects of ECT on Quantified EEG

James S. Lawson, Ph.D., Department of Psychiatry, Queen's University, Kingston ON K7L 3N6, Canada; Donald W. Brunet, M.D., Nicholas J. Delva, M.D.

Summary:

Objectives: To examine the following questions about the effects of ECT on QEEG: (1) Are effects uniform across the cranial surface? (2) Are effects the same for different treatment electrode placements? (3) Are effects uniform across the EEG frequency spectrum? (4) How long do effects persist? (5) Are effects related to clinical outcome? (6) Are effects related to cognitive deficit? (7) Does pretreatment QEEG predict seizure threshold?

Method: Forty-four subjects suffering from major depression were assigned in a random double-blind fashion to one of three electrode placement groups: bitemporal (BT), bifrontal (BF), or right unilateral (UL). QEEG and clinical assessment were done before treatment, after treatment #6, and three months after the final treatment.

Results: QEEG power increased at post ECT #6 and seven days post ECT uniformly for all groups, but reverted to pretreatment levels by three months post ECT. There were no localized effects. The greatest power increase occurred in the theta band. There was no increase in the beta band. Effects were not related to clinical outcome or cognitive side effects. There was a modest negative correlation between pretreatment EEG power and seizure threshold.

Conclusions: These EEG effects are of great theoretical interest, but appear to be of limited clinical relevance because of their failure to predict clinical response or cognitive side effects.

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A Naturalistic Review of Maintenance ECT

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Summary:

The is a naturalistic review of the use of maintenance ECT (MECT) during the first 4 1/2 years of a university ECT service. The decision to use MECT was based upon the recommendations of the ECT team, the wishes of the referring psychiatrist, medical insurance restrictions, and the patient and family (including issues such as distance from the hospital). A total of 56 patients, ages 30–84, received MECT (12 male/44 female). Patients could be classified under five different clinical groups, each with its own characteristics. (1) Of 14 patients with major depression, 18 had a good clinical response and three had an partial response. (2) Of nine patients with bipolar disorder, three had a complete response and four had a partial response. (3) Of 10 patients with Parkinson's disease plus depression, five had a good response and four had a partial response. (4) Of three patients with schizophrenia, two had a good response and one had a partial response. (5) Of 10 patients with a combined depression and Axis 2 disorder, one had a good response and five had a partial response. Issues related to partial improvement or treatment failure in the different groups will be discussed. Different approaches to MECT, including electrical energy and treatment frequency, may be needed for bipolar patients and patients who also have Axis 2 disorders or other comorbid psychopathology. Noncompliance will also be addressed.

NR290 Tuesday, May 20, 12 noon-2:00 p.m.

Challenges in Using the Medical Outcome Scale for Mental Health Clinic Outpatients

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Summary:

The short form of the self-administered Medical Outcome Scale (MOS-20) is an instrument to assess quality of life in six health areas. It was has been used to assess patients with many chronic medical conditions in a wide variety of clinical settings, and a few studies have used it in acutely ill populations. This pilot study utilized the MOS-20 with patients at a county mental health clinic, a population not previously reported on in conjunction with this assessment tool. A group of 191 new patients completed the MOS-20 at the time of psychiatrist evaluation, then six months (n = 102) and one year (n = 48) later, coinciding with their clinic appointments. At the initial assessment MOS-20 measures of physical, role and social functioning, and health perception showed significant deficits as compared with published norms. None of the scales demonstrated statistically significant improve-

ment at either follow-up time, although some positive trends existed, consistent with clinical improvements documented in progress notes. The high rate of drop-outs may have skewed the data away from those patients who would have shown improvement. The challenges of administering the MOS-20 in this patient group are discussed. Longitudinal studies to correlate MOS-20 data with psychiatric clinical observations may require an outpatient population with higher appointment compliance rates.

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Longitudinal Risperidone Use and Side Effects in an Urban Mental Health Clinic

Peggy E. Chatham-Showalter, M.D., Department of Psychiatry, Lehigh Valley Hospital, 1243 S Cedar Crest Blvd, #2800, Allentown PA 18103; Maureen MacFarland, R.N., Ralph A. Primelo, M.D.

Summary:

Risperidone was approved in December 1993 as a novel antipsychotic with a mild side-effect profile. At an urban mental health clinic, the charts of all 175 patients prescribed risperidone from January 1994 through June 1996 were concurrently reviewed through December 1996. This was a psychiatrically more complex population than included in Phase 2 or 3 studies. Over 80% of these clinic patients had prior neuroleptic treatment, which had been discontinued for poor therapeutic response or side effects. During the review period, 16% of patients received risperidone as their sole psychotropic medication. Approximately half the patients had a primary psychotic disorder and half a primarily affective disorder. Of the 152 patients who remained in the clinic's treatment during the study period, 73% continued the medication at least six months (mean duration 18.6 months at the end of the study period), remarkable for this population. Risperidone was discontinued for persistent or recurrent positive psychotic symptoms in only 8% of patients. Side effects prompted discontinuation in 19% of patients as follows: extrapyramidal symptoms 3%, sedation 3%, nonspecific "just don't like it" 3%, nausea 2%, headache, weight gain, galactorrhea, dizziness, hypomania, hives, and fear of tardive dyskinesia each 1%. These rates compare quite favorably with prior clinical experiences with chronic treatment-refractory patients on multiple medications.

NR292 Tuesday, May 20, 12 noon-2:00 p.m.

Fluvoxamine Therapy for Schizophrenia Patients with OCD

Pinkhas Sirota, M.D., Abarbanel Men Hlth Ctr 6A, 15 Keren Kayemet, Bay Yam 59100, Israel; Ilya Reznik, M.D.

Summary:

Introduction: Obsessive compulsive disorder (OCD) is a frequent comorbidity of major psychoses e.g. schizophrenia (SCZ). In previous studies, nonselective serotonin reuptake inhibitors (NSRI) such as clomipramine were used with some success, but only discrete case reports were presented in the current literature. The aim of our study was to evaluate the effect of selective serotonin reuptake inhibitors (SSRI's) in the treatment of OCD in schizophrenic patients when the drug is added to a standard neuroleptic.

Method: Twelve patients (nine males and three females), aged 27–59, (mean ± SD: 38.2 ± 9.2 years) participated in the study. The subjects were interviewed according to the guidelines of SADS-L. Diagnosis of SCZ and OCD was established according to DSM-IV criteria. The severity of SCZ was evaluated using the PANSS. The severity of OCD was assessed using the Y-BOCS. They were treated with conventional neuropleptics (phenothiazines or buthyrophenomes) and received additional fluvoxamine in doses of 100–150 mg/day for eight weeks. Clinical changes were assessed by Y-BOCS, PANSS and CGI. During the ongoing study, two patients were hospitalized twice and one of them received a combined treatment for 12 weeks, each time.

Results: A significant improvement in PANSS scoring, especially in positive symptoms and general psychopathology, was noted. CGI decreased only moderately (one or two points), and Y-BOCS ratings showed a moderate improvement in OCD symptomatology.

Discussion: Comorbidity of SCZ and OCD represents one of the most severe types of mental disorders. Our pilot open-label study disclosed that coadministration of fluvoxamine and neuroleptics probably augmented the efficacy of neuroleptics on specific schizophrenic psychopathology, and affective symptoms and OCD symptoms were improved moderately. Thus, therapy-resistant SCZ patients, probably could be more successfully treated with larger doses of fluvoxamine. Further investigation is needed to elucidate the efficacy of fluvoxamine in treatment-resistant schizophrenic patients with OCD symptoms.

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Therapist-Patient Sexual Relations: Result of a National Survey

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Summary:

Objective: The study was conducted to measure various parameters and implications of patient-therapist sexual relationships.

Methods: A structured questionnaire was sent to all psychiatrists, psychologists, and social workers who are members of the Psychiatric Society, Psychological Association, and Psychotherapy Association in Israel, respectively. The questions were whether the recipient therapist had treated patients who experienced sexual relations with the former therapist, and inquired into the implications.

Results: 50.5% of the 1,817 recipient therapists answered the questionnaire, and 29% reported that at least one of their patients had been sexually intimate with the previous therapist. Most cases involved female patients (91%) and male therapist (92%). Responding therapists reported that about 25% of the patients had not been adversely affected by the sexual contact.

Conclusions: Similar numbers for the gender of the offending therapist and exploited patient were obtained for both current Israeli and previous U.S. studies. This may suggest that such parameters are influenced by common norms of both societies and by various parameters determined by the psychotherapeutic dyadic situation. It seems, however, that there is less awareness of the phenomenon and its consequences in the younger, democratic, immigrant country (Israel) with less-established social and ethical orders.

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Front-Loading Ambulatory Care for Bipolar Disorder

Mark S. Bauer, M.D., VA Medical Center/116A, 830 Chalkstone Avenue, Providence RI 02908; Linda McBride, M.S.N., Nancy Shea, R.N., Christopher Gavin, B.S.

Summary:

Objective: We hypothesized that easy access to ambulatory services for bipolar disorder would improve several important process and outcome variables. An exclusively clinic-based program was developed that included (1) algorithm-driven somatotherapy, (2) standardized psychoeducation, and (3) easy access to a single primary nurse provider to enhance continuity of care.

Methodology: An *a priori* study using mirror-image design was used to compare pre-program data under standard clinical care to data after one year in the experimental program. Data from the first 103 patients to complete one year are reported here.

Results: The program resulted in increased patient satisfaction and increased intensity of medication treatment without increased side effects. While scheduled ambulatory clinic visits increased as expected, emergency room use and psychiatric triage use decreased significantly. For high utilizers, psychiatric hospital days and total mental health expenditures decreased significantly.

Conclusions: Easy access to ambulatory care may have beneficial effects on important process and outcome variables for bipolar disorder. Candidate mechanisms include on-demand access, continuity of care with a single primary provider, and improved medication delivery. Augmenting, rather than limiting, ambulatory access for major mental illnesses such as bipolar disorder may reduce overall mental health expenditures.

NR295 Tuesday, May 20, 12 noon-2:00 p.m.

Cost of Care by a Psychiatrist Versus Split Treatment

Mantosh J. Dewan, M.D., Department of Psychiatry, SUNY Health Sciences Center, 750 East Adams Street, Syracuse NY 13210

Summary:

Managed care advocate split treatment (physician plus therapist) over treatment by a single psychiatrist (medication plus therapy) as a preferred, cost-effective model. The theoretical and economic bases for these two models are examined. Theoretically, psychiatry espouses the biopsychosocial model and medicine has embraced the primary care model. Split treatment is counter to both these basic, well-accepted models. Theory would therefore support the single psychiatrist providing comprehensive care over the fragmented, split treatment model.

Split treatment is reportedly cost-effective. Costs were compared using schedules from Medicare and three of the largest managed care companies; VBH (largest), Merit (3rd), and USBH (6th). Costs for 10 psychotherapy sessions alone are $1008 (psychiatrist), $859 (psychologist), and $687 (social worker). Treating a patient with medication alone (five sessions, initial plus four half-hour) averaged $309. Split treatment consisted of 10 sessions with a therapist and five sessions for medication management with a psychiatrist. Compared with the cost of a psychiatrist providing both therapy and medication, which averaged $1008, split treatment cost $1168 with a psychologist and $999 with a social worker.

Preference for split treatment should be reconsidered. Holistic care (psychotherapy and medication) by a psychiatrist is theoretically a superior model. It costs slightly more than split treatment with social workers (+$9) and less (–$160) than split treatment with psychologists.

NR296 Tuesday, May 20, 12 noon-2:00 p.m.

The Perception of Effectiveness: Physician Use of Lobotomy in a California State Hospital, 1947-1954

Joel T. Braslow, M.D., Department of Psychiatry, UCLA Sepulveda VA, 16111 Plummer Street, Sepulveda CA 91343

Summary:

Objective: Physicians often use therapies with questionable or unproven efficacy. The aim of this project is to assess some of the ways in which physicians convince themselves of a therapy's effectiveness by way of an historical example.

Method: I explore doctors' use of lobotomy in a California state hospital and base my analysis upon the surgical reports and records of 245 lobotomy patients. I tabulated patient diagnostic and demographic characteristics and performed a qualitative analysis of medical record texts using historical methods.

Results: Institutional exigencies powerfully reinforced the appearance of the treatment's utility in three ways. First, the institutional culture made opposition to lobotomy virtually unthinkable. Second, lobotomy allowed physicians to transform behaviors that disrupted the smooth running of the institution into surgically treatable diseases of the brain. Third, physicians measured the effectiveness of lobotomy by its ability to eliminate these "chronically disturbed behaviors," reinforcing the institutional criteria by which these patients were originally deemed lobotomy candidates. A patient's gender was the most important social factor in determining whether a patient became a lobotomy case. While men outnumbered women at Stockton (resident women fluctuated between 39% and 48%), physicians lobotomized many more women than men (85% versus 15%).

Conclusion: Institutional and cultural factors can strongly influence physicians' perceptions of effectiveness.

NR297 Tuesday, May 20, 12 noon-2:00 p.m.

Practice of ECT in Veterans Affairs Medical Centers

Jagannathan Srinivasaraghavan, M.D., Department of Psychiatry, VA Medical Center, 400 Fort Hill Avenue, Canandaigua NY 14424; Richard D. Weiner, M.D.

Summary:

Objective: The aim of the study is to understand utilization and practice patterns of ECT in Veterans Affairs medical centers in Fiscal Year 1996 (Oct 1, 1995–Sep 30, 1996).

Method: A response to an ECT survey questionnaire was sought from all V.A. medical centers. Follow-up phone and fax were used to obtain responses.

Results: All 156 V.A. medical centers in operation in Fiscal Year 1996 responded to our survey (100%). The 83 hospitals not performing ECT (24 medical centers have no psychiatry beds) referred 159 patients for ECT, nearly three-fourths of referrals were to another V.A. facility, and five facilities plan to start ECT in Fiscal Year 1997. The 73 hospitals equipped to provide ECT treated 697 patients with 6,273 treatments. Approximately 38% of patients were at least 65 years old, and 19% received some maintenance ECT. Depressive disorders were the commonest referral for ECT in 84%. Multiple monitored ECT was practiced in 16% of hospitals in a mean of one-third of the patients. All but one hospital used brief pulse devices routinely. Some unilateral ECT was utilized at 44% of hospitals. Methohexital was routinely used for anesthesia in 63% of hospitals. Anticholinergic premedication was routinely used in all cases in 42% of hospitals and not at all in 21% of hospitals. Ambulatory ECT was practiced in 12% of hospitals, where a mean 13% of treatments accounted for ambulatory ECT. Routine EEG monitoring accompanied ECT in 88% of hospitals. The OR recovery room was the commonest site for ECT. Seven serious adverse events were reported, including two cases of status epilepticus, one myocardial infarction, and one aspiration pneumonia, but no deaths. In the last five years ECT utilization remained the same in 47% of hospitals, while 37% saw an increase and 16% saw a decrease.

Conclusions: 1.) Fifty-four percent of V.A. hospitals with psychiatric beds have ECT services. 2.) ECT utilization is relatively low, consistent with other public sector hospital data. 3.) Practice of ECT reflects contemporary ECT guidelines.

NR298 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Neuroendocrine Effects of Intravenous Meta-Chlorophenylpiperazine in Three 4-Methylenedioxymethamphetamine Users

Una D. McCann, M.D., BPB, National Institute of Mtl Hlth, 10 Center Drive/MSC 1272, Bethesda MD 20892; Melissa M.

Mertl, B.A., Dennis L. Murphy, M.D., Robert M. Post, M.D., George A. Ricaurte, M.D.

Summary:

Objective: To determine whether the direct 5-HT agonist, *m*-CPP, can be used to detect lasting alterations in serotonin function in individuals previously exposed to the central serotonin neurotoxin and drug of abuse, MDMA.

Method: Twenty four abstinent MDMA users (16 males and eight females) and 25 controls (17 males and eight females) underwent pharmacological challenges with intravenous *m*-CPP (0.08 mg/kg) and saline placebo in a single-blind fashion. Repeated blood samples were collected for later analysis of plasma cortisol and prolactin.

Results: Cortisol and prolactin responses in male, but not female, MDMA users were found to be significantly blunted when compared with responses in same-sex control subjects.

Conclusions: Alterations in *m*-CPP-induced cortisol and prolactin responses in abstinent male MDMA users suggest lasting alterations in 5-$HT2_C$ receptor function possibly reflecting MDMA-induced serotonin neurotoxicity. Failure to detect neuroendocrine alterations in female MDMA users may be due to the smaller sample size, differences between males and females with regard to their MDMA histories, or gender-based differences in the pharmacokinetics or pharmacodynamics of MDMA and/or *m*-CPP.

NR299 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Comparison of Morphine and Methadone Maintenance in Pregnant Opiate Addicts

Petra Etzersdorfer, M.D., University of Psychiatry, Wahringergortel 18–20, Vienna 1090, Austria; Gabriele Fischer, M.D., Harald Eder, Reinhold Jagsch, M.A.G., Kathrin Schmidl-Mohl, M.D., Wolfgang Gombas, M.D.

Summary:

A majority of studies demonstrate the advantage for mother and child in using methadone maintenance in pregnant opiate addicts. It is also proven that infants born to methadone-maintained mothers are more severely affected in their neonatal withdrawal syndrome than infants with an intrauterine exposure to heroin. Over a period of 50 months, the drug-addiction outpatient clinic in Vienna investigated 52 pregnant opiate addicts who were given during pregnancy either methadone or slow-release morphine. The subjects (mean age: 26 years, mean duration of pregnancy before starting maintenance treatment: 19 weeks) were consecutively enrolled in an open study design. The oral opioid at time of delivery was in 50% of the subjects methadone (mean daily dosage 45 mg), in 43% morphine (mean daily dosage 340 mg), and 7% were successfully detoxified and drug-free. The mean birth weight in the methadone group was 2850 g, in the morphine group 2880 g. No significant differences occured in comparing the mean duration of withdrawal syndrome in the newborns; it was 16 days in the methadone group and 20 days in the morphine group. No significant correlation between withdrawal syndrome and mean daily dosage of methadone ($r = 0.53$, $p = 0.2$) and morphine ($r = 0.39$; $p = 0.14$) could be found. Both substances are safe during pregnancy and yield to a comparable outcome in regard to birth weight of the infant and neonatal withdrawal syndrome.

NR300 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Buprenorphine Maintenance in Pregnant Opiate Addicts

Gabriele Fischer, M.D., Department of Psychiatry, University of Psychiatry, Waehringer Guertel 18–20, Vienna 1090, Austria; Kathrin Schmidl-Mohl, M.D., Petra Etzersdorfer, M.D., Harald Eder, Reinhold Jagsch, M.A.G., Wolfgang Gombas, M.D.

Summary:

The use and effects of methadone during pregnancy have been well investigated. Alternative substances like morphine have been used during pregnancies in opiate addicts and showed safety for the unborn child. Both methadone and morphine improved the situation for mother and child in comparison to heroin exposure but yielded to an enhanced neonatal withdrawal syndrome. Reisinger reported in 1995 at the CPDD about low-dose buprenorphine maintenance in pregnant opiate addicts, in which no withdrawal syndrome occured in the newborn. At the drug addiction outpatient clinic in Vienna seven opiate addicts with a mean duration of pregnancy of 28 weeks were maintained on sublingual buprenorphine during pregnancy. The subjects were switched from a mean daily dosage of 430 mg slow-release morphine to a mean daily dosage of buprenorphine of 9 mg. The subjects were integrated into an established program with obstetricians and pediatricians and until delivery followed on an outpatient basis, seen three times a week. Supervised urine samples were examined weekly for toxicology to exclude illegal drug consumption. Buprenorphine was well tolerated in the females. Our preliminary results demonstrate that the newborns showed an decreased opiate withdrawal syndrome in comparison to morphine or methadone exposure during pregnancies.

NR301 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Effect of Varying Methadone Doses on Heroin Use

Chandresh Shah, M.D., Dept of Psych SVC (116), VA Outpatient Clinic, 351 East Temple Street, Los Angeles CA 90012; Adonis Sfera, M.D., Lena Simitian, Pharm.D.

Summary:

Methadone (MTH) is widely used in maintenance treatment of opioid dependence. The fear of overdose, dependence, and diversion has resulted in prescribing lower doses, at times at the expense of its efficacy. To study effects of different doses of MTH on use of heroin, we selected 30 patients who had been using heroin in spite of their daily treatment with 50 mg of MTH. Their daily dose was gradually increased up to 80 mg/day. During this course of treatment their randomly selected urine samples were analyzed for heroin. There were 29 male and one female patient. They were 46.25 ± 1.96 years old. At the dose level of 50 mg/day, all 30 patients were using drug at the rate of 53.83 ± 33.95%. When the dose was increased to 60 mg/day, 24 patients continued using drug at the rate of 35.86 ± 35.58%. Only half of the patients were found to be using drug at a frequency of 32.62 ± 33.83% when the dose level was 70 mg/day. And finally, at the dose level of 80 mg/day, only two patients were using drug 75.00 ± 35.36% of the time.

These data show that increasing dose of MTH is associated with lesser number of patients using heroin at a lower frequency. Further study is needed to establish comparative results.

NR302 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Gene Coding for D2 Dopamine Receptor and Addiction

Philip A.P.M. Gorwood, M.D., Unity 155, Inserm, 2 Place Jussieu, Paris 75251, France; Jean Ades, M.D., Philippe Batel, M.D., Pierre Sokoloff, Ph.D., Jean C. Schwartz, Ph.D., Josue Feingold, M.D.

Summary:

The allele A1 of the gene coding for dopamine receptor D2 significantly increases the risk for alcoholism, according to differ-

ent meta-analyses. We analyzed the role of the allele A1 (Taq1 polymorphisms of the D2 gene) and another marker within this gene (CA repeat) in a sample of male French patients (for two generations) with alcohol dependence (N = 114). The control group was based on matched blood givers (N = 51) with no familial or personal history of any addictive disorder. All subjects were directly interviewed (DIGS).

The frequency of the allele A1 (of D2) was not significantly different between controls and alcoholics, but allele A1 was significantly more frequent in the subsamples of alcoholics with somatic, withdrawal, or social complications, and with comorbid dependence. The link, qualitative and quantitative, between complicated alcoholism and allele A1 is still present when considering censored data and interaction between variables. A linkage disequilibrium was suggested between the (CA) repeat of the D2 and the Taq1 polymorphism of this D2 gene for patients and for controls. The allele A1 appears involved in an addictive trait which partially recovers the diagnosis of alcoholism. The allele A1 is probably associated with this trait through a disequilibrium with another closed mutation.

NR303 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Patterns of Drug Use Risk in Psychiatric Patients

Ihsan M. Salloum, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213; Dennis C. Daley, M.S.W., Jack R. Cornelius, M.D., Levent Kirisci, Ph.D.

Summary:

Objectives: The aim of this study was to evaluate whether there is a differential pattern of high-risk drug-taking situations among psychiatric patients with substance use disorders.

Method: The Inventory of Drug Taking Situations (IDTS), a self-report questionnaire that provides a profile of drug-taking situations over the past year, was administered to dually diagnosed inpatients (n = 75; males = 44; females = 31). The IDTS assesses two major categories of drug use situations: a Personal States category including five subscales that address drug use involving response to psychological or physical events, and a category Involving Other People, composed of three subscales, which assess the influence of other individuals in the drug-taking situation. Logistic regression analysis was employed to evaluate the likelihood of differential patterns of drug-taking situations among hospitalized patients with either psychotic disorders, major depressive disorders, or adjustment and anxiety disorders.

Results: The results revealed that comorbid patients with major depression differed from substance-abusing patients without major depression on two of the three subscales investigating situations Involving Other People. Specifically, they were more likely to report drug use in response to social pressure (odds ratio = 1.03, $p < 0.05$) and were less likely to use drug in response to having pleasant times with others (odds ratio = .96, $p < 0.05$). Psychotic patients, as compared to those with adjustment and anxiety disorders, were more likely to report using drugs in situations involving pleasant emotions (odds ratio = 1.14, $p < 0.05$), and less likely to use drugs in order to test personal control (odds ratio = .96, $p < 0.05$).

Conclusions: Psychiatric patients with comorbid substance abuse may differ in terms of high-risk drug-taking situations. The type of the psychiatric diagnosis may have moderating effect on drug-taking situations. Further studies are warranted to enhance our understanding of drug-taking behavior, which may be useful to refine relapse prevention strategies for these high-risk dual-diagnosis patients.

NR304 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Assessment of the Role of Kindling Mechanism and Somatic Disorders in Development and Course of Alcohol Withdrawal Delirium

Marcin Wojnar, M.D., Department of Psychiatry, Warsaw Medical School, Nowowiejska 27, 00–665 Warswa, Poland; Artur Cedro, M.D., Zdzislaw Bizon, Ph.D., Agata Orlow, M.D.

Summary:

Objective: To evaluate the role of the kindling phenomenon and the influence of physical trauma and somatic disorders as well as alcohol dependence variables on development, severity, and course of DT and withdrawal seizures.

Methods: Medical records of 2186 episodes of alcohol withdrawal syndrome in 1179 patients hospitalized from 1973–1987 in Nowowiejski Hospital in Warsaw were reviewed using a structured questionnaire.

Results: Increasing severity of AWS symptoms was observed in the course of successive episodes of 22.5% of patients. No correlation was found between the occurrence of withdrawal seizures or DT, and the number of prior AWS episodes as well as the length of period of excessive drinking. Delirium tremens was preceded by withdrawal seizures only in 11%, and by physical trauma or disorder in 18% of cases. We found a positive correlation between the severity of DT and occurrence of pneumonia, heart disease, liver cirrhosis, and anemia, as well as the amount of alcohol consumed during the last drinking bout.

Conclusions: 1.) The role of the kindling mechanism in the development of alcohol withdrawal delirium and withdrawal seizures is restricted to only one-fourth of cases. 2) Somatic disorders or physical trauma trigger DT during alcohol withdrawal and have substantial influence on the course of DT. 3.) The more severe course of DT is correlated with the quantity of alcohol consumed and coexisting abuse of benzodiazepines and barbiturates.

NR305 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

The Alcohol Insensitivity Index: Pilot Study of a Potential Phenotypic Measure

Thomas P. Beresford, M.D., Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver CO 80220; David B. Arciniegas, M.D., John Hewitt, Ph.D.

Summary:

Objective: We sought a method of identifying ethanol insensitivity in large human populations.

Method: We analyzed a mail survey to a pilot sample of 137 adults: 73 females (mean age 40.5 years ± 7.4, range 29 to 63) and 64 males (39.4 years ± 8.6, range 35 to 63). We assessed 1) construct validity, 2) differentiation from chronic tolerance, 3) predicitive utility, and 4) continuous distribution of the responses.

Results: 1) Subjects reporting pleasant/neutral versus unpleasant items drank more days/week ($r = -0.23$, $p < 0.007$), greater amounts/day ($r = -.23$, $p < 0.007$), greater total weekly amounts ($r = -0.20$, $p < 0.02$), and described themselves as heavy drinkers ($r = -0.29$, $p < 0.0006$). Subjects reporting little initial intoxication reported drinking more days/week ($r = -0.18$, $p < 0.03$), drank greater total weekly amounts ($r = -0.18$, $p < 0.03$), and described themselves as heavy drinkers ($r = -0.22$, $p < 0.01$). A clear relationship between the two aspects of ethanol sensitivity existed and was inverse as expected. 2) Regression analysis of current drinking level on sensitivity was significant ($p < 0.03$), suggesting that the effects of chronic tolerance can be measured and can be separated from those of reported initial insensitivity. 3) Sensitivity items were associated in a negative direction with CAGE positive responses ($p < 0.001$; $p < 0.04$) as with specific CAGE items such as cutting down on alcohol use ($p < 0.02$; $p < 0.002$). This suggests that initial insensitivity reports may be indicators of risk for alcohol

problems. 4) Using our scoring method, about one-quarter (27%) were completely initially insensitive on all five items, 19% on one item, 23% on two, 23% on three, and the remaining 8% on four or five.

Conclusion: This early work suggests that ethanol insensitivity can be recognized in large numbers of subjects, is associated with both heavy use and with alcohol problems, can be differentiated from the effect of chronic tolerance, and is continuously distributed. These characteristics may fit the Alcohol Insensitivity Index for use in human genetic studies of AD vulnerability.

NR306 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Heavy Alcohol Use and Cardiac Surgery Outcome

Catherine Villanueva, Ph.D., Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver CO 80220; Adrianne Casebeer, M.A., Laurie Shroyer, Ph.D., Frederick L. Grover, M.D., Karl Hammermeister, M.D., Thomas P. Beresford, M.D.

Summary:

Objective: While heavy alcohol use bears both on cardiac function and medication compliance post-operatively, no studies exist on alcohol dependence affecting cardiac surgery outcome. We asked whether heavy alcohol users who undergo cardiac surgery 1) present more pre-op comorbidity, 2) use more intraoperative resources, 3) present more post-op complications, and 4) have poorer six-month outcome than non-heavy drinkers.

Method: We analyzed data from a multicenter, prospective study of cardiac surgery outcome. From a total of 3,427 cases, we separated 341 self-identified heavy drinkers (HD) and compared them with the non-HD cases (n = 3044), excluding 42 self-identified drug-abusing patients.

Results: 1) Heavy drinkers were significantly more likely to present a history of liver disease, diabetes, current smoking, and hepatomegaly on physical exam (all $p < 0.001$) as well as a prior myocardial infarction ($p < 0.05$). 2) Intraoperative resource utilization did not separate the two groups. 3) Atrial fibrillation was the only post-op complication separating the two groups ($p < 0.006$). Cardiac deaths were fewer in the heavy drinking group. 4) At six months, HD cases were more likely to a) present improved cognitive status ($p < 0.04$), b) be employed ($p < 0.03$), c) have less social support ($p < 0.001$) or friends ($p < 0.02$), and d) have higher diastolic blood pressure (0.001).

Conclusions: Heavy drinkers show more alcohol-related pre-op comorbidities and comparable resource utilization as well as immediate and six-month outcome. These data suggest that attention to pre-op evaluation and outcome with respect to alcohol use resumption is important.

NR307 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Alcoholic Liver Disease and Liver Transplantation: A Survey of United States Programs

Thomas P. Beresford, M.D., Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver CO 80220; David B. Arciniegas, M.D., James Everhart, M.D.

Summary:

Objective: Alcoholic liver disease (ALD) is now the most frequent indication for liver transplant in the U.S. but few data document current practices in selecting patients for this procedure. To describe national trends and practices, we surveyed all liver transplant programs in the United States.

Method: A total of 69 programs listed in the United Network for Organ Sharing (UNOS) directory and that reported at least five initial transplants for adults in 1995 completed the survey with a response rate of over 90 percent.

Results: Thirty-two percent of programs had become more restrictive in the past five years in accepting patients with ALD for transplant, and only 2 percent were less restrictive. Greatest emphasis in diagnosing alcohol dependence was placed on the determination by experts in alcoholism or transplant physicians and less on referral diagnosis or laboratory evaluation. The most frequently reported factors related to the decision to transplant were a period of abstinence of at least six months, social support, and other substance abuse or severe psychiatric disorders. While a minority of programs require an alcohol rehabilitation "contract," those that do are over 20 times more likely than other programs to remove patients permanently from the transplant list after an alcoholic relapse. All programs monitor for drinking relapse after transplantation, and all but two carry on a prevention effort. Very few of the responses were related to program size, percent of transplants for ALD, or increasing restrictiveness for transplanting patients with ALD.

Conclusions: These data characterize current practice as 1) increasingly restrictive, 2) reliant on the expertise of professionals knowledgeable in alcoholism, 3) utilizing histories of recent sobriety, social support, and lack of concomitant drug abuse as prognostic factors, and 4) unlikely to use a rehabilitation "contract." Increased restrictiveness may be a response to the shortage of donor organs, while reliance on a six-month abstinence period, for which no good empirical evidence exists, may reflect the clinical complexities of alcohol dependence.

NR308 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Cocaine as a Risk Factor for Neuroleptic-Induced Acute Dystonia

Peter N. van Harten, M.D., Department of Psychiatry, PC Welterhof, JF Kennedylaan 301, Heerlen XZ 6419, The Netherlands; Jan C. van Trier, M.D., Ernst H. Horwitz, M.D.

Summary:

A prospective study was conducted to test the hypothesis that cocaine is a risk factor for neuroleptic-induced acute dystonia (NIAD). The study sample consisted of a high-risk group for NIAD, males between 17–45 who received high-potency neuroleptics within 24 hours of admission and did not use neuroleptics in the month prior to admission. Patients were excluded if they suffered from a neurodegenerative disorder or were exposed to anticholinergics, benzodiazepines, promethazine, carbamazepine, phenytoin, or L-dopa during the study.

During the two years of the study, 29 patients entered the study, nine cocaine users and 20 nonusers. Patients were followed for seven days. Detection of cocaine use was based on urinary samples. Cocaine users did not differ significantly from nonusers in mean age, mean daily dose, and peak neuroleptic dose. Cocaine-using patients developed significantly more NIAD than did nonusers (relative risk 4.4, Fisher exact $p = 0.01$).

Cocaine is a major risk factor for NIAD and should be added to the list of well-known risk factors. Prophylactic treatment is strongly advised.

NR309 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Coexistence of Tardive Dyskinesia, Parkinsonism and Akathisia and Tardive Dystonia: Their Prevalence and Inter-Relationships

Peter N. van Harten, M.D., Department of Psychiatry, PC Welterhof, JF Kennedylaan 301, Heerlen XZ 6419, The Netherlands; Hans W. Hoek, M.D., Glenn E. Matroos, M.D.

Summary:

This epidemiological study was performed in the Netherlands Antilles, a well-defined catchment area with only one psychiatric

hospital (N = 194; mean age 53.1). The prevalence of tardive dyskinesia, parkinsonism, akathisia, and tardive dystonia was measured, using the Abnormal Involuntary Movement Scale, the Unified Parkinson Disease Rating Scale, the Barnes Akathisia Rating Scale, and the Fahn-Marsden rating scale, respectively. With use of logistic regression the adjusted odds ratios between the various EPS revealed strong connections between the hyperkinetic syndromes (tardive dyskinesia, tardive dystonia, and akathisia). Parkinsonism was found to be inversely related to tardive dyskinesia and to tardive dystonia.

Almost 30% of the patients suffered from two or more EPS. The highest prevalence rates of combinations were tardive dyskinesia combined with parkinsonism 12.9%, and tardive dyskinesia combined with tardive dystonia 9.8%.

The findings suggest that combinations of EPS are common, and that the diagnosis of tardive dyskinesia should alert the clinician to look for akathisia, a distressing EPS that is often neglected.

NR310 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Treatment of Depressed Alcoholics

Alec Roy, M.D., Department of Psychiatry, VANJ Health Care System, 385 Tremont Avenue, East Orange NJ 07019

Summary:

Objective: Depression is common among alcoholics. However, its treatment has been little studied.

Methods: Thirty-six depressed, recently abstinent alcoholics were randomized in a six-week, double-blind, placebo-controlled study of sertraline 100mg daily.

Results: There was a significant group x time interaction for both the Hamilton Depression Rating Scale (HDRS) and the Beck Depression Inventory (BDI). Also, patients receiving sertraline (N = 18) had significantly lower mean HDRS and BDI scores than patients receiving placebo (N = 18). Furthermore, significantly more of the patients receiving sertraline obtained a Clinical Global Impression (CGI) score of "very much improved" or "much improved".

Conclusion: Depressed, recently abstinent alcoholics benefit from antidepressant medication.

NR311 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Ego Defense Mechanisms in Korean Male Cigarette Smokers

Sang Keun Chung, M.D., Department of Psychiatry, Chonbuk National University, 634-18 Keumam-Dong Dokjin-Ku, Chonju 561-182, South Korea; Ik-Keun Hwang, M.D., Hong Bai Eun, M.D., Young-Chul Chung, M.D.

Summary:

Objective: Deficiencies in internal self-regulation are due to inadequate ego defense mechanisms (EDMs) and are important in the understanding of substance abuse. We examined characteristic EDMs and the relationships between EDMs and nicotine dependence in Korean male cigarette smokers (CSs).

Methods: 75 male CSs meeting DSM-IV criteria for nicotine dependence and 75 healthy male nonsmokers (NSs) were evaluated by using Ehwa Diagnostic Test of Defense Mechanisms, semistructured questionnaire. CSs were also evaluated by Fagerstrom Test for Nicotine Dependence. EDMs were analyzed by maturational level.

Results: Acting out (p = .0001) and regression (p = .0132) of immature defenses, controlling (p = .0001) and dissociation (p = .0062) of neurotic defenses, and projection (p = .0172) and denial (p = .0014) scales scores of narcissistic defenses were significantly higher in CSs than NSs (by t-test). There was significantly positive correlation between nicotine dependence and the acting-out scale score (r = .39, p = .005) in CSs.

Conclusion: These findings indicate that inadequate EDMs may be an important cause of self-regulatory deficiencies in CSs. We suggest that multiple therapeutic approaches to strengthen healthy ego functions of self-regulation should be provided in smoking-cessation programs.

NR312 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Alcoholism and Depression in the Community

Jin Pyo Hong, M.D., Department of Psychiatry, Asan Medical Center, Song-Pa/PO Box 145, Seoul 138736, South Korea; Maeng Je Cho, M.D., Yang Sook Ha, Ph.D., Chang Yoon Kim, M.D., Gun Hee Lee, Ph.D.

Summary:

Objective: The purpose of this study was to examine the relationship between alcoholism and depressive symptoms after controlling for possible confounders such as age, education, sex, and marital status in a general population aged 30 and over in Korea.

Method: The sample was drawn from one rural county of 60,014 residents with random stratified-cluster sampling. Two brief screening devices, CAGE for alcoholism and CES-D (Center for Epidemiological Studies Depression Scale) for depressive symptoms were administered. About 1138 residents completed the questionnaires. We used weighted total scores of CES-D after factor analysis, which were believed to reflect depressive state more accurately than simple total score of CES-D.

Results: Demographic variables were closely correlated with CES-D score. Symptoms of depression were more common among the older, less-educated, and female sample. After controlling for effects of demographic variables, three or more positive response group for CAGE showed significantly higher CES-D score than two or fewer group. Using logistic regression, those who showed two or more positive responses for CAGE had 1.67 times the chance of being depressed compared with all others.

Conclusions: While depression and alcoholism are individually major health problems, the results of this investigation suggest that there is significant relationship between the two in the community.

NR313 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Platelet Serotonin-2 Receptor in Alcohol Use Disorder

Young-Cho Chung, M.D., Paik Hospital 85 2-KA, Jurdong, Seoul Choong-Ku 00172, Korea; Hong Bai Eun, M.D., Ik-Keun Hwang, M.D., Sang Keun Chung, M.D.

Summary:

Objective: To find a biological marker of alcoholics, we looked at the binding characteristics of ^{125}I-LSD to the platelets of alcoholics.

Method: We prepared platelet pellets from 25 alcoholics and 10 normal volunteers. Using ^{125}I-LSD as a radioligand (six final concenturations. 50 ~ 500pM), saturation binding experiment was only performed. Specific binding was obtained using 1 μ M ketanserin. Bmax and Kd were calculated through Scatchard plot.

Results: 1) In the comparison of patients vs. controls, Bmax of the former was significantly higher than that of the latter ($P < 0.0017$). But there was no significant difference in the Kd between the two groups. 2) In the comparison of type 1 and type 2, Bmax of the latter was significantly higher than that of the former ($P < 0.0396$), but there was no significant difference in the Kd between the two groups.

Conclusions: These results show that increased density of serotonin receptors can be used as a biological marker for alcoholics; in a more specific way, as a trait marker for type II alcoholics. In

addition, it can be inferred that alcoholism could be the result of serotonin deficiency.

NR314 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Naltrexone Effects on Lorazepam Challenge in Alcoholics

Ede Frecska, M.D., Department of Psychiatry, V.A.M.C., 79 Middleville Road/116A, Northport NY 11768; Robert Hitzemann, Ph.D., Maria Taylor, R.N., Paula Cerveny, N.P., Kathleen Piscani, R.N., Laurel Weissman, R.Ph.

Summary:

Background: An increasing number of studies now indicate that the prophylactic administration of naltrexone is of benefit to some alcoholics in controlling alcohol abuse. The exact ways in which naltrexone alters ethanol intoxication in humans is not yet clear. Benzodiazepine intoxication has effects on mood and psychomotor performance similar to alcohol intoxication. Benzodiazepines bind to the GABAA receptor complex and induce cross-dependence and cross-tolerance with alcohol.

Objective: The study investigated how subjective effects of lorazepam-induced GABA-benzodiazepine receptor complex (GBRC) activation are affected by naltrexone pretreatment in alcoholic patients.

Method: We examined 12 subjects who meet DSM-IV and Cloninger's Type 2 criteria for alcohol dependence over a two-year period. After detoxification, subjects underwent a 50 mg naltrexone/placebo trial, followed 90 minutes later by a 30 μg/kg IV lorazepam challenge. Intoxication measures included several scales sensitive to the effects of alcohol and drugs and lorazepam blood levels.

Results: Lorazepam induced a pattern of sedative sensations similar to those induced by alcohol. Sedative effects of lorazepam were significantly greater during the naltrexone than the placebo trial. Unlike alcohol, lorazepam did not induce subjective stimulation.

Conclusions: The augmentation of lorazepam's sedative effects by naltrexone suggests that these may be mediated through GABAergic mechanisms.

NR315 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Social Consequences of Substance Abuse: The Impact of Comorbid Psychiatric Disorders: A Prospective Study of a Nationwide Sample of Treatment Seeking

Kristinn Tomasson, M.D., Department of Psychiatry, University Hospital, Landspitalinn, 101 Reykjavik, Iceland; Per Vaglum, M.D.

Summary:

Background: The purpose was to study among substance abusers seeking treatment the association between social consequences (accidents, fights, broken relationships, drunken driving arrests, and employment) related to alcohol and psychiatric comorbidity.

Methods: Three hundred and fifty-one patients were administered the Diagnostic Interview Schedule and queried as to social consequences. Then 16 and 28 months later they were asked in a mail survey about the reoccurrence of these consequences.

Results: Social consequences had a high rate of reoccurrence, especially if sobriety was not achieved. Heavy alcohol consumption and polysubstance abuse predicted (OR = 2.9) accidents among men. Polysubstance abuse among men (OR = 3.9) and (simple) phobia (OR = 9.9) among women predicted fights. Among alcoholics, (social) phobia (OR = 4.3) and antisocial personality disorder (OR = 3.0) predicted fights. Broken relationships were predicted by the level of substance abuse. Drunken driving arrests were most prevalent among antisocials.

Conclusion: The above predictors of social consequences related to alcohol should be the focus of studies designed to reduce these events. Currently however, the goal of abstinence should be stressed as the main method for these patients to reduce social consequences related to alcohol and substance abuse.

NR316 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Sertraline with Naltroxene Versus Naltrexone Alone in the Treatment of Alcohol Dependence

Coner K. Farren, M.D., 133 Pawson Road, Branford CT 06405-5035; Dana Catapano, B.A., Stephanie S. O'Malley, Ph.D.

Summary:

In humans, the benefit of treatment of alcohol dependence with opiate antagonists has been proved with a number of successful treatment trials with naltrexone and nalmafene. The benefit of treatment with serotonergic medications has been less successful, despite an encouraging preclinical literature. We recruited nine alcoholics, abstinent from alcohol from between five and 30 days, for treatment with between 50 and 100mg of sertraline in combination with 50mg of naltrexone for a 10-week period, together with standard substance abuse psychotherapy. The results were compared with nine alcoholic controls from the open-label component of a large naltrexone trial, and were closely matched according to gender, family history, age, and baseline alcoholic characteristics.

There was a divergence in outcome between the two groups in time to first drink, 51.8 days (+/– sem 9.5) for the trial group versus 37.9 (+/– 9.7) for the controls, $p < 0.24$; and for time to relapse to heavy drinking, 60 days (+/– 7.2) versus 52.3 (+/– 8.5), $p < 0.31$. The number of drinking occasions was 1.9 (± 4.3) for the 10-week period versus 7.2 (+/– 10.7), $p < 0.18$; while the number of drinks per days in treatment was 0.1 (+/– 0.2) versus 1.41 (+/– 2.6), $p < 0.16$. Although these differences did not reach statistical significance, the trends were encouraging and suggest a role for combination pharmacotherapy in the treatment of alcohol dependence.

NR317 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Stages of Change Among Cocaine-Dependent Schizophrenic Patients

Lisa J. Roberts, M.A., Department of Psychology, University of Washington, 11600 100th Avenue, #A5, Kirkland WA 98034; Andrew L. Shaner, M.D., G. Alan Marlatt, Ph.D., Jeffery N. Wilkins, M.D.

Summary:

Objective: Most schizophrenic substance abusers either do not tolerate or are not helped by standard treatments for substance abuse. It has been suggested that treatment effectiveness could be improved by matching interventions to individual readiness to change addictive behaviors. The Transtheoretical Model of Change, as measured by the URICA, has received considerable attention in the field of addictive behaviors. This study was conducted to determine if it was possible to categorize cocaine-dependent schizophrenics using the URICA and to examine the relationship between stage and cocaine use.

Method: In a prospective study, 64 subjects were assessed using the URICA (for cocaine) and urine toxicology. Follow-up data were collected at three, six, 12, and 18 months after study entry.

Results: In this study, cocaine use was fairly constant over time and no relationship between stage and cocaine use was observed.

Conclusions: This suggests that among schizophrenics, readiness to change is not an important predictor of subsequent cocaine

use. The authors discuss other explanations for this finding and its clinical implications.

NR318 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Caffeine and Nicotine Use Around Alcohol Withdrawal in Veterans Diagnosed with Alcohol Dependence

James J. Kim, M.D., Department of Psychiatry, VA Medical Center, 400 Fort Mill Avenue, Canandaigua NY 14424; Hedy E. Tasbas, M.D., Jagannathan Srinivasaraghavan, M.D.

Summary:

Objective: The goal of the study was to determine the relationship of caffeine and nicotine use during the pre- and post-alcohol withdrawal period (pre-AWP and post-AWP) among patients with a diagnosis of alcohol dependence.

Subjects: All inpatients in a substance abuse rehabilitation unit at Canandaigua Veterans Affairs Medical Center with a history of caffeine or nicotine use or both, in addition to a diagnosis of alcohol dependence, admitted during a six-month period (Oct 1, 1995 - Mar 31, 1996) were the subjects of the study. There were 78 subjects.

Method: Each subject was interviewed for collecting demographic information such as age, sex, marital status, employment, education, and use of alcohol, caffeine, and nicotine.

Results: About 95% of subjects were male. About 52% white, 43% black, and 4% Hispanic. Only 13% were married, 63% employed, and 60% had a minimum of high school education. Sixty-one percent of subjects used increased amount of caffeine from mean 190.8 mg/day during pre-AWP to mean 786.1 mg/day on post-AWP. Nine percent of subjects reduced caffeine use from mean 581 mg/day to mean 336.4 mg/day. Ten percent of subjects showed no change. On the contrary, 47% of subjects reduced cigarette smoking from 41.2 cigarettes/day during pre-AWP to 19.3 cigarettes/day during post-AWP; 22% of subjects showed no change. Only 14% of subjects increased cigarette smoking from 20.5 cigarettes/day to 35.4 cigarettes/day.

Conclusion: A majority of patients with alcohol dependence ingest more caffeine and smoke fewer cigarettes during the period following alcohol withdrawal.

NR319 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Dissociative Phenomena in MICA Inpatients

Zebulon C. Taintor, M.D., Manhattan Psychiatric Center, Ward's Island, New York NY 10035; A. Jonathan Porteus, M.A.

Summary:

While studies of dissociative phenomena in substance abuse and in specific psychiatric populations are burgeoning in the literature, these phenomena have not been explored in MICA populations that represent the confluence of mental illness and substance abuse, a substantial subset of psychiatric inpatients. This ongoing MICA research includes the ACTD-D for DSM-IV Dissociative Disorders, the Dissociative Experiences Scale (DES), Trauma Symptom Checklist (TSC-40), and the Childhood Trauma Questionnaire (CTQ). Each of 67 subjects received the protocol across a month, using intercorrelated dissociative scales as a time-delayed validity check (DES & TSC-40; r = 0.61, p .001). In terms of differentiating a MICA population from others, MICA DES scores (M = 27.41, SD 24.03) are significantly higher than previous findings using similar scales with psychotic disordered inpatients, substance abusers abused as children, and substance abusers not abused as children (all p. 05). CTQ scores revealed a high rate of childhood sexual abuse, and over 25% S_s met SCID-D criteria for a dissociative disorder. Furthermore, analyses of the five SCID-D dimensions (amnesia, depersonalization, derealization, identity confusion, and identity alteration) present both a useful clinical population profile as well as suggesting a natural hierarchy for therapeutic intervention/remediation towards long-term stability and rehabilitation.

NR320 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

HIV-1-Induced Cognitive Impairment Is Associated with Total But Not Free p24 Antigen Level

Karl Goodkin, M.D., Department of Psychiatry, Univ of Miami School of Med, 1400 NW 10th Avenue, #836-A, Miami FL 33136; Frances Wilkie, Ph.D., Benedetto Vitiello, M.D., J. Hampton Atkinson, M.D., Peter N.R. Heseltine, M.D., Daniel Feaster, M.S.

Summary:

A sample of 214 HIV positive subjects (204 men and 10 women) was identified based on complaints of decreased cognitive functioning and deficits on a neuropsychological (NP) test battery developed for HIV-associated neurocognitive impairment, yielding a total of 23 scores summarized as a global z-score. p24 antigen level was analyzed as a free level in serum by an antigen capture assay and by a more sensitive technique—immune complex dissociation. A Spearman correlation coefficient was computed for the relationship between the global z-score and the level of free and total p24 antigen. A significant negative correlation ($r = -0.31$, $p = .03$) was found between the global NP z-score and the total p24 antigen level. However, the correlation of this z-score with the free p24 antigen level was not significant ($r = -.20$, $p = 0.27$). We conclude that total p24 antigen level by ICD technique may prove advantageous over free p24 antigen level for monitoring of NP impairment in HIV-1 infected individuals. CSF levels would be expected to show a stronger relationship. Given that viral load of HIV-1 in the CSF is currently of unproven clinical utility, CSF total p24 antigen level may be appropriate to use as a virological index confirming NP impairment.

NR321 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Neurocognitive Decline in HIV-1 Infection: Relationship to Cortisol

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Summary:

Objective: This study examines whether the stress hormone cortisol is associated with HIV-related neurocognitive decline.

Method: Sixty HIV-1 infected gay/bisexual men were evaluated over a three-year period. Individuals with a history of substance abuse, pre-existing CNS disorder, mild head injury, or learning disability were excluded. All 60 subjects were medically asymptomatic at baseline. A comprehensive battery of neuropsychological tests was administered at each annual visit and included measures of attention, cognitive speed, learning and memory, visuospatial function, executive function, language, motor speed, and general intellectual ability. Standardized scores for the individual test measures were calculated for each subject, based on data derived from our age- and education-matched seronegative control group. Blood samples were also collected at each visit for cortisol measurements.

Results: For analysis purposes, cortisol levels obtained at the last visit in the study period were used to divide subjects into low and high cortisol groups. Analyses of covariance (adjusting for education, antiretroviral use, and baseline performance) were conducted on primary neuropsychological measures gathered at the

last visit. Executive functioning was significantly impaired in the high cortisol group when compared with the low cortisol subjects ($P = .009$). Group differences were not detected in other neurocognitive domains.

Conclusions: The findings suggest that cortisol may be related to neurocognitive disturbances in HIV-1 infection. The clinical significance of cortisol dysregulation in HIV-related dementia warrants further study.

NR322 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Stress and Social Conflict Predict Major Depression in HIV-Infected Men

Jane Leserman, Ph.D., Department of Psychiatry, University of North Carolina, CB7160, Chapel Hill NC 27599-7160; Diana O. Perkins, M.D., Susan G. Silva, Ph.D., Paula Bird, M.S.N., Dwight L. Evans, M.D., Robert N. Golden, M.D.

Summary:

Objective: This paper examines prospectively the relationship of stressful life events and social conflict with major depression among HIV-infected gay men.

Method: We studied 83 HIV-infected gay men every six months for up to four years. All men were asymptomatic at entry. Subjects had at least four visits; 72% had eight or nine visits. Consensus DSM-III-R psychiatric diagnoses, including major depression, were made at a diagnostic conference by reviewing the results of a modified SCID. Stressful events and difficulties were given a severity rating based on an interview to assess the context of each event during the previous six months; stress scores were based on the mean number of moderate and severe stresses during all study visits. The questionnaire to assess social conflict with friends and relatives was averaged for all visits.

Results: Of the 83 men in this study, 23 (27.7%) had a major depression at least once during their study participation. On average, subjects had 1.5 stresses (SD = .84) during each six-month period and tended to score low on social conflict (mean = 2.22, SD = .52, possible range 1-5). Logistic regression showed that men with greater social conflict (p = .007) and stress (p = .04) were more likely to develop a major depression. These results were unchanged when controlling for change in CDC disease stage and demographic variables. When compared with those with scores below the median, men above the median in social conflict had seven times the odds of becoming depressed (CI = 2.2-27.2) and men above the median on stress had about four times the odds of becoming depressed (CI = 1.3-13.5).

Conclusions: As shown in other populations, conflict in social relationships and/or moderate stress may be risk factors for depression among HIV-infected men. These findings indicate the importance of inquiring about social conflict and stresses that are not necessarily related to disease progression among HIV-infected patients.

NR323 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

An Open Trial of Nefazodone in HIV-Positive Outpatients with Major Depression

Andrew J. Elliott, M.D., Department of Psychiatry, University of Washington, 1001 Broadway, Ste 206, Seattle WA 98122; Peter P. Roy-Byrne, M.D.

Summary:

Treatment studies of major depression in HIV+ patients have shown that TCAs and SSRIs are both effective. Recently we reported comparable efficacy for depressed HIV+ patients on imipramine or paroxetine compared to placebo with increased side-effect-related dropout rates on imipramine (12/25; 48%) compared to paroxetine (5/25; 20%). Despite their greater tolerability, SSRIs may still exacerbate some of the most common somatic symptoms seen in HIV+ patients, including sleep disturbance, weight loss, sexual dysfunction, decreased energy, and fatigue. This is a report of an open 12-week trial of 15 subjects treated with nefazodone. The same ratings were obtained (Ham-D and CGI) as in our previous double-blind trial of paroxetine and imipramine to allow for efficacy and side-effect comparison (acknowledging the design limitations of open, nonblinded, and nonrandomized treatment). Results from the first seven subjects completing week 6 show a mean reduction in Ham-D scores from 27.57 to 9.8 (17.77 reduction). This is comparable to our previous study where mean six-week Ham-D scores decreased from 24.12 to 11.32 for paroxetine (12.81 reduction) and 23.80 to 8.93 for imipramine (14.87 reduction). Even more importantly, only 1/15 patients (7%) has dropped out due to side effects, and this was due to a drug-drug interaction. Nefazodone-treated subjects did experience transient dizziness, headache, and dry mouth when initiating therapy, but these resolved and did not affect compliance with treatment. The apparent equal efficacy and possibly greater tolerability of nefazodone for the treatment of depression in HIV+ patients should be investigated in a placebo and active-treatment controlled trial.

NR324 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

AIDS Patients' Preferences About Advance Directives

Cheryl A. Kennedy, M.D., Department of Psychiatry, UMDNJ-NJ Medical School, 185 South Orange Avenue, Newark NJ 07103; James Hill, Ph.D., Debra Kantor, Ph.D., Scott Matthews, Kari O'Connell

Summary:

Objective: To examine the relationship between illness adjustment and health beliefs in hospitalized AIDS patients and their preferences about advance directives.

Methods: In an urban teaching hospital, interviews utilizing structured questionnaires and open-ended, guided interviews assessed patients' health beliefs, satisfaction with health care, and preferences for advance directives. Qualitative information was examined by grounded theory and domain analysis. Quantitative data were analyzed using standard tests of association.

Results: Of 34 interviews (10 female), 30 (91%) thought advance directives were a good idea, but only 11% had documents. Adjustment to illness (70% 'well-adjusted'), age, gender, CD4 count (mean = 260/uL) were not associated with advance directives, but education was (p = 0.02). Over 60% thought doctors should initiate the discussion very early in the illness, and 84% thought it was the doctor's duty to stop life support if the patients' condition was hopeless. Religious people were likely to refuse life support in terminal situations (p = 0.007).

Discussion: While many patients thought advance directives were a good idea, few had such documents. Compassionate care requires that patient preferences about end-of-life decisions be honored. Psychiatrists are in a unique position to assist AIDS patients in developing documents that describe these preferences.

NR325 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Depression Among AIDS Patients in a Nursing Home

Leonid Bilenkin, B.S., Department of Psychiatry, Bronx-Lebanon, 1276 Fulton Avenue, Bronx NY 10456; Gopalakrishna K. Upadhya, M.D., Ali Khadivi, Ph.D., Rogelio Thomas, M.D.

Summary:

Objective: To date, little is known about the prevalence of depression among minority patients with AIDS in the inner city. This study examines the prevalence of current depressive symptom-

atology among African-American and Latino patients with AIDS in a skilled nursing facility in the South Bronx.

Methods: 118 subjects who had met the CDC criteria for acquired immunodeficiency syndrome and constituted all of the residents of the nursing home were selected. Ten patients refused to participate in the study and 14 patients met the exclusion criteria for severe dementia (MMSE score < 17). The Short Depression Screen (SDS), a brief depression screening instrument, was administered to the final sample of 94 subjects.

Results: 61% of the sample were males and 39% were females. Mean age was 42. The sample was predominately African American (47%) and Latino (47%). Forty-two patients (45%) had a history of intravenous drug use (IVDU). The prevalence of current depressive symptoms as measured by SDS was 35%. There was no significant difference in the rate of depression across gender or ethnicity. Also, patients with a history of IVDU did not show more depression than the non-IVDU group. Out of 34 patients who were found to be depressed, only 20 (60%) were receiving antidepressant medication.

Conclusion: A high prevalence of depression exists among minority patients with AIDS living in a nursing home. A careful assessment of depression in this population is essential for effective psychiatric intervention and overall medical care.

NR326 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Psychiatrist Outreach to Homebound AIDS Patients

Lawrence B. Jacobsberg, M.D., Department of Psychiatry, Visiting Nurse Services, 220 East 63rd Street, New York NY 10021; Robert P. Parkin, M.D., David C. Lindy, M.D., Neil Pessin, Ph.D.

Summary:

Objective: Patients with HIV/AIDS are often homebound as a result of their illness. Psychiatric teams, consisting of nurses, social workers, and psychiatrists, provide consultation to medical home care services. Since disciplinary boundaries are not clearly defined by the team's work, we sought to identify the role played by the psychiatrist, the only prescribing practitioner on the team.

Method: A 54-item questionnaire, filled out by the treating clinician, provided information on patient demographics, referral, and history. Another questionnaire, filled out by the consulting psychiatrist, recorded the need for medication, the alteration or initiation of psychotropic medication, response, and outcome.

Results: Forty-two patients were evaluated over a three-month period. Psychotropic medication was prescribed in 50% of the cases. Among those cases where medication was employed as an intervention, the recommendation was for an antidepressant (usually an SSRI) in 40%. A benzodiazepine was prescribed for anxiety symptoms in 40% of cases, while a neuroleptic was recommended in 20% (usually in the setting of organicity). Patient demographics, as manifested by different locales, HIV risk factors, and socioeconomic status, differentiated treatment interventions and responses.

Conclusions: Psychiatrists acting as part of mental health consultation teams to homebound HIV/AIDS patients made interventions beyond the realm of medication. When medications were employed, benzodiazepines, antidepressants, and neuroleptics were prescribed.

NR327 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

The Progression of HIV Knowledge, Attitudes and Behavior of Drug and Alcohol Outpatients Through Treatment

Thomas M. Brady, M.S., Department of Psychiatry, University of IL/Chicago, 912 South Wood Street, Chicago IL 60612-7327; Joseph A. Flaherty, M.D., Norman S. Miller, M.D.

Summary:

Objective: To illustrate how knowledge and attitudes about HIV and sexual risk behaviors evolve during the tenure of drug and alcohol outpatients in the first six weeks of abstinence-based group therapy. Although it is fairly easy to change HIV knowledge during a short behavioral intervention and somewhat more difficult to change attitudes, it is very challenging and extremely difficult to change behaviors.

Methods: We surveyed more than 100 outpatients with two instruments, a knowledge and attitudes instrument (McKusker) and the Risk Assessment Battery-RAB (Metzger). Patients were surveyed anonymously in groups during two communicable disease lectures per month offered in our health education program. Between June and December 1996, 175 knowledge and attitude survey questionnaires and 150 RAB questionnaires were collected and analyzed. Endpoints measured included total score for HIV knowledge, two attitude scales of self efficacy in condom usage and vulnerability to HIV infection, and a summary behavior score including measures of sex for drug exchanges, commercial sex, and multiple sexual partners. Exposure variables were number of HIV education sessions and number of weeks in treatment.

Results: HIV knowledge increased significantly ($p = .001$); although self efficacy improved, the results, however, were not significant. HIV risk behaviors decreased in severity with time in treatment, but not with statistical significance. In planning HIV education interventions, we suggest that administrators of drug and alcohol programs should anticipate modest reductions in behavior change.

NR328 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Assessment of Asymptomatic HIV Patients with the Computerized Neuropsychological Test Battery

John Herrera, Ph.D., California Clinical Trials, 8500 Wilshire Blvd, 7th Floor, Beverly Hills CA 90211; Amy Veroff, Ph.D., John J. Sramek, Pharm.D., Standford S. Jhee, Pharm.D., Claudette Francis, R.N., Neal R. Cutler, M.D.

Summary:

Objective: The human immunodeficiency virus (HIV), the etiologic agent of acquired immunodeficiency syndrome (AIDS), directly affects the central nervous system, often causing cognitive, motor, and behavioral changes, and eventually a dementia prior to death. Recent evidence suggests the presence of cognitive impairments early in the course of the disease (i.e., in asymptomatic patients). These findings derive from several sources, including subcortical CNS postmortem results (Neuen-Jacob et al., 1993), early abnormalities in cerebrospinal fluid, computed tomography, magnetic resonance imaging, positron emission tomography, and select neuropsychological tests. In this study, the cognitive function of asymptomatic HIV patients was evaluated using the Computerized Neuropsychological Test Battery (CNTB, see Veroff et al., 1991).

Methods: The CNTB was administered to 50 asymptomatic HIV patients (CD4 count < 400/ml). The CNTB is a computer-based assessment instrument for neuropsychological research consisting of 11 subtests; it has demonstrated high levels of validity, reliability, and sensitivity for a broad range of neurocognitive functions.

Results: The results will be discussed and compared with those obtained in psychiatric and normative populations.

Conclusions: The results of this study have significant diagnostic and treatment implications for patients with HIV.

NR329 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Physicians in a Residence Program: Evaluation of a Substance Abuse Training Approach Using Simulated Patients

Frances R. Levin, M.D., Department of Psychiatry, Columbia University, 722 West 168th Street, Unit 66, New York NY 10032; Patricia Owen, Ph.D., Edward Rabinowitz, M.D., Nicholas A. Pace, M.D.

Summary:

Despite the widespread prevalence of substance abuse among patients seeking medical treatment, physicians often fail to diagnose substance abuse and fail to refer addicted individuals to treatment. One program designed to improve physicians' knowledge and interviewing skills is the Physician in Residence Program (PIRP) at Hazelden's Residential Program in New York City. The PIRP combines didactic and experiential learning in a clinical treatment setting. This study was designed to evaluate the efficacy of the PIRP in training medical house staff. Residents were videotaped while interviewing two actors (*standardized patients*) prior to program entry and at program completion. Two experienced drug counselors rated each of the resident's videotapes using the Alcoholism Intervention Performance Evaluation. This instrument provides an overall score and seven subscale scores. The raters were blind as to whether the residents' interviews were done pre- or post-training. Using intraclass correlation coefficients, inter-rater reliability for the overall instrument was .79. Interviews from 23 residents were evaluated. Improvements were found in various areas including patient education and negotiation of a treatment plan. These changes were consistent with self-reported improvements in interviewing and referral skills. These data suggest that the PIRP provides an effective way to improve residents' substance abuse assessment skills.

NR330 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Buprenorphine for Opioid Detoxification in a Private Practice Setting

Richard B. Resnick, M.D., Department of Psychiatry, New York University, 43 West 94th Street, New York NY 10025-7113; Marc Galanter, M.D., William Matikiewicz, M.D., Elaine Resnick, M.S.W.

Summary:

Buprenorphine detoxification of 39 opioid addicts was conducted in an outpatient private psychiatric setting. Eligibility included: Older than age 18; informed consent; good mental and physical health; refusal to enter a hospital or enroll in methadone maintenance; no prior buprenorphine treatment. Subjects received a modified ASI, Beck Depression Score, Hamilton Anxiety Score, screening for OCD and psychiatric evaluation. Buprenorphine was administered daily, sublingually, under direct observation. Subjects were blind to their dose, with no take-home doses allowed. Initial doses were based on level of opioid dependence, i.e., 1 mg for each $10/day heroin (max = 6 mg); administered when subjects had abstinence symptoms of at least moderate severity. If clinically required, subjects could receive additional doses every two hours on the first day only.

Demographic, other intake variables, and addiction treatment histories will be presented. Twenty-eight subjects (72%) completed buprenorphine administration (10-34 days) and started placebo; 11 subjects (28%) discontinued treatment before placebo. Drop-outs and relapse to heroin occurred at 2 mg or less, when subjects had withdrawal symptoms, low energy being the most difficult. Six subjects had confirmed opioid-free status at three months follow-up and three subjects at 12 months. These findings are comparable to those of methadone and inpatient detoxifications, demonstrating the feasibility and patient acceptance of buprenorphine for detoxification. Expanding buprenorphine to private practice settings has public health benefits, without risk to public safety. We recommend limiting treatment to physicians with advanced training in addiction medicine, restricting the numbers of patients at each facility, and maintaining the same regulations regarding doses, take-home, informed consents, etc., as in NIDA-funded studies.

NR331 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Influence of Addictions Treatment on Perceived Problem and Need for Treatment of Substance Use and Mental Illness Among Dually Diagnosed Inpatients

Jill RachBeisel, M.D., Department of 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 and need for treatment of MI and SA problems, and 2) whether these perceptions changed in response to a brief inpatient dual-diagnosis treatment program (DDP).

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 before and after the DDP. 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 prior to the DDP. Acknowledgement of a SA problem was associated with perceived need for SA treatment ($p < .001$), diagnosis of a substance-induced mental disorder (SIMD) compared with a primary mental disorder (PMD), 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. SIMD patients were more likely to perceive their problem as a SUD rather than a MI after completing the DDP ($p < .001$).

Conclusions: The high level of illness awareness and consent for treatment observed suggests that treatment readiness may be optimal in the inpatient setting and that providing addictions treatment may have a strong impact on aftercare compliance and outcome.

NR332 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Sequential Serotonin Assessments in Cocaine Addicts After Cocaine Discontinuation

Laure B. Buydens-Branchey, M.D., VA Medical Center, 800 Poly Place, Brooklyn NY 11209; Marc H. Branchey, M.D.

Summary:

Our goals were to compare the serotonergic (5-HT) function of healthy subjects and cocaine addicts and to examine whether cocaine addicts would exhibit changes in 5-HT function after a drug-free period. An oral dose of 60 mg of d-1 fenfluramine (FEN) was used as the 5-HT probe. Eleven healthy males completed two days of testing separated by 48 hours, involving the administration of FEN or placebo in random order. Twelve hospitalized

male patients underwent two sets of FEN and placebo challenges that took place a few days and three weeks after cocaine discontinuation. Patients were divided into two subgroups as a function of the presence (FH+) or absence (FH–) of a paternal history of alcoholism or drug abuse. Double deltas (maximum change from baseline after FEN minus change from baseline at the corresponding time point after placebo) were calculated. The FH+ patients (but not the FH–) had a significantly blunted early prolactin (PRL) response when compared with controls (3.8 ± 1.3 ng/ml vs. 12.4 ± 2.4, $p < .01$). Their early PRL response was also significantly reduced when compared with that of FH– patients (3.8 ± 1.3 ng/ml vs. 13.1 ± 1.8, $p < .01$). When the late responses of FH+ and FH– patients were compared, no significant difference was observed. The late responses of the two patient subgroups were also not significantly different from the response of controls.

Conclusion: Our data suggest the existence of an altered 5-HT function in a subgroup of cocaine addicts with a familial history of alcoholism or drug abuse that could be attributed to the effects of cocaine. The greater blunting of the PRL response observed within days of cocaine discontinuation followed by a greater rebound of this response after three weeks could indicate an increased vulnerability to the disruptive effects of cocaine in these patients.

NR333 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Utilization of Consultation Services in an Addiction Unit

Vasant P. Dhopesh, M.D., Department of Psychiatry, VA Medical Center/116A, University & Woodland Avenue, Philadelphia PA 19104; Bruce J. Berg, M.D., Elmer Yu, M.D., Gerald A. Groves, M.D.

Summary:

Background: On our Veterans Affairs inpatient substance abuse treatment unit we find that a large proportion of patients require consultation, a service that consumes the time and resources of the staff. The objective of this study was to document the number of consultations and to determine whether consultation was requested for preexisting or new conditions.

Methods: From the beginning of July to the end of November, a record was maintained of all consultation requests along with the type of consultation and whether the consultation was for a preexisting or new condition. Demographic information such as age, race, routes of drug administration, and duration of substance abuse were recorded.

Results: All 137 patients were males and ranged in age from 24 to 67 years with the mean of 41.8 ± 7.9 years; 71.5% were black, 26.3% were white, and 1.5% other. Also, 107 or 78% were polysubstance abusers. Of the 137 patients 109 (80%) received at least one consultation. Of these 109 patients, (40%) had one consultation and 65 (60%) had more than one consultation, mean 2.8 ± 1.1. Thirty-two patients (13%) had four or more consultations. Forty-nine of the consults (45%) were for dental problems and 30 (28%) were dermatological conditions. The total number of consultations obtained for preexisting conditions was 171, and 59 consultations were requested to investigate new conditions. There were no statistically significant differences in the utilization of consultations between intravenous drug users (IVDU's) and non-IVDU's, between IVDU's and alcoholics, or between polysubstance abusers and alcoholics.

Conclusions: 1.) Our survey confirms the observation that a significant percentage of patients on our substance abuse treatment unit utilize consultation services. 2.) Although the majority of requests for consultations are for preexisting conditions and are not urgent, the large number of consultations suggests that these patients have genuine and multiple medical problems that require additional investigation and intervention. 3.) The impact of consultation services on the cost of health care and on the staffing of the unit needs to be considered in planning for the healthcare needs of substance-abusing patients.

NR334 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

State-Dependent Personal Memories During Intoxification Reported by Patients with Alcoholism

Richard J. Esposito, M.S., Yale Psychiatric Institute, PO Box 208038, New Haven CT 06520; Ralph E. Hoffman, M.D., Marc I. Rosen, M.D., Rockholz Peter, M.S.S.W.

Summary:

Objectives: Experimental studies have demonstrated that alcohol has state-dependent effects on learning and memory. We therefore sought to determine if alcohol intoxication triggers selective retrieval of memories that could alter patterns of alcohol use.

Methods: Eighteen alcoholic patients were studied along with a comparison group of 12 patients who abuse cocaine, a drug not associated with memory state-dependence. Patients underwent a semistructured interview to elicit information about recurrent personal memories (RPMs) experienced when intoxicated. RPMs experienced during craving were also studied as a comparison condition.

Results: Fourteen out of 18 (78%) alcoholic patients reported RPMs during intoxication compared with four of 12 (33%) cocaine-abusing patients; this difference in prevalence was statistically significant ($\chi^2 = 5.93$, $p < .015$). For the alcoholic patients, these experiences occurred more frequently than during craving (paired t-test = 2.77, $p < .013$), generally reflected prior disturbing events and were often reported to promote continued drinking.

Conclusions: The association of recurrently experienced personal memories with intoxication in alcoholic patients suggests but does not establish pharmacologic state-dependence. Further studies of this memory phenomenon are indicated.

NR335 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Toxicological and Psychosocial Profile of Ecstasy Abusers and Non-Abusers in Military Conscripts

Julio Bobes, M.D., Department of Psychiatry, University of Foviedo, Julian Claveria 6, Oviedo 33006, Spain; Pilar A. Saiz, Ph.D., Maria P. Gonzalez, Ph.D., Manuel Bousono-Garcia, M.D., Jose R. Perez-Carral, M.D.

Summary:

Objectives: To describe the prevalence of MDMA consumption and the toxicological and psychosocial profile of 1854 young male conscripts from Asturias (Spain).

Subjects and Method: The WHO questionnaire for drug consumption, the EPQ-A, the Zuckerman Sensation Seeking Scale, and the Dupuy PGWB Index were administered to the total intake (mean age = 20.179, SD = 2.371).

Results: Comparisons are shown below:

	MDMA Consumers [Mean (SD)]	MDMA Nonconsumers [Mean (SD)]	p
N	226	1628	
EPQ-N	12.4558(5.708)	11.4650(5.728)	.015
EPQ-P	6.9292(4.578)	3.9889(3.058)	.000
Thrill & Adventure Seeking	7.0177(2.422)	6.2899(2.736)	.000
Disinhibition	8.1504(1.650)	6.5338(2.118)	.000
Experience Seeking	6.5531(1.743)	4.8059(1.818)	.000
Boredom Susceptibility	5.9513(1.933)	4.9380(2.134)	.000
Total Sensation Seeking Scale	27.6593(5.226)	22.5835(6.113)	.000
PGWB Index	63.8982(14.437)	58.5111(13.3000)	.000

Conclusions: The consumer profile indicates that these people are high sensation seekers with emotional instability, high levels of psychoticism, and impulsivity. Furthermore, these individuals believe that they have a poorer general well-being.

NR336 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Quality of Life in 274 Schizophrenic Outpatients Undergoing Risperidone Maintenance Treatment

Julio Bobes, M.D., Department of Psychiatry, University of Foviedo, Julian Claveria 6, Oviedo 33006, Spain; Miguel Gutierrez, M.D., Juan Gibert, Ph.D., Maria P. Gonzalez, Ph.D., Marisa Herraiz, M.D., Antonio Fernandez, M.D.

Summary:

Objectives: To assess the quality of life and level of disability of schizophrenic outpatients in Spain.

Patients: A nationwide sample of 274 schizophrenic patients undergoing maintenance treatment with risperidone was assessed four times (at baseline, 2, 4 and 8 months) during 1996. Instruments used were the BPRS, UKU, CGI, SF-36 and Disability Diagnostic Scale.

Results: Mean age was 34.5 years (SD 10.6), 67% were male, 70% were paranoid subtype, and mean length of evolution was 10.9 years (SD 8.9). Results at four months are presented, and data at eight months are currently being processed. The mean dose of risperidone at baseline was 5 mg/day increasing to 5.5 mg/day at four months. From baseline to four months, clinical scores decreased as follows: BPRS from 24.2 to 15.0. With reference to quality of life, significant improvements from baseline to four months were seen on all scales of the SF-36. Women showed a significantly greater improvement on the role emotional scale. Paranoid patients improved significantly more than nonparanoid patients on the following scales: role physical, general health, social functioning, and role emotional. Global disability level decreased from 52.5 to 38.1.

NR337 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

The Association Between Animal Cruelty and Psychiatric Disorders

Roman Gleyzer, M.D., Department of Psychiatry, UTMB at Galveston, 301 University Blvd/Route 0428, Galveston TX 77555; Alan R. Felthous, M.D., Charles E. Holzer III, Ph.D.

Summary:

Animal cruelty in childhood, though generally viewed as abnormal or deviant, for years was not considered symptomatic of any particular psychiatric disorder. Though currently used as a diagnostic criterion for conduct disorder, research establishing the diagnostic significance of this behavior is essentially nonexistent.

Objective: To test the hypothesis that a history of substantial animal cruelty is associated with a diagnosis of antisocial personality disorder (ASPD) and to assess for associations with other disorders commonly diagnosed in a population of criminal defendants.

Method: The investigators compared the diagnoses of 48 subjects who had histories of substantial animal cruelty with matched subjects without such history. Both groups were comprised of criminal defendants referred for court-ordered psychiatric evaluations. Data were systematically obtained from the files using four specifically designed retrieval outlines.

Results: ASPD was significantly associated with a history of animal cruelty during childhood (37.5% vs. 8.3% in control group; $P < 0.001$). An association was also significant for antisocial personality traits (ASPT), $P < 0.001$. Correlations for malingering and abuse of substances other than alcohol were also found ($P < 0.05$). Mental retardation, psychotic disorders, and alcohol abuse showed no such association.

Conclusion: In the studied population, a strong correlation appeared between a history of animal cruelty in childhood and ASPD/ASPT. There were also associations with malingering and abuse of substances other than alcohol.

NR338 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Newborn Murder in Maternity Wards: A Report of Three Cases and a Discussion on the Definition of Neonaticide

Marcio Gekker, M.D., 3187 Cowley Way, #108, San Diego CA 92117; Mauro V. Mendlowicz, M.D., Katia Mecler, M.D., Talvane M. de Moraes, Mark H. Rapaport, M.D.

Summary:

Objective: Resnick (1970) defined neonaticide as the killing of a neonate by its mother during the first 24 hours after its birth. He suggested that it is committed by young, nonmarried, nonpsychotic women whose motivation is to get rid of an illegitimate child. We demonstrate that a similar pattern can also be found in cases in which a neonate was killed by its mother after the first 24 hours of life.

Method: We performed a review of the judiciary files in the city of Rio de Janeiro, Brazil, looking for cases in which a woman killed her newborn child between the second and 30th day after birth, from Jan. 1, 1900 to Dec. 31, 1996. These cases were presented and discussed.

Results: Three newborns (5.3% of the total of 56 cases) were killed by their mothers at the fourth, fifth, and sixth day after birth. In all three cases, delivery and murder occurred in maternity facilities. In one case, the murderer had been formerly diagnosed as schizophrenic. In the other two cases, nonpsychotic women secretly killed their illegitimate newborns whose unexpected birth was believed to shame them and their families.

Conclusions: The characteristic motivation of neonaticide can also be found in cases in which a child was killed by the mother after the first day of life. However, in these cases, unlike other neonaticide cases, the birth and the newborn killing occurred in maternity facilities. These findings suggest that a subgroup of neonaticides may opt for an assisted delivery and postpone the murder to a more favorable opportunity. Resnick's definition of neonaticide is based only on the most typical cases and ignores the late-occurring varieties. A new definition of neonaticide is required. Meanwhile, we recommend that the identification of a case of neonaticide should not rely exclusively on a temporal criterion, but should also consider the particular circumstances of each case.

NR339 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

A Case-Control Study on the Sociodemographic Characteristics of a Sample of Fifty-Five Neonaticide Women

Mauro V. Mendlowicz, M.D., Department of Psychiatry, University of CA/San Diego, 8950 Villa La Jolla Dr, #2243, San Diego CA 92037; Mark H. Rapaport, M.D., Talvane M. de Moraes, Katia Mecler, M.D., Marcio Gekker, M.D.

Summary:

Objective: To test for Resnick's (1970) empirically derived hypothesis that neonaticide mothers are generally young, nonmarried women, we performed the first controlled study of the sociodemographic characteristics of neonaticide women.

Method: We performed a review of the judiciary files in the city of Rio de Janeiro, Brazil, looking for cases in which a woman killed her newborn child during the first 30 days after birth, from January 1, 1900 to December 31, 1996. The sociodemographic characteristics—age, marital status, occupation, educational status, ethnic origin, number of abortions, and children—were compared with those of a control group of women who delivered children in public hospitals in the same city around the time of the victims' birth. Statistical significance was tested using the chi-square test for categorical variables and Student's t-test for continuous variables.

Results: Fifty-five cases of neonaticide were identified. Neonaticide mothers were significantly younger (mean = 22.7 +/- 5.5 vs. 24.8 +/- 6.2 years; controls; $p = 0.003$), less often married (89% vs. 42% controls; $p < 0.001$), and had a lower educational level than controls ($p < 0.001$). The proportion of non-white women was significantly higher among neonaticide mothers (80% vs. 53% controls; $p < 0.001$). Neonaticide women were usually nulliparous (80% vs. 38% controls; $p < 0.001$) and had no history of abortions (5% vs. 27% controls; $p < 0.001$). The preponderance of mothers in both groups were employed as domestic servants.

Conclusions: Resnick's empirical data have been confirmed in this controlled study. Increased knowledge about the sociodemographic profile of neonaticide mothers can help psychiatrists and social workers to establish intervention programs.

NR340 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Psychosis and Criminal Behavior: Implications for Risk Assessment and Dispositional Planning

Debra A. Pinals, M.D., Forensic Services, Northcoast Behavior Sciences, 1756 Sagamore Road/PO Box 305, Northfield OH 44067; Stephen G. Noffsinger, M.D.

Summary:

Objectives: Dispositional planning for forensic patients necessitates an understanding of psychotic symptoms as precursors of criminal behavior. The purpose of this study was to examine the relationship of psychotic symptoms to violent and nonviolent offenses in persons determined to be NGRI (not guilty by reason of insanity).

Methods: All patients who were hospitalized with a forensic NGRI status at the study site were included. Forensic psychiatrists conducted thorough reviews of medical and legal records to gather information regarding the presence and type of psychotic symptoms at the time of the offense. Symptoms were classified as delusional, psychotic without pervasive delusions, and not psychotic. Offenses were classified a priori as violent to person or not violent to person. Analyses were conducted to examine the relationship between the criminal behavior and psychotic symptoms.

Results: Preliminary results examining 45 patients (37 male, eight female) indicate that of violent NGRI acquittees, 74% had pervasive delusional symptoms and 18% had psychotic symptoms without delusions, whereas in the nonviolent group, 27% had delusional symptoms and 64% had nondelusional psychotic symptoms ($x^2 = 8.94$, $DF = 2$, $p = .01$). In addition, violent offenses committed in conjunction with paranoid delusions were most likely perpetrated on known victims.

Conclusions: These data support previous findings that in psychotic patients, delusional symptoms are significantly associated with violent crimes. A thorough review of psychotic symptoms in NGRI patients may assist clinicians with comprehensive risk assessments and treatment decisions.

NR341 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

A Descriptive Study of the Psychiatric Aspects of Fifty-Five Cases of Neonaticide

Talvane M. de Moraes, 262 Praia Do Flamengo #501, Rio De Janeiro 22210, Brazil; Mauro V. Mendlowicz, M.D., Mark H. Rapaport, M.D., Katia Mecler, M.D., Marcio Gekker, M.D.

Summary:

Objective: To describe psychiatric symptoms associated with the commitment of neonaticide (i.e., the killing of the neonate by its own mother on the day of its birth), in order to distinguish it from the postpartum psychotic disorders.

Method: We performed a review of the judiciary files in the city of Rio de Janeiro, Brazil, looking for cases in which a woman had killed her newborn child during the first 30 days after birth, from January 1, 1900 to December 3, 1996. The circumstances of pregnancy, birth, and murder; the criminal's motivation; and the results of psychiatric evaluation were presented and discussed.

Results: Fifty-five cases of neonaticide were identified. Neonaticides usually tried to keep their pregnancies concealed (80%). Deliveries and crimes generally took place secretly (91%) at night (69%) in theirs employer's house (73%). Fifty-two women (95%) tried to conceal the body through several methods; eventually 25 (45%) failed. After the unravelment of the crime, one-third of neonaticides denied having killed the newborn and attributed the death to natural or accidental factors. Other women admitted having murdered the child for moral (22.1%) or economic (9.3%) reasons or simply because they didn't want him/her (3.5%). Eleven (19.8%) neonaticides alleged they could not recall the moment of the crime. No major psychiatric disorders were diagnosed among the accused. Amnesia allegations were considered malingering.

Conclusions: Despite apparent irrationality, neonaticide generally involves a certain degree of premeditation and should not be confounded with postpartum psychosis. Nevertheless, psychiatric evaluation is recommended in all cases.

NR342 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Correlates of Aggression in Male Prisoners

Eulon R. Taylor, M.D., Department of Psychiatry, TTUHSC, 8602 Peach Street, Lubbock TX 79404; Pamela M. Diamond, Ph.D., Eugene W. Wang, M.S., Lue E. Herrington, M.S.

Summary:

Results presented are from a random sample of 103 inmates receiving services in a specialty program for aggressive mentally ill offenders. Data collected include IQ score, reading level, neuropsychological functioning (EXIT, QED, CLOX, MMSE), personality style (MCMI-III), anger expression (STAXI), psychopathy (PCL-R), adaptive functioning (MCAS), and overt aggression (OAS). Demographic and clinical variables included age, ethnicity, Axis I and II diagnoses, and current medications. Criminal history variables included age at conviction, length of sentence, times in prison, time served, and time lost for disciplinary offenses; dichotomous variables included whether the current offense was violent and/or caused injury. Criterion measures of aggression included

OAS total score and average assaults per year. Bivariate correlations between the two criterion measures and all other variables were performed. The OAS total score was correlated with assaults per year, as were OAS Verbal Aggression and Aggression Against Objects Scales, PCL-R Factor 2, MCAS Behavioral Problems Scale, STAXI Anger-Out scale, and length of sentence. Correlates with OAS total score included PCL-R Factors 1 and 2 and total score, and all MCAS subscales and total score. Conclusions were that the best predictors of assaults are clinician ratings of psychopathy, adaptive functioning, and overt aggression.

NR343 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Coercion in Medical and Psychiatric Admissions: An Empirical Study

Bruce J. Cohen, M.D., Department of Psychiatry, University of Virginia, Drawer D/Blue Ridge Hospital, Charlottesville VA 22901; Steven K. Hoge, M.D.

Summary:

Objective: While patients' perceptions of coercion in the psychiatric admissions process have been studied, medical patients have remained unexamined. We surveyed the prevalence of perceived coercion in a medical population and explored factors associated with this perception. The medical group was then compared to a psychiatric sample.

Method: A total of 172 newly admitted inpatients on a general medical service at a university hospital were interviewed. Using the MacArthur Admission Experience Survey, "high coercion" subjects were obtained (n = 33). They received the more detailed Admission Experience Interview, including scales of perceived coercion and the perception of having been included in a fair decision-making process ("procedural justice"). Subjects were matched for degree of perceived coercion with a group of 206 newly admitted psychiatric inpatients on an acute inpatient service in the same teaching hospital.

Results: Perceived coercion was less common in the medical group (2% vs. 21%). In both groups, the degree of perceived coercion significantly correlated with the degree of perceived procedural justice. Both groups reported similar frequencies of specific types of pressures.

Conclusions: Perceived coercion is less common in medical inpatients, but is related to similar variables as in psychiatric patients. Attention to these variables during the admissions process may facilitate patient care.

NR344 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Impulsivity Related to Suicide Attempts and Self-Aggression in Mentally Disordered Offenders

Francisco Paez, M.D., Clinical Research, Institute of Mexican Psych, Calzada Mexico Xochimilco 101, Mexico City 14370, Mexico; Alberto G. Lopez, M.D., Rogelio Apiquian, M.D., Humberto Nicolini

Summary:

Suicide is 10 times more frequent in jails and is associated with mental disturbance. The aim of this study was to determine the one-year incidence of suicide attempts (SUAT) and self-aggression (SEAG) among institutionalized mentally disordered offenders. Impulsivity was compared between the two groups.

Methods: A total of 123 male subjects were assessed in the psychiatric ward of the South Preventive Prison in Mexico City. A direct interview and record analysis was made to retrospectively obtain the one-year history of SUAT or SEAG among subjects. SUAT and SEAG differentiation was established with a clinical judgment of the presence or absence of the wish to die in the act. Impulsivity was assessed with the Spanish version of the Plutchik impulsivity scale (internal consistency 0.89).

Results: One-year SUAT incidence was 8.9%, while SEAG one-year incidence was 23.5%. The impulsivity rates showed no differences between SUAT and SEAG, but when we compared them against patients without SUAT or SEAG, patients with self-aggressions (SEAG) showed a significantly higher level of impulsivity (17.3 +–4.9 vs 14.6+ –5.5, p = 0.01).

Conclusion: Self-aggression is far more frequent than suicide attempts among mentally disordered offenders and is related to impulsivity.

NR345 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Intermittent Explosive Disorder: A Preliminary Report of 17 Cases

Susan L. McElroy, M.D., Department of Psychiatry, Univ of Cincinnati Col of Med, 231 Bethesda Avenue, ML 559, Cincinnati OH 45267-0559; Cesar A. Soutullo, M.D., DeAnna A. Beckman, M.S.W., Paul E. Keck, Jr., M.D., Purcell Taylor, Jr., Ed.D.

Summary:

Background: Intermittent explosive disorder (IED) is a probably common but little studied impulse control disorder (ICD). We provide preliminary phenomenology and associated psychopathology data on 17 subjects with DSM-IV IED.

Method: Seventeen consecutive subjects who met DSM-IV criteria for IED were self-referred in response to a newspaper advertisement (N = 9), referred by other physician (N = 3), or by staff from a facility for violent difficult-to-place felons (N = 5). Structured interviews were used to collect phenomenological characteristics prior to, during, and after the explosive episodes. The Structured Clinical Interview for DSM-III-R (and subsequently DSM-IV) (SCID) [3] was used to evaluate comorbid psychiatric disorders.

Results: The age (mean ± SD) of our subjects was 35 ± 7 years. The male:female ratio was 13:4. The mean age of onset of IED was 14 ± 8 years. Most subjects (N = 15) had IED episodes at least once a month. The mean duration of episodes was 24 ± 23 minutes. Subjects displayed very high rates of comorbid Axis I disorders: 15 (88%) of the patients with IED had lifetime diagnoses of a major mood disorder (47% bipolar disorder), 10 (59%) a substance use disorder, 8 (47%) an anxiety disorder, 8 (47%) another ICD, 4 (24%) an eating disorder, and 2 (12%) a somatoform disorder. Most subjects described various affective symptoms associated with their explosive episodes.

Conclusion: Our subjects provided a very consistent description of their explosive episodes. IED was highly comorbid with mood, substance use, anxiety, eating, and impulse control disorders. We also found striking phenomenological similarities between IED explosive episodes and bipolar disorder mood swings. IED is a bonafide ICD that may be related to mood disorders, especially bipolar disorder, and perhaps may represent another form of "affective spectrum disorder."

NR346 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Chronicity in PTSD and Predictors of Course of PTSD in Patients with Comorbid Anxiety Disorders

Caron Zlotnick, Ph.D., Department of Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Meredith Warshaw, M.S.S., M. Tracie Shea, Ph.D., Jennifer Allsworth, B.A., Teri B. Pearlstein, M.D., Martin B. Keller, M.D.

Summary:

Objective: To date, studies on the course of PTSD have been limited to retrospective designs to assess the illness (e.g. Breslau & Davis, 1992; Kessler et al., 1996) or have relied on self-

report measures of post-traumatic morbidity (e.g. McFarlene, 1988). Using data from a prospective longitudinal, multicenter design study of patients with specific anxiety disorders, we examined the course of post-traumatic stress disorder (PTSD) and the role of various factors in the maintenance of PTSD in patients with a comorbid anxiety disorder.

Method: The initial evaluations assessed psychiatric disorders, including PTSD, using structured diagnostic interviews. PTSD was not an inclusion criterion for this study. The Longitudinal Interval Follow-up Evaluation was used to collect detailed information on course of symptoms of PTSD illness and other disorders at various time intervals.

Results: Of the 54 subjects in episode of PTSD at intake, the likelihood of full remission from PTSD during five years of follow-up was .18, and .60 for partial remission from PTSD. Variables associated with a longer time to remit from an episode of PTSD were a history of alcohol abuse ($\chi 2 = 5.09$, $\beta = .05$, $p = .02$), and a history of childhood trauma ($\chi 2 = 4.10$, $\beta = -1.65$, $p = .04$).

Conclusion: Our findings with other research findings confirm clinical impressions that a substantial number of persons, especially those with histories of childhood abuse or alcohol abuse, endure prolonged episodes of PTSD.

NR347 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

A New Screening Measure for Domestic Violence

David P. Bernstein, Ph.D., Department of Psychiatry, Mt. Sinai Hospital, 130 West Kingsbridge Road, Bronx NY 10468; Edward A. Walker, M.D., Judith Stein, Ph.D., Martha A. Medrano, M.D., Murray B. Stein, M.D.

Summary:

Objective: To provide initial validation for the Traumatic Attachments Inventory (TAI), a new screening measure assessing victimization by domestic partners.

Methods: A total of 121 items were written by the author reflecting experiences described in the partner violence literature. All items were written in gender-neutral language and introduced by instructions asking subjects about their current sexual partner or most significant recent partner. This pilot version of the scale was given to 234 subjects at three sites: a community-based sample of 87 male and 51 female substance abusers, a general psychiatric sample of 21 male and 62 female patients, and a shelter-based sample of 13 female domestic violence victims. Exploratory and confirmatory factor analyses were then performed using EQS.

Results: A six-factor solution involving 34 items was found to be optimal: I. Partner drug and alcohol problems (6 items). II. Sexual assault (5 items), III. Warmth and affection (6 items), IV. Physical assault (5 items), V. Physical fights (4 items), and VI. Emotional assault (8 items). Fit indices for the confirmatory model were good for both male and female subjects (females: Sandor-Bentler $x^2 = 703.24/509$ df, Robust Comparative Fit Index = .93, males: $x^2 = 623.50/509$ df, RCFI = .90).

Conclusions: These preliminary findings support the validity of the TAI as a screening measure for a broad range of domestic victimization experiences. Ongoing research investigating the reliability and validity of the scale will be discussed.

NR348 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Serotonin Response to Trauma and Axis II Disorders

David P. Bernstein, Ph.D., Department of Psychiatry, Mt. Sinai Hospital, 130 West Kingsbridge Road, Bronx NY 10468; Larry J. Siever, M.D., Rachel Yehuda, Ph.D., Robert A. Grossman, M.D.

Summary:

There is increasing evidence that childhood trauma can produce lasting changes in both biology and behavior. However, little is known about the impact of different types of trauma (e.g., abuse versus neglect) on neurobiological function or the degree to which such biological alterations underlie the psychological effects of maltreatment. In this study, we examined the relationship between childhood trauma and the cortisol response to fenfluramine, a marker of serotonergic (5-HT) activity, in 30 personality disordered patients (male, N = 20, female, N = 10). Patients' maltreatment histories were assessed by the Childhood Trauma Questionnaire (CTQ), a reliable and valid retrospective measure of child abuse and neglect. DSM-III-R personality disorders were determined by the SIDP interview. The peak cortisol response to fenfluramine challenge was positively associated with emotional neglect scores on the CTQ ($r = .45$, $p = .01$), but inversely associated with sexual abuse scores ($r = -.34$, $P = .07$). When emotional neglect and sexual abuse were partialled from each other, their respective relationships with peak cortisol were strengthened: emotional neglect partialling sexual abuse, $r = .50$, $p < .01$, sexual abuse partialling emotional neglect, $r = -.41$, $p < .05$. Cluster analysis revealed that the patients could be classified into three groups, defined by histories of childhood trauma, peak cortisol levels, and gender; the three clusters also differed in their personality disorder symptoms. These findings suggest that personality disorders may be associated with distinct patterns of biologic response to childhood trauma.

NR349 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Physiological Response to Trauma and Subsequent PTSD: A Prospective Study

Arieh Y. Shalev, M.D., Department of Psychiatry, Hadassah University, PO Box 12000, Jerusalem 91120, Israel; Tali Sahar, M.A., Sara Freedman, M.A., Tuvia Peri, Natali Glick, M.D., Dalia Brandes, Scott P. Orr, Ph.D., Roger K. Pitman, M.D.

Summary:

Objective: This study prospectively examined the relationship between heart rate (HR) and blood pressure (BP), recorded immediately following a traumatic event, and the subsequent development of post-traumatic stress disorder (PTSD).

Method: Eighty-six trauma survivors who were admitted to an emergency room (ER) of a general hospital were followed for four months. HR and BP were recorded in the ER. HR, anxiety, depression, and PTSD symptoms were assessed one week, one month, and four months later. The Clinician-Administered PTSD Scale defined PTSD status at four months.

Results: Twenty subjects (23.3%) met PTSD diagnostic criteria at the four-month assessment (PTSD group), and 66 (76.7%) did not (non-PTSD). Subjects who developed PTSD had higher HR levels at the ER (95.5 ± 13.9 (SD) vs. 83.3 ± 10.9 beats per minute (BPM)), $t = 4.4$, $p < 0.001$) and one week later (77.8 ± 11.9 vs. 72.0 ± 9.5 BPM, $t = 2.25$, $p < 0.03$). The groups did not differ in one- and four-months HR, nor in initial BP. Repeated measures ANOVA for HR showed a significant group effect ($p. < 0.02$), a significant time effect ($p < .0001$), and a significant group by time interaction ($p < 0.0001$). Time and group by time interaction remained significant when adjusted for the effects of age, trauma severity, immediate response, and peri-traumatic dissociation.

Conclusion: Elevated heart rate, shortly after trauma, predicts the later development of PTSD. The role of peripheral adrenergic activation and interactions among stress hormones after trauma should be further explored.

NR350 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Children as Homicide Victims in Homicide-Suicide Events

Maria D.D. Llorente, M.D., Department of Psychiatry, University of Miami, 1201 NW 16th Street, Miami FL 33125; Donna Cohen, Ph.D., Carl Eisdorfer, M.D., Maria A. Gadia, M.D.

Summary:

Introduction: Homicide-suicide(H/S) events are devastating and particularly tragic when the homicide victim is a child or adolescent. This study evaluates H/S events that involved victims aged 19 or younger, identifies risk factors, and describes antecedent motivations.

Methods: Records of medical examiners' offices from four Florida districts (population = 4 million) were reviewed (1988–94) and 161 H/S events were identified; 18 (11%) involved victims under age 19. Data gathered included demographic information, investigative reports, autopsy/toxicology results, hospital/criminal records, news accounts, and suicide notes. Frequency distributions were calculated.

Results: For victims aged 3-12, 72.7% were Hispanic, 54.5% were female, 57.1% of the perpetrators were depressed, and 81.8% were precipitated by divorce/custody. For those aged 13–19, 45.5% were Hispanic, 81.8% were female, 60% of perpetrators had histories of verbal discord, and 63.6% involved an amorous relationship. One hundred percent of victims were killed by gunshot wound; 89% of perpetrators were male.

Conclusions: "Subtypes" of H/S events occur and age of victim is useful for classification schemes. Pre-teens are more likely to be killed by a depressed father involved in an ongoing divorce/custody dispute. Teen H/S more often involve a female who is killed by an enamored male with previous verbal discord. Hispanic youngsters appear to be at particular risk.

NR351 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Neuroleptics in Nursing Homes: Outcome of Discontinuation

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Summary:

Introduction: OBRA-87 mandates that physicians periodically attempt to discontinue neuroleptics in nursing home residents (NH), if possible, although little is known about the clinical outcome. This study sought to: longitudinally determine prevalence of neuroleptic discontinuation, examine factors that maintain drug-free status, and determine use of other psychotropic drugs.

Methods: Records of all residents taking neuroleptics in nine nursing homes were reviewed at baseline, 6 months (T2) and 12 months (T3). Residents whose neuroleptics had been discontinued at T2 were re-examined at T3 and information recorded regarding all medications initiated, reasons for use of psychotropic drugs, and patient disposition.

Results: Of 240 residents on neuroleptics at baseline, 64 (26.7%) neuroleptic drug discontinuations had occurred by T2. At 12 months, 17 residents (60% female) remained free of psychotropic medications; another 20 were off neuroleptics but on other psychotropics, most commonly lorazepam (80%). Twenty-seven residents (42%) were restarted on neuroleptics, most commonly for recurrence of delusions (14).

Conclusions: Most (73%) NH residents taken off antipsychotic drugs will be back on psychotropic medication within six months, with almost half back on neuroleptics for recurrence of psychotic symptoms, usually delusions. Lorazepam is the non-neuroleptic psychotropic most used. Female residents are more likely than males to remain drug-free.

NR352 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Psychosocial Stressors Among Homeless Children: Relationship to Child Mental Health Problems

Bonnie T. Zima, M.D., Department of Psychiatry, UCLA-NPI, 300 Medical Plaza, Box 956967, Los Angeles CA 90095; Regina Bussing, M.D., Marina Bystritsky, M.A., Barbara J. Genovese, M.A., Thomas R. Belin, Ph.D.

Summary:

Objective: The purpose of this study was to describe the level of exposure to severe psychosocial stressors among sheltered school-age homeless children and the relationship of stressors to child mental health problems.

Methods: A cross-sectional study of 169 sheltered homeless children, age 6–12 years, in Los Angeles County.

Results: Almost one-half (N = 77;49%) of children had been a victim or witness to serious violence; 12% (N = 19) had experienced either a death of a parent or sibling, 49% (N = 77) had parents who were divorced or separated, 35% (N = 55) had been separated (> 1 wk) from their mother, and 8% (N = 13) had been in foster care. White children were more likely to be a victim or witness to violence than children from minority backgrounds ($p = .02$) and older children were more likely to be a victim of violence ($p = .003$). Children who had been a witness to violence were more likely to screen positive for major depression ($p = .05$).

Conclusion: School-age sheltered homeless children were exposed to a disproportionately high level of severe psychosocial stressors; among these stressors, being a witness to violence was related to having symptoms of major depression. Psychiatric evaluation of homeless children should include inquiry into stressful lifetime events.

NR353 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Childhood Maltreatment in Psychiatric Inpatients

Taruna Ahluvalia, M.A., Department of Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; David L. Pogge, Ph.D., David P. Bernstein, Ph.D., Susan R. Borgaro, M.A., John M. Stokes, Ph.D.

Summary:

Objective: Most studies on child abuse have used reports of specific abusive events in defining maltreatment, rather than self-perception of having been abused. This study examines whether subjects' recall of specific abusive events (i.e., historical reports) concurs with their perception of having been maltreated (i.e., judgments), and also whether or not historical and judgment reports differentially relate to symptomatology.

Method: The Childhood Trauma Questionnaire (CTQ) and the Youth Self-Report (YSR) were completed by 179 adolescent inpatients. Historical and judgment items on the CTQ were correlated separately for physical, sexual, and emotional abuse, and physical neglect. Stepwise regressions were computed to predict historical and judgment reports of each type of maltreatment from the YSR symptom scales.

Results: Correlations between historical and judgment items ranged from .52 to .86. Different symptoms were found to predict judgments of abuse vs. maltreatment.

Conclusions: Results indicate that history and judgment reports are neither identical nor associated with the same types of symptoms. This suggests the need to distinguish between these two classes of self-report in future research on child maltreatment.

NR354 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Violently Injured Patients and the Development of PTSD

Sheila J. Eaton, Ph.D., Department of Psychiatry, Wayne State, 4201 St. Antoine Boulevard, Detroit MI 48202; John D. Mesaros, M.D., Shiyoko Slate, B.A., Manuel E. Tancer, M.D., Thomas W. Uhde, M.D.

Summary:

Objective: Violence is a significant precursor of psychological distress. In this study, we examined the relationships between violent injury, victim characteristics, initial distress, and the development of post-traumatic stress disorder (PTSD).

Method: Forty-six patients (ages 16-30) hospitalized for medical treatment of gunshot or stab wounds participated. Patients with preexistent psychiatric or substance dependency determined by structured interview were excluded. Post-admission, one-month, and four-month follow-up assessments were completed for 27 subjects. Primary outcome measures included the Impact of Events Scale (IES), the Stanford Life Events Scale (SLE), and a behavior checklist of stress response symptoms (BCL).

Results: This pilot study found that 16 of the 27 (59%) who followed-up developed PTSD. Assessments yielded the following:

	Baseline	One Month	Four Month
IES	27.4 ± 14.6	30.1 ± 19.3	32.7 ± 18.4
SLE	4.3 ± 1.7	3.6 ± 1.0	4.9 ± 1.8
BCL	17.0 ± 12.1	26.9 ± 17.6	33.0 ± 24.0

Utilizing a logistic regression model, baseline scores on the above measures classified subjects who developed PTSD with 70% accuracy.

Conclusions: In this violently injured population without prior trauma and substance dependency, there was an incidence of 59% PTSD that was accurately predicted 70% of the time by initial scores on three brief and readily administered instruments.

NR355 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Cost of Incidents of Aggression in a Large Metropolitan State Hospital

Mohammed Y. Alam, M.D., Department of Psychiatry, University of Chicago, 5841 S Maryland Avenue/MC 3077, Chicago IL 60637; Asif A. Aleem, Daniel J. Luchins, M.D., Patricia Hanrahan, Ph.D.

Summary:

There has been no research on total financial cost of incidents of aggression among psychiatric inpatients. The purpose of the study was to estimate direct public cost of incidents of aggression in a large state hospital through cost accounting of services utilized for incidents of aggression in one year.

Sample: All patients hospitalized at Elgin Mental Health Center, 1/1/93 - 12/31/1993; average daily census was 650.

Measures: Direct public cost of staff time estimated by multiplying staff time involved in dealing with aggression incidents by their wage rates for activities such as 1:1 observation, mechanical restraints, and psychopharmacology consultations. Workers' compensation for staff who were injured by patients was calculated.

Results: Overall costs for aggression were substantial at $313,831 in 1993 dollars. Largest costs were due to constant observation, at $156,156, followed by restraints at $99,717. Workers' compensation costs totaled $30,676. Security costs were considerable at $22,273. Remaining costs included $2,749 for psychopharmacology consultations and $2,259 for clinical advisory meetings. Costs will be reported for subgroups, forensic versus nonforensic, diagnostic groups, and acute versus chronic units.

Conclusion: Aggression has important economic implications for state mental hospitals. Developing better treatments for aggression should be a major priority. Research is needed on assessing other costs of aggression, such as longer hospitalizations, increased admissions, and need for higher staff ratios.

NR356 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Valproate in Impulsivity and Violent Behavior in a Psychiatric Emergency Hospital

Luis D. Mosca, M.D., Emergency, Hospital Alvear, Juan Bautista Alberdi 6952, Buenos Aires 1440, Argentina; Jorge L. Coppola, M.D., Juan P. Licciardo, M.D.

Summary:

Objective: Valproate is a well established mood stabilizer and anticonvulsant drug that has been used in behavior disorder and aggression in the last years. In this six-month study, we wanted to determine the efficacy of valproate in impulsivity and violent behavior.

Method: Forty inpatients with impulsivity and violent behavior were scored with the Modified Overt Aggression Scale (MOAS). Subjects were administered valproate at dosages ranging from 15-25 mg/kg during six months and were evaluated once a week using MOAS.

Results: Repeated measures MOAS revealed significant reductions in the frequency of aggressive episodes during valproate treatment.

Conclusions: Our results revealed that valproate is effective in treating aggression. Moreover, this treatment appears to be well tolerated and economical.

NR357 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Psychophysiologic Assessment of Breast Cancer Patients and Witnesses

Douglas M. Lanes, M.D., Department of Psychiatry, Harvard Medical School, 228 Maple Street, 2nd Floor, Manchester NH 03103; Stephanie K. Williston, M.S.Ed., Scott P. Orr, Ph.D., Roger K. Pitman, M.D.

Summary:

Objective: We evaluated post-traumatic stress disorder (PTSD) in breast cancer patients approximately one year following tissue diagnosis, and their primary witnesses (significant others), including psychophysiologic responses during mental imagery of their experiences with breast cancer.

Method: Participants were diagnosed by means of the Clinician-Administered PTSD Scale. They then underwent script-driven imagery of their breast cancer experiences, while heart rate, skin conductance, and frontalis and corrugator facial electromyograms were recorded. A physiologic discriminant function derived from the responses of previously published PTSD and non-PTSD comparison groups was used to classify participants.

Results: Of 34 breast cancer patients studied to date, 1 (a physiologic responder) met DSM-IV criteria for current PTSD related to her breast cancer experience; 6 (1 physiologic responder, 5 nonresponders) met DSM-IV criteria for past breast cancer-related PTSD. Of 28 witnesses, 1 (a physiologic nonresponder) met DSM-IV criteria for current PTSD; 6 (2 physiologic responders, 4 nonresponders) met DSM-IV criteria for past PTSD.

Conclusions: Results to date suggest that the incidence of active, physiologically responsive breast cancer-related PTSD is relatively low.

References:

1. Pitman RK, Orr SP, Forgue DF, de Jong JB, Claiborn JM. Psychophysiologic assessment of post-traumatic stress disorder imagery in Vietnam combat veterans. *Archives of General Psychiatry* 1987;44:970-975.

2. Orr SP. An overview of psychophysiological studies of PTSD. *PTSD Research Quarterly* 1994;5:1-7.

NR358 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Serotonin-Related Genes and Impulsive Aggression in Personality Disorders

Antonia S. New, M.D., Department of Psychiatry, Mt. Sinai/ Bronx VAMC, Box 116A, 130 West Kingsbridge Road, Bronx NY 10468; Joel Gelernter, M.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

Summary:

Polymorphisms in human genes involved in serotonin functioning have been identified, including tryptophan hydroxylase (TPH) (Nielsen et al, 1994) and the serotonin transporter gene (SLC6A4; Lesch et al, 1994; Heils et al, 1996).

TPH: The "L" allele of a biallelic polymorphism in the TPH gene has been associated with reduced CSF 5-HIAA concentrations and a history of suicide attempts (Nielsen et al, 1994). Our preliminary data suggest that the "LL" genotype is associated with higher total scores on the Buss-Durkee Hostility Inventory (BDHI) in Caucasian personality disorder patients (45.3 ± 9.8) compared to those with the "UL" or "UU" genotypes (32.9 ± 13.5; t – 2.38, df = 19; $p < .03$) in males but not in females.

SLC6A4: Two polymorphisms in the serotonin transporter gene have been identified: 1) an intronic polymorphism with frequent variants of the allele with 10 or 12 copies of a 17 base repeat, and 2) a polymorphism coding for long or short promotor region with functional significance. Our data suggest relationships between SLC6A4 genotype (intronic and promotor) and impulsive aggression, as well as anxiety-related personality traits. Specifically, an association between the 10 repeat allele of SLC6A4-intronic and the short promotor allele measures are both associated with impulsivity and risk aversion behavior in Caucasian patients with personality disorders.

The identification of genes associated with impulsive aggression could elucidate specific mechanisms involved in these behaviors and lead to the development of new treatment strategies.

NR359 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Gulf Veterans Seeking Department of Defense Care: Relationship to Gender, Absenteeism and Combat Stressors

Charles C. Engel, Jr., M.D., Department of Psychiatry, Uniformed Services, 4301 Jones Bridge Road, Bethesda MD 20814; Robert J. Ursano, M.D., Charles D. Magruder, M.D.

Summary:

In 1994 the Department of Defense (DoD) initiated the Comprehensive Clinical Evaluation Program (CCEP) for Gulf War (GW) veterans with war-related health concerns. This study evaluates the relationship of ICD-9 psychological conditions to gender and occupational impairment and the relationship of combat stressors to psychological conditions among the first 9,798 veterans participating in CCEP. Phase I of CCEP included a thorough primary care assessment. Intensive specialty care assessment (Phase II) was prescribed based on clinical need and included a SCID-NP and Clinical Assessment for PTSD Scale. Nineteen percent of veterans received a psychological condition as a primary diagnosis; 37% had a psychological condition among their diagnoses. The most common diagnoses were depression and anxiety disorders. A total of 11.8% of participants were diagnosed with tension headache, 5.3% with PTSD, and 2.1% with somatization disorder. Psychological conditions were more common among Phase I/II than Phase I only participants, equally common for men and women, and related to increased lost work days. Combat stressors were related to number of psychological conditions and PTSD. Mental disorders are common among Gulf War veterans in CCEP and associated with significant morbidity. Controlled comparisons of Gulf War veterans to civilians and non-deployed Gulf War era veterans are needed.

NR360 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Examination of Family Environment Characteristics Among Couples Involved in Abusive Relationships

Charles D. Magruder, M.D., Clinical Services, DoD HA, 2009 Alabaster Drive, Silver Spring MD 20904; Phuong Colquett, M.A., David Cowan, Ph.D., Robert Mays, Ph.D.

Summary:

Objective: Spouse abuse is a serious public health problem for which the epidemiologic characteristics and possible risk factors need elucidation. This study assesses family environment characteristics among couples involved in abusive relationships in comparison to couples who indicate no signs of abuse.

Methods: Couples in substantiated, abusive relationships, as defined by established protocols, were asked to participate. Control couples, matched by age, ethnicity, and socioeconomic status, were recruited after participation in a primary care spouse abuse screening program. Each partner completed the Family Environment Scale (FES), which has nine subscales. The Mann-Whitney U was used to test for differences.

Results: To this point, 44 case and 18 control couples have participated. Among case couples, no significant incongruence was found between male and female perceptions of the family environment. Women from control couples perceived more conflict in the relationship than males ($p = 0.02$). Many differences were found in comparing men and women from abusive relationships to controls. Men in abusive relationships were more likely to state rules and procedures are used to run family life ($p = 0.04$) and less prone to emphasize ethical issues ($p = 0.01$).

Conclusions: Couples in abusive relationships exhibit different family environment characteristics than other couples. Some of these may result in predisposition to violence.

NR361 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

An Examination of Stress and Social Resources Among Abusive and Non-Abusive Couples in a Military Population

Phuong Colquett, M.A., Birch and Davis, 5205 Leesburg Pike, #300, Falls Church VA 22041; Charles D. Magruder, M.D., David Cowan, Ph.D., Robert Mays, Ph.D.

Summary:

A number of studies suggest that stress is associated with marital discord and violence. Further, various studies indicate that social support can serve as protection from the negative effects of stress and low self-esteem, two factors related to spouse abuse. This study determines the extent to which stressors and social resources are related to couples' involvement in abusive situations.

Method: Couples in substantiated, abusive relationships, as defined by military protocols, and couples free of abuse, as determined by a screening program, were asked to complete the Life Stressors and Social Resources Inventory (LISRES).

Results: A total of 44 case couples and 18 control couples agreed to participate in the study. Using independent samples t-tests and taking into account covariants such as race, age, pay rank and education level, case couples reported significantly ($p < .05$) higher levels of stress related to family and spouse. However, they experienced significantly lower levels of social resources including those related to friends, family, and spouse support.

Conclusions: The compounded effects of high stress and low social support are likely to play a strong part in abuse in relationships. More extensive examination of stress/resources should be considered for spouse abuse.

NR362 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Terrorism in Oklahoma City: Predictors of Distress

Phebe M. Tucker, M.D., Department of Psychiatry, University of Oklahoma, 920 Stanton L. Young Blvd, Oklahoma City OK 73190; Warren Dixon, Ph.D., Gwen Allen, M.S.W., Betty Pfefferbaum, M.D., Sara Jo Nixon, Ph.D., Amar N. Bhandary, M.D.

Summary:

Objective: Risk factors for developing post-traumatic stress symptoms are explored for community members seeking help six months after Oklahoma City's 1995 terrorist bombing.

Methods: Eighty-six adults evaluated for bombing-related distress were surveyed for demographics, exposure, grief symptoms, peri-traumatic reactions (PRPLT) reported retrospectively, current distress (Impact of Events Scale, IES), and coping. To identify immediate reactions predictive of later distress, individual and total PRPLT scores were correlated with total IES scores using Pearson Correlation Coefficient, significant at $P < 0.05$. Additionally, low, middle, and high scoring groups on IES were compared for exposure and coping items to identify those endorsed more frequently by highly distressed (IES); items were flagged when high and low IES scorers differed by more than 40%.

Results: Immediate bombing responses predictive of high distress on the IES were total averaged PRPLT score ($R = 0.59$); four anxiety symptoms (being nervous [$R = 0.56$], trembling [$R = 0.41$], heart beating fast [$R = 0.41$], fearful for family [$R = 0.40$]), and one dissociative symptom ("on automatic pilot" [$R = 0.42$]). High IES scorers were distinguished from low scorers by being strongly exposed to the blast, injuries, or disaster scene; by experiencing more difficulty functioning; by finding counseling helpful; and by increasing consumption of alcohol and tobacco.

Conclusion: This study points to greater exposure and higher peri-traumatic anxiety and dissociation as predictive of later distress in this population seeking help, consistent with other disaster studies. Results point to unhealthy coping styles in some who are highly distressed. Implications for disaster planning are discussed.

NR363 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Psychiatric Consequences of Ethnic Cleansing: One Year After Resettlement

Dolores Vojvoda, M.D., Department of Psychiatry, Yale University, 950 Campbell/VACHS W.H. Campus, West Haven CT 06516; Stevan M. Weine, M.D., Daniel F. Becker, M.D., Leslie Hyman, M.S.W., Dori Laub, M.D., Steven Lazrove, M.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To describe the trauma-related symptoms in a group of Bosnian refugees resettled in Connecticut, one year after initial assessment.

Method: Shortly after their arrival in the U.S. 34 refugees received standardized assessments and testimony interviews by clinicians at the Traumatic Stress Clinic at the Yale Psychiatric Institute. The same 34 Bosnian refugees participated in follow-up assessments one year later.

Results: Fifteen (44.1%) refugees fulfilled the criteria for PTSD at follow-up (this compares with 73.5% at baseline). At follow-up the average PTSD severity score was 12.5 (this compares with 20.6 at baseline). There were no new PTSD cases. Older age was associated with more frequent diagnosis of PTSD and higher PTSD symptom severity. High level of trauma exposure was not correlated with PTSD diagnosis. At follow-up reexperiencing cluster symptoms were present more frequently than on baseline, while avoidance and hyperarousal cluster symptoms decreased in frequency when compared to baseline.

Conclusions: The level of PTSD diagnosis and symptoms remains significant even after one year, though with notable overall decreases. The older refugees appear to be more vulnerable to PTSD, which can be understood in relation to the developmental context of middle and older adulthood.

NR364 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Relationships and Psychiatric Disorders

Robert Kohn, M.D., Department of Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Caron Zlotnick, Ph.D., Gabor I. Keitner, M.D.

Summary:

Objective: The aim of this study was to investigate the relationship between the quality of interpersonal relationships across a range of psychiatric disorders in a community sample. This study examined whether individuals who had a psychiatric disorder within the last 12 months reported fewer positive interactions and/or more negative interactions with their spouse, friends, and relatives compared to those individuals without a lifetime or current disorder.

Methods: Using data from the National Comorbidity Study, diagnoses were obtained using the CIDI diagnostic interview. A 31-item interview measured the respondents' perceptions of their positive and negative interactions with spouse, friends, and relatives.

Results: Logistic regressions showed that, compared to no psychiatric disorder, psychiatric disorders were significantly related to fewer positive and more negative interactions with spouse, relatives, and friends, controlling for demographic variables. Logistic regressions, controlling for demographic variables, found that negative interactions with relatives had the strongest relationship to each of the psychiatric disorders compared to no psychiatric disorders in both married and single persons. Another consistent finding was a significant improvement in the quality of the marital relationships as a function of the amount of time lapsed since the last episode. The presence of comorbidity was unrelated to the quality of interpersonal relationships. These findings were replicated in both treatment-seeking and nontreatment-seeking individuals.

Conclusion: Poor interpersonal relationships are associated with psychiatric illness rather than with a specific type of psychiatric disorder.

NR365 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Epidemiological Study of ADHD in an Egyptian Sample

Mohamed H. Ghanem, M.D., Department of Psychiatry, Ain Shams University, Faculty of Medicine, Cairo Abbassia 00097, Egypt; Maissa N. Farid, M.D., Hayam K. Nazif, M.D., Nancy I. Abu-El-Maaty, M.D.

Summary:

The aim of this study is to estimate the prevalence of attention deficit hyperactivity disorder (ADHD) and its comorbidity in Egyptian children.

Screening of ADHD by observation and Du Paul test was conducted on 3,880 school children aged 5 to 11 years at Heliopolis district, Cairo, Egypt. DSM-IV criteria were used in confirmation of ADHD diagnosis and different disorders comorbid with ADHD.

The prevalence of ADHD is 6.1%. It is 8% in boys and 3.3% in girls. The prevalence of ADHD increased progressively with age to reach a peak of 9.6% at 9 and decreased abruptly to 2.9% at 10. Half of both boys and girls have the combined type. The predominant hyperactivity type is more common in boys while the inattention type is more common in girls. The highest distribution of ADHD is in lower social class. A total of 83% of ADHD children are the first-born child; 70.5% are from large families. Only 11.5% of ADHD children have no comorbidity. The highest disorder comorbid with ADHD is learning disorder (78.7%) followed by 70.5% nocturnal enuresis, 49.5% oppositional defiant disorder, 35% conduct disorder, 26% anxiety disorder, and 22% depressive disorder.

Thus, it is concluded that ADHD is a common problem that affects school children that might be accompanied by several psychiatric disorders the most important of which is learning disability.

NR366 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Prevalence of PTSD in a Community Sample of Older Adolescents

Steven P. Cuffe, M.D., Neuropsychiatry, USC School of Medicine, PO Box 202, Columbia SC 29202; Cheryl L. Addy, Ph.D., Carol Z. Garrison, Ph.D., Jennifer L. Waller, Ph.D., Kirby L. Jackson, A.B., Robert E. McKeown, Ph.D.

Summary:

Recent research shows exposure to trauma is common among youth. The need for researching the impact of trauma and identifying risk factors for being traumatized and developing PTSD is critical. Occurrence and predictors of PTSD in a community-based sample of 490 older adolescents are described. These data are part of a longitudinal study of adolescent depression. Most subjects were ages 16 to 19 and living independently at the time of interview. Sexual abuse was the most commonly reported traumatic event among black and white females, while white males reported witnessing an accident or medical emergency and black males reported witnessing a crime most often. The most commonly reported PTSD symptoms were distressing recollections, avoidance of thoughts, feelings or activities that arouse recollections, irritability/anger, and hypervigilance. Rates of PTSD ranged from 0.3% for white males and 0.8% for black males to 2.9% for black females and 3.5% for white females. Weighted logistic regression analyses identified gender (OR = 22.9), childhood sexual abuse (OR = 4.8), and nontraumatic undesirable life events in the past year (OR = 1.2) as significant predictors of PTSD. Certain types of traumatic events are more predictive of PTSD. Furthermore, the type of trauma varies by sex and race, and prevalence of PTSD varies by sex.

NR367 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Use of the Beck Depression Inventory with French Children

Fabien Durif, M.D., Department of Psychiatry, Hopital Purpan, Place Du Docteur-Baylac, Toulouse 31059, France; Veronique Gentil, M.D., Jean P. Raynaud, Ph.D., Laurent Schmitt, M.D.

Summary:

Objective: To investigate by using the Beck Depression Inventory the incidence of depression in a French adolescent population and to compare results with previous studies of Canadian and American adolescents.

Method: A total of 573 adolescents (282 girls, 291 boys) from a high school, aged from 12 to 19 years completed the full version of the BDI.

Results: The mean score of the total sample is 10.7 (9.1 for boys, 12.3 for girls, $p < 0.01$); 51.2% of the subjects (42.1% of boys, 63.6% of girls) scored above the adult cut-off point for "mild depression", 34.8% were "mildly depressed", 11% "moderately depressed" and 5.4% "severely depressed". Older children obtained higher mean scores (11.5 at 18 years against 9.9 at 12 years $p < 0.01$).

Discussion: Girls and older children tended to have higher mean scores, which confirm Albert & Beck (1975). Whereas for Teri (1982) and Kaplan (1984) sex and age have no significant effects. Incidence of depression (51.2%) corresponds to previous studies, but a large majority of our sample express only depressed mood. However, the incidence of high depression (5.4%) corresponds to the adolescent or adult studies using the BDI or other scales. Although incidence of French adolescent depression (51.2%) is higher than Canadian (39%) (Albert & Beck) or American (49%) (Teri, 1982) incidences, further studies are needed to confirm and explain these differences.

NR368 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Enhancing the Effects of Acupuncture Detoxification with Clonidine in Acute Heroin Withdrawals

Cheng-Jen Chen, M.D., Department of Psychiatry, East Orange VAMC, Tremont Street, East Orange NJ 07019; Alexander Babayants, M.D.

Summary:

Objective: In our previous study we found a special technique of acupuncture that can acomplish detoxification of acute heroin withdrawals with only one treatment. However, this technique has its limitations and is best indicated in mild to moderate abusers. In order to understand whether the combination of medications and acupuncture can further improve the therapeutic effects of acupuncture detoxification, we conducted the following study at our inpatient psychiatric unit.

Method: Nine consecutively admitted heroin addicts were given clonidine 0.1–0.2mg p.o. qid for three days and one acupuncture treatment. Acupuncture detoxification procedure was performed within 24 hours after patient's admission. Nine carefully matched control subjects were only treated with acupuncture—once for each patient—without receiving any clonidine during the three-day observation period.

Results: Age (40.88 ± 4.43 vs 38.33 ± 3.28 y/o), longevity of heroin dependence (15.44 ± 7.76 vs 14.88 ± 8.21 ys), amount of daily dosage (5.00 ± 3.24 vs 5.00 ± 3.24 bags), and withdrawal symptoms before treatment (11.67 ± 5.10 vs 10.11 ± 6.51) were not significantly different between the study group and the control group. However, the residual symptoms immediately after treatment (2.33 ± 1.66 vs 5.22 ± 6.14) and the drop-out rate (22.2% vs 55.6%) were significantly different.

Conclusions: In this study we found that clonidine can enhance a patient's immediate response to acupuncture detoxification for acute heroin withdrawals. It also can decrease patients' drop-out rate during the course of treatment.

NR369 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Seasonal Variation in Bipolar Disorder in Appalachia

Hazel E.A. McBride, Ph.D., Department of Psychology, ARH Psychiatric Center, 102 Medical Center Drive, Hazard KY

41701; Geoffrey S. Duckworth, M.D., Joselito B. Morales, M.D., Roy S. Price, M.S.W.

Summary:

Objective: Seasonal variation has been observed in both depression and mania. The Appalachian region is a distinct subculture with geographic isolation, cultural differences, and consanguinity, all contributing to patterns of mental illness. This study examines climatic factors affecting hospitalization.

Method: The sample consists of all admissions from 1994 to 1995 to the ARH Psychiatric Center in Hazard, which serves 21 counties in eastern Kentucky. The admission diagnoses (from DSM-IV) were compared by season using Chi-square analysis and to mean hours of daylight and to solar radiation using Kendall's coefficient of rank correlation.

Results: Monthly rates of admission for bipolar disorders showed a significant seasonal variation with admission for bipolar disorders being more frequent in the spring and summer and lower in the fall and winter ($p = .0001$). Mean monthly admission figures were also found to be significantly correlated to hours of daylight ($p = .05$) and almost significantly to solar radiation. The correlation rates of depression and all other disorders were not significant.

Conclusions: The positive correlation of bipolar admissions both to season and mean daylight hours supports the theory that manic patients are supersensitive to light. Further research is needed to clarify the pathophysiological mechanisms underlying this association.

NR370 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Memory and Physostigmine in Personality Disorders

Andrea Bergman, Ph.D., Department of Psychology, St. Johns University, 8000 Utopia Parkway, Jamaica NY 11439; Philip D. Harvey, Ph.D., Harold W. Koenigsberg, M.D., Bonnie J. Steinberg, M.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

Summary:

Affective instability characterizes some personality disorders (PD) and may affect the recall of emotionally charged information, particularly during periods of intense affect. Affective responses to cholinergic challenge indicate that increases in depression following physostigmine infusion are associated with affective instability and borderline personality disorder (BPD).

Objective: Based on theories of mood congruent memory, we hypothesize that PD patients, particularly BPD patients, will remember more negative words after randomized physostigmine (0.014 mg/kg intravenous infusion) versus placebo infusion.

Methods: Following infusion, a word list learning task is administered involving five presentations of an 18-item list (6 positive, 6 negative, and 6 neutral valence words).

Results: Preliminary results indicated that, on Trial 5, PD patients ($n = 7$) recalled significantly ($p < .05$) more negative words ($M = 4.86$, $SD = .69$) and more positive words ($M = 4.57$, $SD = .79$) with physostigmine versus placebo ($M = 4.14$, $SD = .38$ and $M = 3.71$, $SD = .95$, respectively); the analysis with neutral words was not significant. A subgroup of BPD patients remembered more negative words under physostigmine than other (nonborderline) personality disorder patients, although the samples were too small for statistical analysis.

Conclusions: These preliminary data raise the possibility that PD patients remember more affectively laden words with physostigmine. These results will be updated in a larger sample and implications for theories and treatments of PD, particularly BPD, will be discussed.

NR371 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Treatment Influence on Axis I and Axis II Disorders

Laura Ferrando, Principe De Vergara 120 6D, Madrid 28002, Spain; Emmanuelle Weiller, Julio Bobes, M.D., J. Gibert, G. Saiz, Y. Lecrubier

Summary:

The main objective of this study was to assess the evolution of Axis II disorders in patients with Axis I disorders after a 10-week antidepressive treatment.

Fourty-six outpatients of both sexes aged 18 to 65 were included in this study. The main Axis I diagnoses obtained with a brief diagnostic structured interview (MINI, *Sheehan et al 1995*) were the following: major depressive episode ($n = 21$), dysthymia ($n = 10$), panic disorder ($n = 3$), any phobic disorder ($n = 9$), and generalized anxiety disorder ($n = 3$).

Among patients with Axis I disorders, 82.6% presented an Axis II disorder as assessed with the SCID-II (Cluster A: 43.5%; Cluster B: 39.1%; Cluster C: 65.2%). Additionally, substantial comorbidity between Axis II disorders was observed. After 10 weeks of antidepressant treatment (fluoxetine 20–40 mg or moclobemide 300–600 mg, flexible dosage) 67.4% of patients had no more Axis I diagnosis and 28.9% had no more Axis II disorder. Among "responders" on Axis I ($n = 31$), the mean number of positive items on the SCID-II significantly decreased for all Axis II disorders except for obsessive-compulsive, histrionic, and narcissistic personality. On the contrary, no significant change on the mean number of positive items was observed in patients who did not improve on Axis I ($n = 15$).

The high frequency of Axis II disorders we observed in patients with Axis I disorders raises the need to better study the relation between Axis I and Axis II disorders. Our findings suggest that most Axis II disorders comorbid with Axis I disorders may not be stable and may be improved by psychotropic treatment.

NR372 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Stability of Personality Disorders with Treatment for Chronic Depression

Robert M.A. Hirschfeld, M.D., Department of Psychiatry, University of Texas, 301 University Boulevard, Galveston TX 77555–0429; James P. McCullough, Ph.D., James M. Russell, M.D., Martin B. Keller, M.D.

Summary:

This study investigated the stability of personality disorders in a sample of patients with chronic and double depression who were adequately treated with pharmacotherapy. The specific questions included:

(1) Does the presence of a personality disorder predict a poor response to pharmacotherapy in chronic and double depression?
(2) Are independent assessments of the presence of DSM-III-R personality disorders stable over six months?
(3) Does successful response to pharmacotherapy for chronic depression result in improvement of comorbid personality disorders as well?

The data for this investigation came from the Chronic and Double Depression Maintenance Study, a ten-site collaborative program involving acute, continuation, and maintenance treatment with sertraline or imipramine in patients with chronic or double depression. Of these ten centers involved in the study, six participated in this investigation and contributed a total of 123 patients. Assessments were made of personality disorders using the SCID II, at: baseline, week 24 (test/retest, reflective of previous year), and week 28 (reflective of past month). Assessment at week 28 was to observe whether the features of personality disorder would improve concomitantly with those of successfully treated depression.

Results:
(1) There was no difference in response rates among those with chronic depression or those with double depression on the basis of having a personality disorder or not.
(2) When personality disorders were clustered or looked at individually, the results did not change. With regard to the test-retest (24 weeks) Kappa scores were modest: .42 for any personality disorder and .29, .57, and .42 for cluster A, cluster B, cluster C, respectively.
(3) 62% of those who responded positively to pharmacotherapy for depression *also* recovered from their personality disorder.

This study demonstrates that personality disorders can be reliably assessed in samples of patients with chronic depression, and that the features of personality disorders respond positively to pharmacotherapy.

NR373 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Applicability of Personality Disorder Criteria to Hospitalized Adolescents: An Internal Consistency Evaluation

Daniel F. Becker, M.D., Menninger-SFBA, 1783 El Camino Real, Burlingame CA 94010; Carlos M. Grilo, Ph.D., Leslie C. Morey, Ph.D., Martha Walker, B.A., William S. Edell, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To examine the applicability of personality disorder criteria to adolescent inpatients by evaluating internal consistency and criterion overlap.

Method: Subjects were 38 adolescents and 28 adults who were assessed with the Personality Disorder Examination at the time of admission to the Yale Psychiatric Institute. Assessments were reliable (average kappa = .84). *Within*-category cohesiveness (internal consistency) of the personality disorder criteria was evaluated by examining intercriterion correlations as well as Cronbach's alpha coefficient. In addition, *between*-category criterion overlap was evaluated by examining "inter-category" intercriterion correlations between all pairs of disorders. Separate analyses were conducted for adolescents and adults, and the groups were compared.

Results: Internal consistency was found to be lower in adolescents than in adults, as measured by intercriterion correlation and by coefficient alpha, with the largest differences being identified for antisocial, histrionic, and narcissistic personality disorder criteria. Inter-category analysis indicated that diagnostic overlap may be greater among adolescents than among adults.

Conclusions: Overall, our psychometric analysis suggests that the DSM approach to categorizing personality disorders may have limitations. In both adolescents and adults, modest degrees of within-category cohesiveness (internal consistency) and between-category criterion overlap were observed. Comparatively, we found lower internal consistency of personality disorder criteria in adolescents, and less discriminant validity. Our data raise questions about the construct validity of these disorders—or the applicability of these criteria—within this age group.

NR374 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Fate of Borderline Psychopathology: Nine-Year Follow-Up Study in Japan

Norimasa Ikuta, M.D., Department of Psychiatry, Okura Hospital, 2-10-1 Okura, Setagaya-ku, Tokyo 157, Japan; Kuninao Minakawa, M.D., Yuko Miyake, Ph.D., Naoki Moriya, M.D., Ken Murakami, M.D., Aya Nishizono-Maher, M.D.

Summary:

Objective: The purpose of this study is to investigate stability of borderline psychopathology by using a prospective method.

Method: The original sample was composed of 85 nonpsychotic female patients, aged 18 to 30, who consecutively visited the Keio University Hospital in Tokyo from 1986 to 1989. Thirty-two patients were diagnosed as having borderline personality disorder(BPD) by using the Diagnostic Interview for Borderline (DIB). They were also diagnosed as having comorbid DSM-III/Axis I disorders such as major depression (59%) and/or eating disorders (34%). At follow-up, new raters re-administered the DIB and the Structured Clinical Interview for DSM-IV/Axis I disorders (SCID-IV).

Results: Eleven (34%) of the 32 BPD patients had participated in the follow-up study by December 1996. Mean total score of the DIB decreased from 9.0 to 4.8. Six persons no longer met diagnostic criteria for BPD. Six of the 11 persons still showed high scores in the interpersonal section of the DIB, whereas only two persons showed high scores in the impulse-action pattern section of the DIB.

Conclusions: About half of the BPD patients showed considerable improvement after nine years. Interpersonal difficulties were most durable among five areas of the DIB.

NR375 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

A Partially Heritable Oppositional Factor Predicts Adult Antisocial Symptoms Separately from a Conduct Factor in an Adoption Study

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Summary:

Objective: Our group has previously shown that adverse adoptive home environment and a biologic background of antisocial personality (ASPD) predict conduct disorder, adolescent "aggressivity," and adult ASPD. We have now examined these data to see if uncorrelated symptom combinations (factors) from the juvenile outcomes control for the predictors of ASPD in that original model.

Method: The data originated from a retrospective adoption study. Probands with a biologic background for ASPD or alcoholism were heavily over-sampled. Symptoms were ascertained by proband and adoptive parent interview. We performed, by gender, separate rotated principal component factor analyses on the combined conduct and aggressivity symptoms (females: N=87, males: N = 88). We used linear regression to examine the relationship between the resulting factors and other variables.

Results: In both genders, oppositional-defiant symptoms correlated mainly with one factor and conduct symptoms with a second. Both factors were strongly predictive of adult ASPD symptoms. In men, only the oppositional-defiant factor was associated with ASPD biologic background. The conduct factor was weakly associated with adverse home environment. In women, both factors were associated with ASPD biologic background and the oppositional factor was also associated with a biologic-environment interaction. After controlling for the two factors, ASPD biologic background and adverse environment were no longer associated with adult ASPD. This suggests that the factors serve as intermediaries for those variables in ASPD prediction.

Conclusions: A biologic diathesis for ASPD may manifest early in life primarily as oppositional-defiant symptoms. This is not reflected in the current diagnostic criteria.

NR376 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Cognitive Impulsivity and Behavioral Abnormalities in Patients with Personality Disorder

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Philip D. Harvey, Ph.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

Summary:

Impulsivity is a central feature of the diagnostic definitions of many personality disorders. There are both cognitive and behavioral components of impulsivity. While cognitive impulsivity has been studied in detail in children with behavior disorders, there has been little research in this area in adults. In children, cognitive impulsivity is often correlated with aggressive behavior, but not other aspects of behavioral impulsivity. In this study, 33 patients with borderline personality disorder (BPD), 43 patients with schizotypal personality disorder (SPD), and 43 patients with personality disorders other than SPD or BPD were examined with a computerized "3–7" version of the continuous performance test (CPT) and self-report ratings of impulsive and aggressive behavioral traits. The CPT was scored with a system developed to identify cognitive impulsivity in children with attention-deficit hyperactivity disorder, identifying errors of commission that were impulsive in nature, as compared to random. Similar to the previous studies, errors of commission by the adult patients to stimuli other than a 7 that followed a 3 were extremely rapid (mean RT = 150 msec as compared to 375 msec for correct detections) while other errors of commission were slower in RT than correct detections. While patients with SPD had significantly more errors of omission than the other two groups ($p < .05$), the frequency of impulsive errors of commission did not differ across the three samples of subjects. Similar to previous studies of children, ratings of aggressiveness, but not behavioral impulsivity, were correlated with impulsive CPT errors across all three samples of patients. These findings suggest that cognitive and behavioral impulsivity are not necessarily intrinsically correlated, even in adults with personality disorders. Researchers studying impulsivity and its treatment should be careful to specify whether they are focusing on cognitive or behavioral aspects of the condition.

NR377 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Money Management for Mentally Ill Individuals

Patricia Hanrahan, Ph.D., Department of Psychiatry, University of Chicago, 5841 S. Maryland Avenue MC3077, Chicago IL 60637; Daniel J. Luchins, M.D., Kendon J. Conrad, Ph.D., Michael D. Matters, Ph.D., Courtenay E. Savage, M.A., Marc S. Shinderman, M.D.

Summary:

Severely mentally ill (SMI) individuals often have difficulties in managing money from their Social Security payments, which contributes to homelessness and rehospitalization. Representative Payee programs help SMI individuals to budget Social Security payments for necessities, such as rent and food; however, very little evidence is available concerning the effectiveness of these programs. The purpose of the study is to examine the implementations of a Representative Payee (RP) program under the auspices of a community mental health center with regard to 1) Criteria for referral to the RP program, and 2) program outcomes, particularly re-hospitalization.

Design. This retrospective study includes SMI individuals who were enrolled in the RP program at Community Counseling Centers of Chicago for one year, and who had one year of service utilization data. Enrollment criteria are being determined through chart reviews (N = 40). Pre and post data on utilization of state hospitals is currently available for 34 subjects.

Results. Enrollment in the RP program was associated with substance abuse dependency, 53%; history of homelessness, 32%; and frequent hospitalizations, 24%. Days spent in state hospitals before and after participating in the RP program decreased markedly, from 84 days (SD = 116) to 5 days (SD = 13), $p < .001$.

Conclusion. Findings from this pre and post, retrospective study must be viewed as tentative in the absence of a more rigorous design. However, the preliminary findings suggest that the RP program is quite effective in reducing hospital stays.

NR378 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

The Austen Riggs Follow-Along Study: A Preliminary Report on Dynamic and Descriptive Change

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Summary:

Objective: Dynamic formulations help the therapist focus treatment. Certain formulation methods yield quantifiable ratings, which can detect longitudinal change. The Austen Riggs Center has started a naturalistic follow-along study of adults entering intensive residential treatment. This initial report examines 10 subjects who have completed three years of follow-along after beginning either short- or long-term (less than or greater than three months) treatment.

Methods: Subjects had chronic and recurrent Axis I and II disorders. At entry and every six to 12 months following, subjects received dynamic interviews, Relationship Anecdote Paradigm (RAP) interviews, and symptom assessments. Defensive functioning was rated using the Defense Mechanisms Rating Scales (DMRS). The Standardized Wish and Fear List rated progression of dynamic motives according to Erikson's eight developmental stages. The Psychodynamic Conflict Rating Scales (PCRS) scored specific conflicts. Symptoms were examined using the SCL-90-R and diagnostic measures.

Results: Graphic presentation of the cases showed that defenses, motives, and conflicts progressed more slowly and with less variation over time than did symptoms. Clear dynamic improvement trends were generally evident after two years.

Conclusions: Change in dynamics and symptoms apparently have different characteristics. Dynamic change occurs more slowly than symptom change but may attend stable symptom improvement with greater length of treatment.

NR379 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Treatment of Substance Abusing Schizophrenic Patients: Two-Year Progress Report

Andrew P. Ho, M.D., Department of Psychiatry, West Los Angeles VAMC, 627 N Maple Drive, Beverly Hills CA 90210; John W. Tsuang, M.D., Andrew L. Shaner, M.D.

Summary:

Objective: Substance abusing schizophrenic patients are difficult and expensive to treat due to their low outpatient treatment retention and high hospital utilization. Development of effective treatment may depend on our ability to assess incremental program improvements.

Method: This is a treatment outcome study of 179 such patients consecutively entering the Dual Diagnosis Treatment Program (DDTP) at the West Los Angeles VA Medical Center during a two-year period from 9/1/1994 to 8/31/1996. We divided the 24 months into four consecutive six-month periods for analysis (periods 1 to 4). We used treatment retention rate and hospital bed days of care (BDOC) as measures of treatment outcome.

Results: Increases in number of new patients entering treatment occurred from period 1 through 4 (N = 20, 42, 50, 67). Incremental improvements in 30-day and 90-day treatment retention rate oc-

curred from period 1 to 4 (30-day: 30% to 66%, Chi-Square = 6.63, p = 0.005; 90-day: 10% to 37%, Chi-Square = 4.17, p = 0.019). We also found reduction in acute psychiatric BDOC per patient in the 180 days after initiation of treatment compared to before treatment (from 24.5 to 9.1 days, t = 4.75, p < 0.001).

Conclusions: Useful program evaluation required longitudinal assessment of treatment outcome. This approach enhanced ongoing refinements in treatment of substance abusing schizophrenic patients at the DDTP.

NR380 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Medical Cost Offset in Depressed Primary Care Patients in Two Health Maintenance Organizations

Don P. Buesching, Ph.D., Health Economics, Eli Lilly and Company, Lilly Corporate Center/DP 2646, Indianapolis IN 46285; Timothy R. Hylan, Ph.D.

Summary:

Recent research among depressed outpatients in an HMO suggests that change in depressive symptoms has little impact on the medical expenditures of depressed patients who have physical comorbidities and poor functioning. To further elucidate this relationship, we examine medical costs in two depressed populations: outpatients in an HMO in the Northeast treated with antidepressants (AD's) and outpatients in an HMO in the West who were treated or untreated for depression. Among the 1,661 patients in the Northeast starting a new episode of AD treatment, 42% experienced a median cost increase of $1,124 while the remainder had a median decrease of $1,328 comparing 12-month periods prior to and after initiation of therapy. Depressed patients with comorbid cancer were the only sub-group to evidence a significant cost offset for total medical costs. However, several factors, including having at least six months of AD therapy, were significantly associated with offset in office-based services. The 1,102 patients in the West were part of an earlier prospective study where data on comorbidities and functional status were collected. Initial findings show that costs are higher in the 12-month post period than they were in the 12-month pre period for both the treated and untreated.

NR381 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Modification of EEG Sleep Parameters Under ECT in Drug-Resistant Major Depressives: Preliminary Results of Correlation with Clinical Improvement

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Summary:

Background: Shortened Rapid Eye Movement (REM) latency, increased REM activity and density, reduced slow wave sleep and abnormal temporal distribution of REM and delta sleep are the most prominent features of sleep profile in depressive patients. Most antidepressant medication and sleep deprivation are known to suppress REM sleep whereas electroconvulsive therapy (ECT) does not. Very little is known about changes in sleep variables during ECT treatment in depressive patients, but shortened REM latency after ECT seems to be a marker of relapse.

Objectives: Our aims are to describe EEG sleep changes occuring under ECT treatment, to correlate clinical remission with polygraphical sleep changes, and to evaluate REM latency as a marker of treatment response.

Methods: We include hospitalized patients with major depressive disorder according to DSM-IV criteria, resistant to pharmacological treatment and without serious somatic disease. EEG sleep recordings are done in the psychiatric ward at baseline, during and after ECT treatment. The clinical course of depression is evaluated by two rating scales: Carroll rating scale for depression, and MADRS.

Results: In ECT-treated patients studied we found a reduced REM sleep, both in minutes and in percentage of total sleep time, an increased stage 2 sleep time, and a decreased time spent awake after sleep onset.

Conclusion: ECT seems to affect sleep measures at all levels, including sleep continuity, sleep architecture, and REM sleep measurements.

NR382 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Neurometric EEG Predicts Pharmacotherapeutic Outcome in Depressed Outpatients: A Prospective Trial

Stephen C. Suffin, M.D., Department of Psychiatry, Veterans Administration, 16111 Plummer Street/116A, Sepulveda CA 91343; Nick M. Gutierrez, M.D., Sarla Karan, M.D., David Aurua, M.D., W. Hamlin Emory, M.D., Arthur Kling, M.D.

Summary:

Objective: Can Neurometric EEG (N-EEG) features (retrospectively associated with medication response in adult and adolescent depressed patients) prospectively predict response to medication.

Method: We have, to date, studied seven treatment-refractory, medication-free outpatients in a blinded [to evaluators and electroencephalographer] design. This paradigm allowed outcome assessment of N-EEG medicine response prediction versus unguided medication selection processes with the same clinicians. Patients with DSM-IV diagnoses of major depression, dysthymic disorder, depressive disorder NOS, and bipolar disorder were studied. Patients with diagnoses that physically could confound the N-EEG were excluded. A physical examination and laboratory studies within normal limits were necessary to be a study patient.

Results: Groups [clinician's choice, N-EEG guided] did not differ in mean age [47, 44 years], gender composition [3:1, 2:1 M/F], or initial Hamilton/Beck (H/B) scores [H 24/24, B 25/30]. Post-treatment difference in H/B scores [19/5, 23/8] and mean CGI scores [1, 3] were markedly different and nearly achieved statistical significance despite the small number of patients tested to date [Fisher's Exact, one tailed].

Conclusion: N-EEG has predicted medication response in depression and there has been normalization of the N-EEG features with clinical improvement.

NR383 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Outcomes of Psychiatric Hospitalization: 1988–96

Paul B. Lieberman, M.D., Day Hospital, Butler Hospital, 345 Blackstone Avenue, Providence RI 02906; Stephen A. Wiitala, Ph.D., Elliott E. Binette, M.A., Sandra McCormick, M.S.W., Stephanie Goyette, M.S.

Summary:

Objective: To compare hospital outcomes for depressed patients between 1988 and 1996.

Methods: Between 1988 and 1996, 266 depressed patients in three cohorts were evaluated at admission, of whom 161 (78.2%) were evaluated at discharge and 119 (68.9% of those followed) one month later, using measures of symptoms (BPRS, HRSD), global functioning (GAF), self-concept (Rosenberg Self Concept Inventory), ego defenses (Bond Defense Inventory), work and social functioning (Strauss-Carpenter Level of Function, Interview Schedule for Social Interaction), and readmission.

Results: Lengths of stay significantly declined (26.5 v. 19.5 v. 8.3d; p < .01). The most recently hospitalized group (LOS = 8.3 ds) was the most impaired at admission. Additionally, this group

showed higher *residual* discharge HRSD scores and lower residual GAF ($p < .01$) than the other groups, although this difference was no longer significant at one month. Other measures did not differ at discharge among the groups. At one month, the shortest-stay group showed lower quantity and quality of work functioning ($p < .01$), but higher levels of social contact ($p = .09$). Readmission rates were equal. Within the shortest-stay group, there were no differences in outcome comparing patients treated in a partial hospital with those not so treated.

Conclusions: A significant "deregression" in ego functioning occurs rapidly and equally across lengths of stay. Nevertheless, patients hospitalized briefly are discharged more symptomatic and at a lower level of functioning. Thus, although patients' ego defenses, self-esteem, and difficulty thinking improve, residual symptoms may impair post-hospital functioning.

NR384 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Economic Outcomes Associated with Initial Treatment

Eric T. Edgel, Pharm. D., Health Economics, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Timothy R. Hylan, Ph.D.

Summary:

Objective: To examine the economic outcomes associated with initial treatment choice after a diagnosis of depression.

Method: Retrospective database analysis was used to classify patients into one of four treatment cohorts: diagnosis-only, psychotherapy, drug therapy, and combination therapy. Sample selection bias was accounted for using a two-stage process where treatment choice was estimated using a multinomial logistic regression model in the first stage and total and mental costs were estimated in regression models in the second stage. Log-predicted costs from the second stage were compared across all observations and in observations whose initial provider was a nonpsychiatric physician to determine the relative costs associated with each cohort.

Results: Significant differences ($p < 0.008$) in total costs were found between the combination therapy and psychotherapy cohorts in the analysis that included all observations ($n = 9, 110$). In the analysis that included patients who initiated therapy with a nonpsychiatric physician ($n = 2, 673$) the drug therapy cohort was found to be significantly more costly as compared to the diagnosis-only cohort. (63)

Conclusions: There is not a significant difference in total health costs between depressed patients who initiate treatment with psychotherapy and depressed patients who initiate treatment with drug therapy.

NR385 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Post-Discharge Medication Compliance in Adolescent Psychiatric Inpatients

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Summary:

Psychotropic medications have become a first-line intervention in the treatment of seriously disturbed adolescents, particularly in the inpatient setting. While the goal of symptom reduction during the course of hospitalization is primary, the assumption is that pharmacological treatment will continue following discharge, and is essential to the prevention of relapse. Research on medication compliance in adult patients has identified side effects as a critical factor in noncompliance, but no similar data are available regarding adolescent patients. In this study 97 adolescent inpatients who were discharged from a private psychiatric hospital with a plan that included continued treatment with medications were contacted 12 to 18 months post discharge and interviewed for medication compliance, compliance with other aspects of the discharge plan (e.g., psychotherapy, family therapy, etc.), and the experience of medication-related side effects. Overall medication compliance was extremely poor (35%), although the rate of reported side effects was quite low (24%). Moreover, the rate of side effects in noncompliant patients was only 38%. Stepwise regression analysis revealed that failure to comply with one's discharge plan more generally, $R^2 = .29$, $p < .001$, $t = 5.3$, was a stronger predictor of medication noncompliance than was the experience of side effects, $t = -1.6$, $p = .13$, $R^2_{incremental} = 0$. Further, diagnosis, medication type, age, and gender were unrelated to medication compliance. These data suggest that factors other than side effects, including perhaps personality characteristics, are more likely to predict compliance in this patient population.

NR386 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

A Double-Blind, Placebo-Controlled Study on Gradual Withdrawal of Antiparkinsonian Medication in Chinese Schizophrenia Patients

Alfred Hin Tat Pang, M.D., Department of Psychiatry, Chinese University, Prince of Wales Hosp, 11th Flr, Shatin NT, Hong Kong; Gabor S. Ungvari, M.D., Helen F.K. Chiu, M.D., Linda C.W. Lam, M.D., Dicky W.S. Chung, M.D., Tony Leung, M.Sc.

Summary:

Antiparkinsonian (AP) withdrawal studies conducted so far have shown inconclusive findings regarding the use of anticholinergic APs in the maintenance treatment of schizophrenia. In 21 double-blind, placebo-controlled AP withdrawal studies, 8% to 95% of chronic schizophrenic patients required continuous AP medication. There are also no reliable data in Chinese patients. Fifty-eight (29 pairs) of matched Chinese patients with chronic schizophrenia underwent gradual withdrawal of AP (dose range 2–12 mg) at a rate of 1 mg every two weeks. Monthly assessments of their clinical and motor status were carried out by blind raters. According to Brief Psychiatric Rating Scale (BPRS), Hamilton Depression Rating Scale (HDRS), Abnormal Involuntary Movement Scale (AIMS), Simpson-Angus Scale (SAS), Barnes Akathisia Rating Scale, and nursing staff's assessment using NOSIE-30]. Withdrawal of AP was possible in 25 (90%) patients. Our results suggest that the vast majority of patients with chronic schizophrenia do not require prophylactic AP treatment.

NR387 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Immediate Naltrexone Decreases in Alcohol Intake Urges as Predictor of a Good Outcome

Jorge F. Perez-Cruet, M.D., Department of Psychiatry, Oklahoma City VAMC, 921 NE 13th Street, Oklahoma City OK 73104; Tomislav Iricanin, M.D.

Summary:

Objective: The main objective of this study was to determine predictors of a good outcome in chronic alcohol dependent patients treated with naltrexone.

Method: Eighteen male subjects were studied after they had been thoroughly evaluated for inclusion as patients in our outpatient substance abuse clinic. All patients met the criteria for severe, chronic alcohol dependence according to DSM-IV criteria. Clinical indicators included: self-reports of use of alcohol; reports of increase or decrease of urges of drinking alcohol; reports of other professionals; laboratory indicators: MCV, SGOT, SGPT, GGTP,

urine ethanol; employment status; participation in therapeutical modalities; and social adjustment.

Results: Group I: Five patients reported immediate elimination of urges to drink after the initial doses of naltrexone. Group II. Six patients reported occasional drinking and at times a reduction in urges to drink alcohol. Group III. Five patients reported no decrease in urges or continued drinking alcohol. Group IV. Two patients stopped taking the medication because of severe side effects such as nausea, feelings of increased anxiety and fatigue. Patients in Group I showed an excellent outcome with full employment and improvement in all clinical indicators. Group II, showed longer periods of abstinence but outcomes varied with relapses and readmission in three patients. Group III and IV dropped out of treatment with poor outcomes.

Conclusion: Alcoholics treated with naltrexone who reported an immediate cessation of urges to drink showed excellent outcomes.

NR388 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Comparisons of Antidepressant Prescribing and Use Patterns in Privately Insured and Medicaid Populations

Timothy R. Hylan, Ph.D., Global Health, Eli Lilly and Company, Lilly Corporate Center/DP 2646, Indianapolis IN 46285; Cathy A. Melfi, Ph.D., Anita J. Chawla, Ph.D., William H. Crown, Ph.D., Thomas W. Croghan, M.D., Don P. Buesching, Ph.D.

Summary:

Background: Duration of antidepressant treatment is an important indicator of successful medication management of depression. Published guidelines for treatment of depression include a recommendation of four to nine months of continuous use of an antidepressant following symptom resolution to prevent relapse or recurrence of the depressive episode. The purpose of this study is to compare depressed Medicaid recipients to those with private insurance, specifically with respect to antidepressant use patterns and types of antidepressants prescribed.

Methods: Using data from privately insured and a state Medicaid database, we examine antidepressant use patterns based on the timing and number of all prescriptions for antidepressants during the six months following an initial diagnosis of depression and treatment with a tricyclic antidepressant (TCA) or one of the three selective serotonin reuptake inhibitors (SSRIs) fluoxetine, sertraline, or paroxetine. We compare groups based on type of antidepressant as well as antidepressant use patterns.

Results: The privately insured patients are much more likely to receive SSRIs rather than TCAs relative to Medicaid patients. In both datasets, fluoxetine has the highest rate of continuous use of the three SSRIs considered. In the Medicaid dataset, sertraline and paroxetine have lower rates of continuous use than both fluoxetine and the TCAs. Privately insured patients are far more likely to have continuous use of antidepressants than are Medicaid patients.

NR389 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Combined ECT and Neuroleptic Therapy in Treatment-Resistant Schizophrenia

Worrawat Chanpattana, M.D., Department of Psychiatry, Srinakarinwiroth University, Vajira Hospital, Samsen Dusit, Bangkok 10300, Thailand; Ronnachai Kongsakon, M.D., Wanchai Buppanheran, M.D.

Summary:

Objective: To determine the therapeutic efficacy of combined ECT and neuroleptic therapy in treatment-resistant schizophrenia (TRS).

Methods: Fifty-nine TRS patients suffering acute exacerbations were administered the Global Assessment of Functioning (GAF), Brief Psychiatric Rating Scale (BPRS), and the Mini Mental State Exam (MMSE). Each patient underwent acute treatment using ECT and flupenthixol (dose range 12–24 mg/d). Bilateral ECT was used throughout this study. After the first sign of clinical improvement, all patients had to pass a three-week stabilization period during which their clinical improvement had to be sustained.

Results: Thirty-one patients passed the stabilization period and nine patients left the study and were not included in the analysis. The ECT responders had younger age, shorter duration of illness and duration of the current episode, less FHx, more paranoid type, and use lower dose flupenthixol. The positive and depressive symptoms had better responses; the negative symptoms were poorer (all $p < 0.05$).

Conclusions: Combined ECT and neuroleptic had good therapeutic efficacy in TRS (62% response rate). A double-blind, randomized study is needed. A consensus in the definition of TRS is urgently required.

NR390 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Telephone/Computer Administered PRIME-MD

Leslie V. Taylor, M.D., Dean Foundation, 2711 Allen Boulevard, Middleton WI 53562; Kenneth A. Kobak, Ph.D., Susan L. Dottl, Ph.D., John H. Greist, M.D., James W. Jefferson, M.D., Diane Burroughs, B.A.

Summary:

The PRIME-MD, a screener for psychiatric disorders designed for use by primary care physicians, was converted for administration over the telephone by a computer using Interactive Voice Response (IVR) technology. Diagnoses obtained by the computer were compared to those obtained over the telephone by a trained clinician using the Structured Clinical Interview for DSM-IV (SCID). Primary care physicians also administered the clinician-administered version of the PRIME-MD face-to-face to a subset of patients. Subjects included outpatients from primary care clinics, psychiatric patients with OCD or social phobia, patients from eating disorder and alcohol treatment clinics, and community controls. Prevalence rates were similar, both for the presence of any diagnosis (IVR 61.9%; physician 57.1%; SCID 61.0%) and for the most individual diagnoses (e.g., major depression: IVR 26.0%; physician 27.6%; SCID 24.8%). Twice as many primary care patients reported alcohol abuse and social phobia symptoms to the computer as to the physician or clinician. Compared to the SCID, both the computer- and physician-administered versions of PRIME-MD demonstrated high and approximately equivalent sensitivity and specificity. Results support the validity of the IVR PRIME-MD, which provides a cost-effective and time-efficient source of diagnostic information to improve treatment planning.

NR391 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Preliminary Test-Retest Reliability of the Structured Clinical Interview for DSM-IV Childhood Diagnoses

Frederick J. Matzner, M.D., Child Psychiatry, St. Luke's-Roosevelt, 1111 Amsterdam Avenue, New York NY 10025; Raul R. Silva, M.D., Matthew Silvan, Ph.D., Mizanur Chowdury, M.D., Lisa Nastasi

Summary:

Objective: The Structured Clinical Interview for DSM-IV, Childhood Diagnoses (KID-SCID) is a new semistructured instrument designed for clinical research studies. It is based on the adult SCID, which has good reliability and utility. The KID-SCID is easy to use, has utility as a training tool, and has demonstrated excellent interrater reliability. This study examines preliminary test-retest

reliability of disruptive behavior and anxiety diagnoses in a clinic population.

Method: Subjects consisted of all patients (n = 15; 11 male, 4 females; mean age 12 years, range 7–17) who received the Disruptive Behavior and Anxiety Modules of the KID-SCID during the course of two separate clinical evaluations at a child psychiatry clinic. These modules are part of this clinic's standard psychiatric evaluation. A chart review extracted KID-SCID diagnoses, and the kappa statistic was used to determine the chance-corrected agreement between the first and second interviews.

Results: Kappa scores consisted of:
Disruptive behavior disorders: attention deficit/hyperactivity disorder .84, conduct disorder .84, oppositional defiant disorder .63.
Anxiety disorders: social phobia 1.0, separation anxiety disorder .66, and post-traumatic stress disorder .44.

Conclusion: Preliminary reliability is shown to be good, with three diagnoses showing excellent reliability. A larger reliability study is now under way, examining more females and children from each age group. This instrument shows promise for its intended purpose.

NR392 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Prevalence of Kraepelin's Paraphrenia in a Psychiatric Hospital

Berta Rios, M.D., Department of Psychiatry, Hospital 12 Octubre, Avenida de Andalucia, S/N, Madrid 28041, Spain; Natividad Vicente, M.D., Enriqueta Ochoa, M.D.

Summary:

The term "paraphrenia" was used by Kraepelin in 1909 to designate a subgroup of nosological entities independent from "dementia praecox" and characterized mainly by their beginning after the age of 40, multiple delusional semisystematized ideas, and hallucinations without formal disorders of thought or personality deterioration.

Objective: To determine the prevalence of this diagnosis among inpatients in a psychiatric hospital.

Method: All clinical records of inpatients of Hospital Psiquiátrico of Madrid between June 1985 and June 1995 were reviewed. Those records closer to the first Kraepelin's definition were selected. Then we analyzed sociodemographic data, psychopathology, and course items.

Results: Paraphrenia diagnosis fits in 0.17% of inpatients as a whole, and in 1.6% of those diagnosed with schizophrenia. A total of 92% were female and mean age was 53 years. The more relevant psychopathological features were: persecutory delusions (92%), delusions of grandeur (81%), elation (74%), hallucinations (84%), and the absence of intellectual deterioration (100%).

Conclusions: The results of our study suggest that a small but significant percentage of inpatients fits Kraepelin's concept of paraphrenia, with well determined psychopathological features.

NR393 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Dissociative Symptoms and Aggression in Outpatients

Margaret L. Kaplan, Ph.D., Department of Psychiatry, Montefiore Hospital, 111 East 210th Street, Bronx NY 10467; Miriam Ehrensaft, M.A., William Sanderson, Ph.D., Scott Wetzler, Ph.D., Gregory M. Asnis, M.D.

Summary:

Given the prevalence of dissociative symptoms in psychiatric outpatients, it is important to determine what behaviors may be associated with pathological dissociation. Whereas numerous studies have found a link between high dissociative symptoms and aggressive self-injurious acts (i.e., self-mutilation and suicide attempts), little attention has been paid to whether dissociation is also related to outwardly directed aggressive behavior. In the present study, 122 individuals seeking outpatient treatment at Montefiore Medical Center completed the Dissociative Experience Scale (DES), the Harkavy-Asnis Suicide Survey (HASS), and the Buss-Durkee Hostility Inventory (BDHI). Patients with high DES scores (above 25) (n = 35) were compared with those with low DES scores (below 25) (n = 87) on various types of inward and outwardly directed aggressive behavior. Outpatients with high DES vs. low DES scores reported more assaultive behavior toward others ($t = 3.21$, $p = .002$), and more irritability ($t = 3.60$, $p < .001$), and negativity ($t = 2.56$, $p = .01$) on the BDHI. High DES patients reported more suicidal ideation ($x^2 = 3.67$, $p = .05$) and suicide attempts ($x^2 = 10.22$, $p = .001$), but not more homicidal ideation, plans, or attempts than low DES patients. Our findings suggest that high dissociative symptoms are associated with an increased risk for both self-destructive and outwardly directed aggressive behavior. The possible links between dissociative symptoms and different types of aggression are discussed.

NR394 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Effects of Amphetamine on Working Memory in Schizotypal Personality Disorder

Richelle M. Kirrane, M.D., Department of Psychiatry, Mt. Sinai Medical Center, One Gustave Levy Place, New York NY 10029; Robert L. Trestman, M.D., Michael J. Serby, M.D., Vivian Mitropoulou, M.S., Larry J. Siever, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how amphetamine may improve working memory in schizotypal personality disorder and how a complex relationship between working memory and dopaminergic activity in schizotypal personality disordered patients is implied.

Summary:

Background: Cognitive impairment is common to schizophrenia and schizotypal personality disorder (SPD). It has been hypothesized that decreased dopamine in the prefrontal cortex may be responsible. While limited data show amphetamine to improve cognitive dysfunction in schizophrenic patients, confounds including neuroleptic effects and intractable psychosis complicate the study of these patients. Patients with SPD (SPDs) being less so affected, present an ideal group in which to study cognitive impairment.

Method: We administered amphetamine 30 mg orally to 12 SPDs and 14 other personality-disordered patients (OPDs) in a placebo-controlled manner. We assessed visuospatial working memory using the Dot test (measure: cm error in position memory). Change in position error was measured at 10, 20, and 30 seconds delay. We also measured plasma homovanillic acid (HVA) at baseline and after amphetamine. Change in psychotic symptoms was assessed using the Positive and Negative Syndrome Scale (PANSS).

Results: No significant improvement in visuospatial working memory was noted at 10 or 20 seconds, but at 30 seconds six of 12 SPDs showed an improvement of greater than 1 cm (derived from the OPD mean + 1.5 SD) with amphetamine. None of the 14 OPDs showed this improvement ($X^2 = 6.5$, $df = 1$, $p < .01$). There was an inverse correlation between baseline performance and improvement on amphetamine, with patients who performed worse at baseline demonstrating greater improvement after amphetamine ($r = -.69$, $p = .001$). Regarding dopaminergic activity and visuospatial working memory, in the SPD sample, there was a positive correlation between HVA response on placebo and placebo-corrected performance ($r = .63$, $p = .02$) suggesting that patients with naturalistic variability in plasma HVA showed a

greater improvement in response to amphetamine. There was an inverse correlation between placebo-corrected HVA and placebo-corrected improvement on working memory ($r = -.54$, $p = .06$), raising the possibility that patients whose HVA was least reduced improved most, suggesting that these patients experienced greater net dopaminergic effects of amphetamine. Positive symptoms were unchanged.

Conclusion: These data suggest that amphetamine may improve working memory in SPD and imply a complex relationship between working memory and dopaminergic activity in SPD patients.

References:

1. Siever LF, Kalus OF, Keefe RSE: The boundaries of schizophrenia. *Psychiatric Clin North Amer,* 16:217-244, 1993.

2. Siegel BV Jr, Trestman RL, O'Flaithbheartaigh S, et al: D-amphetamine challenge effects on Wisconsin Card Sort Test. Performance in schizotypal personality disorder. *Schizophrenia Research* 20(1-2):29-32, May 1996.

NR395 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Diurnal Dopamine Rhythm in Nonpsychotic Relatives of Schizophrenic Probands

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Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how similar to schizophrenic patients, the diurnal rhythm in brain dopamine activity may also be attenuated in the nonpsychotic relatives of schizophrenic probands.

Summary:

Background: A diurnal variation in the major dopamine (DA) metabolite homovanillic acid (HVA) in plasma is well known, with a peak during early morning and a trough during early afternoon. Several lines of evidence suggest that this diurnal rhythm in plasma HVA (pHVA) is due to a diurnal variation in brain DA activity. In drug-free schizophrenic patients, the diurnal pHVA rhythm has been shown to be attenuated (Doran et al. 1990). Since the nonpsychotic relatives of schizophrenic probands are known to manifest at least some DA abnormalities of schizophrenia (in relation to the attenuated positive and negative symptoms in relatives) (unpublished data), a possibility is raised that the pHVA rhythm may be affected in relatives, as well.

Methods: pHVA was studied in the nonpsychotic first-degree relatives ($n = 52$) of schizophrenic probands and in a comparison group of subjects without a family history of schizophrenia ($n = 20$). All subjects were physically healthy. Before the study day, subjects observed a low monoamine diet for 72 hours, fasted overnight, avoided strenuous activity and smoking in the morning, and arrived at the medical center by 8:30 a.m. Using a heparin-lock, blood samples were collected at 9:30 a.m., 10:00 a.m., and 10:30 a.m. for the measurement of pHVA.

Results: pHVA declined significantly in both study groups consistent with its known diurnal rhythm. However, the decline was less pronounced in the relatives than in the comparison subjects (repeated measure ANOVA, group by time interactions, $F = 6.97$, $p = 0.004$). This difference did not appear to be due to a noradrenergic component of pHVA or due to renal HVA excretion, suggesting that it may be related to brain DA neuronal activity.

Conclusions: The results suggest that, similar to schizophrenic patients, the diurnal rhythm in brain DA activity may also be attenuated in the nonpsychotic relatives of schizophrenic probands. Furthermore, the results provide additional evidence that the DA abnormalities of schizophrenia may have genetic antecedents.

References:

1. Amin F, Davidson M, Davis KL: Homovanillic acid measurement in clinical research: a review of methodology. *Schizophr. Bull.* 18:123–148, 1992.

2. Doran AR, Labarca R, Wolkowitz OM, et al: Circadian variation of plasma homovanillic acid levels is attenuated by fluphenazine in patients with schizophrenia. *Arch. Gen. Psychiatry* 47:558–563, 1990.

NR396 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Symptom Dimensions and Psychosocial Outcome in Schizophrenia

Beng-Choon Ho, M.D., Department of Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52242; Peg C. Nopoulos, M.D., Arndt Stephan, Ph.D., Michael A. Flaum, M.D., Sue Oliver, M.S., Nancy C. Andreasen, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how negative symptoms measured at index hospitalization are a portent of poor psychosocial outcome. Conversely, severity of psychotic or disorganized symptoms at intake does not appear to predict subsequent psychosocial outcome.

Summary:

Background: Many studies have validated the grouping of schizophrenic symptoms into three independent dimensions: negative, psychotic, and disorganized. Negative symptoms are an important prognostic indicator. When present at the onset of the first episode, they suggest that the patient will develop significant psychosocial impairment. The predictive values of the psychotic and disorganized symptom dimensions, on the other hand, have been less certain.

Methods: In this study of 50 first-episode schizophrenic patients, we examined the relationship between the severity of these three symptom dimensions at index hospitalization (measured using the SANS and SAPS) and psychosocial functioning at two-year follow-up.

Results: Negative symptom severity was positively and significantly correlated with later occupational impairment, financial dependence on others, impaired relationship with friends, impaired ability to enjoy recreational activities, and global assessment of functioning (r's = 0.30 to 0.45; p's < 0.02 to 0.001). There were no statistically significant correlations between the levels of psychotic symptoms or disorganized symptoms and two-year psychosocial outcome measures. Analyses using multivariate regression statistics also revealed similar findings.

Conclusion: Negative symptoms measured at index hospitalization are a portent of poor psychosocial outcome. Conversely, severity of psychotic or disorganized symptoms at intake does not appear to predict subsequent psychosocial outcome.

References:

1. Arndt S, Andreasen NC, Flaum M, et al: A longitudinal study of symptom dimensions in schizophrenia. *Archives of General Psychiatry,* 52:352–360, 1995.

2. Hwu HC, Tan H, Chen CC, Yeh LL: Negative symptoms at discharge and outcome in schizophrenia. *British Journal of Psychiatry,* 166 (1):61–67, 1995.

NR397 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Nefazodone Treatment of Depression Requires Less Use of Concomitant Anxiolytic and Sedative/Hypnotic Drugs

Jean Lian, Bristol-Myers Squibb, 777 Scudders Mill Road, Plainsboro NJ 08536

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that in a population of depressed patients from the California Medicaid system, use of concomitant medications in nefazodone-treated patients was substantially lower than that in patients receiving other newer antidepressants.

Summary:

Objective: The use of concomitant anxiolytic, sedative/hypnotic, and additional antidepressant drugs in depressed patients receiving nefazodone was compared with use in patients treated with other newer antidepressants (fluoxetine, sertraline, paroxetine, venlafaxine).

Methods: The patient population analyzed in this study was from a 5% random sample of the 5.2 million eligible patients in the California Medicaid system from 1/1/93–5/31/95. Patients within this sample with at least one pharmacy claim for an antidepressant or with a diagnosis of depression on a medical or hospital claim were analyzed for the cost of concomitant drug use during the 30-day period following initiation of antidepressant therapy from 2/1/95–5/31/95.

Results: Nefazodone (n = 119 patients) was associated with a total cost for concomitant medications of $2.44/patient (1.20 for anxiolytics, 0.27 for sedatives, 0.97 for other antidepressants). Treatment with fluoxetine (n = 418), sertraline (n = 352), paroxetine (n = 208), and venlafaxine (n = 268) resulted in much higher use of concomitant therapies, with total costs of $11.48, $13.83, $15.53, $14.88, respectively. The majority of the expense was associated with the use of anxiolytics (fluoxetine = 70%, sertraline = 64%, paroxetine = 81%, venlafaxine = 66%).

Conclusion: These data demonstrate that nefazodone treatment is associated with less concomitant drug use in depressed patients, including those exhibiting symptoms of anxiety.

References:

1. Thompson D, Buesching D, Gregor KJ, Oster G: Patterns of antidepressant use and their relation to costs of care. *Am. J. Man. Care* 2:1239–1246, 1996.

2. Sclar DA, Robison LM, Skaer TL, et al: Antidepressant pharmacotherapy: economic outcomes in a health maintenance organization. *Clin. Ther.* 16:715–730, 1994.

NR398 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

The Efficacy of Ziprasidone in the Treatment of Positive, Negative and Depressive Symptoms of Schizophrenia

Paul E. Keck, Jr., M.D., Department of Psychiatry, University of Cincinnati, 231 Bethesda Ave, Medical Bldg, Cincinnati OH 45267; Edmund P. Harrigan, M.D., Karen R. Reeves, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how ziprasidone 80–160 mg/day is effective in the treatment of positive, negative, and affective symptoms of schizophrenia and schizoaffective disorder with the attendant side-effect burden associated with neuroleptics and some of the newer antipsychotics.

Summary:

Objective: To investigate the efficacy of ziprasidone in the treatment of schizophrenia and schizoaffective disorder. Ziprasidone, an effective antipsychotic, has a unique collection of receptor affinities. In conjunction with a high $5HT_2/D_2$ ratio, it has potent affinity for $5HT_{1A}$, $5HT_{1D}$ and $5HT_{2C}$ receptors and moderately inhibits norepinephrine and 5HT reuptake.

Method: Ziprasidone 4–160 mg/day was administered to patients with an acute exacerbation of schizophrenia and schizoaffective disorder in four- and six-week clinical trials.

Results: Ziprasidone 80–160 mg/day was significantly more effective than placebo, and ziprasidone 160 mg/day was similar to haloperidol 15 mg/day in improving positive symptoms. Similarly, the improvements in negative symptoms were significantly greater than placebo. In patients with baseline MADRS ≥ 14 and BPRS anxiety-depression cluster scores ≥ 18, improvements with ziprasidone 160 mg/day at six weeks and 120 mg/day at four weeks, respectively, were clinically and statistically significantly greater than placebo. Discontinuation due to adverse events was rare. The most frequently reported adverse events were somnolence, constipation, nausea, and dyspepsia. Notable was the low incidence of movement disorders, including akathisia, and weight gain, cardiovascular effects, and laboratory abnormalities.

Conclusions: Collectively, these results indicate that ziprasidone 80–160 mg/day is effective in the treatment of positive, negative, and affective symptoms of schizophrenia and schizoaffective disorder without the attendant side-effect burden associated with neuroleptics and some of the newer antipsychotics.

References:

1. Azorin JM: Long-term treatment of mood disorders in schizophrenia. *Acta Psychiatrica Scandinavica* 91:20–23, 1995.

2. Carpenter WT: Serotonin-dopamine antagonists and treatment of negative symptoms. *J Clin Psychopharm* 15:30S–35S, 1995.

NR399 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

The Economic Impact of the Treatment of Depression

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand that the economic benefits to an employer in terms of improved work hours and performance far outweigh the costs of treating depressed patients.

Summary:

Objective: To demonstrate the economic benefits of antidepressant treatment to an employer in terms of improved work hours and performance at work.

Methods: Six hundred thirty-five chronically depressed patients were randomized to treatment with sertraline or imipramine in a 2:1 ratio for 28 weeks. Using work-related questions from clinician-rated depression questionnaires, measurements of hours worked and work performance at baseline, week 12, and week 28 of the clinical investigation were utilized in the following model: *Net Economic Benefits = Income x Change in (hours worked x work performance) - Treatment Costs.*

Results: In a preliminary analysis, 332 depressed patients received antidepressant treatment and completed at least 28 weeks of treatment. Work hours significantly improved from 28 to 38 hours per week ($p < 0.001$). On average, productivity at work, based on an aggregate score of three items, improved from 49% to 90%. Total productivity (hours worked x work performance)

more than doubled in the acute treatment period, increasing from 35% at baseline to 86% at week 12. The improvement in total productivity was sustained after an additional 16 weeks of continuation treatment.

Conclusion: Since treatment costs represent 5% of an average worker's salary, the economic benefits to an employer in terms of improved work hours and performance far outweigh the costs.

References:

1. Finklestein SN, Berndt ER, Greenberg PA, et al: Improvement in the subjective work performance after treatment of chronic depression: some preliminary results. *Psychopharm Bulletin* 32(1):33–40, 1996.

2. Berndt ER, Finklestein SN, Russell JM, Greenberg PE: Measurement of work productivity in depressed patients: a reliability study. Presented at American Economics Association Meeting, San Francisco, 1995.

NR400 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Infant Outcome After Sertraline Exposure

Alexis M. Llewellyn, B.A., Department of Psychiatry, Emory University, 1639 Pierce Drive, Ste 4003, Atlanta GA 30322; Zachary N. Stowe, M.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how there are no adverse effects of infant exposure to sertraline up to 24 months of age and also demonstrate the preservation of the purported benefits of breast feeding with sertraline treatment.

Summary:

Objective: To assess the health and development of children who were breastfed while their mothers were treated with sertraline monotherapy for major depression. The postpartum period is a time of increased vulnerability for the development of major depression. The treatment of postpartum depression is often complicated by a woman's desire to breast feed. The benefits of breast feeding have been well documented and all professional organizations support breast milk as the ideal form of nutrition for infants. The limited data on breast feeding and paucity of infant follow-up studies render a careful risk-benefit discussion speculative.

Method: We conducted a preliminary follow-up study at 12 months and 24 months of infants exposed to sertraline during nursing compared with formula-fed infants of depressed mothers treated with sertraline. A total of 16 mother-infant dyads were matched for gender, birth weight, type of delivery, gestational age, maternal demographics, and the severity and duration of mother's depression. Infants exposed to prescription medications during pregnancy were excluded from the present study. Outcome variables included: illness density ratio, and weight and length percentiles obtained from pediatric records, achievement of developmental milestones by parental report. In an attempt to control for the effects of maternal depression, variable assessment occurred during three phases: I. postpartum not depressed, II. depressed not treated, III. depressed and treated.

Results: The immunological benefits of breast feeding were not affected by sertraline exposure; breast-fed infants demonstrated fewer respiratory infections, less gastrointestinal disturbance, and fewer cases of otitis media. No significant differences in the achievement of developmental milestones were reported.

Conclusion: These preliminary data failed to identify any adverse effects of infant exposure up to 24 months of age and demonstrated preservation of the purported benefits of breast feeding with sertraline treatment.

References:

1. Wisner KL, Perel JM, Findling RL: Antidepressent treatment during breastfeeding. *Am J Psychiatry.* 153(9):132:7, 1996.

2. Altshuler LL, Burt VK, McMullen M, Hendrick V: Breastfeeding and sertraline: a 24-hour analysis. *J Clin Psychiatry.* 56(6):243–5, 1995.

NR401 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Paroxetine Versus Nortriptyline in Ischemic Disease

Steven P. Roose, M.D., Clin. Psychopharmacology, NY State Psychiatric Institute, 722 West 168th Street, Pl 98, New York NY 10032; Bruce Pollack, M.D., John Kennedy, M.D., J. Craig Nelson, M.D., James McCafferty, M.D., Ivan Gergel, M.D.

Educational Objectives:

To inform the clinician of new data on the comparative efficacy and safety of SSRIs and TCAs in treatment of depressed patients with ischemic heart disease.

Summary:

The need to find a safe and effective treatment for depressed patients with ischemic heart disease is critical because depression following myocardial infarction increases risk for mortality, and unfortunately, tricyclic treatment in patients with ischemic heart disease may also increase the risk of death. The question is whether an SSRI is a safe and effective alternative to tricyclics in this patient population.

We report the first prospective, double-blind study comparing the safety and efficacy of an SSRI, paroxetine, with a TCA, nortriptyline, in depressed patients with ischemic heart disease.

Patients were randomly assigned either paroxetine or nortriptyline. Both medications were effective; 60% of the paroxetine and 61% of the nortriptyline group achieved a 50% reduction in baseline HRSD and a final HRSD ≥ 8. Paroxetine did not affect heart rate, blood pressure, cardiac conduction, or heart rate variability. Nortriptyline induced a statistically significant increase in heart rate and orthostatic drop, and a significant decrease in R to R variability. There was a significantly greater rate of dropout due to serious cardiovascular events in the nortriptyline group compared with the paroxetine group (Fisher exact, $p > .03$).

Paroxetine and nortriptyline are both effective in depressed patients with ischemic heart disease. However, the increased heart rate associated with nortriptyline may cause an increase in cardiac work, and if so, have an insidious, but detrimental effect that would not be appreciated after only six weeks of drug exposure. The high rate of serious adverse events associated with nortriptyline in this study further documents that despite robust efficacy, tricyclics are problematic in patients with heart disease.

References:

1. Glassman AH, Roose SP: Risks of antidepressants in the elderly—tricyclic antidepressants and arrhythmia: revising risks. *Gerontology* 40:15–20, 1994.

2. Roose SP, Glassman AH: Antidepressant choice in the patient with cardiac disease: lessons from the Cardiac Arrhythmia Suppression Trial (CAST) studies. *J Clin Psychiatry* 55:83–87, 1994.

NR402 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Dysthymia: An Outcome Study of Combined Group Therapy and Medication Treatment Versus Medication Treatment Alone

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Batchelder, Ph.D., Lisa Wallner Samstag, M.A., Richard N. Rosenthal, M.D., Arnold Winston, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe important treatment outcome areas in combined psychotherapy/psycopharmacology of dysthmia; to describe preliminary findings for an outcome study comparing medication treatment versus combined group and medication treatment.

Summary:

There is increasing evidence that patients with dysthymia respond to treatment with antidepressant medications, including SSRI medications, and to some degree to psychotherapy. However, even patients successfully treated with medication often have significant residual dysfunction, including persistent depressive symptoms and impaired psychosocial and interpersonal function. We present outcome data for a prospective, randomized, 36-week study comparing antidepressant treatment alone vs. combined antidepressant and group therapy for treatment of dysthymia. Following an eight-week trial of fluoxetine, one-half of subjects were randomly assigned to receive additional group psychotherapy. All patients remained on medication until week 24, at which time medication was discontinued, until follow-up at week 36. Group therapy consisted of a manualized 16-session group treatment with cognitive, interpersonal, and experiential orientation. Data on the first 31 patients studied from intake to termination (week 24) will be presented.

Basically, both samples showed significant improvement over time, with combined treatment showing significantly greater improvement on the GAS, CGI, and the Inventory of Interpersonal Problems (high subscale). Additionally, we assessed how many patients in either condition improved in all three areas of 1) symptomatology 2) global functioning, and 3) personality variables. We found that 33% of patients in combined treatment improved in all three areas, compared with 0% of patients on medication alone. These data provide preliminary evidence that group therapy may provide some additional benefit to medication-responding dysthymics, particularly in the areas of interpersonal and psychosocial functioning.

References:

1. Markowitz J: Psychotherapy of dysthymia. *Am J Psychiatry* 151:1114–1121, 1994.

2. Hellerstein DJ, Yanowitch P, Rosenthal J, et al: A randomized double-blind study of fluoxetine versus placebo in treatment of dysthymia. *Am J Psychiatry* 150:1169–1175, 1993.

NR403 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Compliance of Naltrexone in the Treatment of Alcohol Dependence

Kee Namkoong, M.D., Department of Psychiatry, Yale University, Satu, 1 Long Wharf, New Haven CT 06511; Conor K. Farren, M.D., Patrick O'Connor, M.D., Stephanie S. O'Malley, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to demonstrate how the Medication Event Monitoring System is a useful measure of medication compliance for use in clinical trials.

Summary:

Medication compliance is a critical issue in clinical trials of treatments for alcohol dependence. This study examined the utility of two methods for monitoring medication compliance, the Medication Event Monitoring System (MEMS) and pill counts (PC). The MEMS records the time of each pill bottle opening and yields several indices of compliance. PC yield a single index of compliance: total number of pills presumed taken. Compliance data were examined for 85 alcohol-dependent patients participating in a 10-week, open-label trial of naltrexone 50 mg qd and psychotherapy.

Consistent with studies of other pharmacotherapies, PC yielded a higher estimate of compliance (91.9 ± 9.6%) than did the MEMS (84.3 ± 20.2%, $p < .005$). However, the MEMS compliance rate was significantly correlated (ps < .01) with treatment outcome (i.e., % days abstinent; average alcohol amount consumed daily; rs = .31, −.30), whereas the PC compliance rate was not (rs = .18, −22; ps > .05). In addition, the MEMS permitted an examination of the relationship between time of dosing and compliance. Earlier dosing was found to be associated with better compliance ($r = -.33$, $p < .005$). These findings suggest that the MEMS is a useful measure of medication compliance for use in clinical trials. (Supported by NIAAA grants K02-AA00171, RO1-AA09538)

References:

1. O'Maley SS, Jaffe A, Chang G: Naltrexone and coping skill therapy for alcohol dependence. a controlled study. *Arch Gen Psychiatry* 49:881–887, 1992.

2. Melnikow J, Kiefe C: Patients' compliance and medical research: issues in methodology. *Journal of General Internal Medicine* 9:96–105, 1994.

NR404 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

A Placebo-Controlled Trial of Sertraline Treatment for Pediatric OCD

Robert Wolkow, M.D., Pfizer, Inc., 235 East 42nd Street, New York NY 10017; John S. March, M.D., Allan Z. Safferman, M.D., Joseph Biederman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be aware of results indicating that sertraline is a safe and effective treatment for children and adolescents with obsessive compulsive disorder.

Summary:

Objective: The safety and efficacy of sertraline in children and adolescents 6-17 years old with obsessive compulsive disorder were evaluated in a 12-week, multicenter, double-blind, placebo-controlled trial.

Method: Sertraline was flexibly titrated up to a maximum dose of 200mg once daily during the first four weeks of double-blind therapy, after which patients were continued on this dose of sertraline for eight more weeks. The primary efficacy measures were the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS), the NIMH Global Obsessive Compulsive Scale (NIMH), and the Clinical Global Impressions (CGI) scale.

Results: One hundred and eighty-seven patients—107 6-12 years old and 80 13-17 years old—were randomized to either sertraline (N = 92) or placebo (N = 95). In intent-to-treat analyses (using last observation carried forward) of the change from baseline to final visit, patients treated with sertraline showed significantly greater improvement than placebo-treated patients on the CY-BOCS ($p = 0.005$), the NIMH ($p = 0.019$), and the CGI Improvement ($p = 0.002$) scales. Significant group mean differences emerged at week three and persisted for the duration of the study. Neither age nor gender significantly affected response to treatment. The incidences of insomnia, nausea, agitation, and tremor were significantly elevated compared with placebo in patients receiving sertraline. Eleven percent of sertraline and 2 percent of placebo-treated patients discontinued prematurely due to adverse events. There were no differences in the incidence of clinically significant vital sign, laboratory, or electrocardiogram abnormalities between the sertraline and placebo treatment groups.

Conclusions: Results of this double-blind, placebo-controlled multicenter study demonstrate that sertraline is a safe and effective treatment for children and adolescents 6-17 years old with obsessive compulsive disorder.

References:

1. Greist J, Chouinard G, DuBoff E, et al: Double-blind parallel comparison of three dosages of sertraline and placebo in outpatients with OCD. *Arch Gen Psychiatry.* 52:289-296, 1995.

2. McDougle C, Goodman W, et al: The psychopharmacology of OCD. *Psychopharmacology.* 16(4):749-765, 1993.

NR405 Wednesday, May 21, 9:00 a.m.-10:30 a.m.

Relapse Prevention with Fluoxetine in Anorexia Nervosa: A Double-Blind Placebo-Controlled Study

Walter H. Kaye, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh PA 15213-2593; Theodore E. Weltzin, M.D., L.K. George Hsu, M.D., Mae S. Sokol, M.D., Claire Mc Conaha, B.S.N., Katherine H. Plotnicov, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand strategies for the treatment of anorexia nervosa and the effect of SSRIs on symptom reduction.

Summary:

Anorexia nervosa, an often chronic disorder with high morbidity and mortality, has no definitive treatment. Several lines of evidence raise the possibility that a serotonin-specific medication might be useful in the treatment of anorexia nervosa. First, anorexics have persistent serotonin disturbances after weight restoration. Second, anorexics also have obsessional behaviors. Third, several open treatment trials suggest fluoxetine may have beneficial effects in anorexia nervosa.

Most studies on the treatments of anorexia nervosa have sought to determine whether some intervention increases the rate of weight gain in hospitalized patients. This strategy is of questionable value, since factors such as a ceiling on caloric intake or the structure of inpatient treatment may confound results. Instead, we wondered whether medication could prevent relapse in anorexia nervosa by helping patients maintain a healthy and normal weight in an outpatient setting after inpatient weight restoration.

We completed a double-blind, placebo-controlled trial of fluoxetine in 35 patients with restrictor-type anorexia nervosa. Most anorexics were started on fluoxetine (n = 16) or placebo (n = 19) after inpatient weight restoration, discharged from the hospital, and followed for one year as outpatients. Subjects responded significantly better to fluoxetine than they did to placebo. Ten of 16 (63%) subjects successfully responded to fluoxetine, whereas only three of 19 (16%) responded to placebo (p = .006). Fluoxetine administration was associated with a significant weight gain and a significant reduction in core eating disorder symptoms, depression, anxiety, and obsessions and compulsions. This is the first controlled study to show that fluoxetine improves outcome in anorexia nervosa by reducing symptoms and helping maintain a healthy body weight in outpatient treatment.

References:

1. Kaye WH, Weltzin TE, Hsu LKG, Bulik CM: An open trial of fluoxetine in patients with anorexia nervosa. *Journal of Clinical Psychiatry*, 52(11):464-471, 1991.

2. Kaye WH, Nagata T, Hsu LKG, et al: Successful outcome of restricting type anorexia nervosa after the double-blind placebo-controlled administration of fluoxetine. Submitted.

NR406 Wednesday, May 21, 12 noon-2:00 p.m.

Support for the Dopamine Transporter as a Possible Susceptibility Locus for Bipolar Disorder

John R. Kelsoe, Jr., M.D., Department of Psychiatry, University of CA/San Diego, 9500 Gilman Drive/MC 0603, La Jolla CA 92093; A. Dessa Sadovnick, Ph.D., Helgi Kristbjarnarson, M.D., Patricia Bergesch, Zofi Mroczkowski-Parker, Mark H. Rapaport, M.D., Pamela Flodman, M. Anne Spence, Ph.D., Ronald A. Remick, M.D.

Summary:

The dopamine transporter (DAT) mediates the reuptake of dopamine and thereby plays a key role in the regulation of dopaminergic neurotransmission. It is also the site of action of amphetamine, cocaine, and other stimulants. Evidence implicating abnormalities of dopamine in mania, and the manic-like effects of stimulant drugs make this gene an attractive candidate locus for bipolar disorder. We have tested DAT for its possible role in bipolar disorder by examining five polymorphic DNA markers at or near DAT for linkage and association in bipolar families. We examined families from three populations: 21 families from the general North American population (UCSD/UBC families), three large Icelandic families, and Old Order Amish family 110. A maximum lod score of 2.38 was obtained under a dominant model, with the microsatellite marker, D5S392, in one general population family. In the combined families, under a recessive model, a maximum lod score of 1.76 was obtained at a Taq1 RFLP polymorphism in the DAT gene. Support was also provided from several nonparametric analyses including the Affected Pedigree Member method ($p < 0.001$), the Extended Sib Pair method ($p < 0.0008$), and the Transmission Disequilibrium Test ($p < 0.024$). These results provide suggestive evidence that DAT is a susceptibility gene for bipolar disorder.

NR407 Wednesday, May 21, 12 noon-2:00 p.m.

Health-Related Quality of Life and Early Treatment Response in Depression

Jeffrey M. Pyne, M.D., Department of Psychiatry, UCSD, 9500 Gilman Drive MC 0603, La Jolla CA 92093; Kelly N. Yoo, Shahrokh Golshan, Ph.D., Robert M. Kaplan, M.D.

Summary:

This study examines the relationship between a health-related quality of life (HRQL) measure, the Quality of Well-Being (QWB), and early treatment response of inpatients diagnosed with primary major depression. We examined the relationship between the QWB and acute changes in depressive symptoms and compared the QWB scores to other predictors of treatment response. Thirty-four inpatients with primary major depression were recruited. Diagnoses were made by consensus using the SCID-IV. Measures included: weekly Hamilton Rating Scale for Depression (HRSD), Beck Depression Inventory (BDI), and QWB. Baseline data averages weeks 1 (pre-hospital) and 2 (first hospital week). Response is defined as 50% decrease in HRSD-17 compared to the baseline HRSD. Twenty-three patients were responders. Responders' change in HRSD was positively correlated with change in the Social Activity (SAC) subscale of the QWB (p = .04). Using commonly cited predictors of treatment response and the QWB in a logistic regression model, baseline BDI, age of first depression, and baseline SAC were the most significant variables, predicting 81% of the cases.

The above results are consistent with previous literature and provide additional validity to the use of the QWB in assessing HRQL in patients with depression. Future studies will examine the cost-utility function of the QWB.

NR408 Wednesday, May 21, 12 noon-2:00 p.m.

Assessment of Affective Temperament in BP-I Disorder: Preliminary Data from a French Multicenter Study "EPIMAN"

Hagop S. Akiskal, M.D., Department of Psychiatry, Univ. of California, San Diego, 9500 Gilman Drive, La Jolla CA 92093-0603; Elie G. Hantouche, M.D., Jean-Philippe Fraud, M.D., Jean-Michel Azorin, M.D., Marc Bourgedis, M.D.

Summary:

This paper presents the preliminary results of a French multicenter study in progress on 100 hospitalized manic patients (EPIMAN). The aim of EPIMAN is to show the feasibility of validating a broader definition of "dysphoric mania."

Methodology: It involves 1) training French psychiatrists in five sites (n = 22 investigators); 2) construction of a protocol based on criteria of DSM-IV, McElroy et al, and Swann et al, as well as scales like Beigel-Murphy and Ahearn-Carroll, modified HAM-D_{13}/$_{17}$, family history, and comorbidity; 3) prospective follow-up during a period of 12 months. For assessment of affective temperaments (hyperthymic, dysthymic, cyclothymic, and irritable) semistructured interviews and self-questionnaires were constructed in French version and based on Akiskal's definitions. Temperament assessment was programmed after regression of acute manic episode (at least after four weeks from admission).

Results: Preliminary results are presented on 77 hospitalized manic patients. The rate of "dysphoric mania" or DM (defined by the presence of two depressive symptoms for "probable DM" and ≥ 3 for "definite DM") is 38%. Temperament assessment in "dysphoric mania" (DM) versus "pure mania" (PM) showed the following: 1) female over-representation (83% vs 54%, p = 0.008); 2) no difference on hyperthymic temperament (9.1 vs 11.1, p = 0.16); 3) higher level on depressive temperament in DM (9.6 vs 5,8, $p < 10^{-4}$); 4) higher level on cyclothymic temperament in DM (9.7 vs 6.8, p = 0.016); 5) higher level of "irritable temperament" only in the subgroup "probable DM" (7.3 vs 4.4 in PM, 4.1 in definite DM, p = 0.02).

Conclusions: Dysphoric mania represents a distinct form of acute mania that is best characterized by female over-representation and high levels on depressive and cyclothymic temperaments and probably on irritable temperament as well.

NR409 Wednesday, May 21, 12 noon-2:00 p.m.

The Immune Immodulating Effects of Lithium in Normal Volunteers

Mark H. Rapaport, M.D., Department of Psychiatry, UCSD UN Cal San Diego, 8950 Villa Jolla Drive, 2243, La Jolla CA 92037; Lewis L. Judd, M.D.

Summary:

Previous *in vitro* and *in vivo* studies of immune immodulatory effects of lithium in animals and humans suggest that lithium may nonspecifically stimulate immune function. In this study we evaluated the immodulatory effects of lithium on 19 normal volunteers who took lithium for 30 days. Ten men and nine women were in this study; their mean age was 36.8 years. We hypothesized that lithium would be a nonspecific activator of immune function. ELISA essays for IL-2, IL-4, IL-6, IL-10, IFN-γ, SIL-2R, and SIL-6R were performed. Chronic lithium treatment caused a statistically significant increase in IL-4 174.65 pg/ml ± 120.9 pg/ml baseline vs 351.5 pg/ml ± 375.7 pg/ml, p < .03. IL-10 also increased 652.8 pg/ml ± 908.2 pg/ml vs 939.4 pg/ml ± 772.9 pg/ml, p < .03. We did not see statistically significant changes in IL-6, IFN-γ SIL-6R, or IL-2. This suggests that lithium specifically enhanced TH-2 cell activation while not altering TH-1 are general markers of inflammation. We will discuss how these findings may reflect the specific effect of lithium on C-AMP and PI-dependent second messenger systems and immune function.

NR410 Wednesday, May 21, 12 noon-2:00 p.m.

The Characterization and Treatment of Patients with Minor Depression and Subsyndromal Depressive Symptoms

Mark H. Rapaport, M.D., Department of Psychiatry, UCSD UN Cal San Diego, 8950 Villa Jolla Drive, 2243, La Jolla CA 92037; Lewis L. Judd, M.D.

Summary:

Recent epidemiological studies have established that both minor depression (the presence of the 'A' criteria and at least one other symptom of depression) or subsyndromal depression (the presence of two symptoms of depression excluding the 'A' criteria) are associated with functional impairment. This open-label pilot study is the first to characterize the patients with these disorders and look at the effects of open-label treatment with selective serotonin uptake inhibitors. Fourteen patients with minor depression (10 men, 4 women) and 12 patients with subsyndromal depression (9 men, 3 women) were recruited from primary care settings for treatment with fluvoxamine 10-100 mg/day. The patients with MD had a mean age of 49.3 ± 9.4 years, a mean HAM-17 score of 11.5 ± 3.15, a mean IDS-C score of 21.1 ± 5.6, and a mean GAF of 62.7 ± 2.9. The 12 patients with SSD had a mean age of 54.6 ± 14.9 years, a mean HAM-17 score of 11.175 ± 2.8, a mean IDS-C score of 18.5 ± 4.9, and mean GAF of 68.6 ± 3.8. After eight weeks of open treatment, the patients with MD had a mean HAM-17 of 6.25 ± 5.3, a mean IDS-C of 10.8 ± 8.2, and a mean GAF of 75.4 ± 12.02. After eight weeks of treatment patients with SSD had a mean HAM-17 of 3.8 ± 8.1, a mean IDS-C of 5.2 ± 5.1, and mean GAF of 77.1 ± 6.1. This suggests that both groups of patients were responsive to treatment with fluvoxamine. A more complete characterization of these patients, in-depth data on social functioning, and follow-up data off medication will be presented as well.

NR411 Wednesday, May 21, 12 noon-2:00 p.m.

The Course of Bipolar Disorder During Pregnancy

Verinder Sharma, M.D., 32 Fox Chapel Road, London ON, Canada, N6A 4H1 Karen M. Kueneman, B.A., Bhooma Bhayana, M.D., Pierre Mattar

Summary:

Objective: Bipolar women are at a particularly high risk for developing a relapse in the postpartum period, but very little is known about the course of bipolar illness during pregnancy.

Method: Female patients who attended a mood disorders clinic and met the DSM-IV criteria for bipolar I and II diagnoses were mailed a questionnaire to elicit information regarding mood states just prior to and during each pregnancy, and during the postpartum period.

Results: Twenty-four of 34 women who responded to the questionnaire had children. Fifteen had bipolar I and nine had bipolar II disorder. The mean number of children born to each woman was 2.3 (SD = 1.1). There were a total of 55 pregnancies. The women reported experiencing an episode of mania or depression in the month preceding 18 pregnancies (33%). During nine pregnancies the symptoms improved (50% of those reporting episodes before pregnancy), while a worsening of symptoms was described during seven pregnancies (39%). Episodes of illness began during only 11 pregnancies (20%). The women reported a relapse of symptoms during the postpartum period in 23 pregnancies (42%) and there was a worsening of existing symptoms after delivery in

an additional 15 pregnancies (27%). Psychotropic medications were taken during only five pregnancies (9%).

Conclusions: Pregnancy may have an ameliorating effect on the course of bipolar disorder.

NR412 Wednesday, May 21, 12 noon-2:00 p.m.

Hopelessness in Outpatients with MDD

Barbara J. Cannon, M.D., Department of Psychiatry, Mass General Hospital, 15 Parkman/WACC 815, Boston MA 02114; Rosemarie Mulroy, B.A., Michael W. Otto, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D.

Summary:

Introduction: Hopelessness is a core symptom of depression and correlates strongly with suicidal intent, but not all depressed patients feel hopeless. To understand the psychological correlates of hopelessness, we assessed a cohort of drug-free depressed patients.

Methods: A sample of 138 outpatient subjects (65 males, 73 females; mean age 39 ± s.d. = 10.4) with DSM-III-R major depression completed several self-rated measures to assess hopelessness, abnormal cognitions, dysfunctional attitudes, problem-solving abilities, and social dysfunction.

Results: No significant relationships were evident between Beck Hopelessness Scale (BHS) scores and demographic (sex and age) or comorbid anxiety or alcohol or other substance use disorders. The simple regression analysis revealed significant predictors of BHS scores: the Cognitions Questionnaire (CQ), Dysfunctional Attitudes Scale (DAS), the Hamilton Rating Scale for Depression, and the Problem Solving Inventory (PSI). In the stepwise multiple regression equation, however, only the CQ and the PSI offered nonredundant predictability of hopelessness scores, and accounted for 20% of the variance in these scores.

Conclusions: Hopelessness in depressed patients appears to be related to both abnormal cognitions and impaired problem solving. Treatment that targets these areas could reduce hopelessness and perhaps, ultimately, suicide risk.

NR413 Wednesday, May 21, 12 noon-2:00 p.m.

Depression Screening: Ham-D Compared with Prime-MD

Marijo B. Tamburrino, M.D., Department of Psychiatry, Medical College Ohio, 3000 Arlington Avenue, Toledo OH 43699; Rollin W. Nagel, M.A., Denis J. Lynch, Ph.D., Mary Kay Smith, M.D., Osman M. Ali, M.D., Raj A. Narayan

Summary:

The Prime-MD has been suggested as a screening instrument to help family physicians identify common mental disorders, such as depression. In this study, persons screening positive for depression on the Prime-MD were also given the HAM-D over the telephone to compare the two instruments. A total of 481 patients in two family practice settings completed the Prime-MD Patient Questionnaire (PQ). One hundred twenty-five (26.0%) of the subjects scored positive for depression on the PQ. Of these 125 patients, 89 (70.6%) received telephone follow-up with the Prime-MD Mood Module and the HAM-D. Prime-MD Mood Module diagnoses were: major depression, 24 (27%); dysthymic disorder, 7 (7.9%); minor depression, 33 (37.1%); and no depression, 25 (28.1%). The mean HAM-D scores for each diagnosis were: major depression, 21.09; dysthymic disorder, 13.14; minor depression, 11.18; and no depression, 5.61. A one-way ANOVA indicated significant differences between these mean scores ($p < .05$). Post-hoc analysis indicated: 1) the no depression group was significantly lower than each of the three depressed groups; 2) the major depression group was significantly higher than the dysthymic disorder group and the minor depression group. This study's findings support the use of the Prime-MD Mood Module as a depression screening instrument for family physicians.

NR414 Wednesday, May 21, 12 noon-2:00 p.m.

Prime-MD Depression Screening: Anxiety Comorbidity

Marijo B. Tamburrino, M.D., Department of Psychiatry, Medical College Ohio, 3000 Arlington Avenue, Toledo OH 43699; Mary Kay Smith, M.D., Denis J. Lynch, Ph.D., Rollin W. Nagel, M.A., Raj A. Narayan, Osman M. Ali, M.D.

Summary:

Anxiety and depressive symptoms represent the two most common psychiatric conditions in primary care. This study used the Primary Care Evaluation of Mental Disorders (Prime-MD) to identify depressive disorders and explore incidence of comorbid anxiety symptoms and disorders. Patients waiting to see physicians at two primary care sites completed a demographic questionnaire and the Prime-MD Patient Questionnaire (PQ). Those scoring positive for depression received a follow-up telephone call with the Clinician Evaluation Guide (CEG) determining DSM-IV diagnosis. Four hundred eighty-one patients completed the initial screening. There were 363 (76.1%) females, and 114 (23.9%) males with a mean age of 44.2 years, and the majority (64.5%) were employed. The top six complaints endorsed on the PQ were: feeling tired, 258 (53.6%); pain in arms/legs, 222 (46.9%); worrying about things, 202 (42.8%); back pain, 185 (39.4%); headaches, 174 (37.4%); and trouble sleeping, 146 (30.4%). On the PQ, 125 (26%) screened positive for depression with 80.7% of these also positive for anxiety. On the CEG, 64 persons received a DSM-IV depression diagnosis, with 31.25% (N = 20) receiving a comorbid DSM-IV anxiety disorder diagnosis. The authors suggest changes to the Prime-MD to improve accuracy of diagnosis and better distinguish anxiety, depression, and mixed anxiety depression states.

NR415 Wednesday, May 21, 12 noon-2:00 p.m.

Manual-Based Group Therapy for Bipolar Disorder

Linda McBride, M.S.N., 116A, VA Medical Center, 830 Chalkstone Avenue, Providence RI 02908; Mark S. Bauer, M.D., Catherine E. Chase, D.O., Gary S. Sachs, M.D.

Summary:

Objective: The Life Goals Program was developed to improve outcome in bipolar disorder by: (1) supporting more effective participation in medical model treatment and (2) helping patients to meet functional status goals.

Methodology: Phase 1 is a highly structured five-week psychoeducation intervention. Phase 2 is a goal-driven behaviorally oriented intervention devised to assist patients in identifying and meeting functional goals of their choice. The program was developed and then piloted on 29 patients across four therapists and two sites. The goals of this study were to determine whether the procedures could be exported to other therapists, whether procedures were tolerable to patients, and whether we could identify outcome parameters and time course of effects.

Results: Therapists covered a mean of 96% focus points in Phase 1, while content ratings averaged 90% and process ratings averaged 94%. Indices of good to excellent participation were demonstrated in most patients, despite high levels of psychopathology. Several outcome variables showed promise, with the time course to Phase 2 goals measured over months rather than weeks.

Conclusions: The program can be exported with fidelity to its manual-based interventions. Impact of the program must be investigated over months rather than weeks.

NR416 Wednesday, May 21, 12 noon-2:00 p.m.

Disability in the Chronically Depressed

Ivan W. Miller, Ph.D., Department of Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence RI 02903; James M. Russell, M.D., Michael E. Thase, M.D., Andrew Baker, M.P.A.

Summary:

Objective: Depression is at least as disabling as many other chronic medical illnesses. Depressed patients in the Medical Outcomes Study were as disabled as those with congestive heart failure (Hays 95). Despite the debilitative nature of depression, it is often unrecognized by physicians (Wells 1988). In a study comparing sertraline to imipramine, the extent of disability in chronically depressed patients was measured before and after 12 weeks of treatment.

Methods: In a 12-week, double-blind study involving 12 sites throughout the U.S., 635 subjects were randomized in a 2:1 ratio of sertraline to imipramine. The SF-36, SAS, and LIFE scales were administered to monitor disability at baseline and after 12 weeks of treatment.

Results: The patients in this study are as disabled as chronic cardiac patients in the Medical Outcomes Study. Physical functioning, general health perception, and freedom from pain improved from 15% to 30% in the 12-week treatment period. Work by employed patients increased from 28 to 38 hours per week and the percent unemployed decreased from 20% to 14%.

Conclusion: Chronically depressed patients are significantly disabled and this disability responds well to treatment.

NR417 Wednesday, May 21, 12 noon-2:00 p.m.

Sertraline Maintenance Therapy in Chronic Depression

Martin B. Keller, M.D., Department of Psychiatry, Butler Hospital/Brown Univ., 345 Blackstone Boulevard, Providence RI 02906; James H. Kocsis, M.D., James P. McCullough, Ph.D., George A. Trapp, M.D., Alan F. Schatzberg, M.D., Michael E. Thase, M.D.

Summary:

Chronic forms of depression are common, disabling, and undertreated. Acute treatment trials in chronic depression have demonstrated positive outcome for both depressive symptoms and psychosocial functioning. With the exception of one recent long-term study of desipramine pharmacotherapy in patients with chronic depression, there has been no systematic study of maintenance therapy to prevent recurrence in chronic depression.

Objective: To determine the efficacy of maintenance therapy with sertraline in chronic depression.

Method: Patients with DSM-III-R-defined chronic major depression or "double depression" who had responded to sertraline treatment during acute and continuation treatment (28 weeks) were randomized to either continue on sertraline or be tapered to placebo, double blind, for an 18-month study of maintenance treatment. Patients were stratified on probability of recurrence of depression, based on number of previous episodes of major depression and degree of residual symptoms of depression at the time of randomization. Assessments at baseline and monthly visits included the HRSD, MADRS, BDI, CGI, and psychosocial measures.

Results: A comparison of time to recurrence by treatment group was made using a log rank test of Kaplan-Meier estimates. Patients discontinued to placebo demonstrated a significantly shorter time to recurrence of depression compared with patients maintained on sertraline ($p < .05$). Data on demographic and diagnostic characteristics of patients who remained well and those who experienced a recurrence of depression will be presented.

Conclusion: Chronically depressed patients who have continued to demonstrate a therapeutic response through continuation treatment may benefit from maintenance antidepressant therapy.

NR418 Wednesday, May 21, 12 noon-2:00 p.m.

Predictors of Service Use in Bipolar Disorder

Christopher Gavin, B.S., 116 A, VA Medical Center, 830 Chalkstone Avenue, Providence RI 02908; Nancy Shea, R.N., Linda McBride, M.S.N., Mark S. Bauer, M.D.

Summary:

Objective: Many studies have investigated predictors of disease and functional outcome for bipolar disorder. Few have addressed measures of economic outcome. This study investigates predictors of service utilization and resulting mental health expenditures.

Methodology: This study prospectively followed 103 bipolar patients enrolled in a VA treatment program for one year. Inpatient and ambulatory mental health service contacts were recorded and aggregated using the VA Cost Distribution Report. We hypothesized that predictors of illness severity, including current substance dependence, mixed episode, rapid cycling, and history of psychosis, would also predict service utilization, but that other predictors of the latter might also be identified.

Results: Regression analysis investigated several demographic and clinical predictors indicated. Only the presence of a major affective episode at clinic intake and childhood history of physical abuse predicted mental health service utilization. Few types of service contacts differed between those with and without the risk factors for poor disease outcome.

Conclusions: These data indicate that economic outcome may not be driven simply by disease status. This is not surprising since service utilization is likely the product of both disease status and treatment-seeking behavior on the part of patients, which is likely determined by complex patient and provider factors.

NR419 Wednesday, May 21, 12 noon-2:00 p.m.

A Fixed-Dose Comparison of Citalopram Versus Placebo

John P. Feighner, M.D., N Green/Marketing, Forest Laboratories, 909 3rd Avenue, New York NY 10022; Ronald R. Fieve, M.D., John S. Carman, M.D., Lynn A. Cunningham, M.D., Gerri Schwartz, Ph.D.

Summary:

Citalopram, the most selective serotonin reuptake inhibitor available, is approved in Europe at single daily doses of 20 to 60 mg/day. The present study is one of two completed placebo-controlled trials, which were conducted in the U.S. to confirm the efficacy and safety of citalopram in the treatment of patients with moderate to severe depression. In this multicenter randomized trial, patients who were nonresponsive to placebo treatment during the initial one-week, single-blind phase were randomized to citalopram 10 ($n = 131$), 20 ($n = 130$), 40 ($n = 131$), or 60 ($n = 129$) mg/day q.d., or placebo ($n = 129$) treatment for up to six weeks. Both the 40 and 60 mg/day citalopram groups demonstrated significant ($p < 0.05$) improvements in HAMD, MADRS, and CGI endpoint scores compared with placebo. Citalopram was well tolerated with a safety profile similar to that of other SSRIs. Based on these results, both the 40 and 60 mg/day doses of citalopram are effective and well tolerated for the treatment of patients with moderate to severe depression.

NR420 Wednesday, May 21, 12 noon-2:00 p.m.

Effects of Extended Release (ER) Venlafaxine on Anxiety in Patients with Major Depression

John P. Feighner, M.D., N Green/Marketing, Forest Laboratories, 909 3rd Avenue, New York NY 10022; Richard Entsuah, Ph.D., Mary K. McPherson, M.S.

Summary:

Objective: Evaluate the effects of venlafaxine extended release (ER) and venlafaxine on anxiety symptoms in outpatients with major depression.

Methods: Study 1 was a 12-week, randomized, double-blind, placebo-controlled trial. Patients received venlafaxine 37.5 mg twice daily, venlafaxine ER 75 mg once daily, or placebo. The venlafaxine dose could be increased to 150 mg daily after two weeks to increase the response. Study 2 was an eight-week, randomized, double-blind, placebo-controlled trial. Patients received venlafaxine ER 75 mg or placebo once daily. The venlafaxine ER dose could be increased to a maximum of 225 mg/day. Moderate or greater anxiety was a HAM-D anxiety-psychic item score ≥ 2 and severe anxiety was a score ≥ 3.

Results: Study 1: Among patients with moderate or greater ($n = 252$) or severe anxiety ($n = 96$) at baseline, a significant reduction ($p \leq 0.05$ to ≤ 0.001) in the HAM-D anxiety-psychic item scores occurred with venlafaxine ER compared with placebo from weeks 4 through 12. A similar response was observed with venlafaxine. Study 2: Among patients with moderate or greater anxiety ($n = 161$) or severe anxiety ($n = 60$) at baseline, a significant reduction ($p \leq 0.05$ to ≤ 0.001) in HAM-D anxiety-psychic item scores occurred with venlafaxine ER compared with placebo from weeks 1 through 8.

Conclusion: Venlafaxine ER is effective for the reduction of anxiety symptoms associated with major depression at doses of 75 to 225 mg/daily.

NR421 Wednesday, May 21, 12 noon-2:00 p.m.

Differential Female and Male Cerebral Glucose Metabolism Abnormalities in Depression

Timothy A. Kimbrell, M.D., BPB/Bldg 10, Rm 3N-212, Nat'l Inst of Mental Health, 10 Center Drive/MSC 1272, Bethesda MD 20892; Terence A. Ketter, M.D., Robert T. Dunn, M.D., John T. Little, M.D., Mark A. Frye, M.D., Robert M. Post, M.D.

Summary:

Objective: Women compared with men have more widespread and limbic/paralimbic activation during transient sadness induction, higher prevalence of depression, and may have differential responses to pharmacotherapies. We explored differential cerebral glucose metabolism (CMRglu) abnormalities in depressed unipolar women and men when compared with healthy controls.

Method: Twenty-two depressed female and 10 depressed male patients and equal numbers of age- and sex-matched controls were studied with positron emission tomography and 18-fluorodeoxyglucose.

Results: Female and male patients had nonsignificantly lower global CMRglu than the control groups. Female patients compared with controls had decreased (absolute and normalized) left medial temporal, left dorsolateral prefrontal, left thalamus, right cingulate, and right lateral temporal rCMRglu ($p < .005$). Female patients also had increased normalized but not absolute right cerebellum, temporoparietal, and inferior frontal rCMRglu. In contrast, male patients compared with controls had decreased normalized, but not absolute, mesial orbitofrontal, mesial temporal, left lateral temporal, left dorsolateral prefrontal, and right insula rCMRglu. Male patients also had increased normalized, but not absolute, posterior cingulate rCMRglu.

Discussion: The complimentary hypometabolism patterns we noted in female and male depressed patients compared with controls, when combined yield regional differences consistent with prior reports that used mixed gender samples, and are consistent with differential pathophysiologies, perhaps due to the central effects of sex steroids.

NR422 Wednesday, May 21, 12 noon-2:00 p.m.

Effects of Prior Course of Illness on the Neuropsychological Functioning of Patients with Bipolar Disorder

Syed O. Ali, B.S., BPB, NIMH, 9000 Rockville Pike, RM 3N212, Bethesda MD 20892; Earlian E. Smith-Jackson, R.N., Gabriele S. Leverich, M.S.W., Ellen G. Connell, Robert M. Post, M.D., Kirk D. Denicoff, M.D.

Summary:

Objective: This study investigated the association of prior course of illness and neuropsychological functioning in patients with bipolar disorder.

Method: Using a battery of neuropsychological tests, measures of memory, attention, concentration, abstracting ability, intelligence, and psychomotor functioning were assessed in 49 bipolar patients who met DSM-III-R criteria for bipolar disorder. Patients participated in a blind, randomized study comparing the prophylactic efficacy of lithium or carbamazepine in the first year, a crossover to the other drug in the second year, and a third year on the combination of both lithium and carbamazepine. Course of illness prior to study entry was assessed using the retrospective NIMH-Life Chart Method, which characterized the degree of functional impairment caused by periods of mood dysfunction on a monthly basis. Stepwise multiple regression was used to analyze whether prior course of illness variables were associated with neuropsychological functioning.

Results: On memory tests (California Verbal Learning Test), patients with a greater number of weeks ill and a greater number of manic episodes prior to study entry had more impairment. On tests of abstracting ability (Halstead Categories, Wisconsin Card Sorting Test) patients with a greater number of total depressive episodes and a greater number of total hospitalizations had more impairment. Tests of attention and concentration (Cancellation Task) again showed that a greater number of depressive episodes, a longer duration of illness, a greater number of hospitalizations per year, and a greater number of episodes during the year before study entry were associated with more impairment. A greater number of episodes during the year before study entry was associated with poorer performance on intelligence tasks (WAIS-R), whereas a later age of onset of first treatment and first symptom were associated with better performance on intelligence tasks.

Conclusions: The mechanisms by which severity of prior course of illness is associated with impaired neuropsychological performance in bipolar patients require further study.

NR423 Wednesday, May 21, 12 noon-2:00 p.m.

Psychosensory Symptoms in Patients with Bipolar Disorder

Syed O. Ali, B.S., BPB, NIMH, 9000 Rockville Pike, RM 3N212, Bethesda MD 20892; Kirk D. Denicoff, M.D., Terence A. Ketter, M.D., Earlian E. Smith-Jackson, R.N., Robert M. Post, M.D.

Summary:

Objective: This study investigated the relationship of psychosensory symptoms to predicting course of illness as well as therapeutic outcome in patients with bipolar disorder.

Method: Using the Silberman-Post Psychosensory Rating Scale (SP-PSRS), psychosensory symptoms were examined in 51 pa-

tients who met DSM-III-R criteria for bipolar disorder and in 39 healthy normal controls. Bipolar patients participated in a blind, randomized study comparing the prophylactic efficacy of lithium or carbamazepine in the first year, a crossover to the other drug in the second year, and a third year on the combination of both lithium and carbamazepine. Psychosensory scores from bipolar patients were compared with both scores from healthy controls and with a variety of retrospective and prospective course of illness and treatment variables.

Results: Psychosensory symptoms occurred frequently in bipolar patients (mean ± S.D.: 18.41 ± 13.94), but were uncommon in healthy controls (mean ± S.D.: 2.23 ± 2.45). Bipolar II patients experienced more psychosensory symptoms when depressed (mean ± S.D.: 7.96 ± 6.94, n = 23) compared with bipolar I patients (mean ± S.D.: 3.32 ± 4.30, n = 28). Patients with a history of rapid cycling experienced more psychosensory symptoms when depressed (mean ± S.D.: 6.07 ± 5.28, n = 29) compared with patients with no history of rapid cycling (mean ± S.D.: 3.29 ± 3.81, n = 21). However, patients with a history of psychosis experienced fewer psychosensory symptoms when depressed (mean ± S.D.: 3.20 ± 4.62, n = 25) compared with patients without a history of psychosis (mean ± S.D.: 7.54 ± 6.57, n = 26). Psychosensory symptoms were not related to response to carbamazepine, lithium, or the combination of both drugs.

Conclusions: Although the presence of psychosensory symptoms is associated with some bipolar disorder subtypes (bipolar II and rapid cycling patients), they do not appear to predict treatment response or therapeutic outcome. Further studies are needed to assess the theoretical implications of the presence of psychosensory symptoms and their potential implications for therapeutics.

NR424 Wednesday, May 21, 12 noon-2:00 p.m.

Cognitive Side Effects of Lithium, Carbamazepine and Their Combination in Patients with Bipolar Disorder

Kirk D. Denicoff, M.D., BPB, NIMH Bldg 10 RM 3N212, 9000 Rockville Pike, Bethesda MD 20892; Syed O. Ali, B.S., Earlian E. Smith-Jackson, R.N., Allan F. Mirsky, M.D., Robert M. Post, M.D.

Summary:

Objective: To study the cognitive side effects of lithium, carbamazepine, and the combination of lithium and carbamazepine in patients with bipolar disorder.

Method: Outpatients who met DSM-III-R criteria for bipolar disorder were randomized in a double-blind design for an intended one year of treatment with lithium or carbamazepine, a crossover to the opposite drug in the second year, and a third year on the combination of both medications. Patients were administered a battery of neuropsychological tests during each of the three treatment phases. Test variables were compared between the lithium and carbamazepine drug phases, lithium and combination drug phases, and carbamazepine and combination drug phases using Wilcoxon rank sum tests. Patients were tested when clinically stable and when not requiring adjunctive psychotropic medication.

Results: Tests that assessed psychomotor functioning, such as the Trail Making Test A and B and the Purdue Pegboard, demonstrated that patients performed best when on carbamazepine and worst when on the combination. On the Continuous Performance Test (CPT), patients had a longer mean time to respond on the combination compared with either monotherapy. On one of the subtests for the Cancellation Task, patients performed significantly better on carbamazepine compared with the other two treatment phases. No significant difference was found between the treatment phases on the Wisconsin Card Sorting Test, Halstead Categories Test, and the California Verbal Learning Test (CVLT).

Conclusions: Neuropsychological tests measuring attention, concentration, and psychomotor speed demonstrated that patients performed the worst when on the combination of lithium and carbamazepine compared with either monotherapy. On some tests, patients had greater psychomotor impairment on lithium compared with carbamazepine.

NR425 Wednesday, May 21, 12 noon-2:00 p.m.

Thyroid Potentiation in Affective Illness

Mark A. Frye, M.D., BPB/Bldg 10, Rm 3N-212, NIMH, 10 Center Drive/MSC 1272, Bethesda MD 20892; Kirk D. Denicoff, M.D., David A. Luckenbaugh, M.A., Timothy A. Kimbrell, M.D., Robert T. Dunn, M.D., Robert M. Post, M.D.

Summary:

While Joffe and Singer (1990) reported differential response rate of thyroid potentiation with T_3 (53%) versus T_4 (19%), few other comparative data are available on this issue. Forty-two treatment-refractory patients were hospitalized on the 3-West BPB, NIMH research unit and received a double-blind, nonrandomized trial of thyroid potentiation with T_3 (39 ± 2.9 μg/day), $_4T$ (102 ± 18 μg/day) based on physicians' choice for an inadequate response to antidepressant or mood stabilizer regimens. Marked or moderate improvement on the CGI-BP were considered responders. The T_3 potentiation data set included 23 females and 10 males, eight bipolar I, 15 bipolar II, nine unipolar, and one patient with panic disorder, with 70% of the evaluations unconfounded by any medication changes during the trial or two weeks prior. The T_4 potentiation data set included 10 females and five males, 13 bipolar I, and two unipolar patients with 40% of the evaluations unconfounded. The overall antidepressant response rate for T_3 was 11/33 (33%) and for T_4 was 8/15 (53%). Of interest was the trend for females (f) to respond at a higher rate than males (m): for T_3 (f = 10/23, 44% vs. m = 1/10, 10%; $\chi^2 = 3.5$, $p = .06$); for T_4 (f = 7/10, 70% vs. m = 1/5, 20%; $\chi^2 = 3.35$, $p < .07$). T_3 potentiation response was statistically significant by day 4 and unlikely to occur after day 13 if not already present. Responders to T_3 tended to have more diurnal variation than nonresponders ($p = .08$) during the week prior to potentiation. There were no differences in responders versus nonresponders in baseline serum, cortisol, or thyroid indices including T_3, T_4, free T_4, and TSH. These partially controlled observations in treatment-refractory affectively ill patients suggest the potential utility of thyroid potentiation, particularly in females, and the need for further systematic study of T_3 versus T_4 responsiveness.

NR426 Wednesday, May 21, 12 noon-2:00 p.m.

Thyroid Stimulating Hormone and Suicidality in Refractory Mood Disorders

Mark A. Frye, M.D., BPB/Bldg 10, Rm 3N-212, NIMH, 10 Center Drive/MSC 1272, Bethesda MD 20892; Gabriele S. Leverich, M.S.W., Amy L. Danielson, B.A., Ann M. Callahan, M.D., Timothy A. Kimbrell, M.D., Robert T. Dunn, M.D.

Summary:

Recent data suggest an inverse relationship between peripheral TSH and left dorsolateral prefrontal cerebral blood flow. This study investigates the relationship between serum TSH and suicidality in treatment-refractory affective disorder patients. Twenty-eight patients were hospitalized on the 3-West Clinical Research Unit of the BPB, NIMH, and underwent a medication-free lumbar puncture and, on the same day, phlebotomy and, in 25 patients, assessment of suicidal intent using the Scale for Suicidal Ideation (Beck, 1979). The demographics of this group included 11 males and 14 females, eight bipolar I, 11 bipolar II, and six unipolar patients with an average age of 41.1 ± 9.4. There was a positive relationship

between TSH and suicidality in the group as a whole ($r = .526$, $n = 25$, $p = .006$ using the Pearson r). This positive relationship was robust and significant in males ($r = .74$, $p = .007$) but not females ($r = .31$, $p = .28$). There was a positive correlation between age and TSH in the group as a whole ($r = .48$, $p < .01$), again in males but not females. When age was covaried for, the correlation between suicidality and TSH remained significant for the total group ($r = .531$, $p = .008$), more strongly for males than females. There was no correlation between TSH and mood on the Hamilton scale ($r = .13$, $p =$ NS). These results suggest a positive relationship between suicidality and TSH. This marker of relative peripheral thyroid hypofunction has also been linked to prefrontal cortical flow decrements. Further exploration of this relationship is encouraged.

NR427 Wednesday, May 21, 12 noon-2:00 p.m.

Anhedonia and Regional Cerebral Metabolism in Affective Disorders

Robert T. Dunn, M.D., Biological Psychiatry, NIMH, NIH, 10 Center Dr/Bldg 10, Rm 3N212, Bethesda MD 20892; Timothy A. Kimbrell, M.D., John T. Little, M.D., Mark A. Frye, M.D., Mark W. Willis, M.Eng., Robert M. Post, M.D.

Summary:

The cardinal symptoms of depression are depressed mood and anhedonia. Abnormal cerebral blood flow and glucose metabolic rates (CMRglu) in frontal cortex and paralimbic regions have been found in affective disorders. We explored the relationship between patient-reported anhedonia and CMRglu topography in affective disorders.

Fifty-seven treatment refractory affective disorder patients (33 UP, 7 BP I, 17 BP II, age = 39.4 ± 12.7, HAM-D = 16.9 ± 8.7) had medication-free, ^{18}F-deoxyglucose PET scans during an auditory continuous performance task. Anhedonia was evaluated by question #4 of the Beck Depression Inventory. The relationships between anhedonia and absolute or globally normalized regional CMRglu were examined utilizing voxel-by-voxel Spearman rank-order correlation analysis.

Increased right medial prefrontal cortex, right anterior cingulate, left medial temporal gyrus, and left cerebellar normalized CMRglu broadly correlated with increased anhedonia ($p < .001$). Increased normalized CMRglu in left ventral striatum also correlated with increased anhedonia ($p < .005$). Interestingly, all of these brain regions, except the cerebellum, are relatively enriched in dopamine in humans and support intracranial self-stimulation in animals. These preliminary data suggest that abnormal CMRglu in these brain regions may be related to anhedonia, and are consistent with current knowledge of brain reward systems.

NR428 Wednesday, May 21, 12 noon-2:00 p.m.

OCD in an HMO: Prevalence, Treatment and Costs

Lorrin M. Koran, M.D., 710 Alvarado Row, Stanford CA 94305-1049; Jeanne L. Leventhal, M.D., Bruce Fireman, M.S., Alice Jacobson, M.S.

Summary:

Objective: To report the diagnosed prevalence, rate of drug treatment, and nonpsychiatric medical care costs of OCD patients in an HMO.

Method: We utilized computerized records to examine the one-year prevalence of diagnosed OCD in the 1.96 million members aged six or older who were enrolled continuously for 12 months, 5/95 through 4/96, in the Kaiser Northern California HMO. Chart reviews are underway to validate OCD diagnosis. We also examined OCD patients' annual rates of drug treatment and compared their age- and sex-adjusted mean costs for nonpsychiatric utilization with that of Kaiser members with no psychiatric clinic visit, using ordinary least squares regression models.

Results: The prevalence of diagnosed OCD was 1.19/1,000 members (95% CI: 1.14–1.24), higher for adult females than males (1.32 vs. 1.04), and lower for female children aged 6 to 17 than for male children (0.83 vs. 1.53). Twenty-three percent of OCD patients had ≥ 4 psychiatry clinic visits between 5/95 and 4/96 and 54% had a ≥ 8-week trial of a therapeutic dose of a serotonin reuptake inhibitor (65% among those with ≥ 4 visits) (note: some one-visit "OCD" patients may not have OCD; some OCD patients' first visit occurred near the study period's end). The mean annual cost of OCD patients' nonpsychiatric visits was 63% higher ($848 vs. $521), and their laboratory and radiology service costs 56% higher ($176 vs. $113).

Conclusion: The diagnosed prevalence of OCD is lower than household survey data prevalence, and utilization patterns offer opportunities for improving cost-effectiveness of care.

NR429 Wednesday, May 21, 12 noon-2:00 p.m.

Preventing Relapse in Chronic Depressions

Lorrin M. Koran, M.D., 710 Alvarado Row, Stanford CA 94305-1049; Charles Debattista, M.D., Christine Smith, M.D., Robert H. Howland, M.D., Susan G. Kornstein, M.D.

Summary:

Objective: To provide data on longer-term treatment outcome for chronic depressions.

Method: We report 16-week continuation phase results from a double-blind, randomized, parallel group, multicenter trial of sertraline or imipramine in DSM-III-R chronic depression (≥ 2 years of major depression, or major depression + dysthymia). In the 12-week acute phase, we randomly assigned 635 men and women (294 chronic, 341 double depression) to sertraline or imipramine in a 2:1 ratio, ages 21–65; baseline $HAMD_{24} \geq 18$; absent or secondarily important other axis I disorders; and, absent psychotic features, suicide risk, and important medical disease. Continuation patients had responded by acute phase end, or after a 12-week, double-blind crossover to the alternate drug. Because the diagnostic groups exhibited no important baseline differences, they are combined here.

Results: By continuation start, 53% of 239 entering sertraline patients had achieved full remission: CGI improvement (CGI-I) ≤ 2 and $HAMD_{24} \leq 7$; 44% were "responders": CGI-I ≤ 2, $HAMD_{24}$ ≤ 15, ≥ 50% ↓ in $HAMD_{24}$ from baseline, and CGI-Severity ≤ 3. For the 147 entering imipramine patients, these figures were: 58% full remission and 42% responders. At continuation end, 72% of sertraline remitters and 76% of imipramine remitters remained in remission; 38% of sertraline responders and 34% of imipramine responders had achieved remission.

Conclusion: About 3/4 of chronically depressed patients who had achieved remission during acute sertraline or imipramine treatment maintained it during four months of further treatment. About 1/3 of acutely responding patients achieved full remission during four months further treatment.

NR430 Wednesday, May 21, 12 noon-2:00 p.m.

Alcohol Abuse and Bipolar Disorder: Family History

Jose de Leon, M.D., UK/MHRC, Eastern State Hospital, 627 West Fourth Street, Lexington KY 40508; Fernando Mosquera, M.D., Ana Gonzalez-Pinto, M.D., Miguel Guiterrez, M.D., Juan L. Figuerido, M.D., Purification Lopez, M.D.

Summary:

Background: The possibility of a familial relationship between alcohol dependence and bipolar disorder (BD) has been frequently argued. This report compares a group of BD patients with alcohol

dependence (or abuse) with other BD patients with no diagnosis of alcohol dependence.

Method: Subjects are bipolar patients who attended in any of the state of Alava's (Spain) mental health centers, from 1994 until 1996. They were studied with the SCID-P interview and DSM-III-R criteria. Sociodemographic variables and family history with the RDC-FH were rigorously assessed.

Results: A total of 170 BD patients were selected, 19.5% with a diagnosis of alcohol abuse or dependence and 80.5% nonalcoholics. The alcoholism was more frequent in men. The age at onset of BD was earlier in the group of alcohol dependent patients. We found no differences in family history of alcoholism.

Conclusions: The prevalence of alcohol abuse and dependence is quite frequent in our sample and it was in the same range described in previous reports. As in other studies, we found no differences in the family history of either group. This study does not support the hypothesis that alcoholism in bipolar disorder is related to a family history of alcoholism.

NR431 Wednesday, May 21, 12 noon-2:00 p.m.

Psychosis and Bipolar Disorder

Jose de Leon, M.D., UK/MHRC, Eastern State Hospital, 627 West Fourth Street, Lexington KY 40508; Ana Gonzalez-Pinto, M.D., Fernando Mosquera, M.D., Miguel Gutierrez, M.D., Jose L. Perez de Heredia, M.D., Jesus Ezcurra, M.D.

Summary:

Background: The objective of this presentation is to investigate the presence of psychosis in BD diagnosis and its relationship with sociodemographic and outcome data.

Method: Subjects are bipolar patients diagnosed by DSM-III-R criteria, who attended any of the state of Alava's (Spain) mental health centers (310,000 inhabitants) from January 1994 to December 1996. All patients were studied with semistructured SCID-P interview. Sociodemographic data were obtained by interviewing the probands and their relatives. Medical records, which are easily available in Alava, were collected to confirm previous clinical data. Outcome was measured by the GAF and the number of admissions in the previous year.

Results: A total of 170 patients were selected: 80% have never been psychotic, 56% have never had mood congruent psychotic symptoms, and 46% have never had mood-incongruent psychotic symptoms. The bipolar patients with mood-incongruent psychotic symptoms had an earlier age at onset ($p = 0.005$), were more frequently single ($p < 0.005$), and had two or more hospitalizations during the previous year.

Conclusions: Psychosis is frequently presented in bipolar patients. Mood-incongruent psychotic symptoms are frequent and are associated with an earlier age at onset and a worse prognosis.

NR432 Wednesday, May 21, 12 noon-2:00 p.m.

The Relationship Between Head Injuries, Depression and Suicidality in Appalachia

Geoffrey S. Duckworth, M.D., Department of Psychiatry, ARH Psychiatric Center, 102 Medical Center Drive, Hazard KY 41701; Hazel E.A. McBride, Ph.D., Joselito B. Morales, M.D., Roy S. Price, M.S.W.

Summary:

Objective: Few studies have examined the incidence of head injuries in depressed and suicidal populations. This study investigates the relationship between these three factors.

Method: One hundred and four consecutive admissions to the ARH Psychiatric Center in Hazard, Kentucky, were diagnosed by the attending psychiatrist using DSM-IV criteria. All patients were administered a standardized questionnaire by a social worker documenting stressful life events, history of head injury, and family history of psychiatric illness and alcoholism. The relationship of head injuries and suicide to diagnostic category was analyzed using Chi-square analysis with continuity correction. A probability level of .05 was considered to be significant.

Results: Patients with a primary diagnosis of depression or dysthymia were found to be significantly more likely to have suffered a closed head injury than were the other diagnostic groups, while schizophrenics and other psychotics were found to be significantly less likely to have suffered a closed head injury ($p = .039$). Patients with closed injuries were also significantly more likely to have suicide attempts ($p = .0001$) and suicide threats ($p = .0023$).

Conclusions: A positive association was observed between depression, suicidality, and head injuries, but further research is required to clarify the pathophysiology of this association.

NR433 Wednesday, May 21, 12 noon-2:00 p.m.

Risperidone for Bipolar Symptoms in the Developmentally Disabled

Mary C. Chapman, Medical, Gulf Coast Center, 5820 Buckingham Road, Ft. Myers FL 33905; George Woodley, M.D., Barkhat U. Kahn, M.D.

Summary:

The pharmacotherapy of affective disorders in the developmentally disabled is controversial because target symptoms are not necessarily clear, prescribing is based almost solely on clinical judgment, and patients' responses are often independent of whether the behaviors are reactive or endogenous. Conventional neuroleptics often reduce acute symptoms, but their prolonged use has questionable benefit and often causes dysphoria and extrapyramidal symptoms (EPS). Results of several open studies suggest that low doses of risperidone hold promise as an adjunctive mood stabilizer while posing much less risk of EPS. We report the use of adjunctive risperidone or risperidone monotherapy in five developmentally disabled adults to control acute or rapid-cycling bipolar symptoms unresponsive for many years to various combinations of mood stabilizers, anxiolytics, or neuroleptics. The patients, who were severely or profoundly mentally retarded residents of a center for the developmentally disabled, were not challenged by typical environmental factors and were well liked by staff. Three patients received risperidone (4-5 mg/day) adjunctive to lithium or valproic acid and two received risperidone monotherapy (3 or 5 mg/day). Risperidone was associated with marked long-term improvement or remission of manic hyperactivity, agitation, and insomnia, and overall improvement in quality of life in the five patients. Hypomania emerged after initial remission of mania in one of the patients who received risperidone monotherapy; however, it was controlled by addition of lithium. Risperidone is not recommended as a monotherapy for controlling mania but may be effective as an adjunct to mood stabilizers.

NR434 Wednesday, May 21, 12 noon-2:00 p.m.

Depression Awareness in Mental Health Professionals

Gregory M. Asnis, M.D., Department of Psychiatry, Montefiore Medical Center, 111 East 210th Street, Bronx NY 10467; Elizabeth John, M.D., Shehzad Kamran, M.D., William Sanderson, Ph.D.

Summary:

Introduction: Major depression (MD) is frequently undiagnosed and untreated. Since MD is prevalent with a high morbidity and mortality rate, the NIMH established the Depression Awareness Recognition and Treatment (DART) Program to help educate health professionals about MD.

Methods: We report here the outcome of our participation in the DART program (1992–1996) in the NY metropolitan area. Prior to each symposium (n = 18), we administered a questionnaire (16 true/false statements) assessing one's understanding of diagnostic and treatment issues of MD. Demographics such as discipline, years of experience, etc., were assessed.

Results: A total of 1,034 health professionals (304 psychiatrists, 207 psychologists, 396 MSWs, 61 nurses, and 40 OTs) participated. The groups differed significantly on their knowledge of depression. The prevalence of correct responses was 80% for psychiatrists, 81% for psychologists, 73% for MSWs, 69% for nurses, and 69% for OTs, $F = 9.85$ $p < .001$. Follow-up Tukey tests found that psychiatrists and psychologists did not differ from each other but both had significantly greater correct responses than MSWs or nurses. A number of questions had correct rates of less than 70%. For example, question 1 stated that "one could not diagnose MD unless at least one vegetative sign is present (which is false); only 59.5% answered correctly.

Conclusion: Although some disciplines had a greater knowledge base than others, all needed further training in depression. Implications of our findings on education will be discussed.

NR435 Wednesday, May 21, 12 noon-2:00 p.m.

The Altman Self-Rating Mania Scale (ASRM)

Edward Altman, Psy.D., Department of Psychiatry, University of Illinois, 1601 West Taylor Street, 7-East, Chicago IL 60612; Donald Medeker, Ph.D., James L. Peterson, B.A., John M. Davis, M.D.

Summary:

Objective: We describe the development, reliability, and validity of the Altman Self-Rating Mania Scale (ASRM).

Method: The ASRM was completed during medication washout and after treatment by 22 schizophrenic, 13 schizoaffective, 36 depressed, and 34 manic patients. The CARS-M and MRS were administered at the same time to measure concurrent validity. Test-retest reliability was assessed separately on 20 depressed and 10 manic patients who completed the ASRM twice during washout.

Results: Principal components analysis of ASRM items revealed three factors: mania, psychotic symptoms, and irritability. Baseline mania subscale scores were significantly higher for manic patients compared with nonmanic patients. Manic patients had significantly decreased post-treatment scores for all three subscales. ASRM mania subscale scores were significantly correlated with MRS total scores ($r = 0.718$) and CARS-M mania subscale scores ($r = 0.766$). Test-retest reliability for the ASRM was significant for all three subscales ($r = 0.86$, $p < .001$; $r = 0.89$, $p < .001$; $r = 0.88$, $p < .001$). Cronbach's alpha resulted in values of 0.79 for subscale 1 and 0.65 for subscales 2 and 3, respectively. Significant differences in severity levels for some symptoms were found between patient ratings on the ASRM and clinician ratings on the CARS-M. Mania subscale scores of greater than 5 on the ASRM resulted in values of 85.5% for sensitivity and 87.3% for specificity.

Conclusions: The ASRM is a useful and valid self-rating scale for assessing the presence and/or severity of manic symptomatology, and has some advantages over other self-rating manic scales. Differences between patient and clinician ratings suggest some denial or under-reporting of severity levels in manic patients with mild to moderate symptomatology.

NR436 Wednesday, May 21, 12 noon-2:00 p.m.

Personality Variables in Response to Antidepressants

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 examine personality variables in depression.

Method: Eighty depressed (ICD-10: major depression) outpatients (mean age 36) received paroxetine (20 mg o.d.) plus, randomly, either pindolol (2.5 mg t.d.s.) or placebo for six weeks. The Montgomery-Asberg Depression Rating Scale [MADRS] was the chief measure of clinical outcome. Forty-eight subjects completed the Cloninger Temperament and Character Inventory (TCI-125).

Results: Among personality variables, reward dependence and harm avoidance help to predict MADRS score at day 42 for all patients. For patients who received pindolol and paroxetine, novelty seeking and harm avoidance were more predictive of MADRS at day 42 and at six months. For patients who received placebo and paroxetine, self directedness was an additional predictor of MADRS score at day 42. The baseline MADRS score of compliant patients was correlated with harm avoidance scores. Self directedness was an additional predictor of MADRS score at day 42 in this group. In noncompliant patients, reward dependence predicted MADRS score at day 42.

Conclusion: Personality variables may exert a significant influence on the outcome of antidepressant treatment. The association between novelty seeking and the dopaminergic system may be significant in the mechanism of action of pindolol.

NR437 Wednesday, May 21, 12 noon-2:00 p.m.

Study of the ECT Influence in the rCBF by HMPAO-SPECT

Edorta Elizagarate, Department of Psychiatry, Hospital Santiago, Olaguibel 29, Vitoria-Alava 01004, Spain; Maria Artamendi, M.D., Ana Gonzalez-Pinto, M.D., Julia Cortes, M.D., Ignacio Alonso, M.D., Miguel Gutierrez, M.D.

Summary:

Objective: This research studies the regional cerebral blood flow (rCBF) response to electroconvulsive therapy (ECT).

Method: This is a longitudinal prospective study of a cohort of 10 patients with both major depression (CID 10, IC) resistant to pharmacological treatment, or melancholic depression. Patients were given bilateral brief pulse ECT three times a week, for six to 12 sessions, according to the standards of the psychiatric department of the Santiago Apostol Hospital in Vitoria.

Patients were assessed with the Hamilton Depression Scale (17 items), Montgomery and Asberg Scale, Newcastle Scale, the Mini-Mental Scale, and rCBF measured by HMPAO-SPECT.

Results: The pattern of distribution of the regional cerebral flow during the ECT shows changes from the basal pattern in all patients: a) 100% of the patients had a relative increased perfusion of the temporal lobes (9 bilateral; 1 unilateral) and the basal ganglia (7 bilateral; 3 unilateral). b) Other changes from the basal study were areas of decreased perfusion of the occipital lobe (60%) and parietal lobe (30%)

Conclusion: The brain perfusion SPECT study of these patients with major depression shows changes during ECT.

NR438 Wednesday, May 21, 12 noon-2:00 p.m.

Prevalence of Mood Disorders in Hungary

Erika Szadoczky, M.D., Department of Psychiatry, Haynal Imre Medical University, Nyeki Ut 10, Budapest 1021, Hungary; Zsuzsanna Papp, Jozsef Vitray, Zoltan Rihmer, M.D., Janos Iuredy, Ph.D.

Summary:

In a comprehensive epidemiological study the prevalence of mood disorders was assessed by using DIS questionnaire in a

representative Hungarian sample (2950 individuals). The lifetime prevalence for any mood disorders was 22%, for bipolar (cyclothymia, bipolar I and II) 7.9%, for MDD 15%, and for dysthymia 4.2%. The one-month prevalence for any mood disorders was 3.0%, for mania and hypomania 0.8%, for MDD 2.6%, and for dysthymia 0.5%. No sex differences were found among bipolar and pure major depressives either in lifetime or in point diagnoses. Significantly more women than men suffered from comorbid anxiety and depressive disorders. The age of onset for bipolar disorder was the late teens and for major depression and dysthymia the twenties. Two thirds of the subjects with MDD had more than one depressive episode, and 69.4% of those with dysthymia experienced a major depressive episode up to the time of the investigation. Major depression coexisted with dysthymia, GAD, panic disorder, and social phobia significantly more often than chance. A close relationship was found between the DIS suicide variables and the diagnosis of mood disorders.

NR439 Wednesday, May 21, 12 noon-2:00 p.m.

Benefit-Risk Analysis Between Venlafaxine XR and Venlafaxine

Richard Entsuah, Ph.D., Clinical Biostatistic, Wyeth-Ayerst Research, 145 King of Prussia Road, Radnor PA 19087;

Summary:

Comparisons between treatment groups in clinical trials can be done with benefits (efficacy) and risks (side effects) weighted to reflect the relative importance of various clinical outcomes and treatment response distributions. This approach is in line with decision-theoretic methods where the weights are analogous to loss functions. The linear measure and ratio measure, adopted from Chung-Stein et al (1991), simultaneously assess benefit and risk. These were used to compare a new once-a-day formulation (Ven XR) with the conventional formulation (Ven IR) of venlafaxine HCl, the first SNRI (serotonin-norepinephrine reuptake inhibitor) antidepressant.

Benefit-risk was analyzed between Ven XR and Ven IR using the results of a 12-week, randomized, double-blind, placebo-controlled trial in outpatients with DSM-III-R-defined major depression. The efficacy measure was the Clinical Global Impression - Improvement Scale, where responders had scores of 1 (very much improved) or 2 (much improved) at the final-on-therapy evaluation. Risk measures, assessed separately, were nausea/vomiting, dizziness, anticholinergic symptoms, somnolence, nervousness, and insomnia.

The ratio measure benefit/risk ratios between Ven XR and Ven IR were 3:1 for nausea/vomiting ($p < 0.01$) and 2:1 for dizziness ($p < 0.05$). The linear measure showed similar trends in favor of Ven XR, but were marginally significant. These data clearly demonstrate a statistical advantage of at least 2:1 for the benefit/risk of Ven XR treatment over the Ven IR treatment.

NR440 Wednesday, May 21, 12 noon-2:00 p.m.

Prevalence and Significance of Catatonic Symptoms in Mania

Stephanie Kruger, M.D., Department of Psychiatry, Westfal Zentrum, Alexandrinenstr 1, Bochum 44791, Germany; Peter Braunig, M.D., Gerald Shugar, M.D.

Summary:

Objective: This study investigates the prevalence and clinical significance of catatonic symptoms in mania.

Methods: Sixty-one German inpatients with DSM-III-R bipolar disorder, manic or mixed episode, were divided into catatonic (19; 31%) and noncatatonic (42; 69%) groups using the Bräunig Catatonia Rating Scale. The groups were compared for demographic and course parameters and preadmission level of functioning. Current comorbidity was assessed using the SCID of DSM-III-R criteria. Manic symptoms were measured by the Young Mania Rating Scale and the Self Report Manic Inventory, and general pathology by the Brief Psychiatric Rating Scale after admission and again before discharge.

Results: Catatonic manics had lower pre-admission functioning. Mixed mania was more frequent (18; 95% vs 28; 67%). Hospitalization was longer (mean days 112 vs. 64, $p = .002$). The YMRS, the SRMI, and the BPRS were significantly higher on admission and the BPRS remained significantly higher on discharge. There was a higher frequency of anxiety disorder (4, 21% vs. 1, 2.6%, $p = .005$), dysthymia (7, 37% vs. 3, 8%, $p = .005$), prior suicide attempts (12, 63% vs. 7; 18%, $p = .006$), binge eating behavior (11, 58 vs., 4, 10%, $p = .000$), intermittent explosive disorder (4, 21% vs. 1, 3%, $p = .018$) and polydipsia (2, 11% vs. 0, 0%, $p = .039$).

Conclusions: Almost one third of hospitalized manics had significant catatonic symptoms associated with more severe mania, more comorbid pathology, and poorer outcome.

NR441 Wednesday, May 21, 12 noon-2:00 p.m.

Severity of Illness in Mania and Schizophrenia

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Summary:

Objective: This study compared Positive and Negative Syndrome Scale (PANSS) ratings in acutely ill manic and schizophrenic inpatients to determine whether relations between severity of specific symptoms and severity of overall illness differed in these two disorders.

Method: After satisfactory interrater reliability was obtained, the PANSS was carried out on 44 bipolar manic and 93 schizophrenic patients who had undergone diagnostic evaluations based on DSM-III-R criteria using the consensus conference method.

Results: poor impulse control ($r = .66$), hostility ($r = .65$), and suspiciousness ($r = .50$) were most strongly correlated ($p \leq .001$) with an index of overall severity of illness derived from the PANSS total score in the manic group, whereas preoccupation ($r = .51$), unusual thought content ($r = .49$), and emotional withdrawal ($r = .48$) were most highly related to overall severity in the schizophrenic group ($p < .0001$).

Conclusions: Our findings suggest that severity of illness may be associated with different groups of symptoms in bipolar disorder and schizophrenia. The robust relationship of hostility and suspiciousness to overall severity of manic illness may have important clinical implications as these symptoms have been reported to predict poor response to lithium and electroconvulsive therapy.

NR442 Wednesday, May 21, 12 noon-2:00 p.m.

Gender-Based Differences in Depressive Symptoms

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Summary:

Introduction: Previous studies of gender-specific differences in depressive phenomena have observed that whereas women experience relatively greater increases in appetite and weight, depressed men tend to complain of decreases in appetite and weight.

Objectives: The purpose of the present study was to further examine gender differences in the symptoms of depressed patients.

Method: The authors completed a prospective study of 58 patients who were hospitalized with major depressive disorder. Psychiatrists rated depressive severity using the Hamilton Depression Scale. The patients completed the Profile of Mood States (POMS).

Results: The patient cohort included 20 men, and 38 women. The mean HAM-D total scores for the men (28, SD = 5), and the women (29, SD = 6), were similar. The men received higher scores on the Anger/Hostility Subscales of the POMS (18 vs 13). The women had higher scores on the Fatigue Subscale of the POMS (17 vs 15), and on the Anxiety and Somatization Subscores of the HAM-D Scale.

Conclusion: Anger and irritability may be under-recognized symptoms of depression in men, whereas somatization may be a cardinal sign of depression in women.

NR443 Wednesday, May 21, 12 noon-2:00 p.m.

Memory Processes and Executive Functions in Depression and Schizophrenia

Gilles Amar, M.D., Department of Psychiatry, Pitie-Salpetriere, Boulevard de L'Hopital, Paris 13, France; P.H. Fossati, M.D., Na Raoux, Ph.D., J.F. Allilaire, M.D.

Summary:

Objective: The objective of this study is to define the profile of memory failure and executive dysfunction associated with depression and with schizophrenia in order to specify the cognitive processes especially impaired in these two disorders.

Methods: Fourteen schizophrenic patients, 13 depressed patients (DSM-IV criteria), and 14 controls were assessed with a neuropsychological battery including 1) memory tasks (subtest of Wechsler memory, Grober & Buschke's procedure, and 2) frontal tasks (verbal fluency, Nelson's test, and Delis's test). These tasks measured the ability to maintain or shift a mental set, to select actions, and generate categories, which are important elements of executive skills.

Results: Schizophrenics performed poorly in free recall, and showed normal cued recall and recognition. Depressed subjects did not demonstrate memory deficits. Schizophrenic and depressive patients had the same executive impairments. They produced few words in fluency tasks and generated a reduced number of categories with the Delis test. There was no difference between groups on Nelson's test and on perseverative errors.

Conclusion: Schizophrenic patients exhibited a deficit in free recall and executive dysfunction. Cognitive deficits in schizophrenia are characterized by difficulties in selecting and generating actions and retrieval strategy. Depressed patients showed the same executive impairment despite a normal memory function.

NR444 Wednesday, May 21, 12 noon-2:00 p.m.

Anger Attacks in French Depressed Patients

Pauline Morand, M.D., Department of Psychiatry, Hopital St. Antoine, Rue Du FG St. Antoine 184, Paris 75012, France; Guy Thomas, Ph.D., Maurice Ferreri, M.D., Jouvent Roland, Ph.D.

Summary:

The occurrence of anger attacks in depressed patients was first investigated by Fava and coworkers, who developed a self-rating evaluation instrument, the so-called Anger Attacks Questionnaire.

Here, we present the results of a study conducted in 103 French depressed patients who were evaluated with a French translation of the Anger Attacks Questionnaire. The prevalence of anger attacks during the previous month was 46.7%, and the most frequently reported symptoms were feeling of panic (85.1%), tachycardia (83.7%), and feeling out of control (81.3%). Anger attacks were not significantly associated with either age, gender, severity of depression or anxiety, history of suicidal attempts, or mood disorder, but were significantly related to loss of control. Interestingly, a significant association was also observed with history of panic attacks: while not reported previously, this association is striking in the light of Fava's early hypothesis that anger attacks might be a variant of panic attacks.

Three-week treatment with serotoninergic antidepressants induced a significant decrease in prevalence of anger attacks.

Overall, our findings are in close agreement with those of Fava and coworkers, thus confirming the clinical relevance of anger attacks in depressed patients.

NR445 Wednesday, May 21, 12 noon-2:00 p.m.

Hormonal Responses to D-Fenfluramine in Depression: Evidence for Decreased Serotonin Function

Fabrice Duval, M.D., Department of Psychiatry, Centre Hospitalier, 27 rue du 4eme RSM, 68250 Rouffach 00110, France; M. Claude Mokrani, Ph.D., Humberto Correa, M.D.,Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Than Son Diep, M.D.

Summary:

Objective: The aim of this study was to investigate the relationships between adrenocorticotropic hormone (ACTH), cortisol (COR), and prolactin (PRL) responses to dextro-fenfluramine (D-FEN), a specific serotoninergic agonist, and the clinical characteristics of DSM-IV major depressive episode (MDE).

Methods: We studied 49 hospitalized subjects: 33 drug-free MDEs and 16 healthy control subjects (HCs). The changes in ACTH, COR, and PRL after D-FEN (45 mg orally) were expressed as the maximum increment above baseline values (Δ).

Results: ΔPRL was correlated with ΔCOR ($p = 0.45$, $p < 0.002$) and ΔACTH ($p = 0.38$, $p < 0.009$), and ΔCOR was correlated with ΔACTH ($p = 0.64$, $p < 0.0001$). Compared to HCs, MDEs showed lower ΔPRL and ΔCOR values ($p < 0.04$ and $p < 0.07$, respectively). This blunting was related neither to the severity of the depression nor to individual items of the Hamilton rating scale, including anxiety, agitation, retardation, insomnia, and weight loss. However, patients with diminished PRL response to D-FEN were characterized by a course of recurrent episodes without full inter-episode recovery ($p < 0.02$), and a history of repeated suicide attempts ($p < 0.05$).

Conclusion: These results suggest a reduction in central serotonin neurotransmission in major depressed patients, especially those with a history of suicidal behaviors and those without full inter-episode recovery.

NR446 Wednesday, May 21, 12 noon-2:00 p.m.

DST Status and Dopamine Function in Psychotic Depression

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Summary:

Objective: The purpose of the study was to determine whether psychotic symptoms in depression may be due to increased dopamine (DA) activity secondary to hypothalamic-pituitary-adrenal (HPA) axis overactivity (as reflected by cortisol nonsuppression in the dexamethasone suppression test, DST).

Methods: We examined the endocrine response to DST (1 mg orally) and apomorphine (APO, 0.75 mg S.C.)—a dopamine (DA) agonist—in a large group of hospitalized subjects: 133 drug-free patients with either DSM-IV major depressive episode without psychotic features (MDE, n = 57): major depressive episode with psychotic features (MDP, n = 35); schizophrenia, paranoid type (SCZ, n = 41); and 27 healthy controls (HC, n = 27).

Results: Compared with HCs, SCZs and MDEs, the MDP group showed increased activity of the HPA system (i.e., higher post-DST COR levels; all $p < 0.005$). The SCZ group showed lower APO-induced adrenocorticotropic hormone (ΔACTH) and cortisol (ΔCOR) stimulation than HCs ($p < 0.02$ and $p < 0.01$, respectively) and MDEs ($p < 0.0004$ and $p < 0.02$, respectively), suggesting a functional alteration of the hypothalamic-pituitary dopamine receptors in SCZs. MDPs showed no differences in ΔACTH and ΔCOR levels compared with MDEs, and higher ΔACTH levels than SCZs ($p < 0.01$). Moreover, in the total sample and in each group, DST suppressors and nonsuppressors showed no difference in endocrine responses to APO.

Conclusions: Taken together these results suggest that (1) hypercortisolism and increased DA activity may be independent, and (2) in psychotic depression, other pathophysiological mechanisms than DA dysregulation could be involved in HPA hyperactivity.

NR447 Wednesday, May 21, 12 noon-2:00 p.m.

Diagnostic Validity in Pregnancy

Lynn R. Grush, M.D., Department of Psychiatry, Mass General Hospital, 15 Parkman Street WACC 815, Boston MA 02114; Lee S. Cohen, M.D., Jennie W. Bailey, B.A., Paula Tyack, Ph.D., Jerrold F. Rosenbaum, M.D.

Summary:

Introduction: This investigation assesses the predictive validity of both the Hamilton Rating Scale for Depression (HRSD) and the Beck Depression Inventory (BDI) for the diagnosis of depression during pregnancy and the puerperium.

Methods: Data were obtained from an ongoing naturalistic study of major depressive disorder, panic disorder, and obsessive-compulsive disorder during pregnancy and the puerperium. All women had a previous history of at least one of these disorders. All women were assessed at each trimester and at three, six, and nine months postpartum using the HRSD and the BDI. Presence of major depressive disorder was asessed at each of these time points using the Structured Clinical Interview for Disorder (SCID III).

Results: The HRSD had a positive predictive validity of 0.7 during pregnancy (n = 255, sensitivity = .85, specificity = .9) and 0.63 during the first nine months postpartum (n = 245, sensitivity = .74, specificity = .92). HRSD scores > 18 were used to diagnose depression. The BDI had a positive predictive validity of 0.58 during pregnancy (n = 217, sensitivity = .75, specificity = .85) and 0.47 during the first nine months postpartum (n = 158, sensitivity = .44, specificity = .93). BDI scores >16 were used to diagnose depression.

Conclusion: This preliminary report suggests that the HRSD and BDI may be appropriate scales for assessing depressive illness during pregnancy and the puerperium in women with psychiatric disorders.

NR448 Wednesday, May 21, 12 noon-2:00 p.m.

Family Influences on Outcome in Bipolar Illness

Deborah A. Perlick, Ph.D., Department of Psychiatry, NY Hospital/Cornell University, 21 Bloomingdale Road, White Plains NY 10605-1504; John F. Clarkin, Ph.D., JoAnne Sirey, Ph.D., Annette Zygmunt

Summary:

Introduction: We report preliminary results of a cluster analytic approach employed to test hypothesized associations between family caregivers' illness appraisal and patient outcome in bipolar disorder, and to identify subgroups of caregivers whose profiles of illness appraisal may influence patient outcome.

Methods: Two hundred thirty caregivers of patients with SADS/RDC-diagnosed bipolar disorder were assessed on denial, stigma, illness attribution, and social control (Greenley, 1986) at baseline. Patients' clinical status and functioning were reassessed at six and 12 months.

Results and conclusion: The SPSS K-Means Cluster Analysis procedure sorted caregivers into three groups (N = 62, 63, 105) based on illness appraisal scores. One-way ANOVA's and Newman-Keuls tests demonstrated that cluster centers differed at .05 or better for all appraisal variables: Group 1 and 3 caregivers demonstrated high situational and low biological illness attributions, high social control, and low denial relative to Group 2 caregivers, but differed on stigma (1>3). Profile analysis using repeated-measures ANOVA demonstrated that Group 2 patients were less likely to have been hospitalized at six and 12 months and had higher social adjustment relative to Group 1 and 2 patients (all p's < .05). Groups did not differ by subdiagnosis (schizoaffective vs. bipolar). Profile analyses employing ANCOVA to control for potential group differences at baseline will be reported.

NR449 Wednesday, May 21, 12 noon-2:00 p.m.

Irritable and Depressed Mood: Are They Synonymous?

Paul J. Ambrosini, M.D., Department of Psychiatry, Allegheny University, 3200 Henry Avenue, Philadelphia PA 19129; Gary M. Meyers, M.D., Michael D. Bianchi, M.D., Claudia Metz, M.D.

Summary:

Objectives: This study assesses whether irritable mood is analogous to depressed mood for diagnostic purposes. It is hypothesized that a number of patients should exhibit irritability without depressed mood and/or pervasive anhedonia while meeting diagnostic criteria for affective disorders.

Methods: N = 338 adolescents were diagnosed with the Childhood Version of the Schedule for Affective Disorders & Schizophrenia. Irritability was not interchanged with depressed mood for diagnostic purposes.

Results: Irritable mood co-occurs with depressed mood in 58.7% of those with an affective disorder. It was more likely in major (65.4%) than minor (34.9%) depression. A total of 79.4% (27/34) of those with irritability without depressed mood or pervasive anhedonia met diagnostic criteria for an affective disorder. "Irritable minor depression" was significantly more common than irritable major depression (81.5% vs 18.5%). Other disorders that significantly co-occurred in the irritable subjects were oppositional defiant disorder (14/24; 58.3%) and attention deficit hyperactivity disorder (5/24; 20.8%). Overanxious disorder (3/24; 12.5%) significantly co-occurred in the major depressive group.

Conclusions: Irritable mood as an independent depressive symptom is more compatible with minor depression/dysthymia. The validity parameters of irritable depressive subtype remain unexplored.

NR450 Wednesday, May 21, 12 noon-2:00 p.m.

Predictors of Early Recovery in Outpatient Depression

JoAnne Sirey, Ph.D., NY Hospital Cornell University, 21 Bloomingdale Road, White Plains NY 10605-1504; Barnett S.

Meyers, M.D., Martha L. Bruce, Ph.D., Deborah A. Perlick, Ph.D., Patrick Raue, Ph.D., George S. Alexopoulos, M.D.

Summary:

Objective: Predictors of early recovery can guide and promote effective treatment in community settings. This study investigated patient, treatment, and site characteristics associated with improvement.

Method: Eighty-six SCID-diagnosed major depressives seeking treatment at different mental health sites were reassessed three months after intake. Symptomatology was measured using the Mini International Neuropsychiatric Interview (MINI), HAM-D, and CES-D. Antidepressant treatment adequacy was rated using modified NIMH collaborative study criteria. MINI DSM-IV criteria were used to define recovery.

Results: At follow-up, 49% of patients had recovered. Improvement was associated with being employed, married, and higher education. There were no gender, age, or race differences. More severe depressive symptoms (HAM-D; $t = 3.52$, $p < .001$, and CES-D; $t = 2.18$, $p < .05$) at intake predicted recovery. Only 40% of patients received an adequate medication trial. This alone was not associated with recovery. Patients seen at an academic clinic were more likely to recover ($\chi^2 = 5.44$, $p < .05$). Sociodemographics and adequacy of medication treatment did not account for site differences.

Conclusion: SES status and site were independent predictors of recovery using MINI criteria. Most patients did not receive an adequate trial of antidepressant medication. Neither treatment adequacy nor patient characteristics accounted for site differences. Future work will address the multiple factors that contribute to site differences in early recovery.

NR451 Wednesday, May 21, 12 noon-2:00 p.m.

Randomized, Double-Blind Placebo-Controlled Comparison of Once Daily Versus Twice Daily Venlafaxine in MDD

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Summary:

Objectives: Venlafaxine (VEN) and its active metabolite have half-lives ($t_{1/2}$) of about five and 11 hours, respectively; recommended dosing for VEN is bid or tid. The assumption that required dosing and pharmacodynamic effects of psychotropic drugs are determined by their $t_{1/2}$ has been questioned and was studied with VEN, comparing the efficacy and safety of qd vs. bid dosing in 48 patients with major depressive disorder (MDD).

Methods: Twenty-five patients (mean ±SD age 45 ± 15 yrs) received qd and 23 (42 ± 16 yrs) bid dosing: 31 (65%) were women, 37 (77%) had chronic (> 2 yrs) MDD, 30 (63%) had melancholic features, 16 (33%) were bipolar II, and 6 (13%) had a history of hypertension. Mean baseline HAM-D_{21} was 24 ± 4 (QD) and 23 ± 3 (bid). After a one-week placebo lead-in, VEN dosing started at 37.5mg/d and increased by 37.5 mg weekly (as warranted) to a maximum 225 mg/d.

Results: Twenty-one patients in each group completed six weeks VEN. Average maximum dose was 199 mg/d (QD) and 208 mg/d (bid). Mean reduction in HAM-D was 13.8 ± 6.4 (qd) ($p < 0.0001$) and 14.0 ± 5.6 (bid) ($p < 0.0001$). There were no qd vs bid differences observed ($p = 0.89$). Nonmelancholic and bipolar depressives demonstrated earlier onset of efficacy (wk 1, $p = 0.04$ and wk 2, $p < 0.08$, respectively). Side effects were mild/moderate in both groups. Only three patients (6%) dropped for side effects.

Conclusion: VEN given qd (titrated up to 225mg/d) was well tolerated and of comparable efficacy to bid dosing, suggesting that required dosing and pharmacodynamic effects of psychotropic drugs may not be determined solely by their half lives.

NR452 Wednesday, May 21, 12 noon-2:00 p.m.

Gabapentin in Bipolar Depression: A Case Series

L. Trevor Young, M.D., Department of Psychiatry, McMaster University, 1200 Main Street W/Room 3G57, Hamilton ON L8N 3Z5, Canada; Janine Robb, B.Sc.N., Irene Patelis-Siotis, M.D., Cathy MacDonald, R.N., Russell T. Joffe, M.D.

Summary:

The treatment of bipolar depression is not well established. Gabapentin has been suggested to have mood stabilizing and possibly antidepressant properties. Outpatients who met DSM-IV criteria for bipolar disorder type I or II, currently depressed (HamD > 16), and who were refractory to standard mood stabilizers, received gabapentin orally (twice or three times daily for six weeks) in an open fashion alone or in combination with standard mood stabilizers. The mean ± SD age of the subjects (5 men and 10 women) was 39 ± 9 years. The mean dose was 1050 ± 640 mg. There was a significant reduction ($T = 3.00$, df14, $p = 0.01$) comparing the six-week and baseline HamD scores in these subjects. Eight subjects (53%) responded (3 marked i.e. > 50% reduction in HamD; 5 partial i.e. 25% to 50% reduction in HamD). In only one subject was the HamD score higher after six weeks of treatment and this same subject was the only subject to experience hypomanic symptoms (Young Mania Scale score of 13) during the trial. This is one of the first reports to provide preliminary evidence for the acute antidepressant efficacy of gabapentin. This case series requires confirmation and extension in larger-scale controlled trials.

NR453 Wednesday, May 21, 12 noon-2:00 p.m.

A Test of the Phase-Shift Hypothesis of SAD

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Summary:

Objective: This study investigated timing of melatonin rhythm in patients with seasonal affective disorder (SAD) and controls before and after four weeks treatment.

Methodology: The sample consisted of 12 patients with SAD in a winter major depressive episode and 24 never-ill controls. Twelve patients (SAD) and 12 controls (CL) were treated with 2,500 lux full spectrum light from 0600-0800 hrs for four weeks; 12 controls were treated for four weeks by awakening at 0600 hrs with two hours of restriction to dim ambient light (CS). Melatonin and cortisol were measured by RIA.

Results: Melatonin onset did not differ at baseline between SAD and controls. As expected, light significantly phase advanced CL compared to CS. However, phase advance with light in SAD did not differ from that in CL. There was no difference in phase advance between SAD responders and nonresponders. No significant correlation was seen between change in depression and phase advance. No association between phase and emergence of manic symptoms was seen.

Conclusions: Earlier finding of phase delay in SAD compared with controls was not demonstrated, nor was association between phase advance and clinical status. These data provide evidence against the classic phase-delay hypothesis of SAD.

NR454 Wednesday, May 21, 12 noon - 2:00 p.m.

Rapid-Cycling Bipolar Disorder: Does Homozygosity for the COMT Low Activity Allele Represent a Risk Factor for the Development of Rapid-Cycling?

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Summary:

An association study is being carried out to determine the frequency of COMT158^{met} in 60 patients with bipolar disorder (BPD) rapid cycling (RC) variant in comparison with a control sample from the general population of patients with BPD.

Background: (COMT) catechol-o-methyl-transferase enzymatic activity is subject to variability in humans. We and others have recently established that low activity is primarily due to a G A transition at codon 158. An assessment of psychiatric illness in velo-cardio-facial syndrome, a genetic syndrome associated with a microdeletion of chromosome 22q11, which includes the COMT gene, showed that 8/8 patients with the rapid cycling variant of BPD (out of 17 patients with BPD) were found to have the COMT^{met} polymorphism on the complementary chromosome 22. Since the blockade of catecholamine reuptake by tricyclic antidepressants (TCAs) and the blocking of breakdown by MAOIs have been associated with the induction of mania in unipolar and bipolar patients and an increased cycle frequency, we hypothesize that homozygosity for COMT^{met} predisposes to rapid cycling, and possibly represents a risk factor in the use of antidepressants.

Method: Subjects were recruited through advertising in patient advocacy newsletters. All patients were independently interviewed by two research psychiatrists who established DSM-IV consensus diagnoses and concurred on the pattern of cycling pre- and post-antidepressant treatment. Subjects are genotyped blind to psychiatric diagnosis.

Results: Of the 60 ultra-rapid cyclers enrolled, four have been genotyped. All four (100%) were homozygous for COMT158^{met}, the low activity allele, supporting our hypothesis that the presence of this allele may significantly alter the course of BPD. (We expect to have completed the genotyping of the remaining patients in time for presentation at the annual meeting.

NR455 Wednesday, May 21, 12 noon - 2:00 p.m.

Anxiety, Insomnia and Antidepressant Selection

Gregory E. Simon, M.D., Group Health Coop., Center for Health Studies, 1730 Minor Avenue, Suite 1600, Seattle WA 98101-1404; John Heilegenstein, M.D., Wayne J. Katon, M.D.

Summary:

Background: Sedating antidepressants are often recommended for patients with anxiety or insomnia. We examine whether anxiety or insomnia symptoms: 1) show differential response to fluoxetine or imipramine, or 2) predict differences between drugs in overall response or medication discontinuation.

Method: A total of 336 HMO primary care patients beginning antidepressant treatment were randomly assigned to fluoxetine or imipramine. All subsequent care (medication dosage, change, or discontinuation) was managed by the treating physician. The 17-item HDRS and the SCL anxiety and depression subscales were administered prior to randomization and one month later.

Results: Improvement in HDRS insomnia items, HDRS agitation item, and SCL anxiety subscale were essentially identical in the two groups. Baseline insomnia did not predict significant differences between groups in improvement in HDRS (p = .44) or SCL depression subscale (p = .44). Similarly, baseline anxiety did not predict significant differences in improvement in HDRS (p = .19) or SCL depression subscale (p = .31). Patients assigned to fluoxetine were significantly less likely to change or discontinue medication, but this difference did not vary by baseline insomnia (p = .68) or anxiety (p = .25).

Conclusions: Among patients with moderate depression, baseline insomnia or anxiety should not influence the choice of fluoxetine or imipramine as an initial antidepressant.

NR456 WITHDRAWN

NR457 Wednesday, May 21, 12 noon - 2:00 p.m.

A Double-Blind, Placebo-Controlled Study of Sertraline in the Treatment of Outpatients with Dysthymia

Arun Ravindran, M.B., Department of Research, Royal Ottawa Hospital, 1145 Carling Avenue, Ottawa ON K1Z 7K4, Canada; Robert Wiseman, Ph.D.

Summary:

Introduction: There has been little study of the treatment of dysthymia in the absence of major depression. This is the second large double-blind trial of sertraline in dysthymic patients without concomitant major depression.

Objective: To evaluate efficacy and safety of sertraline (STL) and placebo (PLA) in dysthymia.

Method: Outpatients with dysthymia (DSM-III-R) ≥ 5 years, ≥ 12 score on the 29-item Hamilton Depression Scale (HAMD) and without concomitant major depression (DSM-III-R) were randomized in a 12-week, double-blind, parallel group study to STL (n = 158) or PLA (n = 152). Initial daily dosing was 50 mg STL or PLA equivalent with 50 mg increases every two weeks to a maximum of 200 mg, if response was inadequate.

Results: Mean changes from baseline (BSL) to last visit (intent-to-treat) for HAMD-21 and for atypical items, Montgomery-Asberg Depression Rating Scale (MADRS), Clinical Global Impressions of Severity (CGI-S) and Improvement (CGI-I), and the Hospital Anxiety (HAD-A) and Depression Scales (HAD-D) were significantly greater for STL than PLA. At last visit, CGI-I responders (score ≤2) were 60.1% for STL compared with 39.5% for PLA (p < 0.001). More STL (75.3%) than PLA (63.2%) reported adverse events. The most frequent placebo-adjusted adverse events for STL were tremor (13.2%), increased sweating (11.9%), dizziness (8.8%), and abdominal pain (7.4%). Eight of the nine quality-of-life measures showed significantly greater improvement for STL over PLA (p < 0.05).

	21-item HAMD	ATYP Items HAMD	MADRS	CGI-S	HAD-D	HAD-A
STL BSL	21.1	6.6	23.5	4.2	12.2	12.2
% Change	−43.4*	−40.8*	−43.3*	−32.8*	−36.1†	−29.8†
PLA BSL	20.4	6.6	23.1	4.2	11.5	12.1
% Change	−32.9	−27.9	−33.0	−22.8	−11.8	−15.4

*p<0.05, †p<0.01 between groups.

Conclusions: STL is effective and well tolerated for the treatment of dysthymic disorder with significant improvements in quality of life.

NR458 Wednesday, May 21, 12 noon - 2:00 p.m.

A Double-Blind Study of Sertraline and Moclobemide in the Treatment of Outpatients with Atypical Depression

Paul R. Latimer, M.D., Kelowna Hospital, 2268 Pandosy Street, Kelowna BC V1Y 1T2, Canada; Robert Wiseman, Ph.D., Guangrui Zhu, Ph.D.

Summary:

Introduction: Monoamine oxidase inhibitors (MAOIs) have been shown more effective than tricyclic antidepressants in atypical depression, but there has been little study of specific serotonin reuptake inhibitors (SSRIs) in this depressive subtype.

Objective: To compare efficacy and safety of sertraline (STL), a SSRI, and moclobemide (MOC), an MAOI, in atypical depression.

Method: Outpatients with DSM-III-R major depression ≥4 weeks, a Hamilton Depression Scale (HAMD 29-item) score ≥19, and a score ≥4 on the Atypical Depression Diagnostic Scale (ADDS), were randomized to STL (n = 100) or MOC (n = 97) in a 12-week, parallel-group, double-blind trial. Initial daily dosing of 50mg STL or 300mg MOC was increased after four weeks to 100mg or 450mg, respectively, if response was inadequate.

	29-item HAMD	17-Item HAMD	ATYP Items	CGI-S	HAMA
STL BSL	36.4	20.6	13.6	4.5	18.7
	-21.0	-11.5	-8.3	-2.2	-9.1
Change (%)	(-58.0%)	(-56.2%)*	(-60.1%)	(-49.1%)	(-49.6%)†
MOC BSL	36.6	20.4	13.9	4.5	19.1
	-20.1	-11.1	-7.9	-2.1	-9.6
Change (%)	(-54.6%)	(-53.4%)	(-55.6%)	(-45.3%)	(-47.1%)

*p<0.05, †p<0.01 between groups.

Results: Mean changes from baseline (BSL) to last visit (intent-to-treat) were greater for STL than MOC with the treatment differences for HAMD 17-item and HAMA statistically significant. Significant differences favoring STL ($p < 0.05$) were also evident in remitter incidence (HAMD and HAMA ≤7) at week 4 and in quality-of-life measures associated with work behavior. At last visit, responders (CGI-I ≤2) were 75.8% for STL and 67.0% for MOC; ADDS indicated 68.2% STL and 60.6% MOC patients no longer had definite atypical depression. More MOC (85.6%) than STL patients (79.0%) reported adverse events with headache, nausea, and insomnia occurring most frequently with both treatments.

Conclusions: STL was as effective as MOC with similar tolerability in the management of atypical major depression.

NR459 Wednesday, May 21, 12 noon - 2:00 p.m.

Does Severity of Depression Influence Treatment Utilization or Adherence to Guidelines?

Sagar V. Parikh, M.D., Department of Psychiatry, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Elizabeth Lin, Ph.D., Sidney Kennedy, M.D., Paula N. Goering, Ph.D.

Summary:

Objective: Undertreatment of major depression in the community is commonly recognized. However, little is known regarding how the severity of depression relates either to the likelihood or the intensity of treatment, or how treatment matches recommendations from practice guidelines. Our study examines how severity of depression correlates with service utilization and how such utilization may match guidelines.

Method: From an epidemiologic survey (n = 9,953), two subgroups of subjects with major depression in the past year (mild n = 62, severe/psychotic n = 109) were compared on likelihood and frequency of service utilization of the formal health sector/providers and alternative care sector. These visit frequencies were then compared with recommendations of major treatment guidelines.

Results: Formal health care services were utilized by 38.7% of the mild and 55.1% of the severe/psychotic group, a significant difference, but no differences in intensity of service were seen. Furthermore, for those who did use services, only 43% of the mild group and only 60% of the severe/psychotic group met minimal recommendations for visit frequency.

Conclusions: The public health problem of depression includes low overall rates of treatment, a relative mismatch between severity of disorder and intensity of utilization, and poor global adherence to minimal standards of treatment.

NR460 Wednesday, May 21, 12 noon - 2:00 p.m.

Reversed Neurovegetative Symptoms of Depression: A Community Study of Ontario

Robert O. Levitan, M.D., Mood Disorder, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Alain D. Lesage, M.D., Sagar V. Parikh, M.D., Paula N. Goering, Ph.D., Sidney Kennedy, M.D.

Summary:

Objective: To delineate the epidemiology of major depression with reversed neurovegetative features (i.e. hyperphagia, weight gain, hypersomnia) in a large community sample of Ontario, using other patterns of neurovegetative change as a comparison.

Method: A total of 8,116 subjects across Ontario, age 18 to 65, were interviewed using the World Health Organization Composite International Diagnostic Interview. Individuals who met DSM-III-R criteria for major depression were classified into one of four groups based on neurovegetative symptoms experienced over the lifetime (i.e. only "typical" episodes, only "reversed" episodes, "neither," or "both" types). The groups were compared on prevalence, demographics, comorbidity, disability, and health care utilization.

Results: Seventeen percent of individuals with lifetime major depression had experienced the "reversed" symptom cluster during at least one depressive episode. Interestingly, fully one-third of these individuals had also experienced a depressive episode with the "typical" pattern of hypophagia, weight loss, and insomnia at some point; this "both" group was found to have very high rates of comorbidity, substance abuse, and health care utilization. Most of the differences found between the four groups were due to the unique characteristics of the "neither" and "both" groups; individuals who had experienced *only* depression with reversed symptoms lifetime were remarkably similar to those who had experienced *only* typical symptoms lifetime.

Conclusions: Several popularly held beliefs about depression with reversed features did not hold true in this community sample of Ontario. Identifying individuals who have experienced *both* reversed and typical patterns lifetime may be an important consideration in studies of major depression.

NR461 Wednesday, May 21, 12 noon - 2:00 p.m.

The Seasonality of Bulimic Symptoms in Seasonal Depressives and Healthy Controls

Anthony J. Levitt, M.D., Department of Psychiatry, University of Toronto, 2075 Bayview Avenue, North York ON M4N 3M5, Canada; Alan Kaplan, M.D., Robert O. Levitan, M.D., Susan Dickens

Summary:

Objective: This study is designed to examine whether patients with SAD have a seasonal pattern of bulimic symptoms.

Method: SAD patients were recruited as part of studies of light therapy. Age-matched controls were healthy relatives of psychology students. All subjects were interviewed using the Eating Disorders Section of the SCID, and a modified version of the Seasonal Patterns Assessment Questionnaire (SPAQ), which had items added to reflect seasonality of the five major criteria for BN using a five-point scale, similar to the original items of the SPAQ. Only

females (SAD = 78, controls = 29) with no history of any eating disorder were included in this analysis.

Results: As compared with controls, SAD subjects were more likely to report bingeing (52% vs 31%; $\chi^2 = 3.9$, $p < .05$), purging (14% vs 0%; $\chi^2 = 4.9$, $p < .05$), or being preoccupied with body image (35% vs 7%; $\chi^2 = 7.4$, $p < .01$). SAD patients were more likely to report moderate to extreme *seasonal change* in 1) binge frequency (45% vs 3%), 2) feeling eating is out of control (40% vs 3%), 3) purging (22% vs 3%), 4) over concern with body image (40% vs 17%), and 5) feelings of fatness (41% vs 14%; by χ^2, all differences $p < .05$). Overall seasonal changes in bulimic symptoms were highly correlated with overall changes in mood symptoms ($r = .56$, $p < .0001$).

Conclusions: These findings suggest that patients with SAD who do not have eating disorders, have a high degree of seasonal dysregulation in eating behavior, and this dysregulation is closely related to mood. These findings may indicate a shared pathophysiology of SAD and BN.

NR462 Wednesday, May 21, 12 noon - 2:00 p.m.

The Chronological Relationship Between the Onset of Dysthymia and Major Depression Impacts on Outcome

Anthony J. Levitt, M.D., Department of Psychiatry, University of Toronto, 2075 Bayview Avenue, North York ON M4N 3M5, Canada; Russell T. Joffe, M.D., Stephen Sokolov, M.D.

Summary:

Objective: To determine whether the chronological relationship between the onset of dysthymia and the onset of the first major depression influences treatment outcome in patients with double depression (DD).

Method: We examined 77 consecutive unmedicated outpatients who presented with major depression and who had pre-existing dysthymia (i.e. DD). Subjects were administered the Schedule for Affective Disorders and Schizophrenia (SADS-LV), and the Hamilton Rating Scale for Depression (HAM-D) before and after five and 12 weeks of open antidepressant therapy. Response was defined as a 50% decline in HAM-D to score ≤ 8. Subjects were divided into those with the onset of dysthymia before the first major depression (DysB; n = 47), onset of dysthymia after major depression (DysA; n = 12), and those with onset of both condition within two years of each other (Indistinct; n = 18).

Results: There were no significant differences between these three groups in baseline demographics or HAM-D. Using ANOVA for repeated measures, there was a significant group effect on HAM-D at week 5 ($F = 3.0$; $p < .05$) and week 12 ($F = 3.4$; $p < .05$), with the DysA group having significantly higher HAM-D than the DysB and Indistinct group (LSD test, $p < .05$). Response rates were lower in subjects with DysA (33%) as compared with DysB (57%; $\chi^2 = 3.6$, $p = .06$) and Indistinct (78%; $\chi^2 = 5.9$, $p < .02$).

Conclusions: These findings suggest that the onset of dysthymia after the first major depressive episode may adversely affect response to subsequent treatments in patients with DD.

NR463 Wednesday, May 21, 12 noon - 2:00 p.m.

Longitudinal Study of 5HT Function in Depression

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Summary:

Objective: Previous work has shown that depressed patients have blunted neuroendocrine responses to i.v. administration of the 5-HT reuptake inhibitor, clomipramine. In order to examine the state vs. trait nature of this observation, we performed a longitudinal study of depressed patients at baseline and after completion of acute and maintenance phases of treatment.

Methods: 25 patients meeting DSM-III-R criteria for major depression received a standard clomipramine (CMI) challenge test at baseline, following six weeks treatment with desipramine, and following the completion of at least six months of maintenance treatment, in a medication-free state of remission.

Results: Both responder (n = 17) and nonresponder (n = 8) groups showed trends toward decreased prolactin responses to CMI following acute treatment. There was a significant decrease in cortisol response in the responders ($p = .02$), and a trend toward a decrease in the nonresponders ($p = .10$). After maintenance therapy and medication washout, responders did not show any significant change from baseline in prolactin or cortisol responses to CMI challenge.

Conclusions: These results suggest that 5-HT dysregulation in depressed patients may persist even after recovery from acute illness and may represent an underlying biological vulnerability.
This work was supported in part by PHS grants MH-42145, MH-33127, MH-19111, and RR-00046.

NR464 Wednesday, May 21, 12 noon-2:00 p.m.

Growing Old and the Risk of Major Depression

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Summary:

Objective: To examine the relationship between age and the experience of major depressive episodes in a cohort of persons aged 50 and older.

Method: Data on symptoms of DSM-III-R major depressive episodes were examined for the 1994 cohort (n = 2,730) of the Alameda County Study (age range 46–102, $\bar{x} = 65$). In addition to age, we examined gender, education, marital status, social isolation and social support, perceived physical and mental health, chronic medical conditions, functional impairment, life events, financial strain, and neighborhood quality.

Results: The point prevalence of major depressive episodes was 6.6% for men and 10.1% for women, with a trend for prevalence to increase with age. When the effects of the other psychosocial risk factors were controlled, there were no significant age effects. Multivariate analyses demonstrated that the initial age effects were due almost entirely to chronic health problems and functional impairment. Analyses of data from the 1994–1995 follow-up study replicated the findings from the 1994 cross-sectional survey.

Conclusion: The implications are clear: healthy, normal functioning older adults are at no greater risk of depression than younger adults. In addition, apparent age-related effects on depression are attributable to physical health problems and related disability. Furthermore, the risk factors for depression among the elderly appear to be the same as for younger populations.

NR465 Wednesday, May 21, 12 noon-2:00 p.m.

Citalopram in the Treatment of Moderate to Severe Depression

Joe Mendels, M.D., N Greene/Marketing, Forest Laboratories, 909 3rd Avenue, New York NY 10022; Ari Kiev, M.D., Louis F. Fabre, Jr., M.D., Gerri Schwartz, Ph.D.

Summary:

Citalopram is the most selective serotonin reuptake inhibitor available, marketed in 48 countries, with worldwide exposure estimated at over 4,000,000 patients. The present study is one of two completed placebo-controlled trials that were conducted in the U.S. to establish the efficacy and safety of citalopram in the treatment of outpatients with major depression. This multicenter study used a fixed-flexible, parallel-group design in which patients were titrated from 20 to 80 mg in a two-week period. After a one-week washout, eligible patients were randomized to receive either citalopram (n = 89) or placebo (n = 91) in a double-blind manner for four weeks. The citalopram group (average daily dose at endpoint, 52 mg/day) showed clinically and statistically significant improvement compared with the placebo group by trial weeks one or two, and at endpoint based on both HAMD (mean change from baseline) and CGI scores. The citalopram-treated patients had elevated incidences of nausea, insomnia, and dry mouth compared with placebo subjects. Based on these results, citalopram can be judged effective and well tolerated for the treatment of major depression, with a possible rapid onset of effect.

NR466 Wednesday, May 21, 12 noon-2:00 p.m.

The Course of Psychomotor Agitation During Pharmacotherapy of Depression: Analysis from Double-Blind Controlled Trials

Sharon L. Blomgren, M.D., DC 1046, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Gary D. Tollefson, M.D., Mary E. Sayler, M.S.

Summary:

Objective: Psychomotor agitation, a common clinical feature of major depression, may first emerge or intensify during pharmacotherapy. Whether agitation is inherent to the disease state or is a drug-induced phenomenon is a complicated assessment.

Method: We analyzed data from double-blinded clinical trials involving 4737 patients with major depression assigned to fluoxetine, a comparator antidepressant (predominately tricyclic antidepressants), or placebo. Item 9 of the Hamilton Depression Rating Scale was used to assess the degree of psychomotor agitation.

Results: The majority of patients exhibited some degree of baseline psychomotor agitation. The rate of increase in agitation from baseline following randomization was comparable between fluoxetine, placebo, and TCAs. Substantial emergence of psychomotor agitation occurred at a similar incidence across treatment groups. Improvement in agitation occurred statistically significantly more often ($P < .001$) among fluoxetine-treated than placebo-treated patients. Fluoxetine-treated and TCA-treated patients demonstrated comparable improvement rates.

Conclusion: Data from this large series of clinical trials suggested that neither fluoxetine nor TCAs induced psychomotor agitation at a higher incidence rate than seen during the natural course of depression over time (placebo cohort). In fact, pharmacotherapy was typically associated with diminished agitation, likely as part of the response to treatment.

NR467 Wednesday, May 21, 12 noon-2:00 p.m.

Fluoxetine Therapy in Depression in the Older Patient: Effects on Anxiety, Agitation and Insomnia

Sharon L. Blomgren, M.D., DC 1046, Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN 46285; Rosalinda Terner, R.Ph., Michael Wilson, M.S.

Summary:

Objective: Depression is not a normal consequence of aging, although it occurs often and extracts a substantial price in terms of quality of life, hospitalization, disability, morbidity, and nursing home costs.

Method: To evaluate the efficacy and tolerability of fluoxetine in patients aged 55 and older, a meta-analysis was conducted on six trials including 744 patients diagnosed with major depression and randomized to either fluoxetine or placebo. Four trials lasted six weeks, one lasted eight weeks and one lasted 12 weeks. Patients were categorized as anxious or nonanxious using the HAMD anxiety/somatization factor; the efficacy of fluoxetine in treating depression and its effect on anxiety, agitation, and insomnia were evaluated within anxious and nonanxious subgroups.

Results: 1) Patients treated with fluoxetine showed improvement in symptoms of depression, evidenced by the HAMD-17, regardless of baseline anxiety. 2) 77.2% of the patients completed the trial. 3) There were minor differences in adverse events reported by the anxious and nonanxious subgroups; however, there were no differences between the groups in the rates of discontinuation attributed to adverse events. 4) Although nonanxious patients (treated and untreated) improved more than anxious patients (treated and untreated), baseline anxiety level did not impact fluoxetine's effectiveness ($p = .688$).

Conclusion: We conclude that fluoxetine is effective in treating depression in patients aged 55 and older regardless of the presence of baseline anxiety.

NR468 Wednesday, May 21, 12 noon-2:00 p.m.

Residual Symptoms in Responders to Fluoxetine

Andrew A. Nierenberg, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street WAC 815, Boston MA 02114-3117; Bronwyn R. Keefe, B.A., Vinita C. Leslie, M.A., Jonathan E. Alpert, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Antidepressants have unequivocal efficacy, but many patients continue to have residual symptoms despite a robust response. The purpose of this study is to assess residual symptoms in responders to fluoxetine.

Methods: We treated 234 outpatients (mean age 39.6 ± 9.6 years; 54.5% female) diagnosed with major depressive disorder (MDD) as assessed with the Structured Clinical Interview for DSM-III-R-Patient Edition (SCID-P) and SCID-II for personality disorders. Patients were treated with fluoxetine 20 mg/day for eight weeks. We assessed 112 (47.9%) full responders (final Hamilton Depression Rating Scale-17 item version-HDRS ≤ 7) with the mood disorders module at the end of the trial.

Results: Only 17.9% of full responders had no SCID MDD symptoms, while 25.9% had at least one, 24.1% had two, and 32.2% had three or more symptoms. No statistically significant relationships were found between residual symptoms and baseline comorbid Axis I or Axis II disorders.

Discussion: We found that less than 20% of full responders to fluoxetine by HDRS criteria had no SCID MDD symptoms, and that over half had two or more subthreshold or threshold symptoms. While depressed patients benefit from antidepressants, other strategies may be needed to address residual symptoms.

NR469 Wednesday, May 21, 12 noon-2:00 p.m.

Motor Activity and Variation of Mood in Depression

Matthias R. Lemke, M.D., Department of Psychiatry, University of Kiel, Niemannsweg 147, Kiel 24105, Germany; Alesia Broderick, M.S., Martin Zeitelberger, M.D., Wolfgang Hartmann, M.D.

Summary:

Objective: Diagnostic criteria for major depression include diurnal variations of symptom intensity. These variations are subjectively experienced by the patient or directly observed by others. Circadian variation of symptom intensity may include changes in spontaneous motor activity. Therefore, motor activity and self-experienced intensity of symptoms were studied at different times of the day in patients with major depression.

Methods: Inpatients (n = 21) were included if they fulfilled DSM-IV criteria for major depression, melancholic type, and experienced diurnal variations of mood. Motor activity was measured by actigraph (activity-based monitoring) (ZAK, Germany) from 7 a.m. to 9 a.m. and p.m. on three consecutive days. Patients recorded their self-experienced mood and drive on a visual analogue scale (VAS) and Multiple Affective Adjective Checklist (MAACL, German version: EWL) during this time period.

Results: VAS and MAACL (EWL) scores for self-experienced mood and drive were significantly lower in the morning ($p < 0.01$). Counts of activity units were significantly greater in the morning ($p < 0.01$) and showed an inverse correlation with VAS and MAACL (EWL) scores ($r_s = 0.65$, $p < 0.01$).

Conclusions: Activity measured by actigraphy was higher in the morning than in the evening hours. However, patients perceived their own mood and drive being lower in the morning. Neuronal serotonergic activity has been implicated in alterations of motor activity and mood. Increased motor activity may represent an observable, psychobiological behavioral equivalent of self-experienced depressed mood in major depression.

NR470 Wednesday, May 21, 12 noon-2:00 p.m.

Enhanced Corticotropin Response to Corticotropin-Releasing Hormone as a Predictor of Mania in Euthymic Bipolar Patients

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Summary:

Objective: Abnormalities in corticotropin (ACTH) and cortisol levels before and after corticotropin-releasing hormone (CRH) stimulation have been reported in bipolar patients. The aim of this study was to determine whether the hormonal response to CRH is associated with outcome in bipolar disorder.

Method: The ACTH and free cortisol responses to the injection of 100 ug of synthetic human CRH and plasma cortisol-binding globulin (CBG) levels were measured in 42 lithium-treated patients suffering from RDC bipolar I disorder in remission, and 21 age- and sex-matched normal controls. A one-year follow-up was conducted to assess any possible relationship between outcome and the hormonal response.

Results: Bipolar patients showed higher baseline ($p < 0.02$) and peak ACTH concentrations ($p < 0.04$) than controls. A higher area under ACTH concentration curve after CRH stimulation ($p < 0.03$) and higher plasma CBG levels ($p < 0.04$) significantly predicted manic/hypomanic relapse within six months by multiple regression analysis.

Conclusions: CRH challenge test could be a good predictor of manic or hypomanic relapse in remitted bipolar patients.

NR471 Wednesday, May 21, 12 noon-2:00 p.m.

Citalopram Versus Amitriptyline in Depressed Elderly

Kerstin Overo, D.Sc., Marketing, Forest Laboratories, 909 Third Avenue, New York NY 10022

Summary:

The enhanced sensitivity of the elderly to side effects (e.g., anticholinergic effects) of tricyclic antidepressants (TCAs) has made treating depression in this group problematic. The selective serotonin reuptake inhibitors (SSRIs) have been reported to produce fewer such side effects than TCAs. The therapeutic actions and safety of citalopram, the most selective of the SSRIs, were investigated in a group of 365 elderly patients (age ≥ 65) diagnosed with major depression (MADRS ≥ 22) in a double-blind, parallel group, multicenter comparison of citalopram (n = 179, 20 or 40 mg once-daily) and amitriptyline (n = 186, 50 or 100 mg/day). Patients who did not respond to placebo during a one-week, single-blind phase were randomized to receive citalopram or amitriptyline for eight weeks. Both treatments produced equivalent time-related declines in severity of depression so that by eight weeks slightly more than 50% of patients completely recovered (MADRS ≤ 12). By contrast, patients receiving amitriptyline had a greater incidence of anticholinergic effects, including a greater ($p < .001$) percentage of patients reporting dry mouth (34% vs. 7%), as well as a higher ($p < .03$) incidence of somnolence (16% vs. 8%). Based on these results, we conclude that citalopram is an effective antidepressant with potential advantages over amitriptyline in the treatment of the depressed elderly.

NR472 Wednesday, May 21, 12 noon-2:00 p.m.

Previous SSRI Treatment and Efficacy of Sertraline for OCD: Combined Analysis of Four Multicenter Trials

Steven A. Rasmussen, M.D., Psychiatry Outpatient, Butler Hospital, 345 Blackstone Blvd, Providence RI 02906-7010; Lee Baer, Ph.D., David Shera, Ph.D.

Summary:

Efficacy data from four double-blind, placebo-controlled trials of sertraline in the treatment of OCD were combined to determine if there were significant differences in outcome for patients who had previously received trials of SRIs (SSRIs or clomipramine) versus those who were SRI naive. Several previous meta-analyses suggested superior efficacy of clomipramine compared with the SSRIs. However, a confounding factor was that the later SSRI trials had significant numbers of patients who had previously failed trials of CMI or other SRIs. The current study was designed to compare the effect sizes of SRI-naive patients treated with sertraline versus the effect sizes obtained in the collaborative clomipramine multicenter trial. Between 635 and 728 patients on sertraline (number of treatment completers varying by study week) were included in this combined analysis.

A significantly ($p < .001$) greater response was found by week 4 in SRI-naive patients compared with patients having previously taken any SRI on both primary outcome measures (percent of responders on the CGI scale and the mean score on the Yale Brown Obsessive Compulsive Scale). The unadjusted week 10 effect size for sertraline was estimated at 1.53 SD, which was identical to the week 10 effect size in the collaborative clomipramine study. These results suggest that sertraline has comparable efficacy to clomipramine in SRI-naive patients and supports the hypothesis that the greater relative efficacy found for clomipramine was largely due to these earlier studies including only SRI-naive patients.

NR473 Wednesday, May 21, 12 noon-2:00 p.m.

The Clonazepam Switch to Sertraline in Panic Disorder

Marcio V. Versiani, M.D., Department of Psychiatry, Federal University Rio Janeiro, R Visconde de Piraja 407 s 805, Rio de Janeiro 22410, Brazil; Egidio Nardi, M.D., Sandra Pinto, Ph.D.

Summary:

Objective: To evaluate the possibilities and/or advantages of substituting sertraline for clonazepam in the maintenance treatment of panic disorder.

Method: Thirty patients diagnosed with panic disorder with agoraphobia according to the Structured Clinical Interview for DSM-IV and who were being treated with clonazepam (mean daily dose-2.6 mg/day) for more than two years (mean-2.4 years), were switched to sertraline. Sertraline (100 mg/night) was initiated concomitantly with the clonazepam dose, which was tapered off over three months. Biweekly assessments using rating scales were done during six months (three months sertraline + clonazepam withdrawal and three months sertraline alone).

Results: In 21 cases, clonazepam was tapered to zero despite moderate or mild anxiety symptoms. In 14 out of these, sertraline was raised to 200 mg/night to control the reemergence of panic attacks. Four patients dropped out. In five cases, clonazepam was maintained or reinstituted (mean 1.5 mg/day) due to moderate or severe withdrawal, rebound and/or relapse phenomena. Patients on sertraline alone had lower ratings on symptomatology and fewer unwanted effects than when they were on clonazepam.

Conclusions: Sertraline seems to be a promising alternative for panic disorder patients on maintenance with clonazepam.

NR474 Wednesday, May 21, 12 noon-2:00 p.m.

Hoarding Predicts Poor Response in OCD

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Summary:

Several factors have been associated with poor response to treatment in obsessive-compulsive disorder (OCD), including severity of illness, chronicity, and schizotypal personality, but few investigators have looked at specific symptoms. For these reasons we assessed response predictors in 38 nondepressed subjects with OCD who completed 12 weeks of paroxetine therapy (n = 20), 12 weeks of placebo (n = 8), or 12 weeks of cognitive-behavioral therapy (n = 10). Clinician and self-rated measures were gathered at baseline, during, and after treatment. Seventeen (45%) subjects were considered responders (Clinical Global Improvement score of 1 or 2, and a 40% decrease in the Yale-Brown Obsessive-Compulsive Scale score). Responders had lower obsessive-compulsive scores on the Symptom Checklist-90-Revised, a lower checking score on the Maudsley Obsessive-Compulsive Inventory, were less likely to have had prior drug therapy, and suffered more obsessive-compulsive symptoms in general. They were much less likely to have hoarding obsessions and corresponding compulsions (p = .003). The latter finding was confirmed with regression analysis. We conclude that hoarding is an important symptom that specifically predicts poor treatment response in patients with OCD.

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A Follow-Up Study of DSM-III-R GAD with Syndromal and Subsyndromal Major Depression

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Summary:

Recent studies have documented the extensive overlap of both the syndromes and symptoms of generalized anxiety disorder (GAD) and major depression (MD). Mixed symptom patients can be a diagnostic puzzle, and the prognostic implications of mixed symptomatology are unclear due to a lack of published follow-up data in individuals diagnosed with both disorders, in which panic was excluded.

Thirty-nine patients with a modified DSM-III-R diagnosis of GAD with depressive symptoms (23 with syndromal MD) were interviewed approximately 18 months after entering an 11-week clinical trial, utilizing a battery of instruments that included the SCID-Up-R, Ham-A, Ham-D, and SCL-90. Analyses were conducted at categorical and dimensional levels.

Three groups emerged at follow-up. The largest, almost 60% (n = 23) remained syndromal for GAD, of whom 58% (n = 13) also had syndromal MD (nine ongoing, four emergent). Importantly, all of the patients who remained syndromal for MD at follow-up remained syndromal for GAD as well. Six patients were completely asymptomatic at follow-up. Finally, the remaining group (n = 10, 26%) manifested subsyndromal GAD both with (n = 3) and without (n = 7) subsyndromal MD. The clinical significance and prognostic implications of these findings compared with studies of "pure" GAD and MD will be discussed.

NR476 Wednesday, May 21, 12 noon-2:00 p.m.

Long-Term Experience with Clonazepam in Patients with Panic Disorder

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Summary:

Background: Naturalistic longitudinal studies provide the opportunity to assess the effectiveness of treatment interventions as applied in clinical settings over time and thus can be viewed as complementary to randomized trials.

Objective: This study examined the use patterns and efficacy of the high-potency benzodiazepine (HPB) clonazepam in panic patients treated and followed naturalistically in the Massachusetts General Hospital Longitudinal Study of Panic Disorder over a two-year period.

Methods: 204 patients with panic disorder (PD) entered the study after undergoing structured clinical assessment to establish the panic and comorbid diagnoses. Of these, 46% were receiving clonazepam alone or in combination with an antidepressant. Treatment was not controlled at initial evaluation nor during the follow-up period. The main variables assessed in this analysis included global severity of the panic disorder (CGI) and stability of clonazepam dose.

	Clonazepam Alone (mean ± SD)	Clonazepam plus Antidepressant (Mean ± SD)	Other Treatment (Mean ± SD
Number of patients	57	36	111
CGI—Baseline	3.26 ± 1.22	3.56 ± 1.28	3.47 ±1.17
CGI—Endpoint	2.46 ±0.87	2.33 ±0.99	2.25 ±1.21
Dose of clonazepam—Baseline (mg/d)	1.39 ±0.97	2.00 ± 1.26	——
Dose of clonazepam—Endpoint (mg/d)	1.59 ± 1.24	1.99 ±1.17	——

Results: The mean age for the total sample was 39.5 years, and 59% was female. There were no significant differences between groups on any demographic, diagnostic, or severity variables. All treatment groups tended to improve over time without significant differences between groups. Clonazepam doses remained stable over time.

Conclusions: Results of this study suggest that treatment with the HPB clonazepam for panic disorder was associated with achievement and maintenance of therapeutic benefit similar to that obtained for alternative treatments, without the development of tolerance as manifested by dose escalation or worsening of clinical status.

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Multi-Dimensional Outcome and Quality of Life in Panic Disorder: The Effects of Sertraline Treatment

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Summary:

Successful treatment of panic disorder requires improvement not only in the traditional primary outcome measure of panic attack frequency, but also in a series of other quality-of-life measures that reflect the multidimensional nature of the disorder. A total of 342 patients were treated in two randomized, double-blind, flexible-dose, 10-week, multicenter treatment studies with sertraline (50-200 mg) or placebo for the treatment of panic disorder (DSM-III-R) with or without agoraphobia. Assessment of the primary efficacy measures of panic attack frequency, phobic avoidance, CGI, and anticipatory anxiety, which are presented elsewhere, demonstrated significant benefit for sertraline over placebo. Sertraline treatment also yielded significantly greater improvement over placebo on nonpanic measures that contribute to the overall distress and disability associated with panic disorder. Evaluation of quality of life with the Q-LES-Q scale showed significant improvement in overall QOL for sertraline treatment compared with placebo ($p < .001$) at endpoint. These results and those from a multidimensional analysis of the MC-PAS will be presented. The results of these combined studies suggest that sertraline treatment yields multidimensional improvement in a variety of disability and quality-of-life measures, in addition to its significant antipanic efficacy.

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Nefazodone in the Treatment of Social Phobia

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Summary:

Objective: To evaluate the efficacy of nefazodone in the treatment of social phobia.

Methods: Sixteen patients (11 women, five men) with a primary diagnosis of social phobia were studied in a 12-week open trial of nefazodone treatment. Patients had been referred for treatment to a university-affiliated anxiety disorders clinic (in Hamilton, Canada). Patients were evaluated using the Structured Clinical Interview for DSM-IV Disorders (SCID). Symptom course during treatment was assessed using the Brief Social Phobia Scale, the Clinical Global Improvement Scale, and self-report measures of social/performance anxiety, depression, and disability.

Results: The mean age of presentation at the clinic was 34.6 years, with a mean duration of illness of 19 years. The mean dose of nefazodone at the completion of the trial was 462.5mg daily. Of the 16 patients who have completed the trial, 13 (81%) are judged to have been responders (a rating of markedly improved or moderately improved on the CGI), three (19%) were nonresponders (a rating of minimally improved or no change on the CGI). Ratings on the psychometric symptom measures improved significantly across treatment, as did ratings of disability.

Conclusions: Nefazodone may be an effective treatment for social phobia worthy of further investigation with a placebo-controlled design.

NR479 Wednesday, May 21, 12 noon-2:00 p.m.

Shyness and Behavioral Inhibition in Anxiety Disorders

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Summary:

Objective: Both childhood behavioral inhibition (CBI) and extreme shyness are potential precursors of adult anxiety disorders. This study examines the degree of CBI and shyness in an anxiety-disordered population as well as investigates the relationship of these constructs to particular anxiety disorders.

Methods: A sample of 280 SCID-diagnosed patients with a primary DSM-IV anxiety disorder diagnosis completed a battery of psychometric measures that included the Retrospective Self-Report of Behavioral Inhibition (RSRI) and the Revised Shyness Scale (SHY), as well as self-report measures of anxiety, depression, and disability.

Results: Patients with anxiety disorders report statistically significantly more CBI and shyness than normal controls (based on published data). The RSRI scale was strongly correlated with phobic avoidance, while being modestly correlated with depressive symptomatology and state anxiety. The SHY scale was also significantly correlated with phobic avoidance, depressive symptomatology, and anxiety. Scores on the RSRI differed among primary diagnostic groups, with people with panic disorder reporting significantly less CBI than people with obsessive-compulsive disorder or social phobia. Scores on the shyness measure also differed among primary diagnostic groups, with social phobics reporting more shyness than patients with either obsessive-compulsive disorder or panic disorder.

Conclusions: Behavioral inhibition may be a developmental precursor of adult anxiety disorder. Both CBI and shyness may be particularly relevant for the development of social phobia.

NR480 Wednesday, May 21, 12 noon-2:00 p.m.

Symptom Structure in OCD: Factor Analytic Evidence for Subgroups

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Summary:

Although descriptions of coherent symptom groupings in OCD have a long history in the psychiatric literature, OCD is currently considered a unitary diagnosis. Recent studies, despite their limiting use of a priori symptom groupings, have demonstrated discrete symptom subgroups. The present study was unique in its examination of individual (including previously uncategorized) symptoms, as identified by 64 items of the Yale-Brown Obsessive Compulsive Scale (YBOCS) symptom checklist, administered to a sample of 203 OCD patients. Existing models of symptom structure were initially tested using confirmatory factor analysis, and were not replicable. Exploratory factor analysis was then performed. This procedure ultimately yielded five coherent and interpretable symptom subgroups. These were, in order of significance: symmetry/perfectionism, contamination/washing, pure obses-

sions, magical thinking/spectrum, and harm-avoidance checking. These factors and their interrelationships are discussed. In conclusion, these results represent empirical evidence for distinct subgroups within OCD and for the inadequacy of groupings based solely upon overt behavioral similarities (e.g., "checking"). Such findings have potentially important implications for investigation of etiology (e.g., genetics), clinical diagnosis, and prediction of treatment response.

NR481 Wednesday, May 21, 12 noon-2:00 p.m.

Plasma Anti-5HT and 5HT Antibodies Raised in Panic Disorder

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Summary:

A recent report indicated elevations of serotonin (5-HT) antibodies in patients with primary fibromyalgia, a condition associated with panic disorder. We wanted to assess if antibodies directed at the 5-HT system were elevated in patients with PD compared with healthy volunteers. Sixty-three patients with panic disorder and 26 healthy volunteers were diagnosed by the SCID. Employing ELISA, we measured anti-5-HT and 5-HT anti-idiotypic (directed at 5-HT receptors) antibodies. To include all subjects in one experiment, three different batches were run. For plasma 5-HT anti-idiotypic antibodies, there was a significant batch effect overall but no batch by diagnosis effect. Following Z-score transformation of each separate batch and combining all scores, there was a diagnosis effect with elevations in patients. Neither sex nor age as covariates affected the results. For plasma anti-5-HT antibodies, although there was a batch effect, no significant batch-by-diagnosis effect was evident. Patients demonstrated elevated Z-score antibody levels. Covaried for sex and age, the result falls below significance to trend levels. The data raise the possibility that psychoimmune dysfunction, specifically related to the 5-HT system, may be present in PD. Potential interruption of 5-HT neurotransmission through autoimmune mechanisms may be of pathophysiologic significance.

NR482 Wednesday, May 21, 12 noon-2:00 p.m.

Adjunctive Treatments in Bipolar and Schizoaffective Disorder: Comparisons of Risperdone, Conventional Neuroleptics or Clonazepam Combined with Mood Stabilizers

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Summary:

Objective: We compared responses to mood stabilizers alone, combined mood stabilizers, and mood stabilizers plus adjunctive treatments in inpatients with bipolar and schizoaffective disorder.

Methods: Records of all patients with discharge diagnoses of bipolar disorder (n = 50) or schizoaffective disorder (n = 5) were reviewed and treatment outcome assessed. Treatments included mood stabilizers alone (lithium, valproate, or carbamazepine; n = 16), mood stabilizer plus conventional neuroleptic (n = 19), mood stabilizer plus risperidone (n = 10), mood stabilizer plus clonazepam (n = 9), and valproate plus lithium (n = 6).

Results: Treatment response (moderate or marked improvement on the Clinical Global Impression scale) was highest in patients receiving the mood stabilizer plus risperidone (90%), followed by valproate plus lithium (67%, NS), mood stabilizer plus conventional neuroleptic (58%, p = 0.10), mood stabilizer alone (56%, p = 0.10), and mood stabilizer plus clonazepam (44%, p = 0.057). These between-group differences in outcome were not significantly associated with such factors as age of onset, years ill, subtype frequency (pure manic vs. mixed vs. rapid-cycling vs. depressed), or concurrent psychosis, except for the increased prevalence of schizoaffective disorder in the risperidone-treated sample; these data are, however, liable to type II error.

Conclusion: In a study limited by a small sample size, there appeared to be benefits of adding risperidone to mood stabilizers and of combining mood stabilizers in patients with bipolar and schizoaffective disorders. These preliminary findings need to be examined in larger samples.

NR483 Wednesday, May 21, 12 noon-2:00 p.m.

Personality Traits and Disorders in Body Dysmorphic Disorder

Katharine A. Phillips, M.D., Brown University, Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906; Susan L. McElroy, M.D.

Summary:

Background: Individuals with body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, have been postulated to have schizoid, narcissistic, and obsessive-compulsive personality traits. One study found a high rate of personality disorders—in particular, avoidant, paranoid, and obsessive-compulsive—in patients with BDD. However, data on personality disorders in BDD are very limited, and there are no published studies on personality traits in this disorder.

Methods: 118 subjects with DSM-IV BDD (62 [52.5%] females and 56 [47.5%] males, mean age 33.6 ± 10.8 years) participated in this study; 76 (64%) were participants in a phenomenology study of BDD and 42 (36%) in a medication treatment study of BDD. One hundred subjects completed the NEO-FFI (a validated self-report measure of normal personality traits), 51 completed the Rathus Assertiveness Scale (a validated self-report measure of assertiveness), and 44 were assessed for personality disorders with the SCID-II.

Results: 28 (63.6%) subjects had at least one personality disorder, with avoidant (45.5%), paranoid (20.5%), and obsessive-compulsive (18.2%) most common. Thirteen (29.5%) had one personality disorder, two (4.5%) had two, and 13 (29.5%) had three or more. On the NEO-FFI, mean scores were in the very high range on neuroticism, the low range on extraversion and conscientiousness, the low-average range on agreeableness, and the average range on openness to experience. On the Rathus Assertiveness Scale, 12 (23.5%) subjects scored in the unassertive range.

Conclusions: The rate of personality disorders was relatively high, with avoidant personality disorder most common. The high neuroticism scores and low extraversion scores are consistent with this finding.

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Prevalence of Body Dysmorphic Disorder in Dermatology Patients

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Summary:

Background: Accumulating evidence suggests that many patients with body dysmorphic disorder (BDD), a distressing or impairing preoccupation with an imagined or slight defect in appearance, respond to psychiatric treatment. However, a majority seek

dermatologic treatment (e.g., for minimal acne or slightly thinning hair), with which many are dissatisfied. The rate of BDD among patients seeking dermatologic treatment is unknown, however, and most dermatologists are unfamiliar with BDD. This study assessed the prevalence of BDD in patients seeking dermatologic treatment.

Methods: A brief self-report questionnaire that screens for BDD that has adequate sensitivity and specificity in a psychiatric setting was validated in 49 patients in a dermatologic setting. Because the physical defect must be nonexistent or only slight for BDD to be diagnosed, the interrater reliability of a defect severity scale was also determined, with four raters rating the severity of dermatologic lesions in 50 slides. The rate of BDD was then assessed in 171 patients seeking dermatologic treatment, 123 of whom had nonexistent or minimal defects.

Results: The self-report questionnaire had adequate sensitivity (100%) and specificity (92%), and the defect rating scale had acceptable interrater reliability (ICC = .88). Among the 123 patients with minimal defects, BDD was present in 19 (15.4%; 14 females, five males, age 34.5 ± 15.8) (among all 171 patients, the rate of BDD was 11.1%). Similar rates were found in a general dermatology setting (nine of 54 patients [16.7%]) and an academic cosmetic surgery setting (10 of 69 patients [14.5%]). Facial acne was the most common concern (n = 9).

Conclusions: These data suggest that BDD may be relatively common in dermatologic settings.

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The Brown Assessment of Beliefs Scale: Reliability and Validity

Jane L. Eisen, M.D., Butler Hospital, Brown University, 345 Blackstone Boulevard, Providence RI 02906; Katharine A. Phillips, M.D., Lee Baer, Ph.D., Douglas A. Beer, M.D., Katherine D. Atala, M.D., Steven A. Rasmussen, M.D.

Summary:

Objective: The authors developed and evaluated the reliability and validity of the Brown Assessment of Beliefs Scale, a clinician-administered, seven-item scale designed to assess delusions across a wide range of psychiatric disorders.

Methods: The Brown Assessment of Beliefs Scale was developed after reviewing the literature on the assessment of delusions. The scale was administered to 50 subjects by four raters: 20 subjects with obsessive compulsive disorder, 20 with body dysmorphic disorder, and 10 with a mood disorder with psychotic features. Audiotaped interviews of scale administration conducted by one rater were independently scored by the other raters to evaluate interrater reliability. Test-retest reliability was assessed over a one-week interval. Other insight instruments as well as scales that assess symptom severity were administered to assess convergent and discriminant validity. Sensitivity to change was evaluated in a multicenter treatment study of sertraline for obsessive compulsive disorder.

Results: Interrater and test-retest reliability for the total score and individual item scores was excellent, with a high degree of internal consistency. Scores on the Brown Assessment of Beliefs Scale generally were not correlated with symptom severity but were correlated with other measures of insight. The scale was sensitive to change in insight in obsessive compulsive disorder but was not identical to improvement in severity.

Conclusions: The Brown Assessment of Beliefs Scale is a reliable and valid instrument for assessing delusionality in a number of psychiatric disorders. This scale may help clarify whether delusional and nondelusional variants of disorders constitute the same disorder and whether delusionality affects treatment outcome and prognosis.

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Insight in Body Dysmorphic Disorder Versus OCD

Jane L. Eisen, M.D., Butler Hospital, Brown University, 345 Blackstone Boulevard, Providence RI 02906; Katharine A. Phillips, M.D., Steven A. Rasmussen, M.D., Douglas Luce

Summary:

Background: Body dysmorphic disorder (BDD), a preoccupation with an imagined or slight defect in appearance, has been postulated to be related to—or even a form of—OCD. However, it has also been suggested that patients with BDD have poorer insight and are more often delusional than those with OCD, which may have treatment implications. Insight in these disorders has never been compared using a reliable and valid measure of delusionality.

Methods: 37 untreated patients with BDD (16 male, 21 female, age 33.8 ± 9.4 years) and 32 untreated patients with OCD (13 male, 19 female, age 34.0 ± 9.4 years) were evaluated with the Brown Assessment of Beliefs Scale (BABS). The BABS is a reliable and valid seven-item, semistructured, clinician-administered scale that assesses current delusionality. Items are conviction, perception of others' views, explanation of differing views, fixity, attempt to disprove beliefs, insight (recognition that the belief has a psychiatric etiology), and ideas/delusions of reference. Total score ranges from 0 to 24, with higher scores indicating greater delusionality.

Results: Subjects with BDD had a significantly higher mean total score (14.5 ± 5.1, range 3–24) than subjects with OCD (8.8 ± 4.4, range 1–17) ($p < .001$). Scores of BDD subjects were significantly higher on all but two BABS items. In addition, nine (24%) BDD subjects but no OCD subjects were classified as delusional ($p < .01$). Degree of delusionality was correlated with BDD severity ($r = .48$, $p < .01$) but not with OCD severity ($r = .31$, $p = .09$) (illness severity was similar in both groups).

Conclusions: These results suggest that degree of insight differs in BDD and OCD, with insight in BDD often poor or absent, and insight in OCD often good.

NR487 Wednesday, May 21, 12 noon-2:00 p.m.

Long-Term Prognosis of Panic Disorder

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Summary:

The purpose of this research is to investigate the long-term outcome of panic disorder (PD) and identify factors to predict outcome. Two hundred eight patients meeting DSM-III-R criteria for PD (those with or those without agoraphobia) and those suffering panic attacks with agoraphobia were selected, and at least 30 months had passed since diagnosis. Among them we obtained 121 patient self-assessments. Thirty-six percent of all patients experienced at least one panic attack during the follow-up. Forty-two percent suffered from agoraphobia irrespective of severity. Ninety percent, however, were not significantly disabled at work. These results imply that PD is a persistent disorder, but the impairment due to it is relatively slight. Multiple regression analysis indicates that poor educational background, lower age at onset, higher symptom number at intake, and nausea at onset are related to higher attack frequency. Drug doses are determined by the following factors: dizziness at onset, paresthesia at onset, trembling at intake, and depression at intake. Presence of heart pounding at intake, dizziness at onset, and trembling at onset increase scores on the global assessment scale. The rate of working performance as a dependent variable is predicted by severity of agoraphobia at intake and feelings of choking at intake. Heart pounding at intake, lower age at onset, and poor educational background are related to higher phobic avoidance frequency.

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Cognitive-Behavioral Therapy Versus the Combination with Fluvoxamine in the Treatment of OCD

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Summary:

The purpose of this comparative treatment study was to investigate whether the effects of cognitive therapy or exposure in vivo with response prevention for obsessive compulsive disorder (OCD) could be enhanced by adding fluvoxamine before the start of these treatments.

A total of 117 patients were randomized over the following five conditions: cognitive therapy, exposure in vivo, fluvoxamine with cognitive therapy, fluvoxamine with exposure in vivo, and a waiting-list control condition. The trial lasted for 16 weeks. Thirty-one patients dropped out. Outcome was assessed by the Anxiety Discomfort Scale, the Yale-Brown Obsessive Compulsive Scale, and the Padua Inventory-Revised.

In contrast to the four treatments, the waiting-list control condition did not result in a significant decrease of symptoms. After 16 weeks of treatment, all four treatment packages were effective on these OCD ratings, but they did not differ among each other in effectiveness.

The effect of cognitive therapy or exposure in vivo with response prevention can not be enhanced by adding fluvoxamine to these treatments.

NR489 Wednesday, May 21, 12 noon-2:00 p.m.

Are Anger Attacks in Unipolar Depression a Variant of Panic Disorder?

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Summary:

Previous studies have shown that anger attacks occur in approximately 40% of outpatients with major depressive disorder (MDD). It has been hypothesized that these attacks may be related to panic attacks and to cluster B personality disorders.

Objective: The prevalence of panic disorder and other anxiety disorders was assessed in depressed outpatients with and without anger attacks. We also examined whether anger attacks were associated with higher rates of other comorbid Axis I and Axis II disorders.

Methods: 333 outpatients (148 men and 185 woman, mean age 40.0 ± 10.4) with MDD were administered the Structured Clinical Interview for DSM-III-R–Patient Edition and the Structured Clinical Interview for Personality Disorders, as well as the Anger Attacks Questionnaire.

Results: There were no significant age or gender differences in the prevalence of anger attacks. Patients with anger attacks were significantly more likely to meet criteria for current panic disorder ($p \leq .05$), while there were no significant differences between the two groups in rates of other anxiety disorders, eating disorders, and alcohol/substance abuse. Those with anger attacks also had significantly higher rates of dependent, avoidant, narcissistic, borderline, and antisocial personality disorders.

Conclusions: These results support the hypothesis that anger attacks may be related to panic disorder, and confirm previous clinical observations linking anger attacks with certain personality disorders, especially borderline and antisocial.

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Correlates of Hypochondriacal Tendencies in Panic Disorder with Agoraphobia

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Summary:

Objective: To compare panic disorder with agoraphobia (PDA) patients with and without secondary hypochondriacal manifestations in order to ascertain what may account for secondary hypochondriasis (SH) in PDA.

Method: Fifty-three PDA patients were administered the Illness Attitudes Scales (IAS), which measure hypochondriacal tendencies and screen reliably for hypochondriasis. Patients who scored in the hypochondriacal range (n = 27; 50.9%) on the IAS were compared with those who did not (n = 26; 49.1%) in terms of results on the following questionnaires: The Hopkins Symptom Checklist-90, Beck Anxiety Inventory, Beck Depression Inventory, Fear Questionnaire, Panic Appraisal Inventory-Panic Consequences Questionnaire (PAI-PCQ), Agoraphobic Cognitions Questionnaire, Body Sensations Questionnaire, and Somatosensory Amplification Scale.

Results: PDA patients with SH scored higher on measures of all variables, and the difference was statistically significant for most variables. The most striking difference was found on the PAI-PCQ for the measure of expected physical consequences of panic attacks, while the differences on the measures of expected social consequences of panic attacks and loss of control as a consequence of panic attacks, were not even significant.

Conclusions: PDA patients with SH exhibit more psychopathological phenomena than PDA patients without SH. The development of SH in PDA may involve greater expectation of harmful physical consequences of panic attacks, that is, a cognitive processing of somatic correlates of anxiety in terms of somatic catastrophe.

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Low Serum Beta-Endorphin Levels in Panic Disorder

Lucia Perez-Costillas, M.D., Department of Psychiatry, University of Granada, Av. Madrid 11, Granada 18071, Spain; Manuel Gurpegui, M.D., Esperanza Ortega, M.D.

Summary:

Objective: To test the possible abnormality of the opioid regulation in panic disorder, and its relationship with trait or state anxiety.

Method: A group of 22 patients (PP; 18 women and four men) suffering from DSM-IV panic disorder (mean age ± SD = 33.8 ± 7.3 years; range: 20–44) were compared with 22 healthy volunteers (HV) matched by gender, age, and education. All participants were assessed at baseline and after 12 weeks; PP were treated with either alprazolam or chlomipramine. Among other measures, the State and Trait Anxiety Inventory (STAI) was administered, and β-endorphin was determined by radioimmunoassay.

Results: Serum β-endorphin levels were significantly ($p < 0.01$) lower in PP (28.4 ± 10.6 pg/ml) than in HV (38.1 ± 10.8) at baseline; although the differences were shortened after 12 weeks, no significant change in β-endorphin levels was observed in either group. At baseline, PP scored significantly higher than HV in both state and trait anxiety, but only their state anxiety decreased to normal values. In PP but not in HV, β-endorphin levels showed a significant negative correlation with both state and trait anxiety.

Conclusions: In panic disorder, it was demonstrated that there is a decrease in serum β-endorphin levels, which could be an expression of an increased vulnerability to the disorder.

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Repetitive Behaviors of OCD and Tourette's Syndrome

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Summary:

Background: Obsessive-compulsive disorder (OCD) is heterogeneous, with some forms related to Tourette syndrome (TS). This is a phenomenologic study designed to investigate the nature of these possible OCD subtypes and the relationship between OCD and TS.

Method: We evaluated 20 adult outpatients with OCD, 21 with TS, and 20 with OCD plus TS using a semistructured interview designed to assess cognitive, sensory, and autonomic phenomena preceding repetitive behaviors.

Results: A higher frequency of cognitions ($p < 0.0001$) and autonomic anxiety ($p = 0.0001$) and a lower frequency of sensory phenomena ($p < 0.0001$) were associated with repetitive behaviors in OCD than in TS. Like the TS group, the OCD plus TS group reported significantly more intentional repetitive behaviors preceded by sensory phenomena ($p = 0.001$), and significantly fewer preceded by cognitions ($p = 0.004$) compared with the OCD group; there was also a trend toward less preceding autonomic anxiety ($p = 0.06$).

Conclusions: The presence or absence of cognitions, sensory phenomena, and autonomic anxiety distinguishes repetitive behaviors in patients with OCD from those with OCD plus TS and TS. These subjective experiences may be useful in subtyping OCD and may represent valid predictors of prognosis and treatment response.

NR493 Wednesday, May 21, 12 noon-2:00 p.m.

Psychotic Symptoms in PTSD

Daniella David, M.D., Department of Psychiatry, VA Medical Center, 1201 NW 16th Street, Miami FL 33125; Gary S. Kutcher, Ph.D., Elizabeth I. Jackson, M.D., Thomas A. Mellman, M.D.

Summary:

Background: Post-traumatic stress disorder (PTSD) has a high rate of comorbidity with other anxiety, mood, and substance use disorders. Few studies, however, have investigated psychotic symptoms in PTSD. We previously reported the prevalent occurrence of psychotic symptoms in a population of combat veterans. The objectives of the present study are to expand these observations in patients with a primary diagnosis of combat-related PTSD and determine associations of psychotic symptoms with comorbid disorders and ethnicity.

Methods: Fifty-three male combat veterans consecutively admitted to an inpatient PTSD unit were assessed for the presence of psychotic symptoms and lifetime Axis I disorders with structured interviews and self-report forms: 91% were Vietnam veterans; 72% were white, 17% were Hispanic, and 11% were black. Associations between the presence of psychotic symptoms and the other study variables were analyzed by chi-square and t-tests.

Results: Forty percent of patients reported at least one type of psychotic symptom in the preceding six months, with the most common being auditory hallucinations (38%). The majority of psychotic symptoms reflected combat themes and guilt, were nonbizarre, and were not associated with formal thought disorder or inappropriate affect. Psychotic symptoms were significantly associated with current major depression ($p < .02$), but not with lifetime alcohol or drug abuse or with self-rated PTSD or dissociative severity. Psychotic symptoms were more common in the black and Hispanic than the white veterans ($p < .002$).

Conclusion: Psychotic symptoms can occur as a feature of PTSD and appear to be associated with major depression and minority ethnic status.

NR494 Wednesday, May 21, 12 noon-2:00 p.m.

Alcohol and the Pituitary in Hippocampal Volume Loss in PTSD

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Summary:

Reduced hippocampal volumes have been reported in individuals with post-traumatic stress disorder (PTSD). Increase in corticosteroids, with cytotoxic effects on hippocampal neurons, has been suggested as a putative mechanism for hippocampal volume loss in these subjects. However, studies to date have been conflicting regarding the role of corticosteroids in the pathogenesis of this disorder. Further, the presence of alcoholism in these individuals has confounded these findings because alcohol is also known to increase corticosteroid levels, potentially producing the same finding.

We performed magnetic resonance image (MRI) based volumetric analysis of the pituitary and hippocampus on 30 individuals, aged 39 to 46: 10 with PTSD and alcohol dependence, 10 with alcohol dependence alone, and 10 normal control subjects.

Subjects with PTSD and/or alcoholism demonstrated a trend toward significantly increased pituitary size compared with normal controls ($F(1,27) = 3.65$, $p < 0.07$). Hippocampus to pituitary ratios were significantly smaller in subjects with PTSD and/or alcoholism than in control subjects ($F(2,27) = 5.1$, $p < 0.01$), with the effect most pronounced in the alcohol-dependence group. Alcohol stimulates pituitary corticotrophs, which appears to result in hypertrophy measurable by MRI in our study subjects. Reductions in the hippocampus to pituitary ratio demonstrated here are consistent with the hypothesis that increased pituitary activity stimulated by alcohol produces corticosteroids cytotoxic to the hippocampus, resulting in volume loss. Though hippocampal volume reductions have been reported in individuals with PTSD, it appears this effect may be attributable to the effect of comorbid alcoholism. Future studies investigating hippocampal volume in subjects with PTSD will need to exclude those with comorbid alcohol disorders in order to eliminate this possible confounding variable.

NR495 Wednesday, May 21, 12 noon-2:00 p.m.

Repetitive Assessment of Impulsivity in a Cohort of 155 Patients with OCD: Twelve-Month Prospective Follow-Up

Elie G. Hantouche, M.D., SHU, St Anne Hospital, 29 Av Georges Bernanos, Paris 75005, France; Myriam L. Bouhassira, M.D., Marc L. Bourgeois, M.D.

Summary:

In phase 3 of the National French Study on OCD, 155 patients suffering from an OCD (DSM-III-R criteria, score on NIMH-OC ≥ 7, not treated) entered a naturalistic 12-month follow-up. Impulsivity was assessed by using BDS (Behavioral Dyscontrol Scale) at

day 0, 6 months, and 12 months later and were given a semistructured interview for OC related disorders (OCRD).

Results: Impulsivity was more intense in females (mean score on BDS 35.6 vs. 31.9; p = 0.06), in patients with history of anxiety-depression (36.3 vs. 32.3, p = 0.04), prior suicidal behavior (38.3 vs. 33.2, p = 0.06), and familial history of OCD (37.1 vs. 33.0, p = 0.07). Moreover, syndromal typology of OCD was not linked to impulsivity. In contrast, presence of coexisting OCRD was significantly linked to higher impulsivity score, especially with "Intermittent Explosive Disorder (40.1 vs. 30.8; $p < 10^{-4}$), "Compulsive Buying" (38.5 vs. 32.4; p = 0.005), "Hypochondriasis" (36.7 vs. 32.1; p = 0.02), "Dysmorphophobia" (37.1 vs. 32.4; p = 0.02) "Depersonalization" (37.7 vs. 32.9; p = 0.05). Paradoxically, impulsivity was augmented in patients with important to severe slowness syndrome (38.3 vs. 31.8, p = 0.001). This mixed association between slowness and impulsivity can be an excellent testimony of the "Dyscontrol" phenomenon.

In 130 patients who had received an anti-OCD treatment (fluoxetine, clomipramine) and followed for 12 months, BDS score was gradually reduced from day 0 (34.1) to 24.8 at M6 (Δ = 22%) and 20.1 at M12 (Δ = 36%). A decrease by ≥ 50% of BDS was observed in 42% of obsessional patients. Finally, the best results on OCD improvement after six months were observed in the subgroup presenting a high level of "impulsivity" (66% were responders) versus 39% in the subgroup with important to severe slowness.

NR496 Wednesday, May 21, 12 noon-2:00 p.m.

PTSD in Community Samples: A Measurement Problem

Carol S. Fullerton, Ph.D., Department of Psychiatry, USUHS, 4301 Jones Bridge Road, Bethesda MD 20814; Brian Crowley, M.D., Robert J. Ursano, M.D., Richard S. Epstein, M.D., Karrie J. Craig, Ph.D., Andrew S. Baum, Ph.D.

Summary:

The assessment of PTSD in disaster and community samples requires specific attention to measurement because of relatively low base rates of the disorder compared with inpatient samples. Using multiple measures offers some advantages for specificity. The DSMPTSD measure compares favorably with Keane's MMPI-PTSD, the Impact-of-Event Scale, and identifies individuals meeting diagnostic criteria. This poster presents the evaluation of this instrument against the SCID in community samples with varying base rates of PTSD.

We examined a community sample of 122 motor vehicle accident (MVA) victims at one and six months post-accident. Internal consistency standardized Chronbach's alpha = 90 for our measure, and 0.83 for the SCID. Three subsamples of 15%, 50%, and 75% PTSD positive on SCID were randomly created. The DSMPTSD, MMPI-PTSD, Impact-of-Event, and SCL-90 measures of PTSD were compared against the SCID PTSD diagnosis. One month post-MVA, at 15% prevalence of PTSD, the DSMPTSD percent correct was 85.1% (sens = 66.7%, spec = 88.6%; Kappa = .99), at 50% prevalence, the percent correctly classified was 72.5% (sens = 56.4%, spec = 87.8%; Kappa = .98), and at 75% prevalence, the percent correctly classified was 67.3% (sens = 56.4%, spec = 100%; Kappa = .97). Similar results were found at six months. The DSMPTSD measure is better than or as good as all other measures with several advantages: obtaining DSM-III-R and DSM-IV diagnoses, high specificity, strong face validity, and practical use for research in community samples.

NR497 Wednesday, May 21, 12 noon-2:00 p.m.

Pilot Study of Nefazodone for Chronic PTSD and Related Sleep Disturbance

Thomas A. Mellman, M.D., Department of Psychiatry, Veterans Affairs Medical Ctr, 1201 NW 16th Street, 116A, Miami FL 33125; Daniella David, M.D., Lydia Barza

Summary:

Background: Serotonergic antidepressants have been found to improve PTSD; however, benefits tend to be modest in chronic cases. A putative function of rapid-eye-movement sleep (REM), aiding the integration of distressing memories, appears inadequate in PTSD. We hypothesized that the sleep profile of nefazodone, a serotonergically active antidepressant that improves sleep maintenance and preserves or enhances REM, would be beneficial for PTSD.

Method: Fourteen patients who were Vietnam combat veterans or Holocaust survivors (n = 2) were enrolled in an open-label, six-week trial. Four had comorbid depression and eight had prior treatment with other antidepressants. Assessments included diary-derived measures of sleep and dreams.

Results: Two patients dropped out due to lack of efficacy, one due to an adverse reaction, and one was lost to follow-up. Of the 10 completers, eight were judged to be moderately or very much improved. PTSD Severity Scale scores were significantly decreased at six weeks. Mean sleep time was comparably increased from baseline at one week and six weeks, but not significantly. Four out of seven dreams reported at baseline were self-rated as having been similar to traumatic experiences, compared with none of the four dreams reported at six weeks.

Conclusion: These preliminary results are promising and controlled trials are indicated. It is possible that dreams being less replicative of trauma with treatment is related to maintaining REM.

NR498 Wednesday, May 21, 12 noon-2:00 p.m.

Personality Disorders and Temperament and Character in PTSD

Jose J. Almanza, M.D., Department of Psychiatry, Hosp Cent Militar, Bvd Avila Camacho Esq Ej Nal, Mexico City 11649, Mexico; Francisco Paez, M.D., Marcos Hernandez, M.D., Genaro Barajas, M.D., Sergio Altamirano, M.D., Humberto Nicolini

Summary:

Several personality disorders have been associated with PTSD. An elevation of the harm avoidance scale of the TCI has been reported in all anxiety disorders. The aim of this study was to compare DSM-III-R personality disorders frequency and temperament and character dimensions between patients with PTSD and a group of exposed, non-PTSD subjects.

Methods: 21 PTSD subjects were recruited from the psychiatry department of the Central Military Hospital in Mexico City, who were exposed to different stressors. Thirty-four control subjects were recruited from an exposed military population with no PTSD symptoms. Psychiatric diagnoses were confirmed using the WHO's Composite International Structured Interview (CIDI). Personality was evaluated with the personality diagnostic questionnaire (PDQ-R) and the temperament and character inventory (TCI).

Results: Histrionic and avoidant personality were significantly more frequent among PTSD patients (p = 0.02). The harm avoidance scale score was significantly higher among PTSD patients (mean 13.2 vs. 9.6, f 10.2, df 1,53 p = 0.01). Self-transcedence scale was significantly lower among PTSD subjects (mean 32.0 vs. 35.4, f 5.7, df 1,53, p = 0.02).

Conclusion: Personality variables could be associated with PTSD regardless of the system of evaluation used.

NR499 Wednesday, May 21, 12 noon-2:00 p.m.

Stability of Temperament in Panic Disorder Patients

Manuel Gurpegui, M.D., Department of Psychiatry, University of Granada, Av. Madrid 11, Granada 18071, Spain; Lucia Perez-Costillas, M.D.

Summary:

Objective: To test the stability of temperament, particularly of the Harm Avoidance (HA) dimension, in panic disorder patients (PP).

Method: A group of 22 PP (18 women and four men; mean age ± SD = 33.8 ± 7.3 years, range 20–44) were compared with 22 healthy volunteers (HV) matched by gender, age, and education. All participants were assessed at baseline and after 12 weeks, during which PP received appropriate treatment. Among other measures, participants filled out the Spanish version of the Cloninger's Tridimensional Personality Questionnaire (TPQ) and the State and Trait Anxiety Inventory (STAI).

Results: At baseline PP scored significantly higher than HV in the HA dimension (26.4 ± 3.7 vs 16.0 ± 6.2; $p < 0.00001$) and its four subscales, but no significant difference was found in Novelty Seeking, Reward Dependence (RD; three subscales), or Persistence. Twelve weeks later, when state anxiety had been normalized, no significant changes within either group were observed in any personality dimension, including HA (25.7 ± 4.2 and 16.1 ± 5.9), but a significant difference emerged in RD between PP and HV (14.8 ± 2.6 vs. 12.8 ± 3.4; $p < 0.05$). The positive correlation between HA and STAI trait anxiety reached significance among HV (at baseline, $r = 0.64$; 95% *CI:* 0.27-0.85) but not among PP.

Conclusions: High scores on the HA dimension is a stable feature of PP. The TPQ shows a high test-retest reliability, both in patients and controls.

NR500 Wednesday, May 21, 12 noon-2:00 p.m.

Compulsive Behavior in GAD and OCD

Mark H. Townsend, M.D., Department of Psychiatry, LSU School of Medicine, 1542 Tulane Avenue, New Orleans LA 70112; Karen Weissbecker, Ph.D., James G. Barbee IV, M.D., Daniel K. Winstead, M.D.

Summary:

The idea that several related disorders, similar in their presentation and their responsiveness to serotonergic agents, constitute an obsessive-compulsive spectrum has gained increasing acceptance. Largely missing from that discussion has been generalized anxiety disorder (GAD), a condition characterized by at least a six-month history of excessive worry and hyperarousal. While the worry associated with GAD is not senseless, like an obsession, it can be intrusive and distressing. Such worry is often accompanied by checking behaviors, making the symptoms of obsessive-compulsive disorder and GAD similar enough that patients with one condition are often misdiagnosed with the other. In this study, 20 subjects with GAD and without OCD, 15 subjects with OCD and without GAD, and 17 subjects without any Axis I disorder were given the compulsion subsection of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).

Mean compulsion scores for the GAD group (7.75, sd = 4.01, range 0–13) and the OCD group (9.32, sd = 4.05, range 3–18) were not statistically separable, while both scores differed significantly from those of normal controls (0.36, sd = 1.07, range 0–4) ($p < 0.001$). The results indicate that checking behaviors, while lacking the functional impairment associated with OCD, occur frequently in GAD, and that GAD might be understood as part of any obsessive-compulsive spectrum.

NR501 Wednesday, May 21, 12 noon-2:00 p.m.

Cortisol Circadian Rhythms During the Menstrual Cycle and with Sleep Deprivation in Premenstrual Dysphoric Disorder and Normal Control Subjects

Suryabanu Javeed, M.D., Department of Psychiatry, Univ of California/San Diego, 7015 Charmant Drive, #211, San Diego CA 92122; Barbara L. Parry, M.D., Richard Haugher, M.D., Paul Cloptim, M.S.

Summary:

The objective of this study is to compare the cortisol rhythms in PMDD subjects during the follicular and luteal phases of the menstrual cycle in a 24-hour period. The aim of this study is to compare the cortisol rhythms during (ESD) and late sleep deprivation (LSD).

Method: In 15 subjects with a DSM-IV diagnosis of PMDD and in 15 NC subjects cortisol was measured every 30 minute from 6 p.m.-9 a.m. during the mid-follicular (MF) and the late luteal phases (LL) of the menstrual cycle, and during a randomized crossover trial of ESD and LSD in subsequent luteal phases. In ESD the subjects slept from 3 a.m.-7 a.m. and in LSD the subjects slept from 9 p.m.-1 a.m.

Results: There were differences across the four conditions. (MF, LL, ESD < LSD) in the mesor, amplitude, acrophase, and nadir. There were, however, no group differences. The acrophase showed interaction effects ($P = < 0.03$) in that the PMDD subjects had an earlier peak in cortisol with LSD and a later peak in cortisol with ESD compared with the NC subjects.

Discussion: The difference in cortisol in PMDD patients and NC could be due to circadian rhythm. Since the cortisol levels in PMDD patients did not differ from normal control subjects, there is no change in cortisol in PMDD patients, unlike MDD where there can be an increase in cortisol in some patients. The cortisol increases with ESD and LSD are like the studies in MDD.

NR502 Wednesday, May 21, 12 noon-2:00 p.m.

PMS, Premenstrual Dysphoric Disorder, and Diurnal Variation in 5HIAA Levels

Anita L.H. Clayton, M.D., Department of Psychiatry, University of Virginia, 2955 Ivy Road, Ste 210, Charlottesville VA 22903; Adrienne E.R. Sheldon-Keller, Ph.D., Catherine A. Leslie, M.D.

Summary:

Ten women have completed a study of association between diurnal variation in 5HIAA levels and symptoms associated with PMDD. Each participant keeps a daily log of 24 symptoms for two months. During two 24-hour admissions (48 hours prior to onset of menses and 48 hours after onset of menses), participants have blood drawn every 90 minutes. Results to date suggest that premenstrual symptoms are best understood as falling into three groups. Four women had low symptoms in the week preceding onset of menses (mean symptom rating = 200), four women had moderate symptoms (mean symptom rating = 274), and two women had severe symptoms (mean symptom rating = 352). These three groups of women also differed in amount of diurnal variation in 5HIAA both premenstrually (3.48, 4.35 and 4.70 ng/ml, respectively) and postmenstrually (1.3, 6.3 and 5.3 ng/ml, respectively). These preliminary findings suggest: 1) PMS can perhaps be defined as a subthreshold symptom presentation of PMDD. Women with symptoms in this intermediate range might be at greater risk of progressing to PMDD. 2) Symptoms associated with PMDD, both at threshold and subthreshold levels, appear to be associated with increases in diurnal variations in 5HIAA, particularly postmenstrually.

NR503 Wednesday, May 21, 12 noon-2:00 p.m.

Effects of Antidepressants: EEG Sleep Studies in Depressed Patients During Dothiepin Treatment

Seung Chul Hong, M.D., Department of Psychiatry, Catholic University/St. Vincent, 93 Chi-Dong Paldal-Ku, Suwon 442060, Korea; Jin-Hee Han, M.D., Sung-Pil Lee, M.D.

Summary:

Objective: Recent studies indicated sleep changes precede general improvement of depressive symptoms after initiation of antidepressant therapy. In light of the notion that the emergence of clinical effect of antidepressants usually needs about two weeks, it is unclear whether these early changes of sleep are true antidepressive effect or the consequence of the nonspecific sedation. The aim of this study was to identify the nature and time-course of sleep changes following antidepressant administration and to investigate possible association between sleep changes and alleviation of depression.

Method: We studied the baseline sleep electroencephalogram variables and treatment-related sleep changes after one week and three weeks of antidepressant (dothiepin) treatment in a group of 11 depressed patients, mostly suffering from a major depressive disorder (according to the DSM-IV). Mean daily dose of dothiepin was 96 ± 4 mg (at 1st week) and 132 ± 4 mg (at 3rd week). Clinical response was measured by means of the Hamilton Rating Scale for Depression (HRSD).

Results: Compared with baseline, the relative value of each stage to total sleep time was as follows: sleep latency and REM sleep decreased significantly at the first week and third week after treatment; REM latency and stage 2 sleep increased significantly at the first week and third week after treatment; sleep changes linked to the antidepressant are correlated with alleviation of depression.

Conclusions: Significant sleep changes were noted after only one week of dothiepin treatment, which was correlated with alleviation of depression. These findings suggest some vegetative symptoms of depression could be changed earlier than was thought previously after antidepressant treatment.

NR504 Wednesday, May 21, 12 noon-2:00 p.m.

Age Differences in Behaviors Leading to Completed Suicide

Yeates Conwell, M.D., Department of Psychiatry, University of Rochester, 300 Crittenden Boulevard, Rochester NY 14642; Paul Duberstein, Ph.D., Christopher Cox, Ph.D., Jack Herrmann, M.S., Eric D. Caine, M.D.

Summary:

Objective: To describe systematically the behaviors leading to completed suicide and to test whether they differ as a function of age.

Method: 141 victims of completed suicide were studied by the psychological autopsy method. Using multiple analysis of covariance and multiple logistic regression, age at death was the principle independent variable; history of suicide attempts, warnings of intent, and specific behaviors in preparing for and implementing the suicide served as outcome measures; gender, an age-by-gender interaction term, living situation, and presence of specific diagnoses were covariates.

Results: Younger age and male gender significantly predicted having used a violent method to commit suicide. Older victims had significantly higher scores on a rating of suicidal intent and were less likely to have given warning in the last week. Older men and younger women were less likely to have ever made a suicide attempt.

Conclusions: Older people at highest risk for suicide present special challenges for prevention. Intervention following development of the suicidal crisis is unlikely to be effective in the elderly. Efforts to treat conditions that predispose to the suicidal state promise to be most effective.

NR505 Wednesday, May 21, 12 noon-2:00 p.m.

Completed Suicide and Remitted Alcoholism

Paul Duberstein, Ph.D., Department of Psychiatry, University of Rochester, 300 Crittenden Boulevard, Rochester NY 14642; Yeates Conwell, M.D., Dorrie-Sue Barrington, B.S., Jack Herrmann, M.S., Christopher Cox, Ph.D., Eric D. Caine, M.D.

Summary:

Background: Substantial research has been conducted on active alcoholism and suicide, but there is little known about the associations of remitted alcoholism and self-destructive behavior.

Method: Using psychological autopsy data (N = 141), we compared suicide victims with active alcoholism and no other active substance abuse/dependence (AA, N = 38) and those with remitted alcoholism and no active substance abuse/dependence (RA, N = 17). Main outcome variables were psychiatric diagnoses.

Results: Victims with AA were more likely to be divorced/separated and less likely to meet criteria for major depression and remitted substance dependence. Significant age-related psychopathology was prevalent among the RAs: 62% of younger (≤ 49 yrs) RAs met criteria for a psychotic disorder, while 78% of the older RAs met criteria for major depression. Corresponding figures for AAs were 18% and 12% (ps < .05).

Conclusion: Remitted alcoholism is present in a substantial minority of suicides. Its association with schizophrenia in younger victims and major depression in older suicides warrants further study. The finding that AAs are more likely to be divorced/separated is consistent with the idea that suicide in AA is often associated with the dissolution of social ties.

NR506 Wednesday, May 21, 12 noon-2:00 p.m.

Predisposition to Suicide Attempts in Appalachia

Joselito B. Morales, M.D., ARH Psychiatric Center, 102 Medical Center Drive, Hazard KY 41701-9421; Hazel E.A. McBride, Ph.D., Geoffrey S. Duckworth, M.D., Roy S. Price, M.S.W.

Summary:

Objective: To identify predisposing factors to suicide attempts in Appalachia.

Method: 104 consecutive admissions to the ARH Psychiatric Center in Appalachia were assessed and diagnosed based on DSM-IV criteria. A standard life events questionnaire documenting life events in the year prior to admission was administered. Chi square analysis with continuity correction was performed, with a probability level of .05 considered significant.

Results: 59% of the 104 admissions were males; 33% have schizophrenia/psychotic disorders, 25% major depression/dysthymia, 15% bipolar disorder, 3% substance abuse disorder, and 13% classified as "other." Also, 34% have a history of suicide attempts. The modal age is 41. A statistically significant correlation was found (a) between history of suicide attempts and the following social factors: family illness/injury, family problems, financial crisis, police/legal problems, having property lost/stolen, having witnessed violence, experienced trauma, victims of abuse; as well as (b) between history suicide attempts and involvement of drugs/alcohol: dual diagnosis, drug/alcohol abuse, parents actively on drugs/alcohol.

Conclusions: A significant number of the population studied has a history of suicide attempts. These predisposing factors need to be seriously considered when developing suicide prevention programs in this population.

NR507 Wednesday, May 21, 12 noon-2:00 p.m.

Variation in Suicide Risk Among Bipolar Families

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Summary:

Bipolar disorders are highly heritable conditions that are associated with a high risk of suicide. We looked at suicide risk in 770 relatives in 79 bipolar families (71 BP I, 8 BP II), which were ascertained for a linkage study. There were 16 suicides in 15 families; 10 suicides occurred in the 27 families that had a paternal pattern of transmission of bipolar disorder ($X^2 = 7.2$, $p < 0.01$). Eighty-nine subjects attempted suicide, 53% with BP I and 28% with BP II. Fifty families had at least one attempter. The risk of attempting suicide was higher among relatives of the 30 probands who had attempted suicide, occurring in 23% of their relatives versus 13% of relatives of probands with no reported attempts ($p = 0.056$). We are examining whether families with and without suicides and suicide attempts vary on other clinical variables (e.g., rates of comorbidity) or genetic variables (e.g., paternal versus maternal transmission of bipolar disorder). In the first 28 families to be genetically evaluated, we found linkage of bipolar disorder to markers on chromosome 18. Since our preliminary data on families with suicides suggest that paternal transmission of bipolar disorder may be associated with high risk of suicide, we are continuing to analyze the possible relationship between paternal parent of origin, linkage to chromosome 18, and suicide risk.

NR508 Wednesday, May 21, 12 noon-2:00 p.m.

Decreased Risk of Suicide in Clozapine Treated Patients with Schizophrenia: A Retrospective Cohort Study

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Summary:

Objective: To compare rates of serious suicide attempts and completed suicides for patients treated with clozapine to projected rates of serious suicide attempts and completed suicides in the general schizophrenic population.

Method: Patients treated with clozapine at an intermediate care facility for the mentally ill were identified using the facility's pharmacy database. A total of 833 patients met criteria and were cross-referenced with an existing patient database to determine patient deaths and medical hospitalizations for the duration of clozapine therapy. All patient deaths were evaluated to determine if cause of death was suicide related. All medical hospitalizations were evaluated to determine if reason for admission was related to a serious suicide attempt. A student's t-test was used to evaluate statistical significance between actual suicide rates and projected suicide rates.

Results: The rates of serious suicide attempts and completed suicides are significantly reduced for clozapine-treated schizophrenic patients compared with rates projected for a standard schizophrenic population.

Conclusion: Clozapine use appears to be associated with reduced rates of serious suicidal behavior and associated deaths in the schizophrenic population.

NR509 Wednesday, May 21, 12 noon-2:00 p.m.

Precarious Job Integration in Self-Attempters: A French Preliminary Report

Francoise Chastang, M.D., Centre Psych Esquirol, C.H.R.U. Cote de Nacre, 14033 Caen, France; I. Dupont, Patrice Rioux, M.D., V. Kovess, E. Zarifian

Summary:

Since the time of Durkheim, aggregate and individual studies have shown an important and complex association between unemployment and suicidal behavior. Unemployment is also a predictor of repeated parasuicide. The aim of this study is to analyze the relationship between parasuicide and precarious job integration, defined for the authors as unemployment or any of the French government measures taken in response to unemployment. A questionnaire was given to 541 self-attempters (63% females, 37% males, mean age = 34 ± 1) who visited the emergency psychiatric unit during the period from December, 6, 1993, to June, 5, 1994. Demographic data, family and individual characteristics, diagnoses, and previous contacts with health services were collected. Univaried and logistic regression analyses were used. We found that 54% of self-attempters were suicidal repeaters. There were more depressive disorders, parasuicides, and drug/alcohol abuse in their families. The relationship with the family psychiatric background was no longer significant when the population was stratified by job integration, suggesting that precarious integration was a confounding factor in this intricate relationship.

NR510 Wednesday, May 21, 12 noon-2:00 p.m.

Inducible Nitric Oxide Synthase in the Brain

Ma-Li Wong, M.D., CNE, NIMH Intramural/Bldg 10, 2D46, 10 Center Drive/MSC 1284, Bethesda MD 20892-1284; Amer Al-Shekhlee, M.D., Peter B. Bongiorno, B.Sc., Samuel M. McCann, M.D., Philip W. Gold, M.D., Julio Licinio, M.D.

Summary:

Inducible nitric oxide synthase (iNOS), a transcriptionally regulated enzyme that synthesizes nitric oxide from L-arginine, has a key role in the pathophysiology of systemic inflammation and sepsis. Transgenic animals with a null mutation for the iNOS gene are resistant to lethality and hypotension caused by *Escherichia coli* lipopolysaccharide (LPS). The regulation of peripheral iNOS has been well studied in sepsis, but little is known about iNOS regulation in the brain during systemic inflammation or sepsis. We show that at baseline there is no detectable iNOS gene expression in the brain, but a detailed neuroanatomical study reveals that early in the course of systemic inflammation there is a profound induction of iNOS mRNA in vascular, glial, and neuronal structures of the rat brain, accompanied by the production of nitric oxide (NO) metabolites in brain parenchyma and cerebrospinal fluid (CSF). We propose that the spillover of nitrites into the CSF has the potential to be a diagnostic marker for systemic inflammation and sepsis. Pharmacological interventions designed to regulate iNOS function in the brain might represent a new treatment strategy in sepsis. Given the role of NOS in behavior, these findings may also explain behavioral alterations caused by systemic illness. Brain iNOS may be relevant to the pathophysiology, diagnosis, and treatment of systemic inflammation and sepsis, and it may explain abnormal behavior in the context of medical illness.

NR511 Wednesday, May 21, 12 noon-2:00 p.m.

The Immune Function and MDD

Doobyung Park, M.D., Department of Psychiatry, Chung-Ang University Hospital, 82-1 Phil-Dong Chung-Gu, Seoul, Korea; Juyeon Cho, M.D., Aeja Park, M.D.

Summary:

Objective: The objectives of this study were 1) to identify the differences of the immune function between major depressive disorder patients and healthy normal controls; 2) to investigate the correlation between several variables, such as age, symptom severity, and immune function in patients with major depressive disorder.

Method: The subjects were 30 patients who met DSM-IV criteria for major depressive disorder and who had been two weeks drug free before this study. Thirty-two healthy young adults were recruited for control. The following immunological functions were observed in the patients on admission and normal controls on the same day: WBC, lymphocyte subpopulations (T cell, B cell, CD4+ cell, CD8+ cell, CD4+/CD8+ cell ratio), natural killer (NK) cell count and percentage, serum immunoglobulin levels (Ig G, Ig A, Ig M), total hemolytic complement activity. The severity of symptoms was assessed by using the Hamilton Depression Rating Scale on each day of immunological examinations.

Results: The percentage of CD8+ cells of depressive patients was significantly lower than that of normal controls, and Ig A concentration of depressive patients was significantly higher than that of normal controls. In the depressive patients group, a positive correlation was found between the percentage of lymphocyte and age, whereas a negative correlation was observed between IgM and the symptom severity.

Conclusions: These findings suggest that altered immunity in major depressive disorder may be related to age and the severity of depressive symptoms. Further investigation of a range of immune functions in major depressive disorders may help to elucidate the pathophysiology of the depressive state that may be manifested in patterns of dysregulation of neuroendocrine, neurotransmitter, and immune systems.

NR512 Wednesday, May 21, 12 noon-2:00 p.m.

Insomnia and Its Impact: A Survey of Enrollees at Five U.S. Managed Care Organizations

Wallace B. Mendelson, M.D., Sleep Research Lab, University of Chicago, 5743 South Drexel Avenue, Chicago IL 60637; Hind T. Hatoum, Ph.D., Chris Kania, M.S., Sheldon X. Kong, Ph.D., Josephine Wong, Pharm.D.

Summary:

Objective: To assess the prevalence and causes of insomnia among clinic visitors and insomnia's impact on patient well-being and health care use.

Methods: A survey was given to 3,447 enrollees of five managed care organizations, with questions on sleep loss, depression, quality of life (QOL), medical encounters, and medication use.

Results: Three levels of insomnia were defined (none; Level I-difficulty initiating or maintaining sleep; Level II-Level I insomnia plus daytime dysfunction). Nearly half (46.6%) of the respondents reported sleep problems; 34.2% reported Level II insomnia. Level II insomnia increased with decreasing income, education, and age, and was more prevalent in women, non-Caucasians, and those with higher rates of comorbidities. Triggers of insomnia most frequently mentioned by Level II insomniacs were recent stressful events (66.4%) and worry (55.3%). Insomnia was significantly correlated with depression, lower QOL scores, and higher frequency of medical encounters. Only 0.9% sought medical help specifically for insomnia; 12.15%, and 11.5% were taking prescription and over-the counter sleep medications, respectively.

Conclusions: Few insomniacs are being treated for their condition. Proper patient education, diagnosis, and treatment of sleep problems are warranted since insomnia is associated with a negative impact on patients' QOL, functioning, and health care resource consumption.

NR513 Wednesday, May 21, 12 noon-2:00 p.m.

Long-Term Health Care Resource Utilization and Cost Before and After Initiation of Risperidone Treatment in Patients with Chronic Schizophrenia

Penny Albright, Ph.D., Janssen Res Foundation, 19 Green Belt Drive, North York ON M3C 1L9, Canada; David L. Keegan, M.D., Patricia M. Vandenbygaart, M.Sc.

Summary:

This presentation provides a long-term follow-up to a retrospective cohort study that looked at changes in health care resource use following the initiation of risperidone in chronic schizophrenia patients. The data were collected from five linked databases in Saskatchewan containing patient, prescription drug, hospital, physician, and mental health services information. Significant decreases were observed in hospital admissions (60%) and length of hospital stay (58%) for 146 chronic schizophrenia patients for a mean of 10 months before and after risperidone initiation. Decreases were also observed in physician visits, mental health service visits, and number of psychotropic prescriptions.

Data are now available for the same 146 patients, observing changes over a mean period of 22 months before and after risperidone initiation, perhaps representing a more appropriate timeframe, considering the cyclic nature of chronic schizophrenia. We continue to see significant decreases in hospital admissions (49%), length of hospital stay (47%), and physician visits (25%). Decreases were also observed in mental health service visits and number of psychotropic prescriptions. Once again, these updated long-term results support the role of risperidone in reducing health care resource use for patients with chronic schizophrenia, translating into substantial cost savings.

NR514 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Independence of Affect Expression and Affect Recognition in Schizophrenia

Richard J. Shaw, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford CA 94305; Melissa Dong, M.A., Kelvin O. Lim, M.D., Murray Alpert, Ph.D., Enrique R. Pouget, B.A.

Summary:

To examine the relationship between affect expression and affect recognition in schizophrenia, we assessed 31 clinically stable, medicated schizophrenic patients diagnosed by SCID-IIIR interview. Affect expression was assessed using two methods: a standard clinical rating scale (SANS) and a computerized acoustic analysis of speech from a recorded interview (VOXCOM). The acoustic analysis, performed at NYU Medical Center, produces quantitative measures of speech characteristics, including frequency, amplitude, length of utterances, and pauses, and provides an objective measure of flat affect. Affect recognition was assessed using the Florida Affect Battery (FAB), a standardized instrument that assesses the ability of subjects to recognize facial expression and emotional expressiveness of speech. The schizophrenics' performance on the affect recognition tasks was significantly impaired when compared with published normative data, indicating deficits in affect recognition ($p < .05$). To examine the relationship between affect expression and affect recognition, we correlated the affect expression measures (SANS and VOXCOM) with the affect recognition measures (FAB). No significant correlations were found, suggesting that the deficit symptoms in schizophrenia, in particular flat affect and alogia, are not related to their ability to discern emotions in others.

NR515 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A Clinical Lab for Psychiatry: Vocal Acoustic Measures of Flat Affect and Alogia

Murray Alpert, Ph.D., Department of Psychiatry, NYU Medical Center, 550 First Avenue, New York NY 10016; Enrique R. Pouget, B.A., Richard J. Shaw, M.D., Melissa Dong, M.A., Kelvin O. Lim, M.D.

Summary:

Although many behavioral items in the DSM can be objectively measured, practice has emphasized clinical ratings. In this report, we evaluate the feasibility of supplementing clinical ratings of flat affect with objective acoustic measures of voice. Thirty-one interviews with schizophrenic patients were recorded at the Stanford/VA Mental Health Clinical Research Center (MH 30854), where the patients were also assessed by reliable raters (ICC, r = 0.8) with the SANS, BPRS and Gerlach EPS scales. The speech samples were analyzed at NYU Medical Center with a special purpose computerized facility.

There were significant correlations between global ratings of flat affect/alogia and acoustic fluency measures. However, correlations between ratings and acoustic measures of such items as response latency or speech poverty were much weaker. Also, ratings were more confounded by extrapyramidal signs. Ratings of items were more strongly associated with global ratings than with the acoustic measures, suggesting that the ratings items were derived from "top-down" global impressions. Thus, reliable ratings need not be valid. Acoustic analysis may provide clinicians with a useful and quantitative measure of flat affect. Development of these measures and operational definitions of the clinical construct of flat affect may enhance psychiatric diagnosis and assessment of the treatment of negative symptoms.

NR516 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A Bridging Study of Once Daily Iloperidone in Schizophrenia Patients

Neal R. Cutler, M.D., California Clinical Trials, 8500 Wilshire Blvd, 7th Floor, Beverly Hills CA 90211-3109; James E. Shipley, M.D., Jerome F. Costa, M.D., Laura Zumpano, Mindy F. Gellock, Jameel Hourani, D.O., Stanford S. Jhee, Pharm.D., John J. Sramek, Pharm.D.

Summary:

Objective: Preclinical studies of iloperidone suggest potential antipsychotic activity with reduced EPS liability. This four-period (I-IV) bridging study was designed to determine the safety and tolerability of single daily doses of iloperidone in schizophrenic patients.

Methods: Twenty-four schizophrenic inpatients received iloperidone with dose escalations occurring every three days in Study Period I, every two days in Study Period III, or daily in Study Period IV (n = 8 per period). Study Period II, originally designed to determine the maximum starting dose, was canceled, as the optimal initial dose was determined in Study Period I.

Results: Doses of iloperidone up to 32 mg were well tolerated by patients on a slow (every three day) titration schedule, and an administrative decision was made to limit the top dose for future periods to 24 mg/day. Doses up to 24 mg were well tolerated in patients with more rapid (every two day or daily) titration. Adverse events were primarily mild in intensity. A very low incidence of extrapyramidal symptoms was observed.

Conclusions: The doses tolerated by patients in this study were 10 times higher than single doses previously tolerated by healthy subjects and four times higher than the reported dose for efficacy (8 mg/day) in schizophrenic patients.

NR517 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A Bridging Study of Once-Daily MDL 100,907 in Schizophrenia Patients

Neal R. Cutler, M.D., California Clinical Trials, 8500 Wilshire Blvd, 7th Floor, Beverly Hills CA 90211-3109; Linda Elkins, Ph.D., Lutrecia Church, M.A., Jerome F. Costa, M.D., John J. Sramek, Pharm.D.

Summary:

MDL 100,907 is a potent and highly selective 5-HT_{2A} antagonist currently in development for the treatment of schizophrenia.

Objective: This bridging study was designed to evaluate the safety and tolerability of fixed doses of MDL 100,907 in five consecutive panels of schizophrenic inpatients and to determine the maximum tolerated dose (MTD) for once daily (QD) dosing in this population.

Methods: Thirty schizophrenic inpatients were enrolled in the study and participated in a three-day, single-blind, placebo washout prior to the seven-day treatment period. The doses for the five panels (n = 6 per panel) were 20, 40, 80, 100, and 125 mg MDL 100,907, administered QD.

Results: In Panels 1 and 2 (20 and 40 mg/day), MDL 100,907 was well tolerated, with patients experiencing only mild adverse events. In Panel 3 (80 mg/day), four of six patients experienced moderate lightheadedness. This defined the minimum intolerated dose. Because of these adverse events, the dose for Panel 4 was revised downward to 60 mg/day. At this dose, only one patient experienced a moderate adverse event (headache).

Conclusion: The MTD for QD dosing was defined as 60 mg.

NR518 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Computerized Assessment of Psychosis Severity Questionnaire

Robert G. Stern, M.D., Department of Psychiatry, FDR VA Hospital, Route 9A, Bldg 14, Room 8, Montrose NY 10548; Ronald G. Fudge, Ph.D., James Crichton, M.A., Cecile E. Sison, Ph.D., Benedict J. Connolly, M.A., Miklos F. Losonczy, M.D.

Summary:

Objectives: We attempted to develop and validate a computer-driven, patient self-rated questionnaire, COSAPSQ, which should provide a reliable, rapid, and inexpensive method to assess illness severity in patients with schizophrenia.

Design and Methods: After giving informed consent and receiving instructions in the use of the keyboard, patients with DSM-IV schizophrenia or schizoaffective disorder completed the COSAPSQ-V2 questionnaire (version 2 consisting of 61 multiple-choice questions). Binomial correlation analysis assessed the relation between PANSS and CGI scores and COSAPSQ-V2 scores and completion time.

Results: The analysis of the first 29 rating sets showed that patients with a wide range of illness severity (CGI: 3–6;) were able to complete the COSAPSQ-V2 in a mean (±SD) time of 21.6 (±12.8) minutes. COSAPSQ-V2 total scores correlated with PANSS total (r = .6; p < .001), general (r = .7; p < .000) and positive scores (r = .7; p < .000), and with CGI (r = .6; p = .002). Total PANSS negative scores correlated significantly with COSAPSQ-V2 total completion time (r = .6; p = .001) and with individual COSAPSQ-V2 items with correlation coefficients ranging from .4–.6.

Conclusions: These preliminary results confirm that schizophrenic patients are able to complete the computer-driven, self-rated questionnaire COSAPSQ-V2, providing the clinician with a useful measure of illness severity comparable to CGI and PANSS.

NR519 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Speech Processing Impairments Associated with Hallucinated Voices in Schizophrenia

Ralph E. Hoffman, M.D., Yale Psychiatric Institute, PO Box 208038, New Haven CT 06520-8038; Donald M. Quinlan, Ph.D., Jill Rapaport, M.S., Helen Sayward, M.A., Carolyn M. Mazure, Ph.D.

Summary:

Objective: We attempted to replicate and expand upon an earlier study suggesting that schizophrenic patients who report hallucinated "voices" demonstrate specific impairments in processing spoken speech. In addition, we tested the hypothesis that these impairments were not due primarily to disrupted auditory attention.

Methods: Twenty-two schizophrenic patients reporting hallucinations were studied along with 25 non-hallucinating schizophrenic patients and 26 normal controls. Each subject was administered the masked speech tracking task (MST), an auditory continuous performance task (CPT), and a test of verbal working memory (sentence repetition task). MST required subjects to "shadow" (repeat while listening) spoken narrative speech heard binaurally on headphones. Speech stimuli were contaminated with different levels of phonetic noise.

Results: Hallucinating patients again demonstrated significant MST abnormalities relative to the two comparison groups, including reduced number of words correctly reported and an increase in the number of words erroneously perceived. Hallucinators also demonstrated impairments in auditory CPT and sentence repetition performance relative to the other groups. CPT impairments did not fully account for speech-tracking alterations.

Conclusions: These data provide additional evidence that schizophrenic patients reporting hallucinated "voices" suffer from a specific pathophysiological syndrome characterized by impaired speech processing.

NR520 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Schizophrenic Relapse in Medication-Complaint and Non-Complaint Patients

Jose L. Ayuso-Gutierrez, M.D., Department of Psychiatry, Hospital San Carlos, Isac Peral S/N, Madrid 28040, Spain; Beatriz Paya, M.D., Margarita Saenz, M.D., Julia Del Rio, M.D.

Summary:

Why are there so many patients who suffer from relapses, despite the existence of a highly effective preventive treatment?

This study was designed to extend previous research on schizophrenia and to add a detailed investigation of relapse among schizophrenic patients under routine treatment conditions.

The study consisted of 90 consecutive schizophrenic patients (59 male and 31 female) who had suffered a clinical exacerbation and were admitted to Hospital Universitario San Carlos in Madrid.

We have recorded the following items: illness variables, level of family support and level of stress, therapeutic regimen prior to admission, patient's attitude toward health and illness, stressful life events, and current alcohol and drug abuse.

Noncompliance with medication (72%), lack of family support (35%), and alcohol/drug problems (43%) were the most important factors related to schizophrenic relapse. Noncompliant patients did not differ from compliant patients in drug treatment regimens, neuroleptic side effects, family support, or adverse life events. However, noncompliant schizophrenics more often showed a negative attitude toward health and illness as assessed by the scale of Hogan. This low compliance among schizophrenic patients might be caused by the lack of insight into the disease and the need for therapy.

NR521 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Risperidone Versus Conventional Neuroleptics in Forensic Hospital Patients

Patrick J. Devitt, M.D., Dept. of Psychiatry, SUNY, School of Medicine, 750 East Adams Street, Syracuse NY 13210; Prakash S. Masand, M.D.

Summary:

Objective: The efficacy and safety of risperidone and five conventional neuroleptics for treating psychotic symptoms were evaluated in a retrospective study of 42 forensic hospital patients.

Methods: Patient diagnoses were schizophrenia in seven, schizoaffective disorder in 11, paranoid disorder in five, atypical psychoses in five, and other mental disorders with psychotic features, including major depression and bipolar disorder, in 14. Of the 42 patients, 15 were admitted to the hospital for the first time and received risperidone, and 27 patients with multiple previous admissions were switched to risperidone after having received other antipsychotic regimens including haloperidol, thiothixene, perphenazine, fluphenazine, or chlorpromazine. Treatment responses were assessed by means of the Clinical Global Impression scale and staff notes. Most patients received 6 mg/day of risperidone (range, 4–8 mg/day).

Results: Of the 15 first-admission patients treated with risperidone, nine showed moderate to marked improvement, three showed improvement in ward management, and no significant improvement was noted in three. Conventional neuroleptics were associated with marked to moderate improvement in six patients, improvement only in ward management in 13, and no significant improvement in 10; the number of improved patients increased to 19 when this group was switched to risperidone. The incidence of adverse events was twice as high in the neuroleptic-treated patients as in the risperidone-treated patients. Responses to risperidone were not correlated with sex, age, ethnicity, or educational level.

Conclusions: The results indicate that risperidone may be an effective alternative to conventional neuroleptics in forensic patients.

NR522 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Alcohol Metabolism in Three Different Aldehyde Dehydrogenase 2

Sy-Ueng Luu, M.D., Department of Psychiatry, Tri-Service General Hospital, 8, Section 3, Ting-Chow Road, Taipei, Taiwan, R.O.C.; Ming-Fang Wang, M.S., Shih-Jiun Yin, Ph.D.

Summary:

Objective: Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are major enzymes responsible for ethanol metabolism in humans. Our previous study has demonstrated that the polymorphic ADH2, ADH3, and ALDH2 genes can affect susceptibility to alcoholism in Han Chinese of Taiwan (Thomasson et al. Am J Hum Genet 48:677–681, 1991). In this new research, we investigated alcohol metabolism and subjective feelings in three different ALDH2 genotypes.

Method: Male individuals, homozygous for both the ADH2*2 and ADH3*1 alleles, with ALDH2*1/*1, ALDH2*1/*2, or ALDH2*2/*2 genotype, six in each group, were recruited.

Results: The mutant ALDH2*2/*2 homozygotes exhibited significantly higher peak acetaldehyde level and greater AUC than did the normal homozygotes and the heterozygotes after a low dose of ethanol (0.2 g/kg). The mutant homozygotes also displayed significantly higher peak ethanol level and AUC compared with normal homozygotes. Of the 17 subjective feeling items tested, palpitation, facial warming, effects of alcohol, and dizziness were found most pronounced among the mutant homozygotes.

Conclusions: Significantly unpleasant subjective feelings caused by high blood acetaldehyde level after a low dose of ethanol may keep the subjects homozygous for mutant ALDH2*2 avoiding consuming alcohol through learned avoidance, thus completely protecting against development of alcoholism.

NR523 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Additive Effect of Dopaminergic Genes in OCD with Tics

Humberto Nicolini, Clinic, Institute of Mexicano Psych, Calz Mexico-Xochimilco 101, Mexico DF 14370, Mexico; Beatriz Camarena, B.Sc., Carlos Cruz, Ph.D., Francisco Paez, M.D.

Summary:

Disturbances in the dopamine neurotransmitter system have been implicated in the pathogenesis of disorders exhibiting chronic vocal or motor tics such as Tourette's syndrome or obsessive-compulsive disorder (OCD). In this study we examined the dopamine receptor DRD2-TaqI-A allele system and the polymorphism characterized by a varying number of 48-bp repeats (VNTR) in the dopamine D4 receptor (DRD4) gene. Sixty OCD probands with and without tics were genotyped (12 and 48, respectively). Most of the OCD patients with tics, compared with those without tics, showed an increased frequency of the DRD2-A2 (58% vs. 27%, respectively, Fisher's exact test $p = 0.048$) as well as an increased frequency of the DRD4-7-fold variant (48% in OCD with tics vs. 9% in OCD without tics, X^2 Yates corrected = 5.54, $p = 0.018$). Similarly, when both alleles were combined (at least one copy of DRD2-A2 and DRD4-R7), those patients with tics showed a higher frequency of this haplotype (83.3% in OCD with tics vs. 40% in OCD without tics, X^2 Yates corrected = 5.71, $p = 0.016$). These results suggest that this allele combination could be a factor in the phenotypic variance of tics among OCD individuals.

NR524 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Thyroid Hormones and ADHD

Peter Hauser, M.D., Department of Psychiatry, Baltimore VAMC, 10 North Greene Street, Baltimore MD 21201; Rosa Soler, Francoise Brucker-Davis

Summary:

The diagnostic validity of dividing attention deficit hyperactivity disorder (ADHD) into two distinct subgroups, one with and one without hyperactivity, is controversial since there have been no physiological differences demonstrated between these two subgroups. In this study, the relationship between thyroid hormones and symptoms of hyperactivity was examined in subjects with resistance to thyroid hormone (RTH) and their unaffected family members.

Clinical data were collected on 152 subjects; 75 RTH subjects and 77, unaffected family members. Each subject was assessed using DSM-III-R based, structured psychiatric interviews, and Total T3 (TT3), Total T4 (TT4), and TSH concentrations were measured. The total number of ADHD symptoms were assigned to either inattention or hyperactive subgroups using DSM-III-R criteria. The ADHD symptoms were reassigned to inattention or hyperactive/impulsive subgroups using DSM-IV criteria. Pearson R correlation coefficients were calculated separately for the RTH and the unaffected family member groups in order to determine the relationships between TSH, TT3, and TT4 concentrations, and the DSM-III-R and DSM-IV symptom categories of ADHD in both groups. TSH concentrations were not significantly correlated with any of the symptom categories in either group. However, in the RTH group both TT3 and TT4 concentrations were significantly and positively correlated with total symptoms of ADHD (DSM-III-R) as well as symptoms of inattention (DSM-III-R) and symptoms of hyperactivity (DSM-III-R). When DSM-IV criteria were used, which reassigns symptoms of impulsivity from the inattention to the hyperactivity category, only the positive correlation between TT3 and TT4 concentrations and symptoms of hyperactivity/impulsivity (DSM-IV) remained significant. In the group of unaffected family members, the relationship between TT3 concentrations and symptoms of hyperactivity/impulsivity (DSM-IV) was the only significant correlation.

The data support the hypothesis that thyroid hormones may provide a physiologic basis for the dichotomy between symptoms of inattention and symptoms of hyperactivity, particularly when DSM-IV criteria are applied.

NR525 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Serial Correlation of CSF HVA and 5-HIAA in Healthy Humans Undergoing Sequential CSF Sampling for Over Thirty Hours

Mitchel A. Kling, M.D., Department of Psychiatry, Baltimore VA Medical Center, 10 North Greene Street, Baltimore MD 21201; Michael D. De Bellis, M.D., Thomas D. Geracioti, Jr., M.D., Dennis L. Murphy, M.D., Philip W. Gold, M.D.

Summary:

Previous studies have shown significant correlations between single-time-point cerebrospinal fluid (CSF) concentrations of the dopamine (DA) metabolite homovanillic acid (HVA) and the serotonin (5-HT) metabolite 5-hydroxyindoleacetic acid (5-HIAA), which are relevant to psychiatric disorders such as depression and schizophrenia, in healthy subjects studied cross-sectionally, suggesting a physiologic relationship between these parameters. However, it is not known whether temporal correlations occur within the same individual. We examined hourly CSF levels of HVA and 5-HIAA in the same aliquot of lumbar CSF in 11 healthy volunteers (6 M; mean age 35.3 ± (s.e.) 2.6 yr) who underwent continuous CSF sampling for 30 hours via a 20g epidural catheter inserted in a low lumbar interspace through an 18g Tuohy needle under local lidocaine anesthesia at 0900 h. The catheter was connected to a peristaltic pump and fraction collector for continuous collection of CSF at 6 ml/h for 30 h; hourly aliquots (1 ml) were measured for HVA and 5-HIAA by HPLC-EC. Subjects remained at bed rest during the entire study and ate meals at usual times; lights were out from 2300–0700 h.

CSF HVA and 5-HIAA levels showed significant ($p < 0.05$) ultradian variation in all subjects that was well in excess of measurement error (up to 2–3 fold, max/min). A clear diurnal variation was not consistently observed, although both CSF HVA and 5-HIAA levels fell during the night in three subjects. Significant ($p < 0.05$) correlations between simultaneous levels of CSF HVA and 5-HIAA were observed in all subjects. In six of 11 subjects, the Pearson r value for this correlation exceeded 0.9 ($p < 0.001$); in only one subject was $r < 0.5$. Single outliers appeared to account for the lower r values in three subjects. Moreover, even in the time series of subjects with lower correlation coefficients, CSF HVA and 5-HIAA values closely tracked each other for much of the sampling period, although their ratio varied.

These data indicate a close temporal relationship between CSF levels of HVA and 5-HIAA in healthy individuals studied longitudinally over 30-hour periods, suggesting coordinate regulation of DA and 5-HT metabolism in the central nervous system under baseline, resting conditions. Further work will be needed to determine the physiologic significance of this relationship, the implications of its dysregulation, and its status in disorders characterized by disturbances in central DA and/or 5-HT neurotransmission.

NR526 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Clinical and Neuropsychological Improvement Unrelated to SPECT Changes in OCD

Mantosh J. Dewan, M.D., Department of Psychiatry, SUNY Health Sciences Center, 750 East Adams Street, Syracuse NY 13210; John F. Tanquary, M.D., Prakash S. Masand, M.D., Robert Sprafkin, Ph.D., F. Deaver Thomas, M.D., N.M. Szeverenyi, Ph.D., Leslie F. Major, M.D.

Summary:

We hypothesised that SPECT changes would correlate with symptom and neuropsychological improvement in OCD patients treated with medications or behavior therapy (B.Th).

Method: 16 DSM-III-R OCD patients were treated with clomipramine (n = 7) or behavior therapy (n = 9) and studied pre- and post- (after 12 weeks) treatment on SPECT, YBOCs, Wisconsin Card Sort, Trails A & B, and finger tapping.

Results: Compared with normal controls, there were no significant differences on baseline SPECT of OCD patients. Compared with baseline, post-treatment SPECT values *increased* for both groups in L and R frontal, temporal, and parietal areas. There was improvement with medication and B.Th on YBOCs (25 to 14; 22 to 12), Trails A (31 to 29; 40 to 33) Trials B (85 to 69; 76 to 67), and all parameters of Wisconsin Card Sort: number correct, number of errors, perseverative and non-perseverative errors. Finger tapping *worsened*: Left finger tap (47 to 46; 44 to 43) and right finger tap (50 to 49; 51 to 49). Although there were consistent directions of change, all results were statistically nonsignificant.

Discussion: We did not find the expected hyperfrontality at baseline. With treatment, brain activity on SPECT increased in all areas. Clinical and neuropsychological improvements with clomipramine and behavior therapy were not dependent on SPECT brain changes.

NR527 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Lithium Therapy and Hyperparathyroidism

Marion E. Wolf, M.D., Department of Psychiatry, VA Medical Center, 3001 Green Bay Road, North Chicago IL 60064; Mary Holland, R.P.H., Don Grant, R.P.H., Janet M. Mosnaim, Sandra Dempsey, M.D.

Summary:

Lithium is a monovalent cation that influences calcium metabolism in various tissues including the brain, kidney, heart, and parathyroid gland. An association between treatment with lithium and hyperparathyroidism has been recognized, but it remains unclear whether lithium initiated hyperparathyroidism or unmasked an underlying parathyroid disorder. Of 30 reported cases of surgically treated, lithium-associated hyperparathyroidism, 17 patients were found to have a single-cell adenoma and 13 patients had parathyroid hyperplasia. We have examined the characteristics of the hypercalcemia found in 11 chronic affective disorder patients treated with lithium maintenance at our medical center.

Our preliminary findings suggests that the late-onset hyperparathyroid syndrome resembles the clinical picture of familial hypocalciuric hypercalcemia with mild hypercalcemia, hypocalciuria, normal serum phosphate levels, normal urinary cyclic AMP excretion, hypermaganesemia, and absence of nephrolithiasis. Special emphasis is given to a bipolar patient treated with lithium for 18 years and with mild hypercalcemia for the last nine years. Administration of lithium resulted in an improvement of mania or hypomania, but treatment with this agent had to be discontinued because of prominent cardiovascular side effects (bradyarrhythmia, bradycardia, hypertension) that occurred with serum lithium levels within the therapeutic range. Clinical issues concerning the management of late-onset as well as early-onset hyperparathyroidism in patients on lithium maintenance will be discussed.

NR528 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Reversed Circadian Rhythm in Gerbils May Shed Light on Some Sleep and Mood Disorders

John D. Hallonquist, Ph.D., Department of Psychology, University of British Columbia, Kenny Building, Vancouver BC V6T 1Z4, Canada; Penny Gray-Allan, B.Sc., Terry Lao, B.A., Rod Wong, Ph.D.

Summary:

Recently we identified Mongolian gerbils, which are exclusively night-active (*N*) or day-active (*D*) when housed with activity wheels in LD 12:12 (12 hr photoperiod/24 hrs).

Objectives: To determine if *N* & *D* patterns of wheel-running in gerbils reflect circadian differences rather than inverse masking effects of light (Study I) and if such differences result from feedback from activity (Study II).

Methods: In Study I, following 10 weeks in LD 12:12, 15*N* and 10*D* gerbils were exposed to an eight-hour delay of the LD cycle, after which monitoring continued. In Study II, of 10*N* and 6*D* gerbils monitored for 22 weeks in LD 12:12, 6N and 4D animals were prevented from running during weeks 18 and 19.

Results: In Study I, gerbils reestablished their phase relationship to the shifted LD cycle-often following delaying transients. In Study II, phase positions remained stable despite restriction from running.

Conclusions: Study I shows that *N* and *D* rhythms reflect differences in circadian function rather than inverse masking by light. Study II indicates that differences in feedback from activity to the circadian oscillator cannot explain *N* vs *D* rhythms.

Examination of heredity/environment interaction and physiological mechanisms determining phase positions in gerbils may increase understanding of oscillator and entrainment function in the etiology of those human sleep and mood disorders in which displaced circadian rhythms have been observed.

NR529 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

D-fenfluramine Challenge Test in Acute Schizophrenia

Pavel Mohr, M.D., Clinical Research, Nathan S. Kline Institute, 140 Old Orangeburg Road, Orangeburg NY 10962; Jiri Horacek, M.D., Lucie Motlova, M.D., Jan Libiger, M.D., Pal Czobor, Ph.D.

Summary:

Objective: D-fenfluramine has been identified as a highly selective serotonin (5-HT) releaser and reuptake inhibitor. Response of hormones, known to be under 5-HT control (e.g., prolactin), to d-fenfluramine challenge is being used as an indirect measure of the functional state of central 5-HT systems. The objective of our study was to investigate prolactin response to d-fenfluramine challenge in nonmedicated, first-episode schizophrenics. We hypothesized that 5-HT activity can predict response to neuroleptic treatment.

Methods: Inclusion criteria were ICD-10 diagnosis of schizophrenia, first episode or duration of illness shorter than 36 months, and no previous treatment with neuroleptics. So far, 22 inpatients, 12 males and 10 females, at the Prague Psychiatric Center participated in the study. Two d-fenfluramine challenge tests were performed: before and after four weeks of haloperidol treatment. During the tests, prolactin plasma levels were measured. BPRS was administered before and after treatment.

Results: Statistically significant positive correlation was found between pretreatment prolactin response to d-fenfluramine challenge and improvement of psychopathology measured by the change of total BPRS score ($p < 0.0006$).

Conclusions: Our data support the original hypothesis that there is a relationship between 5-HT system activity and treatment response. This research is ongoing; updated results will be reported.

NR530 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Catechol O-Methyltransferase and Tryptophan Hydroxylase Genotypes in Violent Schizophrenia Patients

Pavel Mohr, M.D., Clinical Research, Nathan S. Kline Institute, 140 Old Orangeburg Road, Orangeburg NY 10962; Karen A. Nolan, Ph.D., Herbert M. Lachman, M.D., Jan Volavka, M.D.

Summary:

Objectives: Several different genes have been tentatively associated with violence. The allele encoding the low activity variant of catechol O-methyltransferase (COMT) has been found to predict high risk of violent behavior in schizophrenia. A tryptophan hydroxylase (TPH) polymorphism has been previously linked to aggressive and suicidal behavior in violent alcoholics. The objective of this study was to replicate these findings in a population of violent schizophrenics.

Methods: The subjects were 41 white or non-black Hispanic inpatients (24 males and 17 females) at the Rockland Psychiatric Center, with DSM-IV diagnosis of schizophrenia or schizoaffective disorder. Two groups were selected: violent and nonviolent. The violent subjects had a history of physical assault, violent crime, or threatening behavior, and no history of alcohol or drug abuse. COMT and TPH genotypes were determined. Instruments assessing impulsiveness, intelligence, psychopathy, and socioeconomic status were administered.

Results: In the males, the COMT low activity allele and the TPH L allele were significantly associated with violence (respectively, $p = 0.024$ and $p = 0.028$).

Conclusions: Our results suggest that there are strong relationships between genotype and violence in schizophrenic males. This research is in progress; updated results will be presented.

NR531 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Amygdala Volume and Glucose Metabolic Rate in Autism and Asberger's Disorder

M. Mehmet Haznedar, M.D., Department of Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Place/Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Inbahl Heth, B.A., Tse Chung Wei, Ph.D., Patrick Hof, M.D., Eric Hollander, M.D.

Summary:

Postmortem studies of patients with autism indicate cytoarchitectonic changes in the limbic system. The affected structures include the hippocampus, amygdala and the anterior cingulate cortex. In the current study, we examined the volumetric and metabolic changes in the amygdala in 14 high-functioning patients with autism and Asberger's disorder (12 men, two women, mean age 27.8, SD = 12.0) and 14 sex- and age-matched control subjects (mean age 28.7, SD = 10.3) who had MRI and PET scans. All subjects were free of psychoactive medications and were screened for other neuropsychiatric disorders including seizure disorder. Subjects performed a serial verbal-learning test during the 35-minute, 18-fluorodeoxyglucose uptake period. Two researchers who were blind to the subjects' diagnoses, were trained to outline the amygdala on coronal MRI slices (kappa 0.82). After PET/MRI coregistration, ROI coordinates were applied to the PET scan for each individual, and metabolic three-dimensional maps of the amygdala were reconstructed. Each individual's amygdala was warped to the averaged contour of the normal group. Between-group differences in amygdala metabolism were assessed by statistical test maps (with a resampling technique to control for multiple comparisons).

Neither the volume (amygdala/whole brain) nor the glucose metabolic rate of the amygdala showed between-group differences. This finding will be discussed in relation to hippocampal functions and the earlier reported, highly significant, anterior cingulate cortex metabolic changes in the same cohort.

NR532 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Cavum Septi Pellucidi in Schizophrenia Spectrum Disorders

M. Mehmet Haznedar, M.D., Department of Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Place/Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Jonathan Schwartz, B.S., Erin A. Hazlett, M.B., Jacqueline Spiegel-Cohen, M.S., Larry J. Siever, M.D.

Summary:

Cavum septi pellucidi (CSP) is a developmental anomaly of uncertain clinical significance. In patients with schizophrenia, the incidence of this anomally has been reported to be higher than in the normal population and is believed to reflect abnormalities in the limbic system as well as in the corpus callosum. We examined magnetic resonance imaging (MRI) findings in a total of 97 subjects: schizotypal personality disorder (SPD) = 13 (mean age = 43.3, SD = 12.5); schizophrenia = 42 (mean age 37.5, SD = 12.5); controls = 42 (mean age = 38.9, SD = 12.7). Two trained researchers, blind to diagnosis, used coronal slices (1.2 mm thick) to assess CSP and rated the anomaly on the basis of its severity on a five-point scale (0–4) (kappa 0.82). Ten patients with SPD (83.3%), 32 patients with schizophrenia (76.2%), and 27 controls (64.3%) were found to have a CSP score > 0. As the prevalence of CSP was higher than expected in the controls of this cohort, we carried out volumetric measurements of the anomaly. A simple ANCOVA (age as covariate) on the volume of the anomally comparing controls and patients with schizophrenia and controls and patients with SPD was performed ($F = 6.84$, $df = 1.68$, $p = 0.011$ and $F = 1.65$, $df = 1.43$, $p = 0.20$, respectively). Thus SPD patients were intermediate between controls and schizophrenic patients (mean CSP volume; SPD = 48.1 mm^3, SD = 72.8; patients with schizophrenia = 94.0 mm^3, SD = 255.4; controls = 45.8 mm^3, SD = 103.1). These results are discussed in relation to ventricular size, temporal lobe asymmetry, and callosal size in the same cohort.

NR533 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

PET Studies and Fenfluramine in Impulsive Patients

Larry J. Siever, M.D., Department of Psychiatry, Mt. Sinai School of Medicine, 1 Gustave Levy Place/Box 1230, New York NY 10029; Monte S. Buchsbaum, M.D., Antonia S. New, M.D., Erin A. Hazlett, M.B., Elizabeth Sevin, B.S.

Summary:

Impulsive/aggressive personality disorders have been associated with reductions in serotonergic activity in metabolite and neuroendocrine studies, reflected specifically in blunted prolactin responses to fenfluramine. Serotonin modulates the activity of orbital frontal and cingulate cortex, which may in turn inhibit aggressive behavior. To more directly test the hypothesis that reductions in serotonergic activity modulating orbital frontal and cingulate cortex are associated with impulsive/aggressive behavior, metabolic rate in these and comparison regions was measured by PET following 60 mg fenfluramine and placebo in six impulsive personality disorder patients and six comparison subjects (five normal controls, one nonimpulsive personality disorder patient). In a subset of these subjects (four impulsive patients, two control

subjects) on whom data have been analyzed using the coronal peel method on coregistered MRI, we found blunted fenfluramine responses on the orbital surface, most marked in the anterior granular cortex (controls increase + 0.19, sd = 0.09 with fenfluramine, patients decrease -0.08, sd = 0.30 with fenfluramine). In the medial frontal region, the control group increased relative metabolic rate four times as much on fenfluramine as on placebo (increase + .20 [sd = 0.12]) compared with the patient group increase + 0.05. In the ventral-most anterior cingulate gyrus this effect was twice as big in the control group as in the patient group, (+ 0.12 vs. + 0.06). In the ventral-most anterior cingulate gyrus this effect was twice as big in the control group as in the patient group (+ 0.12 vs. +0.06). For the absolute metabolic rate, the medial frontal region showed a control increase of 8.3 micromoles/100 grams/min., while patients actually showed an absolute decrease of 9.7 micromoles/100g/min. In contrast, in a comparison area hypothesized not to show the fenfluramine blunting, the supraangular gyrus in the parietal lobe of neither controls nor patients evidenced a significant fenfluramine increase. Patients also demonstrated (1.07) significantly lower resting metabolic rate than normals (1.24; $t = 1.84$, $p < 0.05$, 1-tailed), and metabolic rate in this area was partially normalized by fenfluramine. Parallel results were observed for ventral cingulate regions. Preliminary data from our pilot sample, which will be updated, are consistent with the hypothesized reductions in serotonergic modulation of orbital frontal cortex in impulsive/aggressive patients.

NR534 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Frontal Lobe and Startle Eye-Blink Deficits in Schizophrenia

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Summary:

Prepulse inhibition (PPI) refers to the phenomenon that occurs when innocuous, non-startling stimuli (called "prepulses") are presented shortly (30–500 ms) before startle-eliciting stimuli; they reliably inhibit the amplitude of the startle eye-blink response. "Attention to prepulse" paradigms have indicted that the magnitude of the PPI effect can be modulated by selective attention, suggesting that it is not an entirely automatic process, and animal models have implicated the prefrontal cortex in the modulation of PPI. Research has demonstrated that medicated schizophrenic patients fail to show attentional modulation of PPI. This study examined PPI in unmedicated schizophrenic patients (n = 15) and age- and sex-matched normal controls (n = 15) during the FDG uptake period for a PET scan. All patients met DSM-IV criteria for schizophrenia or schizoaffective disorder based on a structured interview. Participants performed an auditory selective attention task involving the presentation of to-be-attended, to-be-ignored, and novel tones, which served as prepulses. Acoustic startle probes were presented 120 ms after the onset of tones and occasionally during the intertone interval. Controls showed significantly greater PPI during attended tones compared with ignored tones, whereas, the patients failed to show this pattern. PET scans were coregistered to MRI for each individual and mean relative glucose metabolic rate was calculated with gray/white segmentation for lateral cortex regions in each hemisphere. A significant diagnosis × lobe × gyrus interaction ($F[5.08, 142.28] = 3.76$, $p < .01$) indicated that patients had lower relative glucose metabolic rates (rGMR) in regions of the frontal (superior, middle, and inferior gyrus, but not precentral) and parietal lobe. In controls, correlational analysis indicated that higher rGMR in the superior and inferior frontal gyrus bilaterally was associated with greater PPI (all r values > .63, $p < .05$). Further, greater PPI in controls was associated with less rGMR in areas 17, 18, and 19, bilaterally. In patients, none of the correlations were significant. These results are the first to provide support for animal models of PPI and suggest that frontal lobe dysfunction is associated with PPI deficits in schizophrenia.

NR535 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Diffusion Tensor Analysis of White Matter Pathways in Schizophrenia

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Summary:

A new visualization technique for analysis of white matter tracts makes direct assessment of large axon masses possible. Diffusion tensor analysis allows quantification of the directionality of restricted diffusion-a physical aspect of water in closely packed bundles of parallel axons in the white matter tracts. It provides a tool to analyze any disruption in the white matter organization in the corpus callosum, in adjacent frontal areas, and in the internal capsule where connections between frontal and striatal areas pass.

Five patients with schizophrenia diagnosed by DSM-III-R criteria (three men, two women, mean age 34, sd = 7.3), and five age- and sex-matched normal controls (41.4, sd = 9.8) served as subjects for MRI and PET-FDG studies. The patients were previously diagnosed with the structured CASH (Comprehensive Assessment of Symptoms and History) interview and were currently being treated with standard neuroleptics. We have used the Line Scan Diffusion Imaging sequence (LSDI) to obtain diffusion weighted images.

Average morphed anisotropy images reveal clear visualization of the corpus callosum and major frontal white matter tracts in both schizophrenic and normal patients. Diminished anisotropy is seen, especially in the frontal regions and white matter adjacent to the putamen of the patients; this effect was confirmed with pixel-by-pixel statistical probability mapping. We next examined the regional interconnectivity in coregistered PET metabolic images by computing the correlation coefficients between metabolic rate in the right putamen and all other points in the PET slice. These differences in correlation reached $p < 0.05$ in frontal regions. Taken together, these two methods are consistent with a hypothesized diminished functional communication in frontostriatal pathways in schizophrenia.

NR536 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Memorization Strategy and CBF

Igor I. Galynker, M.D., Beth Israel Medical Center, 1st Avenue at 16 St/6 Karpas, New York NY 10003; Vanessa Cahn, B.A., Christie Ieronimo, B.A., D. Howard Finestone, M.D., Fukiat OngSeng, M.D., Eamon Dutta, M.D., Dragos Serseni, M.D.

Summary:

Objective: Cognitive activation paradigms are being extensively used in functional brain imaging studies of healthy and psychiatrically ill subjects. However, even during an activation task, rCBF could vary with the subjects' cognitive strategies. The aim of the current study was to examine the effects of cognitive strategy on regional cerebral blood flow (rCBF) during "7/24" activation task that could be solved using either visuospatial or verbal strategies.

Method: The Tc-99m HMPAO scans of 21 healthy subjects who performed modified "7/24" memorization task (MEM group) were compared with those of eight control subjects who did not receive the activation task (CON group). Within the MEM group, rCBF

was compared between subjects who chose visuospatial (VIS) and verbal (VER) strategies.

Results: The MEM subjects had significantly higher rCBF than the CON subjects in the right anterior and posterior temporal cortices and in the left occipital cortex. MEM subjects had higher perfusion in the left posterior temporal cortex and in the right thalamus, though this trend did not reach statistical significance. The left-to-right perfusion ratios were entered into one-way ANOVAs in order to test for gender and strategy effects. Significant strategy effects were noted in the parietal and in the posterior temporal cortices: VIS subjects had higher rCBF in the right hemisphere, while the opposite was true for the VER subjects. The were no significant gender effects present in any of the ROIs. A significant gender strategy interaction was noted in the thalamus: VIS men but not women had higher perfusion in the right thalamus, while the reverse was true for the VER men.

Conclusion: Memorization strategy affects rCBF during "7/24" activation task in normal subjects. The rCBF patterns during commonly used activation tasks could be dependent on the subjects' cognitive strategies.

NR537 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Diminution of CBF After Caffeine: Clinical Evaluation by Means of Neurospect

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Summary:

Objective: The increased use of SPECT for clinical evaluation and measurement of cerebral blood flow (CBF) for assessment of neuropsychiatric disorders must consider that caffeine may produce a diminution of CBF. The purpose of this paper is to demonstrate this hypothesis and quantification and localization of inhibitory effects of caffeine on CBF.

Method: A comparative study was performed in two samples, before and 30 minutes after oral administration of 250 mg of caffeine: 1). In 20 young normal volunteers, CBF was measured using the Xenon-133 inhalation technique. 2). In seven other young volunteers, CBF measurement were obtained by means of SPECT with ECD Tc-99m (Neurolite TM).

Results: Sample I: Administration of caffeine produced, 30 minutes afterwards, a significant reduction of CBF, 8.5 ml/min/100g ($p < 0.0001$) and 9.5 ml/min/100g ($p < 0.0001$) at 2 cm and 6 cm above the orbitomeatal line respectively. This corresponds to a diminution of 25% and 23%, respectively. There is no effect of lateralization. Sample 2: Results demonstrated that the distribution of CBF after ingestion of caffeine was homogeneous, and there were no regional effects on CBF.

Conclusions: The inhibitory effects of caffeine on CBF are demonstrated throughout the cerebral cortex. Caffeine ingestion (coffee, tea, chocolate) should be discontinued before NeuroSPECT.

NR538 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

SPECT in Schizophrenics with Positive Versus Negative Symptoms

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Summary:

Tc99m-HMPAO-SPECT method was used to assess rCBF in 10 schizophrenic patients and 10 normal control subjects of comparable age, sex, social background, and educational status, while two neuropsychological measures were used to assess cognitive function: Wisconsin Card Sorting Test (WCST) and Wechsler Adult Intelligence Scale (WAIS). Meanwhile, Andreasen Scales for positive and negative symptoms have been applied to schizophrenic cases.

Correlations between negative and positive symptoms demonstrated that schizophrenics with predominantly negative symptoms had highly significant decrease of rCBF of the right frontal, both parietal and right temporal lobes than those with predominantly positive symptom. Although the reduction of rCBF was bilateral, the decrease of perfusion was most marked on the right hemisphere. Moreover, both groups did not differ regarding rCBF of the left frontal lobe. These data suggest that multiple brain areas are specifically involved in schizophrenic patients with predominantly negative symptoms.

On neuropsychological measures, schizophrenics with predominantly negative symptoms demonstrated more preservative errors on WCST than those with positive symptoms, although both groups did not differ on total scores.

Correlations between SPECT and WCST were significant within the schizophrenic group as both demonstrated prefrontal lobe dysfunction. The fact that schizophrenic patients have greater right and left prefrontal lobe dysfunction than control subjects gives some initial indication that this deficit is relatively specific to schizophrenia.

NR539 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Outpatient Antidepressant Responders Have Lower Paralimbic Regional Cerebral Glucose Metabolism than Inpatient Nonresponders

Brenda E. Benson, B.S., Biological Psychiatry, National Inst of Mental Hlth, 10 Center Drive/MSC 1272, Bethesda MD 20892; Timothy A. Kimbrell, M.D., Terence A. Ketter, M.D., John T. Little, M.D., Robert T. Dunn, M.D., Robert M. Post, M.D.

Summary:

Objective: To study whether medication responsiveness and illness severity contribute to the variable cerebral glucose metabolism (CMRglu) abnormalities noted in unipolar depression.

Methods: We used F-18-fluorodeoxyglucose and positron emission tomography to compare baseline (medication-free) rCMRglu in eight outpatient venlafaxine/bupropion responders (three men, five women; mean age 38.0, mean Ham-D 12.5) and eight age and gender matched inpatient nonresponders (mean Ham-D 20.2).

Results: Despite similar global CMRglu, responders compared to nonresponders had lower (absolute and normalized) left orbitofrontal cortex, right posterotemporal, and normalized (but not absolute) left mesial temporal, insular, cerebellar, and occipital rCMRglu. Responders compared to nonresponders had only sparse absolute/normalized rCMRglu increases.

Conclusion: Venlafaxine/bupropion responder outpatients compared to nonresponder inpatients had lower right paralimbic and left orbitofrontal (but not dorsolateral prefrontal) rCMRglu. Thus, previously reported paralimbic and orbitofrontal hypometabolism in depressed patients compared to controls could be related to antidepressant responsiveness/illness severity, while dorsolateral prefrontal hypometabolism might be more related to presence of depressive disorder.

NR540 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Cerebellum, Vermis and Brainstem in Schizophrenia: An MRI Study

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Kikinis, M.D., Ferenc A. Jolesz, M.D., Robert W. McCarley, M.D.

Summary:

Objective: The brainstem and cerebellum have been postulated to play an important role in schizophrenia (SZ) and other neuropsychiatric disorders such as autism. The cerebellum traditionally has been associated with the planning and execution of movement, but recent evidence suggests it may also play a role in higher cognitive functions (Leiner et al., 1995). The brainstem has monoaminergic cell groups containing important neurotransmitters postulated to play a role in SZ. There have been, to our knowledge, no quantitative volumetric studies parcellating these structures.

Method: We conducted an MR study of these structures using an automated segmentation algorithm (Wells et al., 1996) to obtain grey and white matter volumes of the cerebellum. MR scans were obtained on a 1.5 Tesla magnet. Double echo spin-echo 3 mm axial slices were obtained to establish total intracranial contents in order to compute relative volumes. For the measurement of specific regions of interest higher spatial resolution SPGR images (1.5 × .9375 × .9375 mm voxels) were used.

Results: We divided the cerebellum from the brainstem in 15 SZ and 15 normal controls (NCLs; matched on age and social class of origin, with all subjects right handed males), and found total brainstem absolute volume, but not relative volume, was larger in SZs than in NCLs (29.9 ± 2.6 vs. 27.8 ± 3.0 ml, p = .056; 1.85 ± .16 vs 1.78 ± .15%, p = .24) and found no significant difference in total cerebellar absolute or relative volumes between SZ and NCLs (137.0 ± 11.6 vs 132.4 ± 13.2 ml, p = .32; 8.5 ± .68 vs. 8.5 ± .68%, p = .96). When we segmented the cerebellum into gray matter (GM) and white matter (WM), we found that GM absolute volume did not differ between SZs and NCLs, but there was a trend for SZ WM absolute volume to be larger than NCLs (33.1 ± 3.3 vs. 31.0 ± 3.7 ml, p = .11). In a subset of these subjects (7 SZs and 10 NCLs) we divided the vermis from the cerebellar hemispheres and then parcellated it into three GM regions and one WM region. We found that SZs had a trend for a larger total (GM plus WM) vermian volume (9.8 ± .87 vs 8.9 ± .89 ml, p = .07), had a larger vermian WM volume (1.1 ± .26 vs. .82 ± .13 ml, p = .03), and larger anterior lobule (I-V) absolute volume (3.8 ± .57 vs. 3.3 ± .43 ml, p = .036) with vermian superior posterior lobules (VI-VII) and inferior posterior lobules (VIII-X) not significantly different (2.3 ± .32 vs. 2.2 ± .27 ml, p = .48; 2.5 ± .23 vs. 2.4 ± .32 ml, p = .44). Inter-rater reliability for brainstem and cerebellar structures was high: Intraclass Correlations were $r_i > .99$.

Conclusions: These data point to the importance of detailed parcellation of the cerebellum, the vermis, and the brainstem in SZ.

NR541 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Midline Cerebral Structures in Schizophrenic Patients: A MRI Study

Professor Giuseppe Bersani, Lasapienza University, 3rd Psychiatric Clinic, Via Del Corallo N25, Rome 00186, Italy; Dr. Cristiana Silvestrini, Dr. Angela Iannitelli, Dr. Pietro Cipriano, Dr. Catia Zucca, Paolo Pancheri, M.D.

Summary:

Objective: Since some observations underline a probable association between neurodevelopmental abnormalities in limbic structures and schizophrenia, the aim of the study was to investigate midline cerebral neuroanatomy in schizophrenic patients.

Method: We evaluated by magnetic resonance imaging 27 men (mean age: 27.5 ± 7.5 SD) meeting DSM-III-R diagnosis of schizophrenia. Subjects were scanned on a MRI unit operating at 1.5 Tesla. We analyzed 4-mm-slice T1-weighted midsagittal spin-echo (SE) sections and T1 and T2-weighted coronal proton density (PD) sections.

Results: Midline abnormalities were found in four out of 27 patients (14.8%), consisting of developmental malformations of the corpus callosum (N = 2) and of the septum pellucidum (N = 2). Regarding callosal modifications, one patient had a thickening callosal splenium, with a PD hyperdense and SE hypodense area (a lipoma); another patient presented a partial callosal agenesis. The septum pellucidum abnormalities were a septal cyst and cavum vergae in one patient, and a cavum septum pellucidum and cavum vergae in the second patient.

Conclusions: The results confirm previous studies, indicating an high prevalence of midline cerebral abnormalities in schizophrenic patients. The finding of a deviant brain development in those areas would further support the hypothesis linking a failure in the normal modulation of the limbic system, to which they project, to schizophrenia.

This study was supported by CNR grant (MRI-Project, years 1995–1997).

NR542 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Obstetric Complications, Age at Onset and Autistic Dimension in Male Schizophrenic Patients

Professor Giuseppe Bersani, Lasapienza University, 3rd Psychiatric Clinic, Via Del Corallo N25, Rome 00186, Italy; Piero Venturi, Paolo Pancheri, M.D.

Summary:

Objective: To elucidate whether the autistic dimension in schizophrenic patients is sensitive to obstetric complications.

Methods: One hundred and eleven consecutively admitted male chronic schizophrenics (DSM-IV) participated in the study. The obstetric history was obtained from 83 subjects and was assessed by means of the Parnas Scale; the age at onset was defined as the age of the first manifestation of psychotic symptoms. The psychopathology was evaluated through the SANS and SAPS; we described some aspects of autistic behavior by taking into account the ratio (Autistic Dimension, AD) between eight items of the SANS (4, 5, 6, 9, 10, 15, 20, 23) and four items of the SAPS (7, 20, 25, 34). Brain morphology was evaluated by computerized tomography scan; the VBR, the third ventricle, the Sylvian fissures, the interhemispheric fissure, and the major intraparietal sulci were considered.

Results: The AD was negatively related to the age at onset (p = 0.008). The AD was lower when obstetric complications' total score was higher (p = 0.008). The AD did not correlate with any neuromorphological measure.

Conclusion: The opposite direction of the relationship between AD and either the obstetric complications total score or the age at onset seems to underline a specific role of obstetric complications in influencing the psychopathological picture in male schizophrenics.

NR543 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A PET Study of Traumatic Response in PTSD

Stephen K. Brannan, M.D., Department of Psychiatry, UTHSCSA, 7703 Floyd Curl Drive, San Antonio TX 78284; Paul Ingmundson, Ph.D., Mark Alfano, Ph.D., Alexander L. Miller, M.D., Helen Mayberg, M.D., Peter Fox, M.D.

Summary:

Our objective was to use PET to image the neural correlates of the hyperarousal symptoms associated with PTSD. By using stimuli and subjects already piloted in the VA collaborative study of the psychophysiology of PTSD, we anticipated identifying the brain areas involved in response to traumatic stimuli.

The subjects were tested for psychophysiologic reactivity both prior to and concurrent with the PET scans. The PET studies used 015 water in a set of eight scans. Two traumatic scripts were used as the activation stimuli (both scripts twice). "Eyes closed rest" scans served as controls. Subjects also had a MRI for anatomic coregestration.

Data were analyzed using intrasubject comparison and image averaging within and across subjects.

The first block of data has been analyzed (with paired image subtraction of "traumatic script"-"eyes closed rest" and discrete, robust activations were observed in midline cerebellum, left basal ganglia, anterior cingulate, insula (R > L), and high frontal areas on the right. A significant decrease was observed in the R hippocampus. These findings confirm our capacity to image such phenomena and identify brain areas likely to be involved in hyperarousal to traumatic stimuli.

NR544 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Toward Localization of Thalamic Pathology in Schizophrenia

William M. Byne, M.D., Department of Psychiatry, Mt. Sinai Medical Center, One Gustave Levy PI/Box 1230, New York NY 10029; Liesl Jones, Ph.D., Eileen Kemether, M.D., V. Haroutunian, Ph.D., Kenneth L. Davis, M.D.

Summary:

Objective: Several studies employing a variety of methodologies have found the volume of the thalamus to be reduced in schizophrenia. To date, however, no study has localized the volume loss to any particular cytoarchitectonic division of the thalamus. The objective of our research is precise localization of thalamic pathology in schizophrenia.

Method: Thalami of schizophrenic subjects and age-matched nonschizophrenic controls were obtained from the Bronx VA/Mount Sinai Schizophrenia Brain Bank. Serial frozen sections through the thalamus were cut, and selected sections stained with either thionin or luxol fast blue and hematoxylin. Computer-assisted morphometry was employed to measure the volume of reliably delineated thalamic subdivisions.

Results: Schizophrenia-associated volume loss differentially affected the various subdivious of the thalamus and ranged from 5 to 33 percent among subdivisions.

Conclusions: Because each cytoarchitectonic division of the thalamus has a unique set of afferent and efferent connections, precise localization of thalamic pathology is necessary for understanding the neural circuitry of schizophrenia.

NR545 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Effects of Anabolic Steroids on Lymphocyte Beta-Adrenergic and Serotonin Receptor mRNA Levels in Male Normal Volunteers

Tong-Ping Su, M.D., Department of Psychiatry, Cheng-Hsin Medical Center, 45 Cheng-Hsin Street, Taipei, Taiwan; Christopher Hough, Ph.D., David R. Rubinow, M.D., De-Maw Chuang, Ph.D.

Summary:

Objective: Previous animal studies have demonstrated that peripheral beta-adrenergic receptors (*B*AR) and 5-HT_{1A} receptors are regulated by gonadal hormones. The aim of this study is to investigate the effect of the anabolic steroid, methyltestosterone (MT), on the mRNA levels of *B*AR and 5-HT_{2A} receptors in human lymphocytes.

Methods: We administered MT to 20 male volunteers and obtained blood (n = 20) and CSF (n = 17) samples at baseline and during high-dose (HD) (240 mg/day) MT condition. Lymphocyte pellets were isolated from 20 ml blood for Northern blot analysis of the levels of *B*AR and 5-HT_{2A} receptor mRNA. The receptor mRNA levels at HD were represented by the ratio to those at baseline. CSF samples were also collected during baseline and HD conditions for measuring the levels of norepinephrine (NE) and serotonin (5-HT) metabolites, i.e. MHPG and 5-HIAA, respectively.

Results: Significant increases in lymphocyte *B*AR and 5-HT2A receptor mRNA levels were found during HD treatment (33% and 29% t_{19} = 2.2 and 2.3, $p < 0.05$, respectively). High-dose MT treatment also resulted in a significant decrease in MHPG ($p < 0.01$) and increase in 5-HIAA ($p < 0.006$) in CSF. The changes in lymphocyte receptor mRNA levels and CSF transmitter metabolite levels suggest that both NE and 5-HT systems are modulated by gonadal hormones.

Conclusions: Consistent with the results of animal studies, administration of anabolic steroids to humans upregulates *B*AR and 5-HT_{2A} receptor mRNA in lymphocyte with a concurrent alteration of NE and 5-HT metabolite levels in CSF. These effects might reflect similar changes in the central NE and 5-HT neurotransmission.

NR546 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Enkephalin Gene Expression After NMDA Receptor Hypofunction Induced by Acute Ketamine

Andrea de Bartolomeis, M.D., Neuroscience, University Med School, "FedericoII" Via Pansini, Naples 80131, Italy; Luigi Aloj, M.D., Giovanni Muscettola, M.D.

Summary:

Objective: Acute administration of ketamine at subanesthetic doses has been used in humans as a pharmacological tool for studying the behavioral and metabolic effects of NMDA receptor hypofunction in normal subjects and schizophrenic patients. NMDA antagonists could effect opioid gene expression directly or through an enhancement of dopamine neurotransmission. We studied the impact of acute subanesthetic ketamine on enkephalin gene expression in subcortical areas in an animal model.

Methods: Sprague-Dawley rats were injected with subanesthetic (12–50 mg/kg, i.p.) doses of ketamine-HCl or with equal volume of 0.9% NaCl, and sacrificed three hours after the injection. Coronal brain sections (12μm, bregma approx. + 1) were pretreated and processed for in situ hybridization histochemistry with a synthetic oligodeoxyribonucleotide (complementary to bases 388–435 of rat preproenkephalin gene) radiolabeled with ^{35}S-dATP.

Results: The densitometry of the autoradiograms (digitized and analyzed using NIH-Image 1.56 program) demonstrated a significant decrease of preproenkephalin mRNA in ventrolateral putamen (ANOVA: $p < 0.008$) of rats treated with a subanesthetic dose of ketamine.

Conclusions: Enkephalin gene expression modulation after acute ketamine administration suggests the involvement of the opioid system in the pathophysiology of behavioral disorders in which a NMDA receptor hypofunction has been proposed.

NR547 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A Double-Blind, Placebo-Controlled Comparison of Venlafaxine and Venlafaxine Extended Release (ER) in Outpatients with Major Depression

Lynn A. Cunningham, M.D., Vine State Clinic, 301 North 6th Street, Ste 330, Springfield IL 62701;

Summary:

Objective: To compare the antidepressant efficacy and safety of venlafaxine and venlafaxine extended release (ER) with placebo in outpatients with major depression.

Methods: This was a randomized, double-blind, placebo-controlled comparison of venlafaxine and venlafaxine ER. Outpatients with DSM-III-R major depression were randomly assigned to venlafaxine 37.5 mg twice daily, venlafaxine ER 75 mg once daily, or placebo for a maximum of 12 weeks. If the response was inadequate after two weeks, the dosage of venlafaxine could be increased to 150 mg daily. Of 278 patients evaluated, 87 received venlafaxine ER, 92 venlafaxine, and 99 placebo.

Results: Venlafaxine ER was superior ($p < 0.05$) to placebo at weeks 2, 3, and 4, continuing through week 12 for all primary efficacy variables. Similarly, venlafaxine was superior ($p < 0.05$) to placebo beginning at week 2 on the HAM-D total and depressed mood item, week 3 on the MADRS total, and week 6 on the CGI severity scales. Venlafaxine ER exhibited superiority ($p < 0.05$) over venlafaxine at week 12 for all primary efficacy variables. The most common adverse event with venlafaxine ER was nausea, which was most frequent during the first two weeks, with a rapid decrease thereafter. No patient had a clinically significant change in blood pressure.

Conclusions: Venlafaxine ER is effective and well tolerated for the treatment of major depression at once-daily doses ranging from 75 to 150 mg.

NR548 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Evidence for a Casual Relationship Between Phantom Limb Pain and Cortical Reorganization in Arm Amputees

Wolfgang Larbig, M.D., Department Med Psychology, University, Gartenstrasse 29, Tuebingen 72074, Germany

Summary:

Objective: Recent studies using noninvasive biomagnetic recording techniques provide evidence that extensive reorganization occurs in the somatosensory cortex following limb amputation. The magnitude of these plastic changes was highly correlated with the magnitude of phantom pain. It remained unclear whether phantom pain is maintained by peripheral and/or central influences. In the present study we examined effects on both cortical reorganization and phantom limb pain.

Method: In nine unilateral arm amputees, five with phantom limb pain and four painfree amputees, we assessed cortical reorganization before and after regional anesthesia of the stump using 40 mg mepivacaine. Somatosensory evoked potentials from 60 scalp EEG electrodes were recorded during pneumatic stimulation of the lower lip of both sides, the first and fifth digit.

Results: Neuroelectric source imaging confirmed more extensive cortical reorganization in the phantom pain group. During axillary brachial plexus blockade, three of five phantom limb pain subjects experienced significant pain reduction. This effect was paralleled by a reduction in cortical reorganization, which remained unchanged in two patients who did not profit from anesthesia and in the pain-free controls.

Conclusions: Our results suggest that peripheral input may maintain both phantom limb pain and cortical reorganization in some amputees.

Supported by the German Research Society

NR549 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Personality Correlates of Response to CCK-4 in Healthy Males

Diana Koszycki, Ph.D., Department of Psychiatry, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Jacques Bradwejn, M.D.

Summary:

Objective: We examined whether behavioral, cardiovascular, and hormonal sensitivity to CCK-4 varied as a function of the personality dimensions of neuroticism (N) and extraversion (E).

Method: Forty healthy male volunteers completed the Eysenck Personality Questionnaire and were challenged with a 50 μg dose of CCK-4.

Results: Analysis of baseline data (T-5 mins) revealed that N correlated positively with self-rated nervousness ($r = 0.33$, $p < 0.05$) and negatively with ACTH ($r = 0.27$, $p < 0.05$), cortisol ($r = -0.22$, $p < 0.10$), and prolactin ($r = -0.32$, $p < 0.05$) levels. An inverse relationship was found between E scores and baseline nervousness ($r = -0.22$, $p < 0.10$) and heart rate ($r = -0.28$, $p < 0.05$). Administration of CCK-4 provoked significant alterations in behavioral, cardiovascular, and hormonal measures. N scores correlated positively with the number of symptoms induced by CCK-4 ($r = 0.31$, $p < 0.05$) and self-rated anxiety ($r = 0.27$, $p < 0.05$), nervousness ($r = 0.26$, $p < 0.10$), and fearfulness ($r = 0.26$, $p < 0.10$). E scores correlated positively with the onset of CCK-4-induced symptoms ($r = 0.40$, $p < 0.01$) and the maximum increase from baseline in prolactin levels ($r = 0.22$, $p < 0.10$) and negatively with the maximum increase from baseline in diastolic blood pressure ($r = -0.29$, $p < 0.05$).

Conclusion: Overall, these results suggest that there is a modest association between the personality dimensions of N and E and response to CCK-4 in healthy subjects.

NR550 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Respiratory Response to CCK-4 in Healthy Subjects

Jacques Bradwejn, M.D., Department of Psychiatry, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Jean-Marc Legrand, M.D., Diana Koszycki, Ph.D., Jason H.T. Bates, Ph.D., Michel S. Bourin, M.D.

Summary:

Objective: CCK-4 is a potent panicogenic agent with well-characterized respiratory actions. In humans, CCK-4 induces dyspnea at a high frequency and in anaesthetized dogs it produces a rapid increase in ventilation. In view of the suspected link between panic and respiratory dyscontrol, we evaluated the effects of CCK-4 on respiration in 30 healthy subjects (aged 19-39) with no personal or family history of psychiatric illness.

Method: Subjects were randomly assigned to a CCK-4 ($n = 15$) or placebo ($n = 15$) challenge. Breathing frequency (f), tidal volume (V), and minute ventilation (V_E) were assessed at baseline and following the challenge.

Results: All of the subjects who received CCK-4 reported dyspnea compared with only one subject who received placebo ($p < 0.001$). Repeated measures ANOVA revealed significant ($p < 0.001$) Time and Drug x Time effects for V_t and V_E. Within-group comparisons revealed significant baseline to postchallenge increases in the CCK-4 group only; between-group comparisons revealed significant postchallenge differences between CCK-4 and placebo for V_t (1.25 ± 0.3 vs. 0.89 ± 0.2) and V_E (19.93 ± 5.1 vs. 12.17 ± 2.9). There was no significant Time or Drug x Time effects for f.

Conclusion: These data suggest that CCK-4 is a potent respiratory stimulant. Consistent with research on ventilatory response to sodium lactate and CO2, CCK-4-induced increases in ventilation were due to an increase in tidal volume rather than breathing frequency.

NR551 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Trauma and HPA Axis Activity in BPD and Normal Controls

Robert A. Grossman, M.D., Department of Psychiatry, Mt. Sinai Medical Center, Box 1230/1 Gustave Levy Place, New York NY 10029; Rachel Yehuda, Ph.D., Larry J. Siever, M.D.

Summary:

Past studies utilizing the dexamethasone suppression test (DST) in borderline personality disorder patients (BPD) have been inconclusive, probably because of the high comorbidity of both major depressive disorder (MDD) and posttraumatic stress disorder (PTSD) with BPD. Both of these disorders are known to affect hypothalamic-pituitary-adrenal (HPA) axis feedback sensitivity in opposite ways. In the present study we used the low-dose DST (0.5 mg dexamethasone) with measurement of pre- and post-DST lymphocyte glucocorticoid receptor (GR) number to study HPA axis negative feedback in normal controls and BPD patients with and without histories of childhood trauma and comorbid PTSD. All subjects were medically healthy and medication-free. Preliminary findings in five subjects, which will be updated at the presentation, show cortisol *hyper*suppression in subjects with BPD (90.6% ± 3.5 vs. 21.1% ± 0) and increased glucocorticoid receptor downregulation in BPD subjects with comorbid PTSD (66.9% ± 38.1 vs. 9.3% ± 17.5).

These findings suggest that cortisol hypersuppression may exist in subjects with BPD regardless of trauma history, whereas increased GR downregulation is particularly related to PTSD symptomatology. Certain individuals with BPD may have a latent increased biological vulnerability to stress, which when activated by childhood sexual or physical abuse is more likely to result in pathophysiological changes similar to those found in PTSD.

NR552 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Reproducibility of ACTH Secretory Response to Corticosteroid Withdrawal and Corticotropin Releasing Hormone and Naloxone Stimulation in Healthy Humans

David A. Graeber, M.D., Department of Psychiatry, VAMC, 2100 Ridgecrest Drive, SE, Albuquerque NM 87108; Richard I. Dorin, M.D., E. Jonathan Lisansky, M.D., Brian B. Roberts, M.D., Clifford R. Qualls, Johannes D. Veldhuis

Summary:

In the present study, we sought to evaluate the reproducibility of ACTH secretory responses to specific stimuli in the absence of cortisol feedback inhibition. We hypothesized that individual subjects generate a characteristic ACTH response that is stable over time, consistent with an individual "set point" for HPA activity. Twelve healthy subjects (mean age 26) were studied under the same protocol on two or more independent study days. We used metyrapone (3g in divided doses) to block cortisol secretion. Human CRH (0.4ug/kg) and naloxone (NAL) (65ug/kg) was infused at 1800 and 1930 respectively, to stimulate ACTH secretion. Frequent (10 min) sampling was obtained and deconvolutional analysis of ACTH secretion kinetics performed. The mean ACTH response (area under the curve above baseline) following MET administration was 137 pmol/L-min with modest correlation between test and retest ($r = .34$, $p = .05$). ACTH response to CRH and NAL (mass/burst) was 219 and 256 pmol/L respectively, with significant between-test correlation for individual subjects ($r = .6$, $p = .01$ for CRH; $r = .71$, $p = .001$ for NAL). Additionally, a highly significant correlation between CRH and NAL stimulated bursts was observed ($r = .9$, $p < .001$).

We conclude that intrasubject variability contributes significantly less to the heterogeneity of ACTH response to CRH and NAL stimulation than the contribution of intersubject variability in healthy humans.

NR553 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Relationship Between the Amygdala and the Midbrain Dopamine System: Implications for Schizophrenia

Julie L. Fudge, M.D., Department of Psychiatry, Univ of Rochester Sch of Med, 300 Crittenden Blvd, Rochester NY 14642-0001; Suzanne N. Haber, Ph.D.

Summary:

Recent evidence suggests that there is an imbalance between cortical and striatal dopamine in schizophrenia. Subpopulations of dopamine cells, which are distinct histochemically and in their connectivities, may explain this imbalance. The input of the amygdala to the dopamine cells is one way the limbic system influences specific dopaminergic output pathways.

Objective and Methods: To determine whether the amygdala has a differential input to subpopulations of dopamine cells, we analyzed the amygdalonigral pathway and correlated this input with the nigrostriatal pathway in macaques using neuronal tracing techniques.

Results: We found that the central nucleus of the amygdala projects to a broad area of dopamine cells in the subregion known as the dorsal tier. In contrast, the amygdala does not project to a more ventral subgroup known as the cell columns. The dorsal tier that receives amygdaloid input projects to the ventral (limbic-related) striatum and cortex. The cell columns that do not receive limbic input from the amygdala project to the dorsolateral (sensorimotor-related) striatum.

Conclusion: The subpopulation of cells known as the dorsal tier is selectively connected to the amygdala, the ventral striatum, and the cortex. These results will be discussed in relation to striatal and cortical dopamine imbalance in schizophrenia.

NR554 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Phenomenology of Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections

Susan J. Perlmutter, M.D., Child Psychiatry, NIMH, 10 Center Dr/MSC 1255, Bldg 10, Bethesda MD 20892;

Summary:

Objective: To present the clinical features of a newly defined disorder, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), which afflicts a unique subgroup of children with obsessive compulsive disorder (OCD) and/or tic disorder who appear to have symptom exacerbations associated with streptococcal GABHS infections.

Methods: Fifty children met working criteria for PANDAS; these are presence of OCD and/or tic disorder, prepubertal onset of symptoms, episodic course of symptom severity, onset or exacerbation of symptoms associated with (GABHS) infection, and presence of neurological abnormalities during symptom exacerbations. All subjects underwent psychiatric and medical assessments, including structured psychiatric interviews, symptom severity ratings, standardized neurological exams, and laboratory studies.

Results: Notable is the early age of onset of OCD and tics, predominance of boys, high rates of psychiatric comorbidity, and episodic course. A review of the subjects' medical and psychiatric records confirmed the association of symptom exacerbations with streptococcal infections. Additionally, in a subgroup of patients followed over time, symptom exacerbations were associated with increased antistreptococcal titers.

Conclusions: Application of the working diagnostic criteria for PANDAS delineates a homogeneous subgroup of patients, which should facilitate clinical and therapeutic studies.

NR555 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Sunnybrook Stroke Study: A Prospective Study of Depressive Symptoms and Functional Outcome

Nathan Herrmann, M.D., Department of Psychiatry, Sunnybrook Hlth Science Ctr, 2075 Bayview Avenue, Toronto ON M4N 3M5, Canada; Sandra E. Black, M.D., Joanne Lawrence, R.N., Christine Szekely, M.A., John P. Szalai, Ph.D.

Summary:

Objective: To assess prospectively the prevalence and clinical correlates of depressive symptoms following hemispheric stroke and their effect on recovery.

Methods: Consecutive admissions to a regional stroke center were eligible. Patients underwent CT and standardized neurological and cognitive examinations at entry. At three months and one year post-stroke, depressive symptoms were assessed with the Montgomery Asberg Depression Rating Scale (MADRS) and the Zung Self-Rated Depression Scale (SDS). Functional outcome was measured with Functional Independence Measure, and handicap was assessed by the Oxford Handicap Scale.

Results: 152 patients were available for assessment at three months and 136 at one year. Marked depressive symptoms were noted in 22% (SDS) to 27% (MADRS) at three months, and 21% (SDS) to 22% (MADRS) at one year. Patients with marked depressive symptoms had more neurological impairment ($p < .008$), were more likely to be female ($p < .05$), and more likely to have histories of depression ($p < .03$). There was no relationship between depressive symptoms and age, lesion volume, or side of lesion. Depressive symptoms were correlated with functional outcome ($r = -.31$, $p < .0001$) and handicap ($r = .41$, $p < .0001$) at three months and one year ($r = -.28$, $p < .001$; $r = .35$, $p < .0001$).

Conclusion: The significant correlation of depressive symptoms and functional outcome underlines the need to monitor and treat mood disorders to optimize stroke recovery.

NR556 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

EEG Evidence of Hemispheric Activation with Contralateral Visual Field Stimulation

Fredric Schiffer, M.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont MA 02178; Carl M. Anderson, Ph.D., Martin H. Teicher, M.D.

Summary:

Objective: In previous work from our group, lateral visual field stimulation altered affect in 49 psychotherapy patients. We attempted to learn if such stimulation could alter EEG activity and affect in a laboratory setting.

Method: We compared EEG and anxiety level changes induced by two pairs of experimental goggles, each taped over one lens entirely and over the middle 60% of the other side, and by two pairs of comparison goggles, allowing monocular vision. Subjects (10 R-handed, seven male) included three patients with PTSD and eight asymptomatic college students. In all, we compared theta and alpha EEG activity in the mean of frontal and temporal leads. Ninety seconds of EEG's were recorded in each condition and, after artifact removal, we calculated a laterality index (LI) = (L – R)/(L + IR) for each pair of randomly presented goggles.

Results: With the experimental goggles the mean laterality index for the 11 subjects was less with the RVF than the LVF. The RVF-LVF differences in LI was –0.109, sd = 0.19, (Wilcoxon Signed-Rank = –26.00, $p = 0.019$) for theta, and –0.033, sd = 0.054 for alpha (Signed-Rank = 21.00, $p = 0.067$). For the comparison goggles the R-L difference in LI was –0.033, sd = 0.08 for theta (Signed-Rank = 9, $p = 0.25$) and 0.002, sd = 0.078 for alpha (Signed-Rank = 0.00, $p = 1$). The absolute differences in anxiety levels (rated on five-point scale) between experimental goggles were significantly greater than those between comparison goggles by Wilcoxon Signed-Rank test, Signed-Rank = 10.5, $p = 0.031$.

Conclusion: Restricting vision to lateral visual fields appeared to activate the contralateral hemisphere and to change anxiety levels from those of the other lateral field.

NR557 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Bedside Neuropsychiatric Findings in Adults with ADHD

Joseph P. Horrigan, M.D., Department of Psychiatry, University of North Carolina, CB#7160, Chapel Hill NC 27514-2877; L. Jarrett Barnhill, Jr., M.D.

Summary:

Objective: Neuroimaging studies have implicated the frontal lobes, especially the frontolateral regions, in the various forms of attention-deficit/hyperactivity disorder (ADHD). No studies have looked at specific bedside neuropsychiatric findings related to frontal lobe functioning in adults with this condition, which was the objective of the study.

Method: 41 adult outpatients (23 males, mean age 34.1 years, and 18 females, mean age 30.1 years) with DSM-IV-criteria ADHD were evaluated and diagnosed at a university-based neuropsychiatric clinic. Each of these never-medicated adults had at least one first-degree relative with ADHD. A complete neurological examination incorporating various measures of frontal lobe functioning was conducted on each patient at the time of diagnosis.

Results: A variety of abnormal findings were detected. Luria hand sequencing tasks revealed dominant-hand deficits in 39% of the patients, while testing of spontaneous word-list generation revealed deficits in 83%. Testing of conjugate eye movements revealed deficits in 29%. On these three tasks alone, 96% of males and 100% of females demonstrated one or more deficits.

Conclusions: Adult ADHD patients appear to have distinct neuropsychiatric deficits, particularly involving frontal lobe functioning, which may be of use during the diagnostic process. Confirmation by more extensive studies is required.

NR558 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Lithium and Neuroleptics in Combination: The Spectrum of Neurotoxicity

Stephen A. Goldman, M.D., Medwatch, Food and Drug Administration, 5600 Fishers Ln/HF-2/Rm 9-57, Rockville MD 20857;

Summary:

Objective: Classifying neurotoxicity in relation to neuroleptic use has been a long-standing concern with clinical, research, and epidemiologic import. This study examines the clinical manifestations of neurotoxicity and current concepts regarding its classification.

Method: The Food and Drug Administration (FDA) Spontaneous Reporting System data base and extant literature were reviewed for lithium/neuroleptic neurotoxicity spectrum cases. Lithium-alone (Li), lithium/haloperidol (LiHal), and lithium/non-haloperidol neuroleptics (LiNonHal) groups, each paired for recovery and sequelae, were established for 237 cases. Data on demographic factors, psychiatric diagnoses, and symptoms/signs/findings were tabulated. Neuroleptic malignant syndrome (NMS) was used as a paradigm for severe neurotoxicity; the cases were evaluated by two strict, published sets of NMS diagnostic criteria and two

"probable" classifications (one published and one established for study) based on these criteria.

Results: Altered consciousness was prominent in all groups. Hypertonia/rigidity was most pronounced in both LiHal groups, possibly reflecting higher relative neuroleptic dosing; Li and LiNon-Hal recovery and sequelae pairs showed lower, similar percentages. Among other physical findings, tremor was either most common or prominent. Neither set of strict criteria diagnosed NMS in more than 30 percent of cases in any group. Expansion of classifications to include "probable" diagnoses resulted in appreciable global group percentage increases for only one set of criteria.

Conclusions: The high percentage of study cases not meeting even "probable" NMS criteria, despite market-clinical morbidity that at times resulted in permanent sequelae, provides a cautionary note regarding the limitations of formulated diagnostic criteria. Data base caveats notwithstanding, study findings support the consideration of a spectrum approach to classifying and diagnosing psychotropic-related neurotoxicity.

NR559 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Minor Depression Following Traumatic Brain Injury: A One-Year Longitudinal Study

Ranjan Dahiya, M.D., Department of Psychiatry, University of Iowa, 200 Hawkins Drive, #2880JPP, Iowa City IA 52242; Robert G. Robinson, M.D., Sergio Paradiso, M.D.

Summary:

Introduction: Prior studies have demonstrated that approximately one-fifth of patients with traumatic brain injuries (TBI) develop major depression. Little is known, however, about the prevalence of clinical correlates of minor depression following TBI.

Methods: 66 patients hospitalized following acute TBI were followed over a one-year period. Patients were examined using a semistructured mental state exam (i.e., the Present State Exam (PSE)), and impairment was measured using the Johns Hopkins Functioning Inventory (JHFI), Mini Mental State Exam (MMSE), and Social Functioning Examination (SFE).

Results: At some time during the one-year study, 10 subjects (15%) met research criteria for DSM-IV minor depression only (i.e., never diagnosed with major depression). Minor depression had a mean duration of 1.5 months compared with 6.2 (SD = 0.4) months for major depression (Wilcoxon χ^2, df = 1 = 13.3, $p < 0.005$). At initial evaluation, 75% of subjects with minor depression had left dorsolateral or basal ganglia lesions compared with 16.7% of nondepressed subjects (two-tailed Fishers exact $p < 0.03$). Subjects with minor depression, however, did not show significant differences in MMSE, JHFI, or SFE scores versus nondepressed controls. Compared with major depression patients minor depression patients were less frequently diagnosed and treated for psychiatric disorder prior to TBI.

Discussion: Minor depression following TBI had a shorter duration and was not associated with intellectual, physical, or social impairment. The pattern of associated factors suggests that minor depression is distinct from major depression following TBI.

NR560 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Social Impairment and Recovery from Stroke

Kengo Shimoda, M.D., Department of Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52242; Robert G. Robinson, M.D.

Summary:

The effect of social functioning and depression on recovery from stroke was examined 142 patients with acute stroke who had follow-up evaluations using a semistructured mental status examination and the Social Functioning Examination (SFE). At three to six-month (short-term) follow-up, patients with impaired social functioning or depression were found to have significantly less recovery in activities of daily living and cognitive functioning than nonsocially impaired and nondepressed patients. On the other hand, at one to two years (long-term) follow-up, depression but not social functioning influenced recovery in activities of daily living.

These data indicate that impaired social function as well as depression may inhibit physical recovery from stroke during the critical first few months of rehabilitation. These data also suggest that early psychosocial intervention as well as antidepressant treatment may play an important role in the quality of life after acute stroke.

NR561 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Slower Reaction Time in Schizophrenia: Relationship to Clinical Symptoms and Cerebral Dysfunction

Jason Willis-Shore, B.A., Department of Psychiatry, UCSF/SF VAMC, 4150 Clement Street/116C, San Francisco CA 94121; Sophia Vinogradov, M.D., John Poole, Ph.D., Beth A. Ober, Ph.D., Greg Shenaut, Ph.D.

Summary:

Generalized slowing of reaction time is a highly significant aspect of cognitive performance in schizophrenia. However, the relationship of this phenomenon to domains of clinical and cerebral dysfunction is not known.

Method: Using 26 medication-free schizophrenic subjects and 17 demographically matched normal controls, we explored the relationship between reaction time (RT) on a lexical decision task and BPRS symptom ratings, IQ, and measures of frontal lobe dysfunction.

Results: RT was much slower in the schizophrenic group compared with normal controls (schizophrenic group: 577 $\pm$ 93 ms; normal controls: 469 $\pm$ 51 ms; $t = 4.4$, $p < 0.001$). Age was significantly correlated with slower RT in the schizophrenic group ($r = 0.40$, $p = 0.02$) and was partialed out of all correlations. We found that in the schizophrenic group, slower RT was significantly associated with Conceptual Disorganization ($r = 0.41$, $p = 0.02$) and Suspiciousness ($r = 0.38$, $p = .03$), but not with Negative or Depressive symptoms. RT was not related to IQ in the schizophrenic group, but this relationship approached significance in the normal control sample ($r = -0.39$, $p = 0.06$). RT and measures of frontal lobe dysfunction were not associated.

Conclusions: Whereas general slowing of reaction time in schizophrenia is related to increased conceptual disorganization and suspiciousness, it appears to be independent of IQ and frontal lobe dysfunction.

NR562 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Gepirone Extended Release (ER) Compared to Placebo in the Treatment of Outpatients with Major Depression

Cal K. Cohn, Ph.D., 5847 San Felipe, Suite 3147, Houston TX 77057; Louis F. Fabre, Jr., M.D.

Summary:

Fifty-three patients were entered into a safety and efficacy trial of two dose ranges of Gepirone ER with placebo outpatients who met DSM-III-R criteria for major depressive disorder. Patients with a minimum of 20 on the 17-Item Hamilton Depression Scale were randomly assigned to Gepirone ER 10-50 mg/day. Gepirone ER 20-100 mg/day, or placebo, for six weeks.

The efficacy analysis compared each Gepirone dose group with placebo. Gepirone ER low dose group (10-50 mg/day) did not

reveal statistically significant results. Gepirone high dose group (20-100 mg/day) showed statistical significance on HAM-D-17 week 2 ($p < .05$), week 4 ($p < .01$), and week 6 ($p < .01$), on HAM-D-28 week 4 ($p < .01$) and week 6 ($p < .01$), and on CGI week 4 ($p < .01$) and week 6 ($p < .01$). Most common adverse events were insomnia, dizziness, nausea, and nervousness. Previous studies have shown that Gepirone ER below 40 mg/day does not produce significant improvement in depressive symptoms. In this study in the high dose group. Gepirone ER average dose exceeds 40 mg/day at week 2-where statistically significant improvement in depression is first seen. In the low dose group Gepirone ER average dose never exceeds 40 mg/day and is uneffective. The conclusion is 40 mg/day is the minimum effective antidepressant dose of Gepirone ER. Gepirone is a 5HT1A partial agonist, which has anxioltyic properties at low doses and antidepressant properties at higher doses.

NR563 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Psychometric Validation and Reliability Testing of a State Scale of Dissociation

Christa Kruger, M.Med., Department of Psychology, University of Warwick, Gibbet Hill Road, Coventry CV47AL, England; Chris J. Mace, M.B.

Summary:

Objective: Pathological and nonpathological dissociative states require clearer definition. To complement existing trait scales of dissociation, the State Scale of Dissociation (SSD) has been developed to measure the degree and variability of dissociative states. Its reliability, construct, and content validity are examined.

Method: Following piloting and item selection, the SSD was administered before and after the Beck Depression and Anxiety Inventories, the Dissociative Experiences Scale, and the Structured Clinical Interview for the Positive and Negative Syndrome Scale to 40 psychiatric inpatients with DSM-IV diagnoses of major depressive disorder, schizophrenia, alcohol dependence, and dissociative disorder, and 40 age-matched controls. Detailed analyses assessed the SSDs reliability and validity.

Results: The SSD showed satisfactory test-retest reliability and inter-item correlations; high internal consistency, item-subscale/item-total/subscale-total correlations and split-half reliability; and divergent validity from the measures of depression, anxiety, and psychosis. Factor analysis confirmed its construct validity.

Conclusions: Previous measures have been relatively insensitive to changes in dissociative status. This demonstration of the reliability, construct, and content validity of the SSD indicates its greater sensitivity. Its applications include future clinical research into neurophysiological changes accompanying dissociative status.

NR564 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Intermittent Explosive Disorder: Revised Criteria for Aggression Research

Emil F. Coccaro, M.D., Department of Psychiatry, MCP Hahnemann, 3200 Henry Avenue, Philadelphia PA 19129-1137; Richard J. Kavoussi, M.D., Mitchell E. Berman, Ph.D., Lauren Y. Weinberg, M.S., Barrie Franklin, Ph.D., Jennifer D. Lish, Ph.D.

Summary:

The study of human aggression has been hindered by the lack of reliable/valid diagnostic categories that identify individuals with significant impulsive aggressive behavior. Intermittent explosive disorder (IED) criteria, which identify some, but not most, aggressive individuals, have several shortcomings limiting their use in clinical/research settings. We revised and broadened IED criteria, then tested their reliability and content/construct validity in a well characterized group of personality disordered subjects with and without reported problems with impulsive aggression ($n = 188$). The IED-REVISED (IED-R) diagnosis had high inter-rater reliability (kappa = .92). IED-R subjects had higher aggression (LHA)/impulsivity (I-7) scores and lower GAF scores than non-IED-R subjects. IED-R criteria were also more sensitive than DSM-IV IED criteria in identifying subjects with impulsive aggressive behavior. In related studies, IED-R subjects: a) displayed diminished central 5-HT responsivity, as evidenced by blunted PRL responses to d-fenfluramine challenge, and, b) demonstrated an antiaggressive response to fluoxetine in a double-blind, placebo-controlled, trial. These data suggest that IED-R criteria can be reliably applied and that they appear to have sufficient initial validity to warrant further evaluation in phenomenologic, epidemiologic, biologic, and treatment-outcome research.

NR565 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Prescribing Practices: Trazodone

John W. Goethe, M.D., Clinical Research, Institute of Living, 400 Washington Street, Hartford CT 06106-3309; Bonnie L. Szarek, R.N.

Summary:

Objective: To examine current prescribing practices for trazodone in psychiatric inpatients.

Method: Medication, diagnostic, and demographic data were recorded for all inpatients between 1/1/96 and 6/30/96. Data were analyzed using descriptive statistics and logistic regression.

Results: Of 1,705 discharges, trazodone was prescribed for 344 (20.2%); 111 of these patients (32.3%) did not have a diagnosis of depression. The mean daily dose of trazodone was 114.39 ± 80.18 mg (median = 50 mg); trazodone was prescribed only at bedtime for 78.2% of patients and "PRN only" for 26.7%. In 68% of the depressed patients, another antidepressant was co-prescribed. Among nondepressed patients, the most frequent diagnoses were dementia (32.4%), substance use (18.9%), and schizophrenia (15.3%). Logistic regression revealed that patients with dementia were 4.64 times more likely to receive trazodone, those with depression 1.91 times more likely, and females 1.23 times more likely (overall goodness of fit = 78.94%).

Conclusions: For this inpatient sample, trazodone was a frequently used drug and was often prescribed for conditions other than depression. Even among depressed patients trazodone appears to have been used most frequently for sedation rather than its antidepressant properties. These data are relevant for formulary management and the determination of treatment guidelines.

NR566 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Effect of Concept Formation Training on the Performance of the Wisconsin Card Sorting Test in Schizophrenic Patients

Young-Nam Park, M.D., Department of Psychiatry, Dongsan Medical Center, 194 Dongsan-Dong, Taegu 700-310, Korea; Hee Choel Kim, M.D., Sung Mi Kim, M.D.

Summary:

Objectives: Schizophrenic patients perform poorly on the WCST. The authors evaluated the effect of concept formation training on the performance of WCST in schizophrenic patients.

Method: Twenty-two DSM-IV schizophrenic patients, who were hospitalized with acute symptoms and completed less than four categories on the pretraining WCST, received a training on a hierarchical cumulative concept formation. In this training, the subjects were trained to classify cards by a single dimension of form, color, and number, respectively. After mastering a single

category classification, the subjects moved to classify cards by two dimensions of form and number. The last step was to classify cards by three dimensions of form, color, and form as for WCST. In one week after the subjects mastered the training, WCST was readministered.

Results: Sixteen patients completed training successfully. There were significant improvements in the total number of correct, total number of errors, perseverative responses, perseverative errors, conceptual level responses, numbers of categories completed, and trials to complete first category after training, but nonperseverative errors and failure to maintain set did not improve.

Conclusions: The results not only confirmed that a subgroup of schizophrenic patients were able to improve their WCST performance by a remedial training, but also showed that schizophrenic patients were able to apply a learned concept to a different task.

NR567 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Personality and Symptom Dimensions in Psychoses

Manuel J. Cuesta, M.D., Department of Psychiatry, Virgen Del Camino Hospital, C/Irunlarrea S/N, Pamplona 31620, Spain; Victor Peralta, M.D., Francisco Caro, M.D., Alfredo Martinez

Summary:

This study is designed to find the correlates of the schizophrenic dimensions in the premorbid personality traits of patients. The sample was 112 psychotic patients who were admitted for recurrence of symptoms. Patients were assessed by means of a semi-structured interview, diagnosed by DSM-III-R criteria, and their symptomatology was evaluated through SAPS and SANS scales. Premorbid personality was dimensionally assessed through the Personality Assessment Schedule (PAS, Tyrer et al, 1988).

Schizoid traits were significantly associated with negative and positive dimensions. Sociopathic traits were related to disorganization dimension. Partial correlational analyses were carried out in order to control the effect of the remaining personality dimensions in the above relationships. Schizoid premorbid traits had significant relationships with negative dimension and in a lesser degree with disorganization and positive dimensions. Sociopathic premorbid traits persisted in their significant association with disorganization dimension. These results were more evident when a subset of more recent onset patients were analyzed. Taken together, a preexistence of vulnerability to schizophrenic dimensions within the premorbid personality of patients could be suggested.

NR568 Wednesday, May 21 3:00 p.m.-5:00 p.m.

MRI and Neuropsychological Measures in Schizophrenia: Partial Least Squares Analysis

Paul G. Nestor, Ph.D., Department of Psychiatry, Brockton VAMC, 940 Belmont Street, Brockton MA 02401; John Barnard, Ph.D., Brian F. O'Donnell, Ph.D., Martha E. Shenton, Ph.D., Ronald Kikinis, M.D., Ferenc A. Jolesz, M.D.

Summary:

Partial Least Squares (PLS) is a novel computational strategy well suited for the challenge of analyzing rich data sets derived from nonindependent measures of distinct domains (e.g., structural MRI and behavioral). However, its utility has not been widely appreciated in biological psychiatry and neuroimaging. PLS operates by performing a principal component-like analysis on the obtained correlational matrix between sets of measures (e.g., anatomical and behavioral measures). By using the correlation matrix instead of individual subject data, as would be the case with a principal component analysis, PLS may be applied to relatively small samples with correlated measures. We used PLS to analyze neuropsychological and MRI frontal and temporal grey matter measures derived from a group of 15 male chronic schizophrenic patients. From the cross-correlation matrix obtained from the neuropsychological (9 tests) and MRI variables (18 volumetric measures), PLS extracted two latent variables (LVs). Each MRI and neuropsychological variable has its own "salience" on each latent variable, which is akin to a factor loading. The set of saliences for LV 1 indicated a positive relationship between volume of temporal lobe structures and performance on verbal learning and categorization. The set of saliences for LV 2 indicated a positive relationship between frontal lobe volume and performance on attention and working memory tests. The covariance between the first pairs of LVs was 3.3, represented by the statistic *d*, the first singular value of the correlation matrix. Permutation tests revealed a highly significant relationship ($p < .05$). The two-pair latent variable solution accounted for a total of 82% of the sum of squares of the cross-correlation matrix. These findings derived from PLS conform with neuropsychological models of attention and memory disturbances in schizophrenia. We conclude that PLS provides a powerful tool to analyze neuropsychological and MRI frontal and temporal grey matter in schizophrenics.

NR569 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Outcome Measures in Initially Untreated Psychosis

David J. Meagher, M.B., Department of Psychiatry, St. Vincent's Hospital, Elm Park, Dublin 4, Rep of Ireland; John L. Waddington, Ph.D., James Mullaney, M.D., John J. Quinn, M.B., Patrice Murphy, M.B.

Summary:

Objective: The effects of pharmacological strategies on the course of schizophrenia can be examined in patients who first became ill in the preneuroleptic era and have experienced prolonged periods of illness untreated by neuroleptic medications. This study investigates the relationship of initial nontreatment to performance on clinical and neuropsychological instruments.

Methods: A total of 109 patients with DSM-III-R schizophrenia were assessed regarding demographic, pharmacological, and clinical variables using the Positive and Negative Symptom Scale, Mini-Mental State Examination, Executive Interview, and Qualitative Evaluation of Dementia.

Results: Duration of illness ranged from 22 to 64 years (mean 43.1). Duration of initial nontreatment ranged from 0 to 29.5 years (mean 8.7). Psychopathological assessment revealed prominent negative symptomatology with little correlation between negative and positive symptoms. Neuropsychological testing revealed cognitive impairment of mixed cortical and subcortical origin and significant disturbance of executive function. Cognitive measures correlated more with negative than positive symptoms. When the effects of age and neuroleptic exposure were accounted for, there was a significant effect of duration of initially untreated illness to predict negative symptom and MMSE scores.

Conclusions: These results indicate widespread cognitive impairments and marked negative symptomatology in chronic schizophrenia. They suggest that positive and negative features represent distinct pathologies and that an increasing period of initially untreated psychosis is associated with poorer long-term outcome.

NR570 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Ziprasidone Metabolism and Cytochrome P450 Isoforms

Donald J. Tweedie, Ph.D., Clinical Research, Pfizer CR, Eastern Point Road, Groton CN 06340; Chandra Prakash, Ph.D., Amin K. Kamel, M.D., D. Cui, Robert D. Whalen, M.D., Jeffrey J. Miceli

Summary:

Objective: Ziprasidone is an effective antipsychotic with a unique collection of affinities at serotonergic and adrenergic receptors; it is extensively metabolized. The major oxidative metabolites are ziprasidone-sulfoxide and ziprasidone-sulfone. The aim of this study was to identify the cytochrome P450 (CYP) isoforms responsible for formation of these metabolites and to predict the potential for *in vivo* drug-drug interactions by investigating inhibition of individual CYP isoforms.

Method: In vitro metabolism of [^{14}C]ziprasidone was studied with human liver microsomes and the metabolites identified by mass spectrometry.

Results: The apparent K_m and V_{max} for formation of the major metabolite, ziprasidone sulfoxide (the sum of sulfoxide and sulfone), by human liver microsomes were 235 μM and 1.14 nmol/mg protein/min, respectively. Isoform-selective inhibitors and recombinant enzyme indicated that CYP3A4 was responsible for the formation of ziprasidone sulfoxide and sulfone. K_i values for the inhibition of specific probe substrates for CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 by ziprasidone, risperidone, and 9-hydroxyrisperidone were determined using human liver microsomes from three subjects. Ziprasidone, risperidone, and 9-hydroxyrisperidone inhibited CYP2D6 to a similar extent (mean K_i 6.9-16μM), and inhibited 3A4 to a lesser extent (K_i 64-80μM). *In vivo* free drug concentrations associated with clinically effective ziprasidone doses are at least 6 500-fold lower than the mean K_i for CYP2D6 or CYP3A4 inhibition.

Conclusions: Ziprasidone is not expected to alter the disposition of co-administered drugs through inhibition of drug-metabolizing enzymes.

NR571 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Steady State Pharmacokinetics of Ziprasidone in Healthy Old and Young Volunteers

Thomas G. Tensfeldt, M.S., Clinical Research, Pfizer CR, Eastern Point Road, Groton CN 06340; Keith D. Wilner, Ph.D., Barbara Baris, Terry A. Smolarek, Ph.D., Ryan Z. Turncliff, B.A., Wayne A. Colburn, Ph.D.

Summary:

Objective: This open-label study compared the steady-state pharmacokinetics of the new antipsychotic, ziprasidone, among healthy young (18–45 years) and elderly (≥65 years) men and women. Ziprasidone, an effective antipsychotic, has a unique receptor profile. The activities at serotonergic and adrenergic receptors, and lack of muscarinic activity differentiate ziprasidone from all other antipsychotics.

Method: There were eight subjects in each of four groups. All subjects received ziprasidone 20 mg twice daily for seven days and a single dose on Day 8. Blood samples were collected on Day 8 immediately before dosing and for up to 96 h after.

Results: Steady state was attained within two to three days of dosing. On Day 8 there were no significant differences between young men and women in mean pharmacokinetic variables, AUC_{0-12}, C_{max}, T_{max}, or K_{el}. Mean AUC_{0-12} in elderly men, elderly women, young men, and young women was 505, 621, 451, and 479 ng.h/ml, respectively; mean C_{max} 71, 102, 67 and 72 ng/ml, respectively; and mean T1/2 was 5.7, 5.3, 3.1, and 4.1, respectively. There were no among-group differences in the incidence or severity of adverse events.

Conclusions: The results of this study indicate that the pharmacokinetics of ziprasidone do not vary significantly according to age or gender and thus no dosage adjustment is required.

NR572 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Effects of Cimetidine or Maalox on Ziprasidone Pharmacokinetics

Keith D. Wilner, Ph.D., Clinical Research, Pfizer Central Res, Eastern Point Road, Groton CT 06340; Robert A. Hansen, Carol J. Folger, Geoffroy Pierre

Summary:

Objective: This open-label study evaluated the effects of cimetidine, an inhibitor of cytochrome P450 3A4 (CYP 3A4), and Maalox® on the pharmacokinetics of ziprasidone in young healthy volunteers. *In Vitro* studies using human microsomes have shown that CYP 3A4 is responsible for the formation of the major metabolites of ziprasidone.

Method: Subjects (n = 10) were randomized to ziprasidone 40 mg alone, ziprasidone 40 mg plus Maalox® 30 ml (Maalox® was also given at bedtime the evening before ziprasidone and 20 min after the midday and evening meals on the day of ziprasidone dosing), and ziprasidone 40 mg plus cimetidine 800 mg (cimetidine was also given for two days before and one day after ziprasidone dosing). On each ziprasidone dosing day (separated by seven days), blood samples were collected immediately before and up to 36 h following dosing for analysis of serum ziprasidone levels and calculation of pharmacokinetic variables.

Results: While Maalox® delayed the occurrence of C_{max} by 3 h, there were no statistically significant differences in C_{max}, $AUC_{0-\infty}$, or K_{el} between the ziprasidone + Maalox® and the ziprasidone groups. In the ziprasidone + cimetidine group, there was a statistically significant increase in $AUC_{0-\infty}$ compared with the ziprasidone only group. However, this increase was only 6% and there were no statistically significant changes in C_{max}, T_{max}, or K_{el} between the two groups. The lack of clinically significant interaction between ziprasidone and cimetidine suggests that the metabolism of ziprasidone is not affected by the CYP 3A4 inhibitor, cimetidine, presumably because alternative metabolic pathways were utilized.

Conclusion: CYP 3A4 inhibitors and Maalox® are unlikely to alter the pharmacokinetics of ziprasidone.

NR573 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Lack of CYP2D6 Inhibition by Ziprasidone in Healthy Volunteers

Keith D. Wilner, Ph.D., Clinical Research, Pfizer Central Res, Eastern Point Road, Groton CT 06340; Steven Demattos, B.S., Richard J. Anziano, M.S., Glen Apseloff, M.D., Nicholas Gerber, M.D.

Summary:

Objective: Ziprasidone is a novel antipsychotic that is effective in the treatment of positive, negative, and depressive symptoms of schizophrenia. Ziprasidone has a unique collection of receptor affinities, potent $5HT_{1A}$ agonism, $5HT_{1D}$ and $5HT_{2C}$ antagonism, and moderate inhibition of norepinephrine and 5HT re-uptake, in conjunction with a high $5HT_2/D_2$ ratio. This single-dose, open-label study investigated whether ziprasidone has the potential to inhibit the activity of the cytochrome P450 (CYP) 2D6 isozyme using dextromethorphan as a model CYP 2D6 substrate.

Method: Healthy young volunteers, who were extensive metabolizes of dextromethorphan (dextromethorphan/dextrorphan urinary ratio ≤0.03), received a single dose of either ziprasidone 80 mg (n = 8), paroxetine 20 mg (n = 8) (a potent inhibitor of CYP 2D6), or placebo (n = 8). Dextromethorphan 30 mg was then administered 2 h later, and urine was collected over the next 8 h for the determination of the dextromethorphan/dextrorphan urinary ratio.

Results: There were no statistically significant changes in the urinary dextromethorphan/dextrorphan ratio in the placebo or zi-

prasidone groups. The mean reductions in the dextromethorphan/dextrorphan ratio from baseline were 0.001, and 0.002, respectively. By contrast, there was a ten-fold increase in the urinary dextromethorphan/dextrorphan ratio for the paroxetine group, which differed significantly from the ziprasidone and placebo groups ($p = 0.0001$).

Conclusions: This study suggests that ziprasidone does not inhibit the clearance of drugs metabolized by CYP 2D6.

NR574 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Working Memory Dysfunction in Schizophrenia

Anne-Marie Shelley, Ph.D., Bronx Psychiatric Center, Albert Einstein/Ward 19, 1500 Watersplace, Bronx NY 10461; Daniel C. Javitt, M.D., Herbert G. Vaughan, Ph.D.

Summary:

Objective: To investigate whether abnormalities of auditory working memory in schizophrenia are due to impaired initial encoding of information or premature decay of accurately encoded information. Auditory working memory abnormalities in schizophrenia are reflected in impaired generation of an event-related potential (ERP) component known as mismatch negativity (MMN) (Shelley, et al 1991, Javitt, et al 1993). In normal subjects MMN amplitude increases with decreasing deviant probability-so by varying deviant probability, MMN can provide an index of initial encoding. By varying interstimulus interval (ISI), MMN can index trace decay over time. If auditory working memory deficits in schizophrenia are due to abnormal initial encoding, MMN amplitude differences between groups should be maximal as deviant probability decreases. If deficits are due to abnormal trace decay, differences should be maximal as ISI increases.

Method: MMN was examined in 15 chronic schizophrenics and 17 normal controls under four conditions of deviant probability (25%, 10%, 5%, and 2.5%) and four ISI conditions (250ms, 500ms, 1000ms, and 3000ms).

Results: Schizophrenics showed less of the normal augmentation of MMN amplitude as deviant probability decreased. ISI had no significant effect on MMN.

Conclusion: The pattern of results suggests that auditory working memory deficits in schizophrenics are due more to abnormal encoding than to abnormal trace decay.

NR575 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Cardiovascular Safety of Sertindole

Mark B. Hamner, M.D., Department of Psychiatry, RH Johnson VAMC, 109 Bee Street (116A), Charleston SC 29401-5703; Chris Silber, M.D., Rita Driscoll, M.D., Mack Randall, B.S.

Summary:

Sertindole, discovered and patented by H. Lundbeck (Copenhagen) and under development in the United States, Canada, and Latin America by Abbott Laboratories, is a novel antipsychotic for the treatment of the manifestations of psychosis.

The QT interval, which represents ventricular repolarization on the ECG, has been found to be prolonged by a number of drugs with different pharmacologic effects. A number of psychotropics have also shown evidence of prolongation of the QT interval. Early in its clinical development, it was noted that sertindole was associated with slight prolongation at the QT interval on the electrocardiogram. Therefore, extensive electrocardiographic recordings (over 14,000 ECG's) were performed during major clinical trials so that the extent of this QT interval prolongation could be precisely assessed. The QT interval prolongation was small (+21 msec or 5.1% compared with baseline) and, importantly, there were no recorded instances of torsades de pointes among 2,194 sertindole-treated patients with 1,024 patient years of exposure. Furthermore, there were few serious cardiovascular adverse experiences and the overall mortality rate was low and consistent with other antipsychotics. An expert panel of cardiologists concluded that sertindole has a favorable cardiovascular risk profile.

NR576 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Nicotine Patch, Smoking and Schizophrenia

Gregory W. Dalack, M.D., Department of Psychiatry, Ann Arbor VAMC, 2215 Fuller Road (116C), Ann Arbor MI 48105; James H. Meador-Woodruff, M.D.

Summary:

Standard smoking cessation treatments achieve mediocre results in the general population, and are less successful among smokers with schizophrenia. Nonpsychiatrically ill groups of heavy smokers, given exogenous nicotine concurrent with smoking, smoke fewer cigarettes, have less carbon monoxide in expired air, and maintain stable nicotine blood levels. If sustained, such smoking reduction may have salutary long-term health effects for those unable to quit. The feasibility and tolerability of such an intervention as a treatment for smokers with schizophrenia is unknown. We used a double-blind, placebo-controlled, cross-over design to measure smoking behavior, psychiatric symptoms, and medication side effects in 10 heavy smokers with schizophrenia during 32 hours of *ad libitum* smoking while wearing 21mg/day or placebo transdermal nicotine patches. Among all 10 subjects, smoking on active patch compared to placebo over 1.5 days did not result in a change in the number of cigarettes smoked, level of carbon monoxide in expired air, or scores on positive and negative symptom scales. There was a significant increase in AIMS score, and a trend toward a decrease in EPS during smoking on active patch. All subjects tolerated the experiment without difficulty. Smoking while wearing the transdermal nicotine patch appears feasible and well tolerated for short periods of time in smokers with schizophrenia. Robust decreases in smoking behavior were not seen over the brief time of exposure.

NR577 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

No Evidence for Autoimmunity in Schizophrenia

Pinkhas Sirota, M.D., Abarbanel Men Hlth Ctr 6A, 15 Keren Kayemet, Bay Yam 59100, Israel; Yoav Cori, M.D., Talia Hahn, Ph.D., Amichai Schattner, M.D.

Summary:

We studied parameters of cellular immunity in 23 schizophrenic patients and compared them to 16 matched healthy controls and to 12 patients with rheumatoid arthritis (RA). None of the patients was receiving neuroleptic drug treatment before the study. We used highly sensitive methods to examine the interferon system by determination of the interferon-induced enzyme 2'-5' oligoadenylate synthetase [2-5A] in peripheral blood mononuclear cells. Tumor necrosis factor alpha (TNF) production was measured in the plasma and in vitro by bioassay of supernatants of stimulated blood cells and of unstimulated cells (spontaneous TNF secretion). In addition, we determined cell-mediated (spontaneous) cytotoxicity, major T cell subsets (CD3, CD4, and CD8 positive cells) and serum neopterin levels. No statistically significant differences could be found between the patients with schizophrenia and the control group in any of the tests used, and no particular subgroup of patients could be identified. In contrast, RA patients had increased serum neopterin and TNF levels, increased LPS-induced TNF production in vitro, increased 2-5A levels, and a decrease in CD8 cells associated with an increase in CD4 cells. Thus, in the group of patients studied, we could find no substantiation for the presence of either autoimmune or occult viral cofactors in the pathogenesis of schizophrenia.

NR578 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Relationship Between Changes in Schizophrenic Symptoms and Cognitive Deficits During Treatment with an Atypical Neuroleptic

Howard H. Chang, M.D., Department of Psychiatry, Taunton State Hosp/Harvard Med, 60 Hodges Avenue, Taunton MA 02780; Ileana Berman, M.D., Demetra Pappas, B.S., Nina Leventhal, B.A., Rogelio D. Bayog, M.D., Joseph Langlois, M.A.

Summary:

Although there is increasing evidence suggesting that negative symptoms are consistently associated with cognitive dysfunction we cannot conclude that cognitive deficits and schizophrenic symptoms share the same etiologic causes. The goal of our study was to determine whether the changes in negative symptoms after treatment with an atypical neuroleptic correspond to changes in cognitive deficits.

Method: A group of 40 actively treated schizophrenic patients were assessed psychiatrically and cognitively before and after receiving an atypical neuroleptic (risperidone or clozapine). The assessments included the Positive and Negative Syndrome Scale for Schizophrenia (PANSS) and a battery of cognitive tests consisting of the Mini-Mental Status Examination (MMSE) and tests of memory, attention, and executive function. After assessing the relationship between schizophrenic symptoms and cognitive scores before and after treatment adjustment, we looked at the association between changes in schizophrenic symptoms and cognitive deficits.

Results: As expected, following treatment with an atypical neuroleptic, our patients improved significantly in negative symptom scores. In addition, patients improved significantly in the positive symptom scores and performed better on some cognitive assessments, particularly on the MMSE. We found that primarily negative and not positive symptoms were correlated with low cognitive scores both before and after medication change. Despite the strong correlations between negative symptoms and cognitive deficits, the changes in negative symptom scores and cognitive performance were not associated.

Conclusions: Our results confirm previous findings that cognitive deficits are associated with negative symptoms. It appears, however, that this association involves complex etiologic elements since the changes in cognitive performance did not parallel changes in negative symptoms. These findings encourage to investigate treatment modalities that specifically target the schizophrenic symptoms and cognitive impairment in schizophrenia.

NR579 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Neuropsychology of Mood Disorder and Schizophrenia Disorder

Joseph Ventura, Ph.D., Department of Psychiatry, UCLA Adult Outpatient, 300 UCLA Medical Plaza Ste2243, Los Angeles CA 90095; William McMullen, Ph.D., Barry H. Guze, M.D., Lorie Humphrey, Ph.D., Michael J. Gitlin, M.D.

Summary:

Objective: Determining the specificity of neuropsychological performance among patients with schizophrenia and mood disorder compared to normals could help isolate those deficits that represent core features of major mental illness.

Method: We assessed cognitive function with neuropsychological tests in patients with schizophrenia (n = 18), mood disorder (n = 6), and in normal controls (n = 8). Neuropsychological measures used included the California Verbal Learning Test (CVLT), Wisconsin Card Sorting Test (WCST), the Controlled Oral Word Association Test (COWAT), Category Exemplar (CE), and the WAIS-R Block Design (BD). ANCOVA using patient age and parental level of education was used to evaluate neuropsychological performance between the groups. A Bonferroni correction was applied to address multiple comparisons in this small sample.

Results: Schizophrenia patients performed significantly lower than the mood disorder patients on the CVLT ($p < .001$) and the WCST ($p < .001$). However, there were no performance differences between the mood disorder patients and normal controls on any of the other cognitive measures.

Conclusions: Patients with schizophrenia showed impairments in verbal memory and in problem solving that were not found in mood disorder patients and normal controls. Differences in neurocognitive deficits among patients with schizophrenia compared to mood disorder patients may help explain differences in functioning observed in these two disorders.

NR580 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

PRN Medication and Seclusion Use in Chronic Psychiatric Inpatients

Cheryl K. Cantrell, M.D., Delaware Psychiatric Center, 1901 N Dupont Highway, New Castle DE 19720; Eric S. Cole, Ph.D.

Summary:

Objective: Seclusion and prn medications can be used in inpatient psychiatric settings both to treat patient agitation and to track agitation levels. The present study examines patterns of seclusion and prn medication administration among subgroups of chronic psychiatric patients.

Method: Over a 53-month period, 48 chronic psychiatric inpatients were tracked for daily frequencies of prn medication and seclusion. Results were tabulated across diagnostic groups as follows: 1) axis I psychosis (N = 25); 2) dementia or personality change due to axis III condition (N = 7); 3) axis I psychosis complicated by dementia or mental retardation (N = 11); and 4) pervasive developmental disorder (N = 4).

Results: Diagnostic group 1 showed the lowest average utilization of both prns (2.9/month) and seclusion (0.14/month). Groups 2 and 3 showed a medium level of both prn rates (7.6/month) and seclusion rates (0.29/month). Group 5 showed the highest utilization of prns (17.9/month) and seclusion (2.50/month) Chi test on the distribution of prns in Group 1 vs Groups 2 and 3 vs Group 5 was significant ($p = 0.050$).

Conclusions: Patients with autistic disorders and psychoses complicated by brain damage and/or mental retardation, show greater utilization of prn medication and seclusion in a chronic state hospital unit than do chronic psychotic inpatients.

NR581 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A Psychiatry Primary Care Clinic and Hospital Stay

Patricio R. Escalona, M.D., Department of Psychiatry, University of New Mexico, 2100 Ridgecrest Drive, SE, Albuquerque NM 87108; Ervin W. Lewis, M.D., Bruce Washburne, David A. Graeber, M.D.

Summary:

We compared the rate of admissions and the lengths of stay of 172 patients with diagnoses of schizophrenia, bipolar disorder, and major depression enrolled in a newly implemented psychiatry primary care clinic, one year prior to and after its implementation. The purpose of the study was to measure the utilization rate of acute inpatient psychiatric treatment in a group of severely mentally ill veterans at a VA medical center. The psychiatry primary care clinic provides a combination of comprehensive psychiatric care and general medical care to a chronic mentally ill population at a VA hospital. The results showed a significant reduction of the average length of stay for the group (7 days shorter, $p = 0.04$) after the implementation of the clinic. There was also a significant decrease in total length of stay per patient (9.5 days shorter, p =

0.03). The rate of admissions per patient also decreased after the clinic implementation, but was not statistically significant (p = 0.33). These preliminary results are encouraging in suggesting an apparent positive effect of a psychiatry primary care clinic in decreasing the utilization of acute inpatient psychiatric treatment. Future studies should be conducted to assess other possible benefits of this kind of clinic.

NR582 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Oral-Facial Dyskinesia in Chronic Institutional Schizophrenic Inpatients

Rebecca E. Adams, M.D., CNC-23, Pilgrim Psychiatric Center, 998 Crooked Hill Road, West Brentwood NY 11717; Michael J. Parrella, Ph.D., Leonard White, Ph.D., William M. Byne, M.D., Philip D. Harvey, Ph.D.

Summary:

This study examined the prevalence of oral-facial dyskinesia in 130 elderly (age < 64) chronic (mean length of illness 48.3 yrs ± 12.4) schizophrenic inpatients, and its relationship to age and gender. Subjects were evaluated individually by at least two experienced clinician raters using the Modified Simpson Dyskinesia Scale; 85.4% were receiving neuroleptics. The prevalence of oral-facial dyskinesia of at least mild severity in at least two oral-facial areas was 47.4%; involvement of the jaw (16.9% of cases) and tongue (16.2%) were the most frequent. Analysis of variance indicated significant relation to age ($F = 4.86$, $p = .009$), with a highest frequencies in the 75- to 85-year-old and 85+ age ranges (significant linear trend for age ($F = 5.31$, $p = .006$); no significant difference was found for gender ($F = .308$, $p = .579$). We conclude that there is a relatively high prevalence of oral-facial dyskinesia, and that the previously reported linear relation to age continues into the older age ranges; there was no significant interaction of age and gender in oral-facial dyskinesia. Most important in these data, however, is the finding that patients who have continuously received neuroleptic medication for over 40 years do not manifest a prevalence of TD that approaches 100%.

NR583 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Empirical Definition of Subtypes of Schizophrenia

Leonard White, Ph.D., Clinical Neuroscience Ctr, Pilgrim Psychiatric Center, Box A, Building 23-5, W. Brentwood NY 11717; Philip D. Harvey, Ph.D., Sonia Dollfus, M.D.

Summary:

We report on a large sample (N = 1,233), cross sectional study of empirically derived subtypes of schizophrenia.

Six clusters were derived describing six subtypes of schizophrenia in the total sample: positive (19.63%), activated (10.6%), negative (18.5%), dysphoric mood (17.0%), preoccupied (8.8%), and residual (25.4%). The residual subtype was most frequent (47.2%) in adult patients living in the community. Dysphoric mood subtype was most common (47.3%) in subjects attending rehabilitation programs. In chronic young adult inpatients, 20.5% were classified as activated subtype, 13.8% as negative subtype, 25.1% as dysphoric mood subtype, 13.8% as residual subtype, and 2.9% as preoccupied subtype. Only 12.3% of elderly chronic inpatients were classified as positive subtype. A high proportion of the elderly chronic inpatients were classified as negative (29.2%) and autistic preoccupation (32.1%) subtypes.

These findings substantiate the discriminant validity of the empirical subtypes. The varying proportions of subtypes identified in different treatment settings in this cross sectional study are consistent with a hypothesis of symptom-based subtypes reflecting phases of the illness.

NR584 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Tolerability and Efficacy of Intramuscular Ziprasidone

Schlomo Brook, M.D., Research Unit, Sterkfontein Hospital, Krugersdorp, South Africa; Rachel Swift, M.D., Edmund P. Harrigan, M.D.

Summary:

Objective: To evaluate the tolerability, safety, and efficacy of three days of treatment with the intramuscular (IM) formulation of the novel antipsychotic ziprasidone. Oral ziprasidone 80–160 mg/day is effective in positive, negative, and depressive symptoms of schizophrenia.

Method: Twelve men with an acute episode of chronic or subchronic schizophrenia received initial doses of 2.5 mg, 5 mg, 10 mg, or 20 mg IM ziprasidone. Over a three-day period, patients received daily doses of IM ziprasidone ranging from 2.5 mg qid to 20 mg tds. Patients were subsequently administered oral zipasidone for two days with an initial daily dose twice the patient's total dose of IM ziprasidone on day 3 (dose range on days 4 and 5 was 40–160 mg/day).

Results: All patients completed the study. Mean baseline to day 5 improvements were observed in BPRS (from 47.8 to 28.9), CGI-severity (from 6.1 to 5.3), and NOSIE (from 39 to 34), with maximum BPRS and CGI-severity improvements occurring on the last IM dose day. Six patients experienced generally mild or moderate adverse events; none discontinued. There were no serious adverse events or acute dystonic reactions. All subjects experienced a decrease in psychomotor agitation from baseline-this effect appeared dose-dependent.

Conclusions: Ziprasidone IM 2.5 mg qid to 20 mg tds was effective in reducing psychomotor agitation and other symptoms of psychosis in patients with an acute episode of chronic/subchronic schizophrenia and was well tolerated. The transition from IM to oral ziprasidone was also well tolerated.

NR585 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

QEEG Topographic Maps in Psychiatric and Neurological Groups

Donald W. Brunet, M.D., Medicine Queen's University, Kingston ON K7L 3N6, Canada; Susan J. Adams, M.B., Marguarita Criollo, M.D., Howard Galin, M.A., James S. Lawson, Ph.D., Duncan J. MacCrimmon, M.D.

Summary:

Objectives: To compare topographic maps of patients in various clinical groups with a database of healthy controls using a novel method of analysis.

Method: Data collection: 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. Data analysis: Each channel was assigned Cartesian coordinates (x, y) so that the response surface could be expressed as a polynomial with 20 parameters. Patient maps were compared case by case with the database, with covariate control of age, sex, and site of ascertainment, and the results aggregated within diagnostic groups.

Results: Multivariate tests of response surface using "jacknife" estimates of error.

Group	Age (yrs)	M/F	Hypothesized Abnormalities	Observed Abnormalities
Database	14–17	273/204	—	—
Depression	16–73	7/19	S^1	S^1, C^2, G^3
Bipolar	32–54	1/5	S^1	None
Schizophrenia	25–63	22/9	S^1, C^2	S^1, G^3
Epilepsy	14–59	7/2	G^3, TP^4	G^3, TP^4, S^1
Head Injury	28–54	6/5	G^3	G^3, S^1, TP^4

[1] Sagittal (hypo- or hyper-frontality); [2] Coronal (lateral asymmetry); [3] Generalized, [4] Total Power

Conclusions: The highly abnormal maps in depression were unexpected. The method of analyzing individual cases, then aggregating, avoids the problem that heterogeneous abnormalities can cancel each other out when mean maps are considered. Frequency analysis and control of drug regimen will be necessary to realize the analytic method's potential as a diagnostic instrument.

NR586 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Role of Immune Measures in Schizophrenic Behavior

Daniel P. van Kammen, M.D., VA Medical Center, 7180 Highland Drive, Pittsburgh PA 15206; Cathy G. McAllister, Ph.D., Mary E. Kelley, M.S., Aleksander A. Mathe, M.D., Walter A. Brown, M.D., Jeffrey K. Yao, Ph.D.

Summary:

Recent studies have shown that the cytokine interleukin-2 (IL-2), but not interleukin 1 (IL-1), in the CSF was elevated in haloperidol-treated patients who relapsed within six weeks following drug withdrawal. This indicated a possible stress sensitivity in the relapsed patients, which could be identified using CSF immune measures. In an attempt to uncover evidence of a direct effect of the immune system on brain function, we examined the relationship between immune measures and behavior in 36 schizophrenic patients. We attempted to control for elements associated with the two proposed mediums of the immune system and brain: the HPA axis (CSF CRF, CSF ACTH, and CSF cortisol), and the sympathetic nervous system (CSF NE). IL-10 was the only immune measure found to correlate with behavioral measures. When all variables were entered into a regression predicting psychosis levels on medication, both IL-10 and cortisol were significant predictors of psychosis levels, indicating a possible direct effect of IL-10 on behavior. However, drug-free data on the same patients and measures revealed that cortisol, but not IL-10, was significantly associated with psychosis. The data indicate that the immune system may have direct effects on schizophrenic behavior during antipsychotic treatment, but not in the drug-free state.

NR587 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Medication Effects on Negative Symptoms in Schizophrenia

Daniel P. van Kammen, M.D., VA Medical Center, 7180 Highland Drive, Pittsburgh PA 15206; Mary E. Kelley, M.S.

Summary:

Recent studies of negative symptoms in schizophrenia have focused on uncovering those symptoms primary to the disease rather than secondary to psychosis. The current study compared negative symptom profiles in 93 healthy male schizophrenic patients on and off treatment. Principal components analysis was performed on all SANS items on haloperidol [mean dose 10.8 ± 6.8 mg/day] and drug free separately to determine if there were meaningful factor scores that were consistent across medication conditions. Of the 30 SANS items, a factor representing affective flattening accounted for similar variance in both conditions. Using repeated measures ANOVA, the negative symptom factor exhibited significant relapse [$F = 4.47$, $df = 1,91$, $p = 0.037$] and relapse by medication [$F = 7.87$, $df = 1,91$, $p = 0.006$] but not medication [$F = 0.11$, $df = 1,91$, p = ns] effects. The relapse effects indicated that relapsers had higher negative symptoms overall, as well as an increase in negative symptoms after withdrawal. However, while the SANS total [sum of 30 items] was correlated with psychosis levels both on and off medication, the negative symptom factor identified was only significantly correlated with psychosis drug free [$r = 0.31$, $df = 91$, $p = 0.002$], when some of the patients ($n = 42$) were exacerbated. The data suggest that the negative symptom factor is both medication independent and not secondary to psychosis in clinically stable patients.

NR588 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A One-Year Prevalence Study of Schizophrenia on Reunion Island in the Indian Ocean

Philip A.P.M. Gorwood, M.D., Unity 155, Inserm, 2 Place Jussieu, Paris 75251, France; Marion Leboyer, M.D., Maurice Jay, M.D., Josue Feingold, M.D.

Summary:

Review of geographical comparisons of the prevalence of schizophrenic disorders found a ten-fold range difference between geographical contiguous groups, with high and low prevalence pockets, and hypothetic north-south gradient in the disease's distribution. We performed a one-year prevalence study of schizophrenia in a limited area of Reunion Island in the Indian Ocean, and analyzed the prevalence variability in contiguous regions of this area. We found one of the highest reported age-corrected (above 15 years) one-year prevalence of schizophrenia (14.9 per thousand, standard error = 0.574 per thousand). A minority of cases were familial (22.3%) as defined by the presence of at least one first-degree relative affected with the diagnosis of schizophrenia.

Large discrepancies in the distribution of prevalence rates of schizophrenia were observed between the five towns analyzed. Interestingly, when a higher prevalence was observed, it was highly correlated with an increase of the percentage of familial cases ($r = 0.989$, $df = 3$, $p = 0.0014$). In particular, the highest prevalence was observed in Saint Bernard (10.4) with a high ratio of familial schizophrenia (61%), whereas the observed prevalence was the lowest in Bretagne (1.78) with a low ratio of familial schizophrenia (14.3%).

Presence of founder effect often described in geographical isolates could explain the high prevalence rate and the heterogeneity between towns observed in our sample.

NR589 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Population Pharmacokinetics of Sertindole

Richard Granneman, M.D., 4PK/AP13A, Abbott Laboratories, 200 Abbott Park Road, Abbott Park IL 60064; Sheckman Wong, Ph.D., Patricia Wozniak, Ph.D., Chris Silber, M.D., Randall Mack, B.S.

Summary:

Sertindole was discovered and patented by H. Lundbeck (Copenhagen) and is currently under development by Abbott Laboratories in the United States, Latin America, and Canada. The pharmacokinetics (PK) of sertindole were evaluated in a Phase III, multicenter, open-label trial to assess the safety of oral 4 to 24

mg doses administered once daily for up to one year in 402 patients with schizophrenia or other psychotic disorders. Demographics were: 62% male, 85% Caucasian, and mean age 40 years (14–73 yr). Plasma samples were analyzed for sertindole and metabolites by HPLC/MS/MS. Steady-state C_{min} means increased proportionally with dose for parent and metabolites. The program NONMEM was used to analyze 884 concentrations in the population analyses of sertindole PK. Estimates were: CL/F = 10.8 ± 0.5 L/h, and V/F = 1150 ± 87 L. Covariates examined included demographics and 36 concomitant drugs. Time on treatment, age, and gender, and most concomitant medications had no effect on sertindole PK. Three major drug-drug interactions were found: fluoxetine and paroxetine reduced CL/F by ≥ 30%; CYP3A inducers increased CL/F 122%. Lower clearances (by ≤20%) were noted for blacks, nonsmokers, and patients concurrently taking a Ca-channel antagonist. The results are consistent with genotyping (n = 29) and *in vitro* data showing that sertindole is metabolized by hepatic CYP2D6 and CYP3A enzymes.

NR590 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Efficacy and Safety of Once-Daily Dosing with Risperidone in Patients with Schizophrenia

Steven G. Potkin, M.D., Department of Psychiatry, Univ of CA Irvine Medical Cntr, 101 City Drive South Route 88, Irvine CA 92717

Summary:

To determine the feasibility of once-daily dosing with risperidone, a double-blind, parallel-group, randomized, multicenter study was conducted to compare the effects of placebo (n = 83) and risperidone 4 mg (n = 85) and 8 mg (n = 78) given once daily for 28 days in 246 patients with schizophrenia. Clinical improvement (≥20% reduction in total PANSS scores) at endpoint was reported in significantly more patients in the risperidone 4 mg group (65%; $p < 0.05$) and 8 mg group (76%; $p < 0.001$) than in the placebo group (47%). Furthermore, both risperidone dosing regimens were associated with greater mean decreases in PANSS total, subscale, and PANSS-derived BPRS scores; the differences versus placebo in PANSS total and the positive subscale were significant ($p \leq 0.05$ and <0.01, respectively). Safety data for patients treated with risperidone were similar to those receiving placebo. Patients reported more subjective extrapyramidal symptoms in the risperidone group. The mean change in total Extrapyramidal Symptom Rating Scale scores from baseline to worst score was similar in all three groups. The percentages of patients reporting adverse experiences were similar in the three treatment groups.

In conclusion, once-daily dosing with 4 mg and 8 mg risperidone was safe and effective in these patients. A regimen of once-daily dosing will increase convenience and patient compliance and contribute to optimizing patient management.

NR591 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

A Cost-Effectiveness Clinical Decision Analysis Model for Schizophrenia

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Summary:

Objective: A model was developed to estimate the medical costs and effectiveness outcomes of three antipsychotic treatments (olanzapine, haloperidol, or risperidone) for patients with schizophrenia.

Methods: Clinical trial results were the basis of parameter estimates in the model with information from medical literature and expert opinion also incorporated. A decision analytic Markov model was used to determine the cost-effectiveness of the three treatments for the different clinical pathways and outcomes that patients treated for schizophrenia experience over a five-year period. Direct medical costs were incorporated into the model and the outcome was expressed using three effectiveness-outcome indicators: Brief Psychiatric Rating Scale (BPRS), Quality-Adjusted Life Years (QALY's), and lack of relapse.

Results: Over a five-year time period olanzapine patients had an additional half-year in a disability-free state (based on BPRS scores), over two additional months of disability-free health state (based on QALY's), and experienced fewer relapses compared with haloperidol patients. The estimated five-year medical cost for olanzapine was $1,460 less than for haloperidol (based on BPRS scores). Compared with risperidone, olanzapine costs $509 less over a five-year period and olanzapine patients had slightly more time in a disability-free state (based on BPRS scores and similar relapse rates).

Conclusions: Olanzapine is cost saving, even with the most conservative estimates, compared with both haloperidol and risperidone for all three effectiveness outcome indicators used in the model.

NR592 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Metabolic Rate in Kraepelinian Versus Non-Kraepelinian Schizophrenia

Lina S. Shihabuddin, M.D., Department of Psychiatry, Mount Sinai, 1 Gustave Levy Place/Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Erin A. Hazlett, M.B., Johannes Schroeder, M.D., M. Mehmet Haznedar, M.D., Kenneth L. Davis, M.D.

Summary:

Positron emission tomography with 18F-deoxyglucose (FDG) and co-registered high resolution magnetic resonance imaging were used to study two subtypes of schizophrenia, the Kraepelinian subtype (n = 10), which is characterized by a poor outcome and chronic deteriorating course, and the non-Kraepelinian subtype (n = 17), which is characterized by a better outcome and remitting course. A sample of 33 age- and sex-matched normal volunteers served as a comparison group. During the period of FDG tracer uptake, subjects performed a serial verbal learning task. Patients in the Kraepelinian subgroup had significantly lower fronto-occipital ratios than non-Kraepelinian or control subjects for the middle and inferior frontal gyri. In addition, Kraepelinian patients had significantly lowers values in the inferior temporal, and inferior frontal gyrus (1.28, 1.26, 1.22 in controls, non-Kraepelinian and Kraepelinian patients, respectively; group by lobe by gyrus interaction, $F = 1.99$, $df = 18,96$, $p = 0.01$). The right striatum also showed lower metabolic rates on exploratory statistical probability mapping. The striatum (caudate plus putamen) assessed by MRI tracing was significantly smaller in Kraepelinian (2.31, sd = 97) than non-Kraepelinian patients (2.55, sd = 106; $F = 4.36$, $df = 1,25$, $p = 0.04$) as traced on their MRI. These findings support the validity of the Kraeplinian/non-Kraeplinian subtypes of schizophrenia and suggest that they have different pathophysiologies and, possibly, different etiologies.

NR593 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Left Ventricular Size Increases with Age and Is Associated with Reduced Parietal and Occipital Cortical Metabolic Rate in Schizophrenia

Adarsh K. Gupta, M.D., Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy P1/Box 1505, New York NY 10029; Monte S. Buchsbaum, M.D., Erin A. Hazlett, M.B.

Summary:

While ventricular enlargement has been widely reported in schizophrenia, its functional implications for specific brain structures have been little studied. Magnetic resonance imaging (MRI) and positron emission tomography (PET) with ^{18}F-2-deoxyglucose (FDG) were used to study ventricular size and metabolic rate in the cortex in 27 unmedicated schizophrenic patients and 32 age- and sex-matched normal controls. During the FDG uptake period, all subjects performed a modified version of the California Verbal Learning Test. PET (30 slice, 3–4 M counts/slice, 4.5 mm FWHM) and MR images (TR 24, TE 5, flip angle 40 degrees, 1.2 mm thickness) were coregistered. Gradient filters were applied to enhance the MRI image and delineate the ventricular edges clearly. Lateral, anterior, and temporal divisions of the ventricles were summed separately and absolute pixel counts were converted into cubic mm volumes. As widely reported, patients with schizophrenia had larger ventricles and this effect was most marked for older patients and the left hemisphere. The increase in ventricular size was significantly correlated with duration of illness in schizophrenics. Ventricular volume showed significant negative correlations with relative metabolic rate in the angular gyrus and primary visual cortex and negative but trend-level correlations across other parietal and occipital areas. Frontal lobe metabolic rate was not correlated with anterior horn volume and temporal lobe metabolic rate was not correlated with temporal horn ventricular volume. It thus appears that ventricular enlargement is associated with diffuse and posterior metabolic change but not changes in immediately adjacent cortex. Ventricular size correlations with metabolic rate in striatal subdivisions, thalamus, and cingulate gyrus as well as neuropsychological function will also be discussed.

NR594 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Skills Training for Substance Abusing Schizophrenics

Andrew L. Shaner, M.D., Department of Psychiatry, Veterans Affairs Medical Cntr., 11301 Wilshire Blvd., B151Z, Los Angeles CA 90073; Lisa J. Roberts, M.A., Thad Eckman, Ph.D., Jeffery N. Wilkins, M.D.

Summary:

Objective: Most schizophrenic substance abusers either do not tolerate or are not helped by standard treatments for substance abuse. We adapted cognitive-behavioral drug relapse prevention strategies originally developed for non-mentally ill substance abusers by using a skills training method originally developed to teach social and independent living skills to schizophrenics.

Method: The intervention consists of three components: 1) basic training (eight psycho-educational sessions); 2) skills training (24 sessions to teach nine relapse prevention skills), and 3) practice sessions (32 sessions paired with the other two kinds of groups during which patients apply newly learned knowledge and skills to real-life situations). Sixteen patients with DSM-IV schizophrenia or schizoaffective disorder and co-occurring substance dependence participated in a feasibility study.

Results: On a test of drug relapse prevention knowledge and skills (assessed through role play), patients scored poorly before the intervention ($X = 37.69$, $sd = 11.85$), but made large and significant improvements by treatment completion ($X = 96.19$, $sd = 7.26$; $F(15) = 437.81$, $p < .0001$). This improvement was maintained at three-month follow-up ($X = 95.88$, $sd = 5.88$).

Conclusions: Subjects acquired and maintained a wide range of drug relapse prevention concepts and skills. If subsequent research demonstrates they actually use these skills, then this manual-driven therapy may play and important role in the treatment of substance abuse among schizophrenic patients.

NR595 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Clinical Actions of Risperidone: Factor Analysis of Data from the North American Trial

Stephen R. Marder, M.D., Department of Psychiatry, UCLA/ West Los Angeles VA, 11301 Wilshire Blvd. (116A), Los Angeles CA 90073; John M. Davis, M.D., Guy Chouinard, M.D.

Summary:

Background: In two double-blind trials conducted in North America, 523 patients with chronic schizophrenia received risperidone, haloperidol, or placebo. In the present study, combined data from the two trials were analyzed.

Method: Patients received placebo, fixed doses of risperidone (2, 6, 10, and 16 mg/day), or 20 mg/day of haloperidol. Factor analysis of scores on the Positive and Negative Syndrome Scale (PANSS) produced five factors (negative symptoms, positive symptoms, disorganized thought, uncontrolled hostility/excitement, and anxiety/depression).

Results: Mean changes (symptom reductions) in PANSS factor scores from baseline to treatment week 6 and 8 were significantly greater in patients receiving 6-16 mg/day of risperidone than in patients receiving placebo or haloperidol. The advantages of risperidone were greatest for negative symptoms, uncontrolled hostility/excitement, and anxiety/depression. Even at the lowest dose, 2 mg/day, risperidone was significantly superior to haloperidol in reducing negative symptoms. The occurrence of extrapyramidal symptoms did not affect the changes in PANSS factor scores at endpoint.

Conclusion: Risperidone produced greater improvements than haloperidol on all five factors. The large between-group differences on negative symptoms, uncontrolled hostility/excitement, and anxiety/depression suggest that risperidone and perhaps other serotonin/dopamine antagonists have qualitatively different effects from those of conventional antipsychotic agents.

NR596 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Attention and Information Processing Deficits in Schizophrenia: Correlates with Clinical Syndromes

Elton T.C. Ngan, M.D., Department of Psychiatry, University of BC, 2255 Wesbrook Mall, Vancouver BC V6T 2A1, Canada; Peter F. Liddle, Ph.D.

Summary:

Objective: Neurocognitive studies have consitentlly demonstrated a decrease in the reaction time of schizophrenic subjects compared to nonpatient controls. The objective of this study is to determine the degree of association between neurocognitive measures of attention and vigilance and symptom profile.

Method: Thirty schizophrenic patients were assessed using a semistructured clinical interview (SANS and SAPS). Following the clinical interview each subject engaged in a simple reaction time task and completed the Stroop test. Syndrome scores were calculated from the SANS and SAPS scores for reality distortion, disorganization, and psychomotor poverty based on results of previous factor analysis studies using SANS and SAPS. Partial correlation coefficients corrected for age were calculated for each syndrome score and reaction time, as well as for each syndrome score and Stroop completion time.

Results: A significant positive correlation was found between psychomotor poverty and both mean reaction time ($r = .379$, $p < .05$) and Stroop performance time ($r = .435$, $p < .05$).

Conclusion: Clinically observable psychomotor poverty symptoms are associated with deficits in simple attention and information processing tasks. Negative or deficit symptoms of schizophrenia may be the clinical manifestation of impaired or delayed cognitive processing. His delayed cognitive processing may represent a core physiological deficit of schizophrenia.

NR597 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Depressive Symptoms in Recent-Onset Schizophrenia Patients Are Associated with a Family History of Depression

Kenneth L. Subotnik, Ph.D., Department of Psychiatry, UCLA, 300 UCLA Med Plaza, Rm 2240, Los Angeles CA 90024; Keith Nuechterlein, Ph.D., Robert F. Asarnow, David L. Fogelson, M.D., Michael J. Goldstein, Ph.D., Jim Mintz, Ph.D.

Summary:

Affective disorders among 286 first-degree and 661 second-degree relatives of 70 DSM-III-R schizophrenia patients with a recent first psychotic episode were examined in relationship to the presence of depressive symptoms in these probands. Depressive symptoms in the schizophrenia probands were examined at the index psychotic episode at study entry and systematically over a one-year follow-through period. The majority of first-degree family members were interviewed in person using semi-structured diagnostic interviews, and family history information was collected on all first- and second-degree relatives. The linear regression findings confirmed the hypothesis that there is an association between depressive symptoms in the early course of schizophrenia and family history of unipolar affective illness. Because the family psychiatric history variables were not normally distributed, a robust "bootstrap" analysis was also performed to generate an empirical distribution of the regression statistics. These regression analyses of 500 randomly generated bootstrap samples from the same data set confirmed the association at $p < .01$. The findings are consistent with a model in which a familial affective liability, when present, exerts a modifying influence on the patient's schizophrenic illness to increase expression of depressive symptoms.

NR598 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Long-Term Treatment of Elderly Psychotic Patients with Risperidone

Michael Davidson, M.D., Chaim Sheba Medical Center, Tel-Hashomer, Israel

Summary:

Objective: Effective management of elderly psychotic patients is often complicated by coexisting illnesses, polypharmacy, and pharmacokinetic changes, which all contribute to a poorer clinical outcome. A study was designed to determine the long-term effects of risperidone treatment in elderly patients.

Methods: A 12-month, open-label, multicenter study of risperidone (flexible doses ≤ 8 mg/day) in elderly psychotic patients is underway. Assessments included the Extrapyramidal Symptom Rating Scale (ESRS), adverse events reports, the Positive and Negative Syndrome Scale (PANSS), and the Clinical Global Impression (CGI) scale.

Results: Data from 106 patients treated for three months (endpoint) are available. The mean daily dose of risperidone at endpoint was 3.7 mg. Severity of extrapyramidal symptoms (ESRS scores) was low at baseline and was reduced during treatment; the mean total score (parkinsonism + dystonia + dyskinesia) was 11.6 at baseline and 10.2 at endpoint. Serious adverse events were recorded in 13 patients; most of these were age-related. Statistically significant improvements in psychopathology (reduced PANSS and CGI scale scores) were observed at endpoint; 57% of the patients were rated as clinically improved (≥20% reduction in PANSS scores). Among the 32 patients who withdrew from the trial, the most common reasons were adverse events (n = 14), insufficient treatment response (n = 8), and treatment deviation (n = 8).

Conclusion: These results suggest that risperidone is safe and effective in elderly psychotic patients.

NR599 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Prolactin Levels and Adverse Events in Patients Treated with Risperidone

David Kleinberg, New York University Hosp., 530 First Avenue, New York NY, 10016; Martin B. Brecher, M.D., John M. Davis, M.D.

Summary:

Objective: A study was designed to characterize the relationship between risperidone, serum prolactin levels, and possible clinical sequelae.

Methods: All randomized double-blind trials of risperidone in patients with chronic schizophrenia were reviewed. The subjects included 837 patients (256 women, 581 men) with paired prolactin data, and 1,884 patients (554 women, 1,330 men) with data on five adverse events possibly associated with increased prolactin levels—amenorrhea, galactorrhea, and gynecomastia in women, and gynecomastia, erectile dysfunction, and ejaculatory dysfunction in men.

Results: Both risperidone and haloperidol produced dose-related increases in plasma prolactin levels in men and women. Among women, the risperidone dose was not correlated with adverse events, nor were the adverse events correlated with endpoint prolactin levels. Among men, the incidence of adverse events was positively correlated with risperidone dose; however, at risperidone doses of 4-10 mg/day, the incidence of adverse events was not significantly higher than in placebo patients. Furthermore, adverse events in men were unrelated to plasma prolactin levels.

Conclusion: Risperidone-associated increases in serum prolactin levels were not significantly correlated with the emergence of possible prolactin-related side effects.

NR600 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Reduced Response of Auditory Steady-State 40HZ in Schizophrenia

Jun Soo Kwon, M.D., Department of Psychiatry, Brockton VAMC, 940 Belmont Street, Brockton MA 02401; Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D., Ronald J. Gurrera, M.D., Robert W. Greene, M.D., Yoshio Hirayasu, M.D.

Summary:

Steady-state 40Hz EEG response can be generated with repetitive auditory stimuli in humans. This oscillatory activity with a frequency in the gamma band is thought to reflect the synchronous electrical discharge in auditory neural network. We used this technique to probe auditory processing in schizophrenia at different rates of stimulation. Fourteen male, right-handed chronic schizophrenics and 14 controls were evaluated. 80 dB click stimuli were delivered in trains of 500 ms duration, with a 700 ms interval between trains of stimuli. Stimulus rates of 20, 30, and 40Hz were used in three separate blocks. EEG was recorded with a 64-channel Geodesic Sensor Net at a 500 Hz sampling rate. Sweeps were averaged at each electrode and filtered 12 –50 Hz. Fast Fourier Transformation was used to calculate the spectral power at the stimulation frequency for each condition. ANOVA was applied with two groups (schizophrenia vs. control), three stimulus rates (40, 30 & 20/sec), and five channels (Fz, Cz, Pz, T3, T4). The results showed that the groups differed ($F = 20.6$, $df = 1$, $p < 0.001$), gamma power decreased with increasing stimulus rate, ($F = 34.1$, $df = 2$, $p < 0.001$), and power was larger at frontal and central electrode sites ($F = 38.2$, $df = 4$, $p < 0.001$). At the 40/sec stimulus rate, the gamma-band spectral power in schizophrenics was significantly smaller than in controls at the midline electrodes. However, at 30/sec and 20/sec stimulus rate, there were no differences of spectral power between schizophrenics and controls. The reduced power at 40Hz suggests a decrease in the ability of networks to maintain synchronous activity of neuronal firing at

higher gamma range frequencies. This kind of synchronous firing may be important for integrative processing between neuronal ensembles.

NR601 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Risperidone in Elderly Patients with Psychotic Disorders

Subramoniam Madhusoodanan, M.D., Department of Psychiatry, St. Johns Hospital, Far Rockaway NY 11691; Ronald Brenner, M.D., John W. Kasckow, M.D., Mark E. Kunik, M.D., Amando Negron, M.D., Nunzio Pomara, M.D.

Summary:

Objective: An open, multicenter study was conducted to evaluate the safety of risperidone in elderly psychiatric patients.

Methods: One hundred three patients with a diagnosis of schizophrenia (75%) or schizoaffective disorder (25%) received risperidone for 12 weeks. The patients' mean age was 71 years (19% were ≥75 years). The starting dose of risperidone was 0.5 mg twice daily, after which it could be increased to a maximum of 3 mg/day during the first week, and then in increments of 0.5 mg twice daily to a maximum of 6 mg/day. Severity of extrapyramidal symptoms was assessed by the Extrapyramidal Symptom Rating Scale (ESRS).

Results: The total ESRS score (parkinsonism + dystonia + dyskinesia) was significantly increased from baseline to worst score during treatment, but significantly reduced from baseline to endpoint. The most frequently reported adverse events were dizziness (22% of patients), insomnia (17%), agitation (15%), somnolence (15%), and injury (12%). Antiparkinsonian medications were used by 33% of the patients. No significant electrocardiographic changes were observed. Mean total and subscale Positive and Negative Syndrome Scale scores improved significantly; greater improvement was seen in patients receiving ≤3 than >3 mg/day of risperidone.

Conclusion: Risperidone was well tolerated and efficacious in elderly patients with schizophrenia or schizoaffective disorder.

NR602 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Haloperidol Improves Memory in Schizophrenia

Daniel N. Allen, Ph.D., Department of Psychology, VA Medical Center, 7180 Highland Drive, Pittsburgh PA 15206; Mark W. Gilbertson, Ph.D., Ethan Barry, B.A., Daniel P. van Kammen, M.D., John A. Gurklis, Jr., M.D.

Summary:

Objectives: Inadequate control of medication effects (antipsychotics and anticholinergics) and symptom severity contribute to inconsistent results of studies examining memory functioning in schizophrenia. This investigation examined influence of haloperidol on memory in schizophrenia while controlling for psychosis severity.

Method: We evaluated 25 male inpatients with DSM-III-R schizophrenia on two occasions separated by three weeks using the Wechsler Memory Scale-Revised (WMS-R) and Bunney-Hamburg Psychosis scale. Thirteen patients were tested twice while clinically stable on haloperidol (maintenance group); 12 were assessed once when clinically stable on haloperidol and again after three weeks medication-free (withdrawal group). Patients were free of anticholinergics at least two weeks before evaluations.

Results: No significant differences were present between groups on age, education, or psychosis severity. Repeated measures ANOVA (test session by group) indicated no significant session effects for psychosis severity. Significant interaction effects were observed for visual and delayed memory indexes ($p < .05$) with a near significant effect for general memory index ($p = .07$). Paired t-tests indicated the haloperidol-withdrawn group did not improve significantly on any WMS-R indexes from session 1 to session 2. The haloperidol maintenance group exhibited significant improvement on all WMS-R memory indexes ($p < .01$).

Conclusions: Haloperidol appears to improve long-term memory functioning in schizophrenia.

NR603 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Visuospatial Working Memory in Schizotypal Personality Disorder

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Summary:

Background: Cognitive processing deficits have been identified as a core abnormality that schizotypal personality disorder (SPD) individuals share with schizophrenic patients. It has been hypothesized that impaired working memory may be a critical component of several of the more complex cognitive deficits found in schizophrenia-spectrum patients. Furthermore, impaired working memory processes have been implicated as an important contributer to the development of schizophrenic symptoms. However, to date, no studies have looked at the relationship between working memory deficits and schizotypal symptomotology. The present study investigates the relationship between working memory function and DSM-III schizotypal symptom clusters in a population of clinically identified patients with a DSM-III personality disorder diagnosis.

Method: Seventeen DSM-III SPD patients, 23 patients with DSM-III non-odd cluster personality disorders, and 25 normal controls were tested on a pen and paper visuospatial working memory task. Each person was given 14 immediate recall trials and 15 trials using a 10-second delay. Performance error was measured in cm as the average difference between the location where each stimulus was presented and the location where it was recalled to have been. Based on previous research, schizotypal symptoms were divided into the following factors: cognitive/perceptual, interpersonal, and paranoid.

Results: SPD patients (mean = 2.85, sd = 1.44) performed significantly worse than both OPD patients (mean = 1.66, sd = .58) and normal control subjects (mean = 1.58, sd = .61) on the working memory task [$F = 10.51$, $df = 2.55$, $p < .001$]. Poor performance was significantly related to greater number of schizotypal symptoms ($r = .34$, $p < .05$). Furthermore, impaired working memory was significantly related to the interpersonal factor (ie. criteria related to social isolation, constricted affect, odd speech, and odd behavior) ($r = .33$, $p < .05$) but was not significantly related to the paranoid or cognitive/perceptual factors (factors comprised of psychotic-like symptoms) ($r's < 1.3$, $p's > .4$).

Conclusions: These results suggest that SPD patients demonstrate working memory impairment, which may be related to the deficit-like symptoms of SPD.

NR604 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Gender Differences in Acute Schizophrenic Symptoms

Julie M. Hannon, B.A., Research Department, Hillside Hospital, 75-59 263rd Street, Glen Oaks NY 11004; Michael Obuchowski, Ph.D., Alyson Andreasen, B.S., Scott P. Smith, M.A., Chris Smith, B.S., David B. Schnur, M.D., Barbara Cornblatt, Ph.D.

Summary:

There is increasing evidence that the course of schizophrenia differs as a function of gender. Several studies have shown that more males than females develop the full blown disorder and that males have an earlier, more insidious onset, display more negative symptoms, and have a poorer prognosis than females. To evaluate whether sample selection strategy influences this effect, gender differences in age of onset and presenting clinical symptoms were examined in 56 unmedicated patients divided into three groups: 14 recent onset adults (8 males and 6 females), 15 recent onset adolescents (8 males and 7 females) and 24 multi-episode patients (16 males and 8 females). All subjects received DSM-IV diagnoses of schizophrenia, based on structured clinical interviews (K-SADS or CASH). Clinical state at admission was assessed according to the Positive and Negative Syndrome Scale (PANSS). No differences in age of onset as a function of gender were found. No differences between males and females were found for either the positive, negative, or general psychopathology PANSS subscales. Subscale items were also analyzed using separate MANOVAs for each set of items. The results of these analyses indicated no significant differences as a function of gender on any of the items with the exception of two in the general psychopathology subscale—that females were higher in depression than males ($F_{1,44} = 6.11$, $p = 0.02$) and males were higher in active social avoidance than females ($F_{1,44} = 5.87$, $p = 0.02$). The implications of these results for sampling selection and for the findings of gender differences in the literature will be discussed.

NR605 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Antipsychotics Affect Suicidality in Schizophrenia

Carolyn Heimberg, M.D., Department of Psychiatry, Dallas VAMC, 4500 S Lancaster Road, 116A, Dallas TX 75216; Richard R. Owen, Jr., M.D., Lynn Mason, R.N., Ellen P. Fischer, Ph.D.

Summary:

Suicidality is frequently encountered in schizophrenic patients. Some reports have linked suicidality in this population to movement disorders, particularly akathisia. Newer antipsychotics available may minimize these motor side effects.

Objective: The relationship of suicidality, movement disorder, and type of antipsychotic treatment was explored.

Method: Data collected as part of a schizophrenia outcomes study was reviewed with attention to suicidality, movement disorders, and medications. The review was retrospective, including chronic in patients and outpatients from community and VA mental health clinics, and included 204 cooperative patients recruited over a 15-month span and followed at six-month and 18-month intervals. Ninety-two percent of patients had complete data sets at six months, and 90% had complete data at 18 months. Medications were adjusted naturalistically, movement symptoms were assessed by standard ratings and patient questionaires, and suicidality was recorded by questionnaire.

Results: A significant relationship was found for type of antipsychotic treatment and both degree of akathisia and degree of suicidality.

Conclusion: This result has significance to patient care in that antipsychotic treatment choice may affect suicidality as well as more obvious side effects.

NR606 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Glial Architecture of Human Cortex: Implications for Neurocognition in Schizophrenia

Bruce Quinn, M.D., Neuropathology, Northwestern Medical School, 303 East Chicago, Ward 6-204, Chicago IL 60611; William M. Byne, M.D., Laurie S. Conklin, B.S., Kenneth L. Davis, M.D.

Summary:

Forebrain astrocytes are typically categorized as fibrous versus protoplasmic astrocytes. Few modern studies address the architectural and cytologic complexity of astrocytes in human forebrain. We have used a battery of novel histotechniques to visualize subtypes of forebrain astrocytes, revealing seven distinct forms in post-mortem cortex. This framework is critical for understanding complex neural-glial interactions in neurodevelopment and neurotransmitter regulation and metabolism in neocortex. One particularly prominent glial form is the "caudate astrocyte," with fibers traversing layers 1 and 2 and unique to these laminae. This astrocytic class appears inconspicuous in the rodent, and much more developed in human neocortex than in squirrel monkey or dolphin. These astrocytes show distinct histopathologies. Fiber tips occasionally reached as far as to "synapse" on capillaries of the middle neocortical lamina. The functional role of subpial caudate astrocytes likely include complex glial functions such as glutamate uptake or monoamine oxidase synthesis for neurotransmitter metabolism. Since the relatively acellular Layer 1 is a unique, rich zone of apical dendrites from multilaminar pyramidal neurons and afferent fibers from thalamus and monoaminergic nuclei, as well as fibers carrying neocortical feedback and control, disruption of caudate astrocyte function could have neurocognitive sequelae in schizophrenia. (Sponsored by the Stanley Foundation.)

NR607 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Schizotypal Personality Disorder: A Replication of Cognitive Deficits

Martina M. Voglmaier, Ph.D., Department of Psychiatry, Harvard Medical School, 1493 Cambridge Street, Cambridge MA 02139; Larry J. Seidman, Ph.D., Dean F. Salisbury, Ph.D., Richard Rhodes, B.S., Robert W. McCarley, M.D.

Summary:

Objective: We previously reported decrements in verbal learning and abstraction in a small group of individuals who met DSM-III-R criteria for schizotypal personality disorder (SPD). The purpose of the current study was to replicate our findings in an independent sample.

Method: A wide array of neuropsychological functions were assessed in a sample of 16 right-handed males who met DSM-III-R criteria for SPD. Functions measured included abstraction, verbal and spatial intelligence, memory and learning, language, attention, and motor skills. Neuropsychological profiles were constructed by standardizing test scores based on means and standard deviations of control subjects ($n = 12$) who were matched for age, education, and parental SES.

Results: SPD subjects showed significant deficits in verbal learning and abstraction functions, against a background of relatively normal cognitive function. SPDs showed a striking decrement on the California Verbal Learning Test (CVLT), a word-list learning measure that requires semantic clustering for more efficient performance, and a reduction in performance on the Wisconsin Card Sort Test, a measure requiring concept formation, abstraction, and mental flexibility.

Conclusions: The results confirm our previous findings of selective neuropsychological deficits in SPD, and are consistent with current hypotheses of left-temporal and prefrontal brain dysfunction in schizophrenia.

NR608 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Volumetric Comparisons of the Cingulate Gyrus in Patients with Schizophrenia and Controls

Patricia A. Fodor, M.D., Department of Psychiatry, University of CO HSC, 4200 East 9th Ave/Box C268-68, Denver CO 80262; Jeanelle Sheeder, B.A., Donald C. Rojas, Ph.D., Peter D. Teale, M.S.E.E., Jack Simon, M.D., Martin L. Reite, M.D.

Summary:

Recent investigational studies have reported significant abnormalities in corticolimbic structures in the post-mortem schizophrenic brain. These findings have been attributed to altered structural architecture, including the anterior cingulate gyrus. We studied the brains of 27 males and 23 females. This group contained 22 schizophrenics and 28 normal controls. MRIs of these brains were obtained at 1.5T, and a T1 weighted 1.7 mm slice thickness coronal image series was used to manually segment the left (L) and right (R) cingulate gyrus (CG). Volumes were then computed. We report the L and R cingulate volumes from the coronal slices extending the length of the corpus callosum. Schizophrenics (LCG = 6.59 ± .23 ml; RCG = 6.56 ± 1.9 ml) have smaller cingulate volumes than controls (LCG = 6.76 ± .31 ml; RCG = 6.89 ± .31 ml), with the size difference being more pronounced in the R hemisphere. Normal males (LCG = 6.67 ± .43 ml; RCG = 7.16 ± .48 ml) have larger cingulate volumes than control females (LCG = 6.36 ± .67 ml; RCG = 6.03 ± .60 ml), with the disparity being greater in the R hemisphere. This inequality also exists between schizophrenic males (LCG = 6.86 ± .40 ml; RCG = 6.66 ± .29 ml) and schizophrenic females (LCG = 6.32 ± .21 ml; RCG = 6.46 ± .27 ml), although the difference is not as pronounced as that in the controls ($F(1,46) = 4.47$, $p < .0399$). These abnormalities may contribute to a disruption in projections to other areas of the limbic system, as well as to the cerebral cortex. This work was supported by NIMH grants MH15442 and MH47476.

NR609 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

The Thalamus in Schizophrenia: Failure to Replicate Reduced Volume

David B. Arciniegas, M.D., Department of Psychiatry, University of Colorado, 4200 E Ninth Ave/Box C 268-68, Denver CO 80262; Jeanelle Sheeder, B.A., Donald C. Rojas, Ph.D., Peter Teele, M.S.E.E., Martin L. Reite, M.D.

Summary:

Thalamic abnormalities resulting in impaired attention and information processing have been suggested to form a foundation for schizophrenic symptoms. Measurements of the thalamus in patients with schizophrenia have shown significantly reduced volumes when compared to normal control subjects (Flaum *et al.*, 1995; Andreasen *et al.*, 1994; Andreasen *et al.*, 1990). If consistent across multiple samples of schizophrenic patients, these results would suggest a necessary role for thalamic abnormalities in the production of the schizophrenic phenotype.

In the current project, magnetic resonance images of the brain were obtained in 51 subjects: 11 males and 11 females with paranoid-type schizophrenia, and 16 male and 13 female normal control subjects. 1.7 mm thick T1-weighted images were obtained through the entire head. Using a locally-designed, semi-automated, manual segmentation routine, the entire brain volume was calculated. Right and left thalami were manually segmented by the first author, who was blind to subject. In analysis of the data, thalamic volume was expressed as a percent of total brain volume in order to avoid interpreting differences arising from variability in total brain volume as actual inter-group thalamic volume differences. Volumetrically, we found no significant diagnostic group or gender differences in thalamic volumes.

These results suggest previously reported thalamic volume reductions are probably not of sufficient magnitude or consistency among all schizophrenic patients to parsimoniously explain the schizophrenic phenotype. Rather, the previously reported differences may be best understood as reflecting one of several contributory but not necessary structural abnormalities producing the schizophrenia phenotype.

NR610 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Predictors of Suicidality in Schizophrenia

Naveed Iqbal, M.D., Department of Psychiatry, Montifore Medical Center, 111 East 210th Street, New York NY 10467; Bruce J. Schwartz, M.D., Edward McGraw, B.A., Stephen Daniel, Ph.D., Syed R. Ahmed, M.D., Faiq A. Hameedi, M.D.

Summary:

Approximately 55% of all schizophrenic patients make at least one suicide attempt in their lifetime and 10% of them successfully commit suicide. Serious suicidal ideation and auditory hallucinations have been reported to be common in depressed schizophrenics. The evaluation of various risk factors for suicide is essential for proper management and treatment of these patients.

The objective of this study is to evaluate risk factors that may be predictive of suicidality in patients with schizophrenia. A sample of 80 patients with a history of schizophrenia were administered the Positive and Negative Syndrome Scale (PANSS), the Suicide Risk Scale (SR), the Impulse Control Scale (ICS), the Past Feeling and Acts of Violence Scale (PFAV), the Harkavy-Asnis Suicide Survey (HASS), and a scale measuring depression (PVP-II).

Within the sample 27% ($n = 21$) of the patients had a history of at least one suicide attempt, and 47% ($n = 37$) had a history of suicidal ideation. Suicide risk was significantly correlated with depression ($r = .68$, $p < .001$), impulsivity ($r = .51$, $p < .001$), aggression ($r = .39$, $p < .001$), anxiety ($r = .27$, $p < .02$), and hallucinations ($r = .26$, $p < .02$). The relationship between depression and hallucinations in increasing the risk for suicide in schizophrenic patients will be discussed.

NR611 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Working Memory Dysfunction in Schizophrenics

Eduardo A. Leiderman, M.D., Department of Psychiatry, Pinero Hospital, Scalabrini Ortiz 3078 6 B, Buenos Aires 1425, Argentina; Sergio A. Strejilevich, M.D., Carlos A. de Lajonquiere, M.D.

Summary:

Objective: There is evidence of spatial working memory dysfunction in schizophrenics that is associated with dorsolateral prefrontal cortex (Brodmann's area 47) pathology. However, working memory deficits that involve other brain regions have been described. The purpose of this study is to examine if schizophrenics show object nonspatial working memory deficits.

Method: Ten schizophrenics and 10 controls with no significant differences in age or educational level participated in this study consisting of one trial in which two nongeometrical figures were presented on a computer screen simultaneously (nondelay condition) and trials with 5 and 30 seconds delay between figure presentation. The subjects had to determine if both figures were identical or not. Distractor tasks were used during the delay.

Results: There were no significant differences in the nondelay condition. Both groups were less accurate on the delay conditions with almost no additional fall on the 30 seconds delay. The accuracy decrease on the 5 seconds delay condition was significantly higher in schizophrenics than in controls ($t = -2.35$, $p = 0.035$).

Conclusions: Schizophrenics have an object working memory dysfunction. This defect may occur principally in the encoding component of the memory process.

NR612 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Tolerability and Cardiovascular Safety of Risperidone

Martin B. Brecher, M.D., Janssen Research Foundation, 1125 Trenton-Harbouton Road, Titusville NJ 08560; Philippe Lemmens, Ph.D., Bart van Baelen

Summary:

Combined data on severity of extrapyramidal symptoms (EPS) from 12 double-blind trials, in which 2,074 patients with chronic schizophrenia received risperidone, were analyzed. Factors associated with increased severity of EPS were increasing dose, lower baseline ESRS scores, and longer duration of psychotic symptoms. EPS severity was greater in patients receiving haloperidol or other antipsychotics than in those receiving risperidone (4–8 mg/day) or placebo. Only four cases of tardive dyskinesia were reported in 3,298 patients participating in 27 trials of risperidone (probability, 0.0034 per treatment year). Data from three short-term, double-blind studies (N = 1,885) and seven long-term studies (N = 1,156) indicate that mean QTc changes in patients receiving risperidone were negative or minimally positive. QT_c changes were similar in patients receiving risperidone, placebo, and haloperidol.

NR613 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

A Study of Treatment Outcome Comparing Dysthymia and Nondysthymia Diagnoses in Brief Psychotherapy

Lisa Wallner Samstag, M.A., Department of Psychiatry, Beth Israel Medical Center, First Avenue & 16th Street, New York NY 10003; David J. Hellerstein, M.D., J. Christopher Muran, M.D., Arnold Winston, M.D.

Educational Objectives:

To describe results of an outcome study comparing dysthymia and nondysthymia patients in brief psychotherapy; to identify significant features of poor treatment efficacy in a population of patients with dysthymia.

Summary:

Objective: We attempted to determine the effect of DSM-III-R dysthymia upon treatment retention and outcome in a variety of forms of brief psychotherapy.

Method: 85 subjects had been treated in a 30-session protocol of manualized individual psychotherapy, having been randomly assigned either to cognitive-behavioral, psychodynamic, interpersonal-experiential, or supportive psychotherapy. Patients were not concurrently treated with psychotropic medications. Forty patients met criteria for dysthymia, whereas a comparison group of 45 subjects met criteria for Axis I disorders other than dysthymia.

Results: Overall outcome was significantly poorer for patients in the dysthymia group than for the comparison group. Significantly more patients in the dysthymia group (53%) than in the comparison group (27%) did not complete the 30-session protocol ($X2 = 5.95$, $df = 1$, $p < .05$). An analysis of pre- and post-therapy scores for treatment completers indicated that significantly more patients within the comparison group (64%) improved their level of functioning following therapy so that their SCL-90R scores fell within the range of the normal population (Fisher = 3.43, $df = 1$, $p < .05$), vs. only 18% of patients in the dysthymia group. There was no significant difference between groups on the IIP.

Conclusions: Findings suggest that brief psychotherapy may not be effective in dysthymia when treatment is not specifically focused on relieving symptoms of chronic depression. In contrast, Markowitz suggests in an uncontrolled study that individual interpersonal therapy specifically focused on alleviating symptoms of dysthymia may lead to positive outcome without medication.

References:

1. Markowitz J: Psychotherapy of dysthymia. *Am J Psychiatry* 151:1114–1121, 1994.

2. Weirzbicki M, Pekarik G: A meta-analysis of psychotherapy drop-out. *Professional Psychology: Research and Practice.* 24:190–195, 1993.

NR614 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

OCD, Response to SSRIs and the Serotonin Transporter Gene

Margaret A. Richter, M.D., Neurogenetics, Clarke Institute of Psych, 250 College Street R-31, Toronto ON M5T 1R8, Canada; James L. Kennedy, M.D., Elizabeth Billett, B.Sc., A. Heils, Ph.D., K. Peter Lesch, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to understand the rationale for genetic etiology in OCD, the methods of genetic association studies, and the potential importance of the serotonin transporter gene as a risk factor in OCD.

Summary:

Obsessive-compulsive disorder (OCD) is a common illness, characterized by anxiety-provoking thoughts and the need to perform rituals. OCD is most commonly treated with serotonin reuptake inhibitors (SRIs), which block the reuptake of serotonin (5-HT) into the presynaptic neuron, a process mediated by the serotonin transporter (5-HTT). The successful use of SRIs in OCD has led to the hypothesis that the 5-HTT may play a pivotal role in the pathogenesis of OCD. We tested this hypothesis from a genetic perspective, based on evidence from family and twin studies. The 5-HTT gene has a 44bp insertion/deletion polymorphism in the promoter region. There is evidence that this polymorphism alters expression of the transporter protein. We typed 72 OCD patients and 72 matched controls, and found no statistically significant difference between the two groups (Chi-square = 4.319; $p = 0.115$; 2df). We observed, however, a trend ($p = 0.066$) towards increased homozygosity in the patient group. We also rated response to SRIs in 78 patients (57 responders; 21 nonresponders). No association was observed between response and the polymorphism in the 5-HTT gene ($p = 0.63$). Given the pharmacological evidence favoring a role for 5-HTT in SRI response, further genetic evaluation of the serotonin transporter in OCD is indicated.

References:

1. Richter MA, Summerfeldt LJ, Joffe RT, Swinson RP: The tridimensional personality questionnaire in obsessive compulsive disorder. *Psychiatry Res* (in press).

2. Lesch KP, Bengel D, Heils A, et al: Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. *Science* 274:1527–1530, 1996.

NR615 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

CCK-B Receptor Gene Alleles Associated with Panic Disorder

James L. Kennedy, M.D., Neurogenetics, Clarke Institute, 250 College Street, Toronto ON M5T 1R8, Canada; Diana Koszycki, Ph.D., Martin A. Katzman, M.D., Nicole A. King, B.Sc., Jacques Bradwejn, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to understand the rationale for genetic etiology for panic disorder, the methods of genetic association studies, and the potential importance of the CCK-B receptor gene in panic disorder.

Summary:

Twin and family studies strongly suggest a genetic etiology for panic disorder (PD). The CCK-B receptor has been hypothesized to play a role in neurobiology of panic attacks. CCK-B receptor agonists reliably induce panic attacks in humans, and PD patients show an enhanced sensitivity to these agonists. Furthermore, CCK-B receptor antagonists decrease response to CCK-B agonists in PD and normals. We therefore examined a genetic polymorphism in the CCK-B receptor gene in 99 DSM-IV PD patients and 99 controls closely matched for ethnic background. The CA repeat length alleles of the CCK-B receptor gene were typed using PCR, with *a priori* collapse from 16 into four categories. The PD patients versus controls showed a significant increase in the allele 5–8 category (chi-sq = 13.8; df = 3; p = 0.004) and an all-allele analysis with df = 15 yielded chi-sq = 26.02; p = 0.038. PD patients showed an excess of alleles 6 and 7, with odds ratios of 2.3 and 1.7, respectively. While these results need to be replicated, they support the hypothesis that CCK-B receptors are involved in the neurobiology of PD. This CCK-B gene polymorphism is neither necessary nor sufficient for the disorder, but may be associated with an important genetic risk modifying factor.

References:

1. Harro J, Vasar E, Bradwejn J: Cholecystokinin in animal and human research on anxiety. *Trends in Pharmacological Sciences* (TIPS) 14:244–249, 1993.

2. Crowe RR, Noyes R, Pauls DL, Slymen D: A family study of panic disorder. *Archives of General Psychiatry* 40:1065–1069, 1983.

NR616 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

Identification of a Putative Alzheimer's Disease Risk Locus on the X-Chromosome

George S. Zubenko, M.D., Department of Psychiatry, WPIC, 3811 O'hara Street/Rm E-1230, Pittsburgh PA 15213–2593; J. Scott Stiffler, B.S., Hugh B. Hughes, M.S., Mark R. Hurtt, M.D.

Educational Objectives:

To gain a perspective on the genetics of Alzheimer's disease; to better appreciate the methods used to detect genetic loci that contribute to the risk of developing Alzheimer's disease; and to review the evidence for the identification and characterization of a putative Alzheimer's disease risk locus on the X-chromosome.

Summary:

The four identified AD susceptibility loci, *APP, PSN1, PSN2* and *APOE*, account for about half of the genetic etiology in AD, indicating that loci having an important impact on the risk of AD remain to be identified. These unidentified loci are likely to contribute primarily to AD cases with typical ages at onset, whose inheritance is multifactorial and heterogeneous. This report describes the initial results of a genomic survey for highly informative DNA polymorphisms (SSTRPs) that exhibit an association with typical-onset AD compared with nondemented controls matched for age at death, gender, and race. To maximize diagnostic accuracy, only histopathologically confirmed AD cases were used and AD cases with other concurrent brain diseases were excluded. Autopsy controls were required to manifest few or absent senile plaques to exclude cases of AD "in evolution."

A novel genome screening approach was developed to achieve this task with considerable economy of effort. After first validating this method using the *APOE* locus as a model, we initiated our survey using SSTRPs that span the X chromosome at an average spacing of 10 cM. An approximate doubling in the allelic frequency of one of these anonymous polymorphisms was observed among 50 AD cases (0.45 ± SE 0.06) compared with 50 autopsy controls (0.22 ± SE 005; $\chi^2 = 8.53$, df = 1, p = 0.003), and a group of 50 nondemented subjects over age 90 (0.27 ± SE 0.05; $\chi^2 = 5.40$, df = 1, p = 0.02). The frequency of this allele among patients with AD was unaffected by the presence or absence of the *APOE* $\epsilon 4$ allele, indicating that the association of the newly identified locus with AD was independent of this *APOE* genotype. These results suggest that this SSTRP may identify the first AD risk locus on the X chromosome.

References:

1. Pericak-Vance MA, Haines JL: Genetic susceptibility to Alzheimer's disease. *Trends Genet* 11:504–508, 1995.

2. Schellenberg GD: Progress in Alzheimer's disease genetics. *Curr Opinion Neurol* 8:262–267, 1995.

NR617 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

Late-Life Depression and Service Use in Primary Care

Barnett S. Meyers, M.D., Department of Psychiatry, NY Hospital-Cornell, 21 Bloomingdale Road, White Plains NY 10605; M. Philip Luber, M.D., Mary E. Charlson, M.D., Pamela G. Williams-Russo, M.D., Tara DiDomenico, M.A., James Hollenberg, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize that depression is associated with both increased medical comorbidity and greater services use in elderly medical outpatients. However, the relationship between depression and greater health services use persists after controlling for comorbidity.

Summary:

This study assesses relationships between a diagnosis of depression, medical comorbidity, and use of medical services in elderly patients served by a university-based internal medicine practice.

Methods: Clinical and demographic information was analyzed on patients age 65 and older using a computerized medical database that systematically records reasons for visits, medications prescribed, and health services utilized. Services use in patients with identified depression was compared with that for patients without depression.

Results: Of the 15,126 practice patients, 3,481 (23%) met the age criterion for inclusion. Only 182 of these individuals (5%) had diagnoses of depression recorded during the study year. Depressed and nondepressed patients were of comparable age (74.5 ± 7.1 versus 74.9 ± 7.5), but depression was associated with significantly higher Charlson comorbidity scores and number of recorded diagnoses. Patients with depression were also prescribed a greater number of medications (14.2 ± 9.8 versus 10.2 ± 9.8) and had a greater number of clinic appointments (6.3 ± 5.2 versus 3.9 ± 3.3) than patients without depression. Regression analyses revealed that a diagnosis of depression and higher comorbidity scores were independently associated with both number of appointments and number of medications prescribed.

Conclusion: Depression is associated with both increased medical comorbidity and greater services use in elderly medical outpatients. However, the relationship between depression and greater health services use persists after controlling for comorbidity.

References:

1. Callahan CM, Hui SL, Nienaber NA, et al: Longitudinal study of depression and health services use among elderly primary care patients. *JAGS* 42:833–838, 1994.

2. Koenig HG, Shelp F, Goli V, et al: Survival and health care utilization in elderly medical inpatients with major depression. *JAGS* 37:588–606, 1989.

NR618 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

Donepezil (E2020) Improves Cognition and Function in Patients with Mild to Moderately Severe Alzheimer's Disease: Results from Phase III Trials

Sharon L. Rogers, Ph.D., Clinical Research, Eisai America Inc., 300 Frank W. Burr Boulevard, Teaneck NJ 07666; Richard C. Mohs, Ph.D., Lawrence T. Friedhoff, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe how donepezil produces a highly significant improvement in cognitive and global function in the absence of significant adverse events or laboratory test abnormalities, and demonstrate clear clinical benefits of donepezil in the treatment of Alzheimer's disease.

Summary:

Objective: To evaluate the safety and efficacy of donepezil in 941 patients with mild to moderately severe Alzheimer's disease (MMSE 10–26, CDR 1 or 2).

Method: One 15-week and one 30-week randomized, double-blind, placebo-controlled study in which 626 patients received donepezil (311 at 5 mg/day, 315 at 10 mg/day) and 315 patients received placebo once daily for 12 or 24 weeks followed by single-blind placebo washout periods, for three and six weeks, respectively. *Safety*: Physical examination, vital signs, laboratory values. *Primary efficacy*: ADAS-cog and CIBI-C (Plus version).

Results: Donepezil was well tolerated at both 5 mg and 10 mg doses with no significant difference between treatment and placebo groups in the overall incidence of adverse events or laboratory abnormalities. Occasional cholinergic adverse events were mild in severity, transient (1–2 days), and resolved during continued donepezil treatment. Highly statistically significant improvement, compared to placebo, was obtained in both treatment groups on measures of cognition (ADAS-cog; $p < 0.0001$) and function (CIBIC-plus; $p \leq 0.006$).

Conclusion: Donepezil produced a highly significant improvement in cognitive and global function in the absence of significant adverse events or laboratory test abnormalities, thus demonstrating clear clinical benefits of donepezil in the treatment of Alzheimer's disease.

References:

1. Rogers SL, Friedhoff LT: The efficacy and safety of donepezil in patients with Alzheimer's disease: results from a multinational, randomized, double-blind, placebo-controlled trial. *Dementia* 7:293–303, 1996.

2. Rogers SL, Doody R, Mohs R, Friedhoff LT: E2020 produces both clinical global and cognitive test improvement in patients with mild to moderately severe Alzheimer's disease (AD): results from a 30-week phase III trial. *Neurology* 46:A217(S14.001), 1996.

NR619 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

Homicidal Behavior and Schizophrenia in Finland

Markku E.J. Eronen, M.D., Forensic Psychiatry, University of Kuopio, Niuvanniemi Hospital, Kuopio 70240, Finland; Pirkko Rasanen, Ph.D., Panu Hakola, Ph.D., Jari Tiihonen, Ph.D.

Educational Objectives:

To assess the motives of the schizophrenic homicide offenders and to estimate the risk associated with schizophrenia and homicides.

Summary:

Objectives: The aim of the study was to assess the motives of the schizophrenic homicide offenders and to estimate the risk associated with schizophrenia and homicides.

Methods: Between 1984 and 1995, 1614 murders and manslaughters were committed in Finland. The police were able to solve 1546 (95.8%) of these homicides. In 1039 cases the homicide offenders were subjected to intensive forensic psychiatric examination, and 100 of these offenders suffered from schizophrenia. Our study is based on the forensic psychiatric reports of these offenders.

Results: Calculation of the odds ratios revealed that the risk of committing a homicide was about five times greater for schizophrenics than it was for the general population. Delusions or hallucinations were the motives for killing in 52 cases; in 20 cases the offenders were delusional or hallucinating, but their symptoms were not clear motives for their violence. There were 19 cases in which no acute psychotic symptoms were reported at the time of the offense, and in nine cases the data were missing. About half of the offenders ($n = 52$) were under the influence of alcohol or drugs while offending.

Conclusions: Schizophrenia appears to have a statistical association with homicidal behavior in Finland, a country with a relatively low crime rate. Although most of the homicides committed by the schizophrenics were associated with delusions or hallucinations, about 20% of schizophrenic homicides were not motivated by acute psychotic symptoms.

References:

1. Eronen M, Hakola P, Tiihonen J: Mental disorders and homicidal behavior in Finland. *Arch Gen Psychiatry* 53:497–501, 1996.

2. Eronen M, Tiihonen J, Hakola P: Schizophrenia and homicidal behavior. *Schizophr Bull* 22:83–89, 1996.

NR620 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

A Sixth-Month Parasuicide Prospective Study in the Emergency Room of a French General Hospital

Francoise Chastang, M.D., Centre Psych Esquirol, C.H.R.U. Cote de Nacre, 14033 Caen, France; I. Dupont, Patrice Rioux, M.D., V. Kovess, E. Zarifian

Educational Objectives:

Parasuicide has been identified as a major public health problem in many European countries. Higher parasuicide rates are found in the younger age group, and more than 50% of the suicide attempters make more than one attempt. Repetition of suicidal behavior substantially contributes to the overall incidence and increases the probability of fatal outcome. The aims of this study are to compare self-attempters with other psychiatric patients, first-attempters with suicidal repeaters, and to investigate the risk factors associated with suicidal behavior.

All patients ($n = 1073$; females = 57%; males = 43%; mean age = 37 ± 0.9) who visited the emergency psychiatric unit during the period from December 6, 1993, to June 5, 1994 were evaluated by a questionnaire. Demographic data, individual and family characteristics, and diagnoses were collected. Univaried and logistic regression analyses were used.

A total of 52% of the patients were self-attempters, significantly younger (mean age = 34 ± 1) and more frequently females (61%); parasuicides were found more frequently in their families and in their personal history. Also, 54% of self-attempters were suicidal repeaters; there were more depressive disorders, parasuicides,

and alcohol/drug abuse in their families. The logistic regression analysis revealed the role of these factors in the repetition of parasuicide. In view of their personal and family history, we may understand the repetition of parasuicide as a response to problems or crisis.

NR621 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

PTSD in Survivors of Rwanda's 1994 War

Athanase Hagengimana, M.D., International Medicine, National University of Rwanda, BP 30, Butare, Rwanda; John Mburu, M.D., Rachel Kangethe, M.D., David Ndetei, M.D., Lawson R. Wulsin, M.D.

Educational Objectives:

To understand the relationship between the prevalence of PTSD and exposure to trauma during the 1994 civil war in Rwanda; to understand the methodological constraints on investigations of psychopathology in Rwanda and other areas of conflict.

Summary:

No previous studies have examined the frequency of post-traumatic stress disorder (PTSD) in survivors of the 1994 genocide and massacres in Rwanda. In a random sampling survey carried out in four regions of Rwanda, July through December 1995, we assessed the frequencies of PTSD and other DSM-IV psychiatric disorders related to exposure to trauma during the 1994 war, using the Standardized Psychiatric Interview and the Harvard Trauma Questionnaire.

Among the sample of 157 citizens aged 8-60, 97% had lost a relative or close friend during the war. The average number of traumatic events experienced by each survivor was 15. Fifty percent (79/157) met criteria for a psychiatric disorder. The most common disorders were grief reaction (24.8%), major depression (22%), PTSD (20.3%), and drug abuse (17%). Four traumatic events were significantly related to the diagnosis of PTSD: forced isolation ($X^2 = 14.98$, $p = .001$), helpless witnessing of atrocities ($X^2 = 8.96$, $p = .02$), rape ($X^2 = 9.96$, $p = .01$), and loss of parents ($X^2 = 16.78$, $p = .0002$).

This preliminary survey suggests that rates of psychopathology among Rwandese survivors of the 1994 war may be higher than rates reported in other studies of trauma survivors. If confirmed, these high rates may raise the rehabilitation priority for psychological disorders in Rwanda. Our study points to the need for a more comprehensive epidemiologic survey of a larger sample to better represent the Rwandan population and to identify high-risk groups for rehabilitation.

References:

1. United Nations High Commission on Refugees: *1995 Report on Rwanda*. World Health Organization, Geneva, 1996.

2. Van der Kolk B: *Psychological Trauma*. American Psychiatric Press, Washington, DC, 1987.

NR622 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

Mental Disorders in a French Follow-Up Study of Rape Victims

Jean-Michel Darves-Bornoz, M.D., Psychiatry, Hopital Universitaire, Clinique Psychiattrique Univ, Tours Cedex 37044, France; Fabrice Pierre, M.D., Christian Berger, M.D., Jacques Lansac, M.D., Andree DeGiovanni, M.D., Philippe Gaillard, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe how in the aftermath of rape several semiologically distinct psychotraumatic syndromes exist.

Summary:

Trauma clinicians are familiar with the life and psychological difficulties of rape victims, but their observations are often refuted as being retrospective and unsystematic.

This study took place in a French forensic center for rape victims. Our aims were to explore the longitudinal course of post-traumatic stress disorder (PTSD) and the prevalence of the disorders over the six-month period following rape, then to group these disorders into syndromes related to but distinct from chronic PTSD. We also aimed to establish some predictive factors for chronic PTSD. Ninety-two rape victims consecutively admitted to the center were regularly interviewed over a six-month period by a psychiatrist using structured interview schedules (ADIS, SI-PTSD, SCID-D) and a clinical questionnaire.

The study confirmed that rape leads to a high proportion of PTSD. Generally speaking, the psychopathology following rape is severe. PTSD at six months is associated with phobic and dissociative disorders. It is further associated with a cluster of symptoms arising after rape that we term borderline-like. Incestuous rape is a predictive factor for PTSD at six months.

We conclude that in the aftermath of rape several semiologically distinct psychotraumatic syndromes exist.

References:

1. Darves-Bornoz JM, et al: Why is dissociative identity disorder infrequent in France? *Am J Psychiatry* 152:1530-31, 1995.

2. Darves-Bornoz JM, et al: Rape-related psychotraumatic syndromes. *Européan Journal of Obstetrics and Gynecology* (in press).

NR623 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

The Relationship Between PTSD and Trauma-Related Disorders and Symptomatology Among Incarcerated Women

Caron Zlotnick, Ph.D., Department of Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence RI 02906

Educational Objectives:

Participants should be able to understand the mental health needs of incarcerated women with PTSD and histories of trauma. Also, participants should be able to demonstrate knowledge concerning recent formulations of PTSD, associated features of PTSD, and the sequelae of childhood abuse.

Summary:

Objective: Although prior studies have shown that the majority of women in jail have been exposed to trauma, research on the mental health needs of these women is virtually nonexistent. The overall purpose of the present study was to identify the specific psychiatric impairments of incarcerated women with PTSD and histories of trauma.

Method: Using structured diagnostic interviews, incarcerated women were randomly selected and assessed for five DSM-IV psychiatric disorders, as well as for current levels of affect dysregulation, dissociative experiences, and somatization. Data on childhood abuse and maltreatment were collected.

Results: Subjects with current PTSD (N = 41) and lifetime PTSD (N = 17) compared with those without PTSD (N = 27) had significantly higher odds of meeting criteria for disorders of major depression ($\chi 2 = 12.22$, $\beta = -0.52$, $p = 0.0005$), lifetime substance use ($\chi 2 = 7.21$, $\beta = -0.34$ $p = 0.007$), and borderline personality disorder ($\chi 2 = 8.15$, $\beta = -0.41$, $p = 0.004$) compared with those without PTSD. Further, subjects with PTSD obtained significantly higher scores on measures of affect dysregulation ($t = 6.95$, $df = 2, 83$, $p = 0.0001$), dissociation ($t = 6.24$, $df = 2, 83$, $p = 0.0001$), and somatization ($t = 5.63$, $df = 2, 83$, $p = 0.0001$) than those without PTSD. In addition, an index of childhood abuse and maltreatment

was significantly related to PTSD and to a greater degree of affect dysregulation, dissociation, and somatization.

Conclusions: Incarcerated women with PTSD present with a range of mental health problems associated with the sequelae of trauma, especially of childhood trauma.

References:

1. Jordan BK, Schlenger WE, Fairbank JA, Caddell JM: Prevalence of psychiatric disorders among incarcerated women. II: convicted felons entering prison. *Arch Gen Psychiatry* 53:513-519, 1996.

2. van der Kolk BA, Pelcovitz D, Roth S, et al: Dissociation, somatization, and affect dysregulation: the complexity of adaptation to trauma. *Am J Psychiatry* 153:83-93 (Festschrift Supplement), 1996.

NR624 Thursday, May 22, 9:00 a.m. - 10:30 a.m.

Correlates of ADHD in the Quebec Child Mental Health Survey

Philippe Lageix, Eating Disorders, Douglas Hospital, 6875 Lasalle Boulevard, Verdun QC H4H 1R3, Canada; Lise Bergeron, Ph.D., Jean-Marie Honorez, Ph.D., Jean-Pierre Valla, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe how the Quebec Child Mental Health Survey shows that an intra-informant bias may exist when the diagnosis is based on parents' responses, but that some correlates remain stable across informants.

Summary:

The Quebec Child Mental Health Survey (QCMHS) is an epidemiological study of a representative sample (N = 2,400) of children and adolescents in the province of Quebec, Canada. Youths' DSM-III-R diagnoses were obtained from parents, children, adolescents, and teachers for children under age 12. Correlates were parent-based. So far, a first set of bivariate analyses have been performed according to informant and two age groups (6-11, 12-14). As for child and adolescent ADHD (parent-based N=116), a number of correlates were evaluated: age, group and gender, physical illness, school difficulties, various life events and their accumulation, single parenting, being an only child, parents' depression and anxiety, parents' stressful events, the frequency of parents' punitive behavior, and other parent-child relationship constructs.

While many correlates of DSM-III-R diagnoses found in the QCMHS merely confirmed results from other surveys, several had rarely been researched in general population epidemiological studies (e.g., parents' stressful events, conjugal relationship, or the child's social competencies) and some had never been mentioned (e.g., being an only child, parent/child relationships). The QCMHS also showed that an intra-informant bias may exist when the diagnosis is based on parent's responses, but that some correlates remain stable across informants.

References:

1. V̊ıl̊ JP, Bergeron L, Lageix P, Breton JJ: *L'étude épidémiologique des variables associées aux troubles mentaux des enfants et des adolescents* Paris: Masson, 1996.

2. Valla JP, Breton JJ, Bergeron L, et al: *Enquête québécoise sur la santé mentale des jeunes de 6 à 14 ans 1992. Rapport Synthêse,* Services d'Editions Interressources, 1994.

NR625 Thursday, May 22, 12 noon - 2:00 p.m.

Clinical Correlates of Mental Retardation in a County Hospital's Psychiatric Emergency Room

Shashi Berdia, M.D., Department of Psychiatry, Nassau City Medical Center, 2201 Hempstead Turnpike Bldg J, East Meadow NY 11554; David I. Mayerhoff, M.D., Jacob K. Ninan, M.D.

Summary:

Objective: To assess the effects of the level of mental retardation (MR) severity, comorbid Axis I and III diagnoses, and violent behavior on admission, discharge, and readmission of MR subjects to the psychiatric ER.

Method: Charts were reviewed on all the MR subjects admitted to a county hospital psychiatric ER over a 13-month period (12/1/93-12/31/94). Specifically, key data on the subjects' nursing and psychiatric assessments, treatment and final outcome, and admission and/or nonadmission to the hospital were extracted from the ER chart.

Results: Sixty-eight charts were reviewed (46 mild or moderate, 22 severe or profound mental retardation). Thirty-five of the 68 subjects were subsequently admitted to the hospital from the ER. Forty-six of the 68 subjects demonstrated mild or moderate levels of MR of whom 18 were admitted to the hospital and 28 were discharged from the ER. In comparison, of the 22 subjects with severe or profound MR, 17 were admitted and five were discharged ($p < 0.01$). Of the 37 subjects who demonstrated violent behavior, 16 were admitted and 21 were discharged, while of the 31 with nonviolent behavior five were admitted and 26 were discharged ($p < 0.05$). Sixteen of the 68 subjects did not carry an Axis I diagnosis and all of these were discharged. Of the 52 that carried an Axis I diagnosis, 33 were discharged and 19 were admitted ($p < 0.01$). Thirty-five of 68 subjects were readmitted to the ER following discharge.

Conclusion: These results demonstrate a significant association between level of severity of MR (i.e., severe/profound MR) and admission to a psychiatric hospital after presentation at the ER. Similar positive associations were found between violent behavior and admission, as well as between comorbid Axis I diagnosis and admission from the ER.

NR626 Thursday, May 22, 12 noon - 2:00 p.m.

Risperidone in the Treatment of Gilles de la Tourette's Syndrome

Mara Stamenkovic, M.D., Department of Psychiatry, University Hospital, Wahringergurtel 18-20, Vienna 1090, Austria; Shird Schindler, M.D., Harald Aschauer, M.D.

Summary:

Objective: The treatment of Gilles de la Tourette syndrome (GTS), a neuropsychiatric disorder that is characterized by the occurence of motoric and vocal tics, is often unsatisfactory. The etiopathogenesis is still unclear, but there are theories about the involvement of neurotransmitters such as D2, 5-HT 2, and alpha-2 adrenoreceptors. Risperidone is a new neuroleptic drug that has a high affinity to dopamine-(D)2 and serotonin (5HT) 2 receptors and a lower affinity to alpha-2 adrenoreceptors. In 1994 we published a case report of risperidone in the treatment of a GTS patient. Van der Linden et al. (1995) published the results of an open pilot study using risperidone in 10 GTS patients. Both investigations showed an amelioration of GTS symptoms. The goal of our investigation was to confirm these preliminary observations.

Methods: We included nine patients (two female/seven male) with an average age of 35 years (± 12.64) over seven weeks, who did not respond to or did not tolerate previous neuroleptic treatments. All patients received risperidone in ascending dosage,

following a washout period of one week. Initial dosage was 2 mg/d with a maximum dosage of 12mg/d. The following rating scales were used: Yale Global Tic Severity Scale (YGTSS), Yale-Brown Obsessive Compulsive Scale (YBOCS), Fischer Somatic and Unwanted Effects Check List (FSUCL), Extrapyramidal Symptom Scale (EPS), and the Clinical Global Impressions (CGI). All scales were assessed at day: –7, 0, 3, 14, 28, 42, 56. Statistical analysis was done using the repeated measurements ANOVA.

Results: Four of nine patients did not finish the study. One patient stopped taking the medication after 14 days because of a general distrust of all medication, the other patient had a history of opiate abuse and had a relapse at day 17. The other two patients dropped out because of side effects, one after 28 days because of akathisia and the other after three days because of drowsiness. At day 14 of treatment with risperidone 4mg/d tic symptomatology (YGTSS) ameliorated ($p < 0,001$), OCD symptomatology (YBOCS) decreased ($p < 0.05$), and CGI improved ($p < 0.001$). At day 56 (end of study) patients received a mean dosage of 7.3 mg/d. At this time point all patients except the four dropouts ameliorated at least 60% of baseline (YGTSS) score.

Conclusion: In our study we found that risperidone was a safe and effective treatment alternative in patients who previously did not respond to or did not tolerate "classical" neuroleptic drugs. In order to confirm these preliminary results it seems necessary to conduct double-blind placebo-controlled trials.

NR627 Thursday, May 22, 12 noon - 2:00 p.m.

How to Diagnose and Treat ADHD in Children and Adults

Sanjay Jasuja, M.D., Stanford Profess Area, CA Institute of Behav Sciences, 701 Welch Road, #203, Palo Alto CA 94304-1709

Summary:

Introduction: Attention-deficit/hyperactivity disorder is a complex condition that has been treated in children for more than 30 years. Contrary to the past belief that children outgrow ADHD/ADD when they reach adolescence, current research shows that only one-third of these cases may outgrow it, the remainder will continue to have it for the rest of their life. There is a question whether ADD is being overdiagnosed or underdiagnosed. Diagnosis and treatment of this disorder is complex.

Purpose: The purpose of this presentation is to present and discuss ways to diagnose and treat ADD in children and adults. The presenter will share his extensive experience using various diagnostic techniques, including the test of the variables of attention or TOVA. The role of comprehensive treatment approach, including, pharmacology, cognitive-behavioral approaches, etc., will be discussed. Current monodrug and polydrug therapies will be presented. Subtle differences in the effects of various stimulants will be pointed out with the aid of bar diagrams from the TOVA. ADD is characterized by difficulties in sustaining attention, easy distractibility, forgetfulness, fidgetiness, history of hyperactivity or hypoactivity during childhood, high impulsivity, impatience, and high emotional reactivity. It is not uncommon for patients to have secondary feelings of anxiety and depression. Comorbidity with bipolar disorder, anxiety disorders, substance abuse, and personality disorders will be discussed. Management of difficult cases will be presented. Diagnostic and pharmacological algorithms and protocols will help to make the discussion of ADD very useful and interesting.

Conclusion: This presentation will discuss current strategies to objectively diagnose and treat ADD in children and adults. Comprehensive treatment approaches, including single and combined psychopharmacology, cognitive-behavioral approaches, etc., will be discussed. Diagnostic algorithms and treatment protocols will also be presented.

NR628 Thursday, May 22, 12 noon - 2:00 p.m.

Self-Perception Profile in Children with Leukemia: Self Versus Parent Report

Valsamma Eapen, Ph.D., Department of Psychiatry, UAE University, PO Box 17666, Al Ain, U. Arab Emirates; Tom Revez, M.D., Chris Mpofu, M.D., Tewfik Daradkeh, M.B.

Summary:

The Self-Perception Profile for Children (SPPC) was administered to 30 consecutive children with leukemia that had been diagnosed in the previous year. Children rated their perception of themselves in the various specific domains of their life, as well as on their sense of global self-esteem and worth. The parent was asked to rate each child's actual behavior and competence using a parallel version of the SPPC, to examine the level of agreement between the child and the parent.

Correlation similarity coefficient revealed excellent agreement between children and their parents in the domains of behavioral conduct (.81) and athletic competence (.81), and moderate agreement on scholastic competence (.65). We noted poor agreement on social acceptance (.45) and physical appearance (.26), where parents rated their children more positively than did the children themselves. This finding is interesting because the child's perception in these two domains is particularly vulnerable to negative affects, given the effects of chemotherapy on physical appearance, and as they view themselves as socially undesirable, or a burden to others.

The implications of this finding for therapeutic intervention to improve self-esteem, and the use of discrepancy score in challenging their negative view will be discussed in the context of cognitive therapy.

NR629 Thursday, May 22, 12 noon - 2:00 p.m.

Obsessive-Compulsive Symptoms in Probands with OCD and Tourette's Syndrome

Valsamma Eapen, Ph.D., Department of Psychiatry, UAE University, PO Box 17666, Al Ain, U. Arab Emirates; David L. Pauls, Ph.D., Mary M. Robertson, M.D.

Summary:

Objective: Cluster analysis was performed to determine whether different constellations of symptoms would differentiate between individuals with obsessive compulsive disorder (OCD) and Gilles de la Tourette syndrome (GTS).

Method: Sixteen individuals each with OCD and GTS, consecutively enrolled from two outpatient clinics, were studied. A two-cluster solution was tested, and analyses were done to determine which of the symptoms were contributing to the inclusion of individual probands into the two separate clusters.

Results: Cluster 1 contained 15 of the 16 GTS probands and seven of the 16 OCD probands ("GTS" cluster). Aggressive obsessions, and compulsions including symmetry, doing things 'just right' and forced touching were more prevalent in "GTS" cluster, while contamination obsessions and washing and cleaning compulsions characterized the second cluster. Membership of OCD probands in the "GTS" cluster was found to be related to familiarity of OCD, with the rate of OCD among relatives of OCD probands in the "GTS" cluster being significantly higher ($p = 0.00009$). A gender difference was noted, with female relatives being more likely to be affected ($p = 0.015$).

Conclusion: The implications of the observed gender difference and the similarity in symptom profile between familial OCD and GTS will be discussed.

NR630 Thursday, May 22, 12 noon - 2:00 p.m.

Impact of Tics on Social Adaptation in Tourette's Disorder

Dinohra M. Munoz, M.D., Department of Psychiatry, Newark Beth Israel, 20 Knickerbocker Road, Tenafly NJ 07670; Raul R. Silva, M.D., E. Steven Dummit III, M.D., Frederick J. Matzner, M.D., Daniel M. Medeiros, M.D., Thomas Hollenbach, Ph.D.

Summary:

Introduction: Patients with Tourette's disorder (TD) often have a host of social difficulties. There have been two reports in the past eight years that looked at social functioning in this population. Systematic evaluation of how different types of tics impact on social adaptation is needed.

Subjects: 35 consecutive patients (25 males, 10 females), aged 9 to 85 (mean, 26.7 ± 16.63), met DSM-III-R criteria for TD. Ethnically: 82.8% were Caucasian, 10.3% Hispanic, and 6.9% Afro-American.

Method: Subjects were systematically assessed during a six-hour interview process. Assessment included the Social Adjustment Scale (SAS) and the Yale Global Tic Severity Scale (YGTSS). We examined the predictive relationships between tic parameters of the YGTSS and social adaptation via the SAS by means of a multiple regression analysis.

Results: In predicting social functioning in work outside the home, greater motor tic frequency predicted greater impairment (Beta = .93; $p < .04$), and poorer adaptation in the social and leisure settings were predicted by the frequency of motor tics (Beta = 1.17; $p < .001$) and number of vocal tics (Beta = .46; $p < .04$). While mean social adjustment scale ratings suggested lower functioning for our TD sample in all but one subscale (family unit) of the SAS, only two subscales yielded significantly lower scores than for the normative population.

Conclusions: In our sample its seems that tic frequency, number, and intensity differentially impact on social adjustment, and motor tics seem to affect functioning in more than one realm.

NR631 Thursday, May 22, 12 noon - 2:00 p.m.

Childhood Sexual Abuse in Medical Students

Barbara A. Warner, M.D., Department of Psychiatry, Wright State University, 37 Rue Laganne #18, Toulouse 31300, France; Jerald Kay, M.D., Ronald J. Markert, M.D., William M. Klykylo, M.D., David G. Bienenfeld, M.D., Paulette M. Gillig, M.D.

Summary:

Objectives: The purpose of the study was to determine the incidence of childhood sexual abuse (CSA) and its correlation with psychiatric symptoms in medical students.

Method: All medical students at a midwestern university (n = 370) were initially mailed a modified version of the Childhood Sexual Experiences Scale (CSES), followed by a second mailing of the modified CSES plus a modified version of the Symptom Checklist-90 (SCL-90).

Results: One hundred sixty-seven responses were received from the initial mailing. The incidence of CSA was nearly the same for women (33%) and men (29%), as was the type of CSA experienced. Eighty-two responses were received from the second mailing. CSA was significantly correlated with an increase in all subscale scores of the modified SCL-90, except the Somatization subscale.

Conclusions: The incidence of CSA in these medical students is higher than that of the general population. Medical students who have experienced CSA are significantly more likely to experience a broad range of psychiatric symptoms than are their nonabused counterparts. Attention in the medical school curriculum to what is taught about sexual abuse and to the sensitivity/empathy with which it is taught is warranted.

NR632 Thursday, May 22, 12 noon - 2:00 p.m.

The Impact of House Officer Rotation on Patient Care

Robert B. Daroff, Jr., M.D., Department of Psychiatry, VAMC, 4150 Clement Street/Box 116C, San Francisco CA 94121-1545

Summary:

Objective: In teaching hospitals, regular rotations of house officers generally create fragmentation and discontinuity of care. At our facility, clinicians normally make efforts to prepare patients for this disruption in care. The objective of this study was to determine if these efforts were sufficient by measuring the impact of house officer rotation on several outcome measures.

Method: The participants included all patients scheduled for one of two weekly psychopharmacology clinics at an urban Veterans Affairs teaching hospital. Eight junior psychiatry residents participate in one of the two clinics in six-month blocks. We measured and compared patient satisfaction, self-reported medication compliance, and no-show rates among patients during the two months before and two months after a July rotation. We used the short form of the Client Satisfaction Questionnaire, modified to include information on medication compliance.

Results: Pooling data from both clinics, 232 out of 376 patients completed the questionnaire, for a response rate of 62%. In both clinics, there were no significant differences in patient satisfaction, self-reported medication compliance, and no-show rates between the periods before and after the July rotation.

Conclusion: The results suggest that with appropriate interventions, the impact of house officer rotation on patient care can be minimized.

NR633 Thursday, May 22, 12 noon - 2:00 p.m.

Schizophrenia or Strangeness Disorder: An Alternative Name

Isaac Charam, M.D., Department of Psychiatry, University Federal Flum, PC Serzdelo Correia 15 AP 703, Rio De Janeiro RT 22060050, Brazil

Summary:

Objective: To facilitate the teaching and diagnosis of schizophrenia, suggesting a didactic new alternative name that is more descriptive and self-evident, as occurs with the name "mood disorder."

Method: We use the dictionaries and historical books of psychiatry to find a new name for the disease.

Results: The best word that is adapted in five languages is the English word STRANGENESS, from STRANGE, the Portuguese ESTRANHO, the French ÉTRANGER, the Italian STRANO and the Spanish ESTRAÑO. The etymology of the five words is the Latin EXTRANEUS, from EXTRA: outside. In German strange is Fremde. The disease causes a reaction of strangeness in people and in the patient himself. Strangeness occurs in all the clinical forms of the disease. In Spanish and Portuguese dictionaries, STRANGENESS and STRANGE signifies: admiration, amazement, astonishment, bizarre, cold, curious, difficult to comprehend, distant, eccentric, erratic, extraordinary, inexplicable, odd, quaint, rare, reserved, singular, unique, unnatural. Other synonyms are also foreign and alien, and then alienated, a significant old word in psychiatry. They are all words that graphically describe the behavior of these patients. In 1903 when Kraepelin coined the term "dementia praecox" he said that it was a "provisorious" reunion of morbid groups. Bleuler, in 1911, said that "unfortunately" he could not create a new name for this morbid group. In DSM-II "hysterical" was changed to "histrionic" due to the

suggestion of women's groups opposed to its original meaning of "wandering uterus". The name that Kraepelin gave to another disease in 1889, manic-depressive insanity, is no longer used. Students of medicine, psychology, or law without knowledge of Greek will have difficulties understanding the meaning of a) paranoid schizophrenia, b) catatonia, c) hebephrenia, and d) simple form of the disease. They could be respectively called a) strangeness delusional-hallucination disorder, b) strangeness incoherence-irresponsability disorder, c) psychomotor strangeness disorder, and d) social impoverishment strangeness disorder.

Conclusion: For didactic use it would be advantageous to have alternatively the new name "Strangeness Disorder" for schizophrenia and its clinical forms. This other name is much more descriptive for the lay person and the patients will come more precociously to the physicians.

NR634 Thursday, May 22, 12 noon - 2:00 p.m.

Integration of Psychiatry: Designing a Problem-Based Medical Curriculum

Mohammed K. Al-Haddad, M.D., Ministry of Health, State of Bahrain P.O. Box 12, Bahrain 00023, Arabian Gulf

Summary:

This paper presents an analysis of a problem-based curriculum in terms of objectives relating to different basic and clinical disciplines. In phase I of the program basic sciences have major input, while psychiatry and other clinical disciplines are better represented in phase II. However, unlike the traditional discipline-based curriculum, the students are exposed to psychiatry as a discipline from the start of training in medicine. Faculty from the department of psychiatry have also contributed to the development of social skills in the early phase of the program. Studies on the effectiveness of this curriculum show a desirable trend.

NR635 Thursday, May 22, 12 noon - 2:00 p.m.

Discrimination in Residency Applicant Selection?

Richard Balon, M.D., Department of Psychiatry, University Psychiatric Center, 2751 East Jefferson, Suite 200, Detroit MI 48207; Rizwan M. Mufti, M.D., Mark T. Williams, M.D., Michelle Riba, M.D.

Summary:

Many health care analysts have warned of a physician glut blaming it on international medical graduates (IMGs). Politicians are not enthusiastic about addressing the overall question of the supply of physicians, including the number of residents. It is possible that medicine has been attempting to address this issue itself. We tested this hypothesis by sending identical requests for residency applications from a USMG and an IMG to 188 psychiatry training programs in the United States. The response rate for the USMG applicant was significantly higher ($p < 0.001$, McNemar's test for paired data). The quality of responses was also different in some cases. Some residency programs in psychiatry are attempting to limit the influx of IMG applicants at the very first level—request for application. The reasons for this practice are not known, but discrimination seems to be a plausible explanation.

NR636 Thursday, May 22, 12 noon - 2:00 p.m.

A Survey of State Financing of Psychiatry Residency Programs

Deborah A. Banazak, D.O., Department of Psychiatry, Michigan State University, B 109 West Fee Hall, East Lansing MI 48824; Jed G. Magen, D.O.

Summary:

With upcoming cuts in graduate medical education funding, it is likely that many psychiatry residencies will be searching for new revenues. State funding of residency programs is one possible avenue. The authors surveyed all ACGME-accredited psychiatry residency programs in order to understand the present dimensions of state funding. Questionnaires were returned from 130 of 200 programs for a 67% response rate. Some programs in both publicly funded and private settings receive large proportions of their budgets from the state. Of all programs in publicly funded institutions responding, 39 programs reported a total residency budget averaging $1,235,378. The average amount received from the state was $598,875. Service commitments are common. Western residency programs had more pessimistic views of state funding, with a higher percentage of programs reporting support as having decreased or remained unchanged. The remaining regions had more increases and more stable state funding responses. State support of psychiatry residency education is an important source of funding at the present time and could be more important in the near future.

NR637 Thursday, May 22, 12 noon - 2:00 p.m.

The Internet in Continuing Psychiatric Education

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Summary:

Psychiatric education can be obtained through multiple sources, with the Internet emerging as a new potential resource. A survey was conducted of the professional staff in the department of psychiatry at the University of Toronto to evaluate their use of the Internet in continuing psychiatric education. The survey questionnaire consisted of multiple-choice questions that examined computer skills, preferred methods of learning, and perceptions regarding the Internet as a tool for education and research. One hundred and eighty-one questionnaires were evaluated. The largest group (77%, n = 139) consisted of psychiatrists. Eighty-three percent (n = 150) of the survey responders were self-taught in using computer software. Preferred methods of learning by the respondents in the order of preference were professional journals, colleagues, and books. Of all the learning resources, respondents indicated that they anticipated increasing their use of the Internet for self-directed searches.

Eighty percent (n = 145) of the survey respondents indicated that they will utilize the Internet to obtain information. Forty-three percent (n = 78) of the respondents indicated that the Internet will change the way that they work and learn. The survey results indicate that while traditional sources of information for psychiatric education will remain widely used, the Internet will become increasingly important as a learning tool.

NR638 Thursday, May 22, 12 noon - 2:00 p.m.

Patients' Experiences of a Representative Payee Program

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Summary:

Objectives: Little is known about the processes and outcomes associated with the representative payee (RP) mechanism, in spite of the fact that RPs are required for persons receiving Social Security income who abuse substances. This study assesses

patients' satisfaction and perceptions of RP services delivered within a PACT model.

Methods: Staff uninvolved in direct treatment interviewed 49 of 51 (96%) patients who had received RP services for three months to two years [mean age = 41.6 (10.4); 63% were black, 63% schizophrenic, 35% affective disorder patients, 63% had a substance use disorder (SUD)].

Results: The majority of patients did not request the team as RP (62%) and were initially unhappy with the arrangement (55%). Affective disorder patients were more likely to have been unhappy initially ($p < .05$). Persons with a previous payee were more likely to have requested ACT as payee ($p < .0001$). At interview, 77% of patients reported being satisfied, and the majority reported that having an RP helped with housing (71%) and substance abuse problems (69%). SUD patients were more likely to report that they received help with substance use problems ($p < .0001$).

Conclusions: This study suggests that patients may initially reject RP arrangements, but appreciate the value of having an RP over time. Diagnosis and previous RP experience may impact on perceptions of current RP arrangements.

NR639 Thursday, May 22, 12 noon - 2:00 p.m.

Medical Inpatient Utilization of Recurrently Readmitted Veterans

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Summary:

Objective: This preliminary study examines medical and surgical inpatient resource use by recurrently readmitted psychiatric patients (RRPs) in a Veterans' Affairs hospital.

Method: All patients admitted four or more times in any calendar year during 1991-1995 to psychiatric or substance abuse inpatient units at Long Beach VA Medical Center were identified and paired with age- and sex-matched controls from the rest of the psychiatric inpatient pool. Demographics and admissions and transfer data for general medical-surgical units and intensive care units were obtained from the DHCP database at LBVAMC. Hospital charges for 1996 were obtained from the finance office at LBVAMC.

Results: RRPs used 2.37 times more general medical-surgical bed-days ($p = 0.0005$) and 2.03 times more ICU bed-days ($p < 0.0001$) compared with age- and sex-matched controls. The cost ratio of RRP:controls in 1996 dollars is $2.32:$1.00 (one average general medical-surgical bed day = $246.63; one average ICU bed-day = 696.40, lowest unit acuity assumed).

Conclusions: Compared with controls of the same age and sex who have also been psychiatrically hospitalized during the study period, RRPs used at least twice as many basic medical and surgical inpatient resources over five years.

NR640 Thursday, May 22, 12 noon - 2:00 p.m.

Adolescent Substance Abuse Prevention

John F. Aruffo, M.D., Department of Psychiatry, Univ of Arkansas Med School, 4301 West Markham/Slot 554, Little Rock AR 72205; Debra L. Hollis, B.A., A.J. Naylor, B.A., Roger A. Webb, Ph.D.

Summary:

Objective: An evaluation was designed to measure the impact of a CSAP funded after-school substance abuse prevention program for high-risk youth. The evaluation included both standardized and program-specific instruments.

Method: Participants were regularly attending students at either an urban site (N = 40) or a rural site (N = 41). Students completed the COMPASS and the Piers-Harris. Teachers, staff, and students also completed behavior scales. The reported analyses are based on Pearson correlations.

Results: At the rural site the students were younger, 13.3 vs. 14.9 years, and had fewer risk factors, 5.4 vs. 7.1. Analysis of the combined sites showed no consistent trends. When analyzed separately, the urban site showed only a correlation between the student and teacher behavior scales ($r = .43$, $p < .05$). The rural site did show changes consistent with expectations. Increased center attendance correlated with decreased teacher-reported and student-reported behavior problems ($r = .46$, $p < .05$), ($r = -.38$, $p < .05$). Higher risk factors correlated with higher substance use ($r = .50$, $p < .01$) and lower GPAs ($r = -.45$, $p < .05$).

Conclusion: Differences in population characteristics and program implementation make multisite analysis very difficult. Combining standardized instruments and program-specific instruments is necessary to analyze these types of programs. Additional analyses are being completed to identify critical factors that impact outcome.

NR641 Thursday, May 22, 12 noon - 2:00 p.m.

Persistence of Depressive Illness in Primary Care Patients with Major Depression: Is a Coexisting Anxiety Disorder a Risk Factor?

Bradley N. Gaynes, M.D., Department of Psychiatry, University of North Carolina, 5034 Old Clinic Bldg/CB #7105, Chapel Hill NC 27514; Kathryn M. Magruder, Ph.D., Barbara Burns, Ph.D., W.E. Broadhead, M.D., Grayson S. Norquist, M.D.

Summary:

Objective: To assess whether a current coexisting anxiety disorder (panic disorder, generalized anxiety disorder, social phobia, and/or agoraphobia) predicts persistent depressive illness at 12 months.

Method: Patients with major depression were identified in a university-based family practice clinic as part of a larger study of depression. Presence of an anxiety disorder and other potential prognostic factors, including depressive severity and medical illness severity, were measured at baseline. Persistence of depression was determined at 12 months.

Results: Of 85 patients with major depression at baseline, 43 had a coexisting anxiety disorder. Social phobia, an anxiety disorder ignored in previous studies of depression outcome, was the most common anxiety diagnosis (88%). Patients with and without coexisting anxiety disorders were similar in demographic characteristics, medical illness severity, and depression severity. The risk for persistent depressive illness at 12 months was increased by 44% (risk ratio = 1.44, 95% CI [1.02-2.04]) in those with a coexisting anxiety disorder. This risk persisted in stratified analysis with other prognostic factors.

Conclusion: A coexisting anxiety disorder is a risk factor for persistent depressive illness in primary care patients with major depression. Social phobia, which prior studies have neglected, may be an important disorder to identify in these patients.

NR642 Thursday, May 22, 12 noon - 2:00 p.m.

Alcohol-Dependent Liver Graft Recipients: A Controlled, Three-Year Follow-Up

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Summary:

Objective: Short-term outcome studies have noted high abstinence rates and good overall functioning in alcohol-dependent

(AD) liver recipients, but these observations have not been extended beyond one year.

Method: We conducted a three-year follow-up study of 42 AD liver transplant recipients and 38 non-AD controls. Both groups were surveyed by an independent clinical research fellow using a structured phone interview, a corroborating interview, random blood and urine alcohol testing, and review of clinic records. The study groups were matched for age, gender and, de facto, for liver disease severity.

Results: Resumption of *any* alcohol use was higher in the non-AD group, 45% versus 18% ($p < 0.01$). Heavy drinking did not differentiate the two, 5% versus 3%. AD recipients were more likely to report that 1) post-transplant drinking would injure their graft ($p < 0.05$), 2) the transplant helped them remain abstinent ($p < 0.02$), and 3) they recalled the pre-transplant counseling against any alcohol use ($p < 0.001$) as well as post-op reminders of abstinence ($p < 0.01$). Post-transplant, demographic variables did not separate the two groups. Rates of depressive or anxiety symptoms or of confusion episodes were the same in both groups. Compliance with anti-immune medication was identical, with up to 75% of both groups having missed one dose but less that 3% of each group having missed two consecutive doses. Vaillant's prognostic factors for sustained abstinence suggested that 1) AD subjects' rate of return to work was about 15% to 20% lower than controls, 2) sustaining personal relationships decreased with time: 70% reporting a relationship in the first year and only 40% in the third year, and 3) 24% of the AD group continued to experience bothersome guilt about pre-op drinking.

Conclusions: Long-term abstinence and compliance rates were high in the AD sample, but factors supporting continued abstinence seem to attenuate with time. These data suggest a need for focused long-term follow-up care for AD recipients.

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The Relationship Between Major Depression and Cardiovascular Disease: Is Homocysteine a Link?

Jonathan E. Alpert, M.D., Department of Psychiatry, Massachusetts General Hospital, WAC-815, 15 Parkman Street, Boston MA 02114; Isabel T. Lagomasino, M.D., Andrea R. Kolsky, B.A., Teodoro Bottiglieri, Ph.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Depression, anxiety, and hostility appear to be independent risk factors for cardiovascular disease. Elevated levels of homocysteine are also a known risk factor for cardiac illness. It is unclear whether the relationship between depressive symptoms and cardiovascular disease is mediated by changes in homocysteine levels.

Objective: We examined the relationships between degree of depression, anxiety, and hostility, and blood levels of homocysteine in a population of outpatients with major depressive disorder (MDD).

Method: 198 (112 women and 86 men; mean age: 40.0 ± 10.5) medication-free subjects were diagnosed with MDD using the Structured Clinical Interview for DSM-III-R—Patient Edition. The Symptom Questionnaire was used to assess depression, anxiety, and hostility, and blood samples were collected for the blind assay of homocysteine.

Results: Homocysteine serum levels were elevated (i.e., two standard deviations above the mean of a normal control group) in 38 (19%) depressed patients. After adjusting for age and gender, we found statistically significant positive relationships between serum levels of homocysteine and depression ($p < .003$), anxiety ($p < .0005$), and hostility ($p < .02$).

Conclusions: Our results suggest that the degree of depression, anxiety, and hostility may be related to elevated homocysteine levels in patients with MDD. Further studies should investigate the nature of these relationships in light of the increased mortality from cardiovascular problems in depression.

NR644 Thursday, May 22, 12 noon - 2:00 p.m.

Adjustment Disorder in Hospitalized Cancer Patients Receiving Bone Marrow Transplantation

Jesus Prieto, Department of Psychiatry, Hospital D'Olot, Mulleres S/N, Olot 17800, Spain; Jorge Atala, Jordi Blanch, Cristobal Gasto, Esteve Cirera

Summary:

Objective: This study determines the prevalence of clinical subtypes, diagnostic stability, and course of adjustment disorder (AD).

Method: A consecutive series of 170 patients were evaluated on admission and weekly until discharge. We used structured clinical interviews and DSM-IV criteria for diagnosis.

Results: Fifty-three (31%) of 170 patients met criteria for AD. Change in AD subtype throughout hospitalization occurred in 12 (23%) of these patients, with an additional 11 (21%) patients developing a major depressive episode from AD. Ten patients were diagnosed with a definitive AD with anxiety (ADA), 13 with AD with depressed mood (ADDM), 17 with AD with mixed anxiety and depressed mood (ADM), and two patients with two nonconsecutive AD. Percentage of cases that resolved during hospitalization were 100% for ADA, 87% for ADM, and 47% for ADDM; mean episode length for these disorders were 2.42 weeks (range: 1–10), 7.33 weeks (range: 1–31), and 20.57 weeks (range: 2–97) respectively.

Conclusion: A considerable degree of subtype instability is observed when serial evaluations are carried out. One-quarter of patients with AD developed a major depressive episode. The duration of individual cases of ADM and ADDM varied greatly. Adjustment disorder needs to be more rigorously defined and validated.

NR645 Thursday, May 22, 12 noon - 2:00 p.m.

Middle-Aged Women with Heart Disease Have Greater Depressive Symptoms

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Summary:

Objective: To assess the prevalence of depressive symptoms in women with heart disease, a group of patients who have been underrepresented in previous research.

Method: Over a 14-month period 181 women were evaluated on the cardiology service of a university medical center and completed a 21-item Beck Depression Inventory (BDI). Sixty-eight patients (38%) had unstable angina, 51 (28%) acute myocardial infarction, 27 (15%) dysrhythmia, 25 (14%) congestive heart failure (CHF), and eight (4%) valvular disease; two (1%) were post-transplant. Mean ± SD age was 60.4 ± 12.5 years (range 22–87).

Results: The mean ± SD BDI score for the 181 women was 12.7 ± 8.9, in contrast to a score of 9.8 ± 7.7 for a group of 338 male cardiology patients evaluated at the medical center during the same time period. Women aged 45–59 ($n = 68$) had a higher BDI (14.1 + 8.9) than women in other age groups: under 45 years, $n = 19$, 11.8 ± 8.8; 60–74 years, $n = 75$, 12.5 ± 9.1; 75 years or over, $n = 19$, 9.2 ± 7.5. Patients with CHF had the highest BDI (15.7 ± 11.4) among the different diagnoses; 65% of women aged 45–59 and 64% of those with CHF had a BDI of 10 or greater.

Conclusions: These data suggest that clinically significant depressive symptoms are common in women with cardiac disease, especially in those who are middle-aged or have congestive heart failure.

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Identification of Domestic Violence Among Hospitalized Patients: Utilization of a Screening Questionnaire by a Psychiatric C/L Service

Stephanie K. Stern, M.D., Department of Psychiatry, Mt. Sinai Medical Center, One Gustave Levy Pl/Box 1228, New York NY 10029; James J. Strain, M.D.

Summary:

Objectives: Using a brief domestic violence questionnaire (DVQ) this study attempted to: 1) determine the prevalence of domestic violence (DV) among inpatients seen by the psychiatric consultation liaison service at a large academic hospital; 2) characterize the DVQ-positive population, and 3) assess the relationship among DV, psychiatric morbidity, and health care service utilization.

Design and Methods: Psychiatric consultation-liaison evaluations on hospitalized patients, which included the DVQ, were completed and summarized on a structured data base form. Unmatched t-tests and Chi-square analyses were conducted, where appropriate, to assess differences between DVQ-positive and DVQ-negative patients regarding psychiatric morbidity and health service utilization.

Results: Seventy-one percent of the patients assessed were female, 30% black, 30% white, and 40% Hispanic. Their mean ($\pm$ SD) age was 41.8 $\pm$ 13.0 years. Preliminary analysis showed that 36% of the patients assessed so far were DVQ-positive. Further analysis of concurrent psychiatric morbidity and health service utilization for the DV-positive patients will be presented.

Conclusions: These preliminary results confirm that the DVQ is an effective instrument for eliciting DV data. The DV prevalence rate detected in this study may underestimate the actual prevalence as some patients may report inaccurately, refuse or be unable to answer when queried.

NR647 Thursday, May 22, 12 noon - 2:00 p.m.

Psychopathology Following Cardioverter-Defibrillator Implantation

Scott J. Crow, M.D., Department of Psychiatry, University Hospital, 420 Delaware Street SE/Box 393, Minneapolis MN 55455; Marcia Justic, M.S.N., JoAnne Collins, B.S.N., Robert Goetz, Stuart Adler, M.D., Barbara Praus

Summary:

Objective: To examine the onset of psychopathology following cardioverter-defibrillator (ICD) implantation.

Method: All first-time ICD recipients in a tertiary care hospital over a 25-month period were asked to participate. The Structured Clinical Interview for DSM-III-R was administered during hospitalization for ICD implantation and again nine to 18 months later.

Results: 35 ICD recipients agreed to participate; 27 were recontacted after nine to 18 months for follow-up assessment (three died, two received heart transplant, one refused, and two could not be located). Rates of lifetime psychopathology were: alcohol dependence in full remission 14.3%; past major depression 5.7%; past panic disorder 2.9%. For current psychopathology, 8.6% had current major depression; 2.9% dysthymia; .7% adjustment disorder with depressed mood; 2.9% panic disorder; and 2.9% organic anxiety disorder. Following implantation, two cases of major depression developed—one in a subject who had adjustment disorder with depressed mood at baseline and one in a subject with a lifetime history of MDD. No new cases of anxiety disorders were seen.

Discussion: In contrast to previous reports, ICD implantation was not associated with the onset of new psychopathology. Lifetime rates of psychopathology in this group were similar to those seen in other studies involving medically ill individuals.

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Treatment of Delirium with Risperidone

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Summary:

Objective: Delirium is an organic psychiatric syndrome characterized by fluctuating consciousness and impairment in cognition, perception, and behavior. The authors treated 11 consecutive delirious patients with the atypical antipsychotic risperidone.

Method: Eleven consecutive patients with delirium were started on 0.5 mg P.O. b.i.d. of risperidone which was increased every three to four days until either improvement or side effects were observe.

Results: The mean duration of risperidone treatment was 8.9 $\pm$ 5.1 days and maximum response was seen at 5.1 $\pm$ 4.3 days. Eight of the 11 patients showed improvement based on the CGI scale.

Conclusion: High-potency neuroleptics such as haloperidol have been traditionally used in the treatment of delirium. Adverse effects have limited its use, especially in the elderly who are more sensitive to the side effects of typical antipsychotic agents. The atypical antipsychotic drug, risperidone, was found to be an effective treatment in medically and surgically hospitalized patients with delirium. The limitations of our study include the small number of patients and lack of a control group as well as the lack of a structured interview or rating scale. Larger studies are needed to explore these preliminary conclusions.

NR649 Thursday, May 22, 12 noon - 2:00 p.m.

Screening for Anxiety and Depression in Women with Breast Cancer

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Summary:

Psychological distress in women with breast cancer is an important factor in their quality of life. Twenty-five percent of women with advanced breast cancer have been diagnosed with depression or anxiety, using the Hospital Anxiety and Depression Scale, HADS-2. Identifying patients with anxiety and depression in an efficient, timely manner is a concern for both psychiatrists and oncologists. We explored the use of several screening instruments to assess the reliability of self-administered questionnaires compared with more time-consuming methods. Our sample consisted of 31 women with breast cancer attending an outpatient breast cancer clinic. Patients were asked to complete the HADS, the VAS, a 100 mm visual analogue scale (0 mm = worst, 100 mm = best I ever felt), and the Brief Symptom Inventory (BSI). We also administered structured clinical interviews, SCIDs.

Patients who had a current DSM-IV diagnosis had a higher total HADS score ($p < 0.01$) and a higher global distress index on the BSI ($p < 0.01$) than patients with no current diagnosis. The VAS showed a trend towards lower scores in patients with a current diagnosis ($p = 0.075$). Our study indicates that the level of reliability of these assessment scales may be comparable in detecting psy-

chological distress. Psychiatrists may assist medical staff in screening large numbers of patients through the use of self-administered scales.

NR650 Thursday, May 22, 12 noon - 2:00 p.m.

Recognition and Management of Psychiatric Distress in Ethnically Diverse Primary Care Patients

Henry Chung, M.D., Chinatown Health, 125 Walker Street, New York NY 10013; Peter J. Guarnaccia, Ph.D., Jean Teresi, Ph.D., Tracey Goldstein, M.S., Mark Olfson, M.D., Barnett S. Meyers, M.D.

Summary:

Objective: In this pilot study, we examine primary care physician recognition and management of psychiatric distress in an ethnically diverse primary care sample composed primarily of Asians and Hispanics. In addition, the relationship of patient and physician sociodemographic factors and diagnostic congruence is investigated.

Methods: 235 consecutive patients in the general medicine clinics in a large ambulatory medical facility agreed to participate and completed the following measures prior to their medical visit: Center for Epidemiologic Studies-Depression (CES-D) scale, a demographic questionnaire, and an acculturation scale. Immediately after the visit, physicians completed a mental health treatment summary. Sixteen PCP agreed to participate in the study; 90% are attending physicians, and 30% have moderate to complete fluency in either Spanish or Chinese (Cantonese or Mandarin).

Results: The sample was mostly female with a mean age of 52 years. Thirty-six percent were Asian, primarily of Chinese descent, and 46% Hispanic, of either Dominican or Puerto Rican descent. Also, 44% of the sample were psychiatrically distressed as measured by the CES-D as compared to 34% by physician judgment ($X = 28.4$, $df = 1$, $p < .01$). The most frequent diagnoses were: adjustment disorder, anxiety disorder, major depression, and dysthymia. Identified patients received counseling (41%), psychotropic medications (36%), an earlier return visit (21%), or referral to psychiatry (16%). Physicians were more likely to diagnose distress in Hispanics (Wald statistic = 4.4, $p = .04$) and for those that lived alone (Wald statistic = 4.5, $p = .03$). Higher patient acculturation status was the only factor that improved diagnostic congruence (Wald statistic = 4.8, $p = .03$).

Conclusions: This study found that primary care physicians ably recognize psychiatric distress and are very active in managing these conditions. However, it appears these physicians assume that distress is more evident in Hispanics and in those living alone. Higher acculturation status improved diagnostic congruence, but racial and language match did not. Further research will be required to understand how primary care patients (particularly low income and racially diverse) express their psychiatric distress in the clinical encounter and how physicians identify patients for intervention.

NR651 Thursday, May 22, 12 noon - 2:00 p.m.

Acculturation, Psychiatric Distress and Major Depression in Ethnically Diverse Primary Care Patients

Henry Chung, M.D., Chinatown Health, 125 Walker Street, New York NY 10013; Peter J. Guarnaccia, Ph.D., Mark Olfson, M.D., Barnett S. Meyers, M.D., Jean Teresi, Ph.D., Tracey Goldstein, M.S.

Summary:

Objective: In this pilot study, we examine the prevalence of and relationship between acculturation status, psychiatric distress, and major depression in an ethnically diverse primary care sample composed primarily of Asians and Hispanics.

Methods: 235 consecutive patients in the general medicine clinics in a large ambulatory medical facility agreed to participate and completed the following measures: Center for Epidemiologic Studies-Depression (CES-D) scale, a demographic questionnaire, and either the Marin Hispanic Short Acculturation Scale or Suinn-Lew Asian Acculturation Scale; 98 patients also completed the the Mini International Neuropsychiatric Interview - Depression scale (MINI-dep), a scale highly specific for major depression.

Results: The sample was mostly female with a mean age of 52 years; 36% were Asian, primarily of Chinese descent, and 46% Hispanic, of either Dominican or Puerto Rican descent. Also, 44% of the sample were psychiatrically distressed as measured by the CES-D. Most Hispanics and Asians were non-English speaking and of low acculturation status. Fifteen percent of the subsample ($n = 98$) met criteria for a current diagnosis of major depression. Acculturation status in both Hispanics and Asians had no relationship to psychiatric distress ($r = 0.03$, $p = .78$ and $r = 0.15$, $p = .20$, respectively). In a multiple regression analysis, being unemployed was the only significant predictor of current psychiatric distress ($F = 3.98$, $p = .05$).

Conclusions: The prevalence of psychiatric distress and major depression are high in this low-income, primary care sample. Contrary to expectations, having a low acculturation status did not appear to predict psychiatric distress in these patients. Because past studies in the U.S. have not included monolingual, Chinese-speaking, primary care patients, this pilot study indicates that this group, like other low-income groups, has significant psychiatric distress. Larger mental health studies in primary care should include these ethnic groups, since they tend to use services in the mental health sector only as a last resort.

NR652 Thursday, May 22, 12 noon - 2:00 p.m.

Older Hispanic Men: At Risk for Untreated Depressive Symptoms?

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Summary:

Objective: This investigation explored the following: 1) comparison of the incidence of depressive symptoms between 437 elderly Hispanic (H) and non-Hispanic white (NHW) elderly men, and 2) the use of antidepressant in H and NHW elderly men.

Method: We examined the use of antidepressants in 223 NHW men and 184 H men. These subjects were administered the Geriatric Depression Scale-Short Form (GDS-S). A GDS-S of ≥ 6 was used to suggest depression. Medication was self-reported and recorded by a trained nurse practitioner.

Results: 1) Elderly H men demonstrated a higher prevalence of depressive symptoms than did elderly NHW men (GDS-S: H men 10.9%, NHW men 7.2% suggesting depression); 2) Elderly H men were less likely than NHW men to be taking antidepressants (1.6% compared to 6.3%); and 3) NHW elderly men compared to HM of similar income, education, and depressive symptoms were more than five times more likely to be taking antidepressants.

Conclusions: Ethnicity is a statistically significant factor affecting the underutilization of antidepressants. Further investigation is needed to develop culturally sensitive intervention methods for depressed elderly HM so that they may receive appropriate psychiatric treatment.

NR653 Thursday, May 22, 12 noon - 2:00 p.m.

Ethnicity and Anxiety Surrounding Breast Cancer Screening Mammography in an Urban Center

Theresa M. Miskimen, M.D., Department of Psychiatry, UMDNJ, Newark Campus, 215 South Orange Avenue, Newark NJ 07103; Arthur T. Meyerson, M.D., Haftan M. Eckholdt, Ph.D., Beverly R. Delaney, M.D.

Summary:

Objective: To determine differences in the level of anxiety between ethnic groups before and after a mammogram.

Method: Women (n = 28, African-American = 46%, Hispanic = 21%, White = 18%, other = 14%) mostly referred by physicians for routine mammograms were interviewed immediately before and after mammograms in a university-based inner-city setting. The Hamilton Anxiety Scale and SCID-IIIR were administered. Subjects under age 18 and over age 65, were excluded, as were mentally retarded, medically ill, and/or subjects on medications.

Results: All mammograms were negative. There was no age or income differences between ethnic groups. ANOVA showed no significant difference between ethnic groups on Hamilton Anxiety score measured immediately before mammograms, but Hispanic women scored higher than African-American women after mammograms ($t = 2.88$, $p < 0.05$).

Conclusions: Participants may not represent the community or typical users of health care systems. Hispanics tended to remain anxious after mammograms even when negative. Consequences of anxiety, including distorted perceptions and confusion, could impede follow-up. This pilot study highlights the importance of designing interventions to address the specific needs of women from certain ethnic groups where anxiety and its consequences during screening procedures may be most pronounced.

NR654 Thursday, May 22, 12 noon - 2:00 p.m.

African-American Women with Breast Cancer

Ruth M. Lamdan, M.D., Department of Psychiatry, Allegheny University Hospital, 3300 Henry Avenue, Philadelphia PA 19129; Kathryn Taylor, Ph.D., Bonnie O'Connor, Ph.D., Jamie Siegel, M.D., Karen Moran, B.S.

Summary:

The lifetime risk of breast cancer (BC) is 13.2% for white women and 9% in African-American (AA) women. Much has been published on the adjustment to BC; however, little is known about adjustment in AA women. AA women are diagnosed at a more advanced stage and have lower survival rates than white women. These biological differences raise questions as to whether psychological adjustment and interventions may also vary for AA women.

Using standard ethnographic techniques, we have analyzed 33 verbatim transcripts from a comprehensive, semistructured interview that we conducted within the first eight months of diagnosis. This is in the context of an 18-month longitudinal study that includes a randomized intervention with 96 AA women with Stage I to IIIa BC.

In looking at religion, life perspective, and problem comparison, we found that 70% said religion played the most important role in coping with BC; age did not affect this coping mechanism. Forty-five percent of the women felt that BC was less of a problem compared with other difficulties they had encountered throughout their lives. Variables of SES do contribute to this hierarchy. Studies of middle class white women show BC was one of the worst stressors in their lives. Specific interview material will highlight our findings.

NR655 Thursday, May 22, 12 noon - 2:00 p.m.

Bosnian Student Survivors at Home and in Exile: A Comparative Study

Steven M. Weine, M.D., Department of Psychiatry, University of IL at Chicago, 1601 West Taylor Street, #423S, Chicago IL 60612; Slobodan Loga, M.D., Ismet Ceric, M.D., Vladimir Gruden, M.D., Alma Dzubur Kulenovic, M.D., Zorana Kusevic, M.D., Ines Matijas, B.S., Amer Smajkic, M.D., Ivan Pavkovic, M.D.

Summary:

Objective: To describe the psychiatric consequences of ethnic cleansing in a group of 111 Bosnian female students, in three different settings, comparing the traumas of siege and exile.

Method: An international collaborative study between psychiatry departments of the universities in Sarajevo, Zagreb, and Illinois at Chicago looked at the sample of 111 student girls aged 18 to 23. The Sarajevo sample consisted of 52 girls, mean age 21.23, and the exile sample (Chicago, Zagreb), consisted of 59 girls, mean age 20.73. The subjects completed self-report anonymous questionnaires that asked about general information, traumatic events, traumatic stress symptoms, general functioning, school satisfaction, traumatic memories, coping styles, cultural identification, and alienation, all drawn from standardized assessments.

Results: The mean frequency of occurrence of different types of traumatic events was significantly higher in the Sarajevan sample, 104.58, compared with the exile sample, 62.25. PTSD diagnosis and symptom severity were not different: 46.2% and 14.1 in Sarajevo, and 40.6% and 14.4 in exile. Global functioning, school satisfaction, cultural identification, and alienation were all similar in both samples. There was a significant difference in traumatic memories coping styles (2.93 in Sarajevan sample and 14.48 in the exile sample, which indicates less-assertive relating with traumatic memories in the Sarajevan sample).

Conclusions: The rate of PTSD diagnosis and severity in the exile sample appeared not to be driven by a higher frequency and number of types of traumatic events, but by factors related to exile, not directly detectable on our assessment scales. The difference in traumatic memory coping across settings could reflect how for these students the psychosocial conditions of siege mitigated against active sharing, whereas those of exiles mitigated for it. Further studies comparing traumas across context are needed.

NR656 Thursday, May 22, 12 noon - 2:00 p.m.

Evidence of Genetic Linkage of Antisocial Alcoholism to the 5HT-1B Gene

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Summary:

Objective: Two recent gene knockout studies have demonstrated that mice lacking the terminal serotonin autoreceptor 5-HT1B show enhanced aggressive behavior and consume more alcohol compared to wild-type mice. We therefore investigated whether the 5-HT1B gene (HTR1B) is linked to alcoholism and impulsive behavior in humans.

Method: 640 Finnish subjects including alcoholic offenders (n = 166), their relatives (n = 261) and healthy controls (n = 213) were psychiatrically interviewed (SCID-II), blind rated for DSM-III-R diagnoses, and typed for an RFLP in the HTR1B and for two closely linked short tandem repeat loci: D6S284 and D6S286. The SIBPAL module of S.A.G.E package was used for sibpair linkage analysis. Association between markers and phenotypes was measured using the PEDASSOCIATION program, which allows the

use of related subjects in association studies. This pedigree randomization method corrects for the fact that observations within the contingency table are not independent when related subjects are included in the analysis.

Results: The frequency of the HTR1B-2 allele in 180 male ASPD alcoholics (DSM-III-R antisocial personality disorder or intermittent explosive disorder) was first evaluated by comparing the ASPD alcoholics to the rest of the sample (n = 350), including male controls and male non-ASPD alcoholics. A significant association was observed (p = 0.01). Further analyses revealed that ASPD alcoholics had a significant excess of the HTR1B-2 allele compared to 264 controls (p = 0.03) or to 86 non-ASPD alcoholics (p = 0.02). Sibpair analysis detected a linkage between ASPD alcoholism and HTR1B (p = 0.039). D6S284 was also weakly linked to ASPD alcoholism (p = 0.055). SSCP analysis of the HTR1B coding sequence detected no functional variants in 140 individuals.

Conclusions: These results suggest that a locus contributing to ASPD alcoholism resides close to HTR1B at 6q13-15, or that there are undetected functional alleles within the coding sequence of HTR1B.

NR657 Thursday, May 22, 12 noon - 2:00 p.m.

18q Locus for Comorbid Bipolar and Panic Disorder

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Summary:

Panic disorder frequently cosegregates with bipolar disorder in some families. In these families, we have proposed that a high risk for panic disorder may be a marker for a genetically distinct subtype of bipolar disorder. We now test this hypothesis on a sample of 28 families previously reported as showing evidence of linkage on chromosome 18. Here, we have re-evaluated these linkage results using the same families, but stratified the sample into three groups: 1) five families in which the bipolar proband of the family had panic disorder (RDC inclusion criteria); 2) six families in which the proband had panic attacks but not panic disorder, 3) 17 families in which probands denied having panic attacks. Only family members with BPI or BPII were included in the analysis. Nonparametric multipoint analysis showed high likelihood of linkage for four markers on 18q for the group of families in which the proband had panic disorder. Scores for the second group were intermediate, while scores for the third group in this region were negative. This study provides evidence for genetically distinct subtypes of bipolar disorder, distinguished clinically by a difference in the risk of comorbid panic disorder in probands and affected family members.

NR658 Thursday, May 22, 12 noon - 2:00 p.m.

MDD: Are Genetic and Environmental Contributions Different in Men and Women?

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Summary:

We examined genetic and environmental contributions to the development of DSM-IV major depressive disorder in a large sample of Australian twins. Subjects were part of the Australian twin registry, which is a volunteer sample of twins from the general population. All subjects were given a semistructured diagnostic interview that evaluated DSM-IV major depressive disorder along with other psychiatric disorders.

A total of 5998 individuals were interviewed (2090 men and 3908 women), and the mean age of the sample was 44 years. Twenty-one percent of women and 16% of men had a lifetime diagnosis of DSM-IV major depressive disorder. We performed model fitting of genetic, familial environmental, and individual environmental factors in the development of major depressive disorder. For both men and women, a model including genetic and individual environmental factors most simply described the data, and the magnitude of these contributions was significantly different between men and women ($\lambda 2 = 4.09$ 1df). We found that 38% of the variance in liability for major depressive disorder was due to additive genetic component in women compared to 17% in men.

In summary, genetic and environmental factors differ in the magnitude of their contribution to the development of DSM-IV major depressive disorder in men and women. But, for both men and women, familial resemblance is primarily due to genetic factors.

NR659 Thursday, May 22, 12 noon - 2:00 p.m.

Systematic Search for Molecular Variants of Catechol-O-Methyltransferase Gene and Association Study with Schizophrenia

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Summary:

Family, twin, and adoption studies of schizophrenia suggested schizophrenia has a genetic component in its etiology. Recent linkage studies indicated suggestive linkage between chromosome 22q11-13 and schizophrenia. Moreover, patients with velocardio-facial syndrome (VCFS), which is characterized cytogenetically with interstitial deletion at 22q11, are liable to psychosis; suggesting 22q11 may harbor susceptible genes for schizophrenia. One of the candidate genes mapped in this region is the catechol-O-methyltransferase (COMT) gene, because it degrades catecholamine neurotransmitters.

We first systematically searched for molecular variants in four coding regions of COMT gene in 50 Chinese schizophrenic patients from Taiwan. At the second stage, we carried out a case-control association study in a cohort of 177 schizophrenic patients and 99 normal controls using molecular variants identified from first stage of the study.

We identified five polymorphisms of COMT gene, i.e. 1526(C > T) at exon 3, 1883(C > G) and 1947(G > A) at exon 4,2359(G > A) at exon 5, and a C insertion at 3' untranslated region. Further association study revealed no differences of allelic or genotypic distributions of these five polymorphic markers between patients and normal controls. Thus, we suggest that the COMT gene may not play a major role in the genetics of Chinese schizophrenic patients.

NR660 Thursday, May 22, 12 noon - 2:00 p.m.

Familial Aggregation of Psychiatric Disorders in Schizophrenic Probands

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Summary:

Objective: It has been suggested that genetic factors in schizophrenia have a wide range of phenotypic expression. The objective

of this study was to compare the risk of psychiatric disorders in first-degree relatives of schizophrenic probands (FDRS) with those of the general population (GP) of Santiago, Chile.

Method: Forty-four schizophrenic probands were selected at random, according to the DSM-III-R criteria. All the FDRS (247) were interviewed using the Composite International Diagnostic Interview and the DSM-III-R checklist.

Results: Psychiatric morbidity was observed in 56.3% of FDRS and in 33.7% of GP, being the difference statistically significant ($p < 0.05$). Affective disorders had the highest frequencies, both in FDRS and GP (28.3% and 16.3%, respectively), the risk was significantly higher in FDRS ($p < 0.05$). Alcoholism and drug abuse disorders had similar risk in FDRS (12.9%) and GP (11.0%). Morbidity risks (MR) for schizophrenia (3.6%) and schizoid-schizotypal personality disorders (2.8%) were significantly higher in FDRS than in GP (1.0% and 1.1%, respectively) ($p < 0.05$).

Conclusions: Results suggest a biological relationship between schizophrenia and schizoid-schizotypal personality disorders. The higher MR for affective disorders in FDRS must be analyzed with caution, considering that some authors postulate that schizophrenia and affective disorders belong to the same continuum.

NR661 Thursday, May 22, 12 noon - 2:00 p.m.

ApoE Gene Variants and Drug-Induced Cognitive Toxicity in the Elderly

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Summary:

Objective: The ε 4 allele, the major susceptibility gene for AD, may have a broader role in reducing the ability of the CNS to successfully recover from metabolic and traumatic brain insults. The ε 4 allele has been associated with persistent cognitive deficits in individuals cardiopulmonary bypass surgery (Newman et al., 1995) and with decreased recovery of neurological functions in patients suffering from intracerebral hemorrhage (Alberts et al., 1995). These findings prompted us to examine the relationship between the ε 4 allele and susceptibility to drug-induced cognitive toxicity in the elderly.

Method: ApoE phenotyping was performed on 80 cognitively intact, medically healthy, normal volunteers (age-range 60–87) who had participated in a recent NIMH-sponsored, placebo-controlled, parallel-group, double-blind study examining the neuropsychological effects of alprazolam and lorazepam.

Results: Delayed recall on the Buschke task was significantly impaired in response to lorazepam (1mg) in subjects with the ε 4 allele compared with placebo at 2.5hr after acute, oral, single-dose administration, but not in individuals without the ε 4 allele. Multivariate regression analysis also revealed that the ε 4 allele was a significant predictor for impairment in the delayed recall task.

Conclusions: These preliminary findings, if confirmed, identify a genetic factor that may increase risk for lorazepam-induced memory deficits in the elderly. Future studies with other benzodiazepines as well as other centrally active agents may evaluate the potential role of the ε 4 allele as a modulator of individual differences in susceptibility to drug-induced cognitive toxicity.

NR662 Thursday, May 22, 12 noon - 2:00 p.m.

D2 Dopamine Gene Receptor Allele and Reward Dependence-Attachment

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Summary:

Meta-analyses of relevant studies suggest that the A1 allele of the D2 dopamine receptor (DRD2-A1) weakly associates in Caucasians with substance use disorders (SUDs). Most patients with antisocial and borderline personality disorders (PDs) have SUDs.

Hypotheses: DRD2 A1 would more strongly associate with these PDs than with SUDs, and with Cloninger's putatively dopaminergic Novelty Seeking personality dimension.

Methods: 46 inpatients with antisocial or borderline PDs or SUDs and 22 nonpatient controls were compared by RFLP genotype, SCID-III-R SUD module, PDQ, and TPQ.

Results: DRD2-A1 was more associated with PD than SUD. It was also more common in patients with antisocial and borderline personality disorder than in controls. However, it was even more common in those with comorbid schizoid, narcissistic, sadistic, avoidant, and passive aggressive PDs.

DRD2-A1 was negatively related to Reward-Dependence, and its subscale, Attachment, but not to Novelty Seeking. Logistic regression analysis indicates that Attachment is the significant ($p = .013$) negative predictor of DRD2-A1, whereas race, patient status, PD, and SUD are not.

DRD2 or a nearby gene may partially control Attachment. Caucasian substance users and members of this insular-to-dangerous group of Personality disorders may have in common finding little reward in bonds with others.

NR663 Thursday, May 22, 12 noon - 2:00 p.m.

Cerebrovascular Risk Factors in Older Depressives: Testing a Small Vessel Brain Disease Model of Pathogenesis

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Summary:

Objective: A theoretical model has been proposed in which later life depression is caused by small vessel brain disease, supported by evidence from neuroimaging (e.g., MRI) and neuropsychological studies. We tested this model by examining the association of cerebrovascular risk factors (CVRFs) with clinical variables among older psychiatric inpatients with major depression, and by comparing the prevalences of CVRFs in these inpatients and in nondepressed controls.

Methods: One hundred thirty psychiatric inpatients age ≥50 years with a primary diagnosis of DSM-III-R major depression (confirmed by the Structured Clinical Interview for DSM-III-R [SCID]) who gave informed consent participated in this study. In addition to the SCID, other assessments included measures of depressive symptom severity (Hamilton Rating Scale for Depression); psychiatric and medical disability (Global Assessment of Functioning and Karnofsky Performance Status Scale, respectively); cognitive function (Mini-Mental State Examination); and CVRFs (based on the American Heart Association Stroke Prediction Chart, scored as a cumulative total of CVRF burden and as presence or absence of individual CVRFs including systolic blood pressure, antihypertensive treatment, diabetes mellitus, cardiovascular disease, cigarette smoking, atrial fibrillation, and left ventricular hypertrophy). Similar procedures were used with 64 community-recruited normal controls age ≥50 years. Data analyses employed comparative statistics and multiple regression techniques to determine associations while controlling for specified covariates.

Results: Among the depressed inpatients, CVRFs were not associated with age of onset of mood disorder, depressive symptom severity, melancholia, psychotic depression, or psychiatric

disability; there was a trend association with cognitive dysfunction, which was not statistically significant when controlled for age, gender, and education. Depressives did not differ from controls in their *cumulative* CVRF score. The depressed group did have a significantly greater prevalence of cardiovascular disease, diabetes, and atrial fibrillation. However, only the associations with diabetes and atrial fibrillation remained significant when controlled for age, gender, and education, and only atrial fibrillation retained a significant association with depression when controlled for medical disability.

Conclusion: These results provide only limited support for a small vessel brain disease model of depressive pathogenesis in later life. Future studies will need to examine these issues in other depressed populations (e.g., primary care settings), along with the potential mediating roles of psychological and psychosocial variables, to delineate better the relationships between CVRFs and depression and to better understand the pathobiological significance of MRI brain abnormalities in older depressives.

NR664 Thursday, May 22, 12 noon - 2:00 p.m.

P300 Latency, Prefrontal Dysfunction and Antidepressant Treatment of Geriatric Depression

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Summary:

Frontal system dysfunction can be conceptualized as a pathophysiological mechanism that predisposes and perpetuates geriatric depression in a subgroup of patients. Since structural brain abnormalities appear to be associated with a chronic course of geriatric depression, and prolonged P300 latency is correlated with initiation and perseveration deficits (IPD), we examined geriatric depressed patients to determine if P300 latency and IPD differentiate responders from nonresponders to antidepressant drug treatment.

Methods: Before initiation of treatment, geriatric unipolar depressives (n = 57) were administered the Mattis Dementia Rating Scale (DRS). P300 latency was measured for a two-tone task. Recovery in 42 patients was associated with treatment with nortriptyline (≥50 mg/daily), paroxetine (≥20 mg/daily), sertraline (≥50 mg/daily), or fluoxetine (≥10 mg/daily) for a period of three or more weeks.

Results: Nonresponders (n = 15) compared to responders to drug therapy had longer latency (F = 32.5; df = 1,54; p < .001; ANCOVA, age adjusted) and greater IPD as reflected in the IP subscale of the DRS (F = 48.9; df = 1,54; p < .001; ANCOVA). A subgroup of patients (n = 17) were also part of a six-week prospective study of nortriptyline at a fixed dose of 75mg/daily for six weeks. Those patients were monitored using weekly Hamilton Depression Ratings (HDRS). At the end of six weeks, recovery was defined by a score of <11 for the 21-item HDRS. Nine patients showed recovery (mean HDRS: 7.1; sd:2.8), whereas eight patients remained unrecovered (mean HDRS: 18.4; sd:3.4). The groups were comparable in their baseline HDRS scores (t = .63; df = 15; p < .55). Patients showing recovery had shorter latency (mean:364.7 ms; sd:30.9) and less IPD (mean:36.2; sd:2.0) compared with patients who failed to recover (mean latency:402.0 ms; sd:38.6; F = 10.0; df = 1,14; p < .01; ANCOVA) (mean IPD:30.0; sd:7.7; F = 9.2; df = 1.14; p < .02; ANCOVA). The percentage change in HDRS score for the entire group at the end of six weeks was negatively correlated with P300 latency (Partial R:-0.777; p < .023; age adjusted). A trend was noted for correlation with IPD (Partial R: -0.435; p < .11; age adjusted).

Discussion: These preliminary findings support the hypothesis that P300 latency predicts response to antidepressant treatment in geriatric patients and is more sensitive than the DRS IP subscale in the symptomatic state. Further investigation in a larger sample using more sensitive measures of IPD is warranted.

NR665 Thursday, May 22, 12 noon - 2:00 p.m.

Inverse Nortriptyline Dose-Response Relationships in Dementia

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Summary:

We evaluated the relationship between drug dose and clinical response for depression in 49 nursing home residents, average age 79.9, who were randomized under double-blind conditions to usual (60 mg/day; n = 35) or low (10 mg/day; n = 14) doses of nortriptyline (NT). Using Clinical Global Impressions of much or very much improved to define categorical responders, 22 of 35 of those assigned to 60 mg and nine of 14 of those assigned to 10 mg improved (Chi sq (1) = .01; ns). However, when the sample was divided into those who were cognitively intact (MMSE > 20) versus those who were impaired (MMSE ≤ 20), significant interactions emerged. For intact patients, 12 of 21 of those given 60 mg versus one of seven given 10 mg improved (Chi sq (1) = 3.88; p < .05); for impaired patients, corresponding figures were one of 14 and four of seven (Chi sq (1) = 6.43; p < .02). Comparable results were obtained using continuous measures of outcome. The inverse relationship between NT dose and clinical response in patients with dementia could not be attributed to either pharmacokinetic differences between intact and impaired patients or cognitive toxicity/delirium in impaired patients given usual doses. These results suggest that the pathogenic mechanisms leading to depression and/or the processes underlying pharmacological responses to nortriptyline differ between intact and demented older adults with depression.

NR666 Thursday, May 22, 12 noon - 2:00 p.m.

Estrogen Therapy Decreases the Frequency of Physically Aggressive Behaviors in Severely Demented Elderly Patients

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Summary:

Objective: To evaluate the efficacy of conjugated estrogens in decreasing aggressive behaviors in severely demented, elderly, long-term-care residents.

Method: A randomized, double-blind, placebo-controlled clinical trial of conjugated estrogens over four weeks. The setting was a severe behavior disturbances unit in a long-term-care facility in Boston, Massachusetts. Subjects were 12 female and one male long-term-care facility residents with dementia (average initial Folstein MMSE score was 4.92 +/- 8.21) and aggressive behaviors. Subjects were referred by their physician or the nursing staff. Participants were randomly assigned to receive conjugated estrogens or placebo over a four-week period. Outcome measures were defined as the difference between the averages of the variable of interest (aggressive behavior scores) on conjugated estrogens and on placebo.

Results: Estrogen therapy decreased the frequency of subjects' physically aggressive behaviors (p < = 0.02), but did not signifi-

cantly decrease the frequency of other types of aggressive behaviors.

Conclusions: This short-term, double-blind, placebo-controlled clinical trial study showed that estrogen therapy resulted in a significant decrease in the frequency of physically aggressive behavior. The patients experienced no adverse side effects from the estrogen during the course of the study.

NR667 Thursday, May 22, 12 noon - 2:00 p.m.

Neuropsychological Functioning and MRI Signal Hyperintensities in Geriatric Depression

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Summary:

Geriatric depression is associated with neuropsychological dysfunction that may have specific structural and/or functional neuroanatomical correlates. The purpose of this study was to examine the relationship between signal hyperintensities on T-2 weighted MR scans–a possible marker of underlying pathology–and neuropsychological test findings in geriatric depressed and normal elderly subjects.

Methods: Elderly DSM-III-R major depressives (n = 41) and normal comparison subjects (n = 38) were participants in an MRI study (1.0T, Siemens) of signal hyperintensities in periventricular, deep white matter, and subcortical gray matter. Hard copies of scans were rated in random order by research psychiatrists (BSG, KRRK) blind to diagnosis employing the modified Fazekas hyperintensity rating scale. Cognitive performance was independently assessed with a comprehensive neuropsychological battery.

Results: Elderly depressives manifest significantly worse cognitive performance on virtually all tests compared with controls ($p < 0.05$). Analyses of covariance (covarying for age and years of education) indicated a significant interaction between hyperintensity location/severity and presence/absence of depression on cognitive performance ($p < 0.05$). Depressed patients with moderate-severe deep white matter hyperintensities demonstrated worse performance on general and delayed-recall memory indices, executive functioning, and language measures than depressed patients without such lesions and normal elderly subjects with or without deep white matter changes. In contrast, periventricular hyperintensities only showed an interaction with language measures, whereas subcortical hyperintensities were unrelated to any measures of cognitive functioning.

Conclusions: Findings validate cognitive changes in geriatric depression and suggest possible neuroanatomic vulnerabilities to developing executive, memory, and language dysfunction when depressed.

NR668 Thursday, May 22, 12 noon - 2:00 p.m.

Neuroanatomical Localization of Magnetic Resonance Hyperintensities of Geriatric Depression

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Summary:

Signal hyperintensities in deep white and subcortical gray matter on brain magnetic resonance imaging (MRI) scans are related to cerebrovascular disease risk factors and probable underlying arteriosclerotic/ischemic histopathology. Increased frequency and severity of signal hyperintensities have been regularly reported in elderly depressed patients compared with normals.

Objective: To examine neuroanatomic localization/lateralization of hyperintensities in late-life depressives and determine whether findings support the relationship between infarct location and depression previously observed in stroke patients.

Methods: T-2 weighted MRI scans (GE 1.0 T) of elderly depressed (n = 35) and normal comparison (n = 31) subjects were reliably assessed for signal hyperintensities in left and right frontal, parietal, occipital, and temporal lobes, basal ganglia subcomponents (caudate, putamen, globus pallidus, internal capsule), and thalamus employing a semiquantitative rating scale that incorporates size and number of lesions in each region of interest.

Results: Comparisons of hyperintensity ratings in elderly depressives and controls revealed uniformly higher mean ratings in depressives. Logistic regression indicated that left frontal deep white matter (Wald statistic = 7.96; $p < 0.005$, Exp[B] = .64) and left putaminal hyperintensities (Wald statistic = 4.65, $p < 0.04$, Exp [B] = .65) significantly predicted depressive group assignment. No relationships with age at onset of depression were demonstrated.

Conclusions: Similarities between hyperintensity locations associated with geriatric depression and infarct location in post-stroke depression studies support a cerebrovascular disease model of late-life depression. Findings also support other structural and functional neuroimaging studies that suggest that frontal and striatal abnormalities, especially left-sided, may have strategic importance in the pathophysiology and expression of depression.

NR669 Thursday, May 22, 12 noon - 2:00 p.m.

Apathy and Activities of Daily Living in Geriatric Depressed Patients With and Without CT-Scan Identified White Matter Disease

Melissa Jenkins, Ph.D., Department of Psychiatry, Brown University, 345 Blackstone Boulevard, Providence RI 02906; Paul F. Malloy, Ph.D., Stephen P. Salloway, M.D., Robert Kohn, M.D., Robert J. Westlake, M.D., Debbie Javorsky, M.A.

Summary:

Objectives: To determine if geriatric depressed patients with CT-scan-identified white matter changes show more apathy and impairment in Activities of Daily Living (ADL) than age- and depression-matched patients without white matter changes.

Method: Noncontrast CT scan ratings by a neuroradiologist were used to group inpatients over age 60 with major depression according to the presence (WMD; N = 20) or absence (CTL; N = 16) of white matter abnormalities. Patients with neurologic illness, dementia, substance abuse, or comorbid psychiatric disorders were excluded. The two groups, which did not differ on age, estimated intelligence, or Mini-Mental Status Examination scores, were compared on ratings of apathy (Apathy Evaluation Scale) and independence in ADL (Lawton and Brody Scales) completed by a family member, and on depression indices.

Results: WMD patients were more apathetic ($p = .04$) and more impaired on Basic Activities of Daily Living ($p = .02$) than CTL subjects. Groups did not differ on self-report, clinician-rated, or informant-rated depression indices. Apathy and ADL ratings were significantly correlated ($r = .51$, $p < .05$), while depression and ADL ratings were not.

Conclusion: White matter abnormalities in geriatric depressed patients may be associated with apathy and ADL impairment.

NR670 Thursday, May 22, 12 noon - 2:00 p.m.

Clinical Significance of White Matter Hyperintensities on MRI in Geriatric Depression

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Summary:

Objective: To assess the clinical impact of MRI-identified white matter hyperintensities in geriatric depressed patients.

Method: Two age-matched groups of geriatric inpatients with major depression were assessed at baseline and after a three-year interval. Dementia, CVA, comorbid neurologic, or psychiatric illness were exclusion criteria. One group (CTL; N = 13) had minimal white matter hyperintensities (WMH) on quantitative MRI, and the other had moderate to severe WMH (WMD; N = 12).

Results: WMD patients had baseline deficits in activities of daily living, which worsened over the three-year interval. Additionally, WMD patients were more likely to die (25% vs. 0%) or need nursing home care (42% vs. 0%) than CTL patients. No between-groups differences in severity of depression were seen at either assessment. At baseline, WMD patients had mild memory deficits suggesting frontal/subcortical dysfunction. At follow-up, a broad range of cognitive deficits including executive, spatial, language, and memory (encoding, storage, retrieval) skills were seen. Despite global cognitive decline, no patient in either group was clinically diagnosed with Alzheimer's-type dementia.

Conclusion: White matter disease may predict poorer outcome in geriatric depressed patients and may be etiologic for non-Alzheimer's-type dementia.

NR671 Thursday, May 22, 12 noon - 2:00 p.m.

Clinical Utility of the Dementia Rating Scale for Evaluation of Patients with Stroke and Non-Alzheimer's Dementia

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Summary:

Objective: To determine the usefulness of the Dementia Rating Scale (DRS) for evaluation of patients with non-Alzheimer's type cognitive impairment.

Method: The DRS was administered to 238 outpatients referred for neuropsychological assessment at three New England medical centers. Patients had Alzheimer's dementia (AD; n = 45), single large vessel stroke (CVA; n = 56), dementia associated with multiple cerebral infarctions (MID; n = 48), white matter disease (WMD; n = 44) of at least moderate severity involving periventricular or subcortical brain areas, and control subjects (n = 45). Total DRS score and subtests assessing attention, initiation, conceptualization, construction, and memory were compared across groups.

Results: All patient groups were significantly impaired on the DRS compared with controls, and all patient groups met criteria for dementia based on performance over two standard deviations below the mean. Among demented patients (DRS < 123). AD patients were most impaired on the Memory index. MID and CVA patients had milder memory impairments, while WMD patients were least impaired. Conceptual ability also was most impaired in AD; yet AD patients actually showed stronger Construction and Attention performance than MID, CVA, and WMD patients.

Conclusions: The results indicate that patients with MID, CVA, and WMD meet criteria for dementia on the DRS, but show a different pattern of impairment than AD patients.

NR672 Thursday, May 22, 12 noon - 2:00 p.m.

A Stress-Diathesis Model of Spousal/Consortial Homicide-Suicide in the Aged

Donna Cohen, Ph.D., Aging/Mental Health, University of South Florida, 13301 Bruce B. Downs Blvd, Tampa FL 33612; Maria D.D. Llorente, M.D., Julie Malphurs, M.A., Carl Eisdorfer, M.D.

Summary:

Objective: To characterize for the first time biopsychosocial, cultural, and environmental factors associated with homicide-suicide of the spousal/consortial type.

Method: A total of 137 homicide-suicides of the spousal/consortial type were identified from 1988-1994 in three medical examiner districts covering six entire counties in west central Florida and one medical examiner district covering Dade County in southeast Florida. Both regions were comparable in total population and had similar high concentrations of older persons. Complete medical examiner files were obtained, and 160 variables in seven areas were coded from death certificates, autopsy reports, toxicology screens, police investigative reports, and newspaper clippings in the files.

There were 12 incident-identification variables (e.g. file number, date of death, type of homicide-suicide); 15 sociodemographic variables; and 24 variables describing physical circumstances (e.g. location of bodies, presence of suicide notes, drugs at the scene); 35 possible antecedent conditions (e.g. illness, separation, adverse life circumstances); 24 possible drug categories classified from toxicology studies at autopsy; and 50 autopsy findings including ICD-codes, height, weight, and number of wounds.

Results: The younger couples in both regions were comparable except for racial composition. There were significant differences between the older couples across the two regions. The west central group were all white, older couples, both in their late 70's, mostly married, with indications of failing health more often in the homicide victim, and indications of depression and alcohol abuse in about half of the perpetrators. Two-thirds of the older group in southeastern Florida were Hispanic, and they were much younger than the west central group, with the perpetrators in their late 60's, and the female victims in their late 40's. The perpetrators had indications of mental disorder in about a third of the sample as well as a history of verbal and physical discord, separation, and previous criminal acts.

Conclusion: Our results challenge the two-level typology developed by Marzuk and colleagues. Although depression and other psychiatric disorders are strongly implicated, our results suggest they are complex, lethal events with multiple interacting antecedents.

NR673 Thursday, May 22, 12 noon - 2:00 p.m.

Increased Medical Utilization in High Anxiety Sensitivity Elderly

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Summary:

Objective: To determine how anxiety sensitivity, a pathologic form of anxiety associated with panic disorder, affects health care utilization by elderly patients presenting to a primary care setting.

Methods: At Cornell Internal Medicine Associates, patients presenting for initial evaluation are asked to complete a questionnaire that includes the *Anxiety Sensitivity Index* (ASI), a 16-item self report for assessing fear of fear and fear-related sensations.

Results: The number of patients 60 years or older was 97 (14%), and 63% were female. High anxiety sensitivity (HAS), ASI score

≥34, was found in 26 patients (27%). Forty-six percent of patients with HAS had more than five visits compared with 21% of all others, yielding an increased relative risk of 1.46 ($p \leq .05$); 54% of HAS patients had more than four prescriptions compared with 25% of all others, yielding an increased relative risk of 1.62 ($p \leq .05$). Subjects were divided into ASI quartile groups and health care utilization measures were compared. The mean number of visits (±sd) by quartile were: lowest quartile 3.75 (±3.22), low-mid quartile 4.44 (±3.57), mid-high quartile 6.88 (±7.31), and highest quartile 5.61 (±3.88). The mean number of medications by quartile was 2.54 (±2.73), 3.88 (±5.09), 4.54 (±5.73), and 5.65 (±5.19), respectively.

Conclusions: High anxiety sensitivity may indicate the presence of pathologic anxiety in patients presenting to primary care clinics and may be a marker for increased health care utilization.

NR674 Thursday, May 22, 12 noon - 2:00 p.m.

Usefulness of Alzheimer's Disease Assessment Scale Late Version for Distinguishing Levels of Function in Advanced Alzheimer's Dementia Patients

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Summary:

Background: This study examined the usefulness of the Alzheimer's Disease Assessment Scale-Late Version (ADAS-L) for assessing cognitive and behavioral impairment in severely demented Alzheimer's disease patients. This scale was designed for use in patients whose impairment was too profound for them to be examined with the ADAS and contains assessments of both cognitive and functional impairments.

Methods: Subjects were 250 geriatric Alzheimer's inpatients who met Clinical Dementia Rating (CDR) criteria for severe impairment (i.e., scores of 3 or 4). They were examined with the ADAS-L, the Mini-Mental State Examination (MMSE), and the Blessed Test of Information, Memory, and Concentration (BT).

Results: Discriminant function analyses used the ADAS-L, the MMSE, and the BT as independent variables predicting the level of impairment on the criterion measure, the Clinical Dementia Rating scale. The ADAS-L surpassed both the MMSE and the BT at accurately distinguishing gradations in functioning at advanced levels of impairment, with 92% accuracy in distinguishing between severe and profound dementia. This finding is at least partially due to the fact that all of the patients with CDR scores of 4 had MMSE scores of 0 and BT scores of 33, reflecting a pronounced floor effect.

Conclusions: These findings provide evidence for the validity of the ADAS-L as an instrument for measuring impairment when dementia has advanced to a point at which standard brief rating scales lose their utility as a source of information about level of functioning.

NR675 Thursday, May 22, 12 noon - 2:00 p.m.

Hopelessness and Suicide Attempts in Elderly Patients with Major Depression

Yeates Conwell, M.D., Department of Psychiatry, University of Rochester, 300 Crittenden Boulevard, Rochester NY 14642; Paul Duberstein, Ph.D., Larry Seidlitz, Ph.D., Christopher Cox, Ph.D., Eric D. Caine, M.D.

Summary:

Objective: Hopelessness is associated with suicidal behavior in adolescent and general adult samples. Little is known, however, about its role in suicide attempts among the elderly. This study tests the hypothesis that hopelessness distinguishes elderly major depressives who made suicide attempts from those who did not.

Method: Using a case-control design, the study compared patients age 50 or older/with major depressive illness admitted to inpatient care following a suicide attempt (DSAs; n = 44) with major depressives whose psychiatric admissions did not follow a suicide attempt (DNAs; n = 52). The Beck Hopelessness Scale was the principal variable of interest.

Results: There were no significant differences between groups in age, gender, marital status, or severity of depression. DSAs reported significantly greater hopelessness in the week prior to their suicide attempts than did the DNAs prior to admission (12.8 ± 6.7 [SD] vs. 10.3 ± 5.5; one sided $t = 1.97$; $p = .026$).

Conclusions: The subjective experience of hopelessness is associated with suicide attempts in depressed older people. These findings have implications both for recognition of depressed elders at highest risk for suicide and for intervention using strategies designed to lower hopelessness.

NR676 Thursday, May 22, 12 noon - 2:00 p.m.

Personality Disorder Predicts Functional Decline in Elderly Depressives

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Summary:

Objective: The authors evaluated premorbid personality disorder (PD) as a predictor of changes in functioning and quality of life among elderly depressives.

Method: Treated elderly patients (N = 35) who no longer met RDC criteria for major depression were assessed for PDs (Personality Disorder Examination); residual depression (Ham-D); disability, health-related quality of life and overall quality of life (respective subscales of the Cornell General Health Questionnaire Quality of Life section); and global functioning (GAS). Subjects were assessed after acute treatment (entry) and at one-year follow-up. Follow-up Ham-D scores were conservatively classified into three categories: no depression (0–3), mild (4–10), and high (>10). A series of two by three ANOVAS was performed using presence or absence of a PD on entry and the three Ham-D follow-up categories as between-subjects factors.

Results: 22.9% of the subjects met criteria for a definite or probable DSM-III-R personality disorder. For all dependent variables except global functioning, the presence of PD interacted with depression severity at follow-up to significantly predict one-year declines in functioning; for global functioning, depression severity at follow-up and personality disorder predicted such change independently.

Conclusions: Patients with mild residual depression and personality disorder may be at risk for impaired functioning despite remission of the acute episode. In treated elderly depressives, personality disorder appears to operate as an "amplification co-factor," exacerbating the impact of residual depression on long-term functioning and quality of life.

NR677 Thursday, May 22, 12 noon - 2:00 p.m.

Effects of Normal Aging on ACTH Response to Corticotropin-Releasing Hormone

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Summary:

We hypothesized that normal aging results in decreased pituitary ACTH response to CRH. This has not been found in other studies, possibly due to compensatory effects of altered sensitivity to feedback inhibition by cortisol. We therefore investigated the effect of age on ACTH response to CRH using metyrapone pretreatment to control for this possibility.

We studied 18 younger (mean age 28 +/- 4 years; 11 males and 7 females) and 16 older (mean age 70 +/- 9 years; 9 males and 7 females) healthy subjects, both with and without metyrapone pretreatment. Human CRH (0.4 ug/kg) and naloxone (65 ug/kg) were administered at 6:00 p.m. and 7:30 p.m., respectively, on both study nights. Serial baseline and stimulated plasma levels of ACTH and cortisol were obtained. Deconvolution analysis was used to define ACTH half life, basal secretion rate, and mass per burst for both age groups on both study nights.

With cortisol feedback inhibition intact (i.e., no metyrapone), there was no age-related difference in ACTH response to CRH ($p = 0.6$) or naloxone ($p = 0.4$). With inhibitory feedback removed by metyrapone pretreatment, however, ACTH responses to CRH and naloxone were both diminished in the older group ($p = 0.01$ and $p = 0.02$, respectively). We therefore conclude that normal aging is associated with decreased pituitary ACTH response to CRH, and a compensatory decrease in sensitivity to cortisol feedback inhibition.

NR678 Thursday, May 22, 12 noon - 2:00 p.m.

Sertraline Treatment of Behavioral Disturbances in Demented Older Adults

William Bondareff, M.D., Department of Psychiatry, University Southern CA, Bldg 10, 1237 N Mission Road, Mol 202, Los Angeles CA 90033; Ill-Woo Han, M.D., Ellen Richter, Ph.D., Laurie La Bree, M.S., Doris Bass, M.S.W.

Summary:

Noncognitive behavioral disturbances, which are often deciding factors for institutional placement of demented elderly persons, are usually transient and responsive to pharmacotherapeutic management. Here, we report our experience with sertraline to treat behavioral disturbances of dementia in an open-label paradigm.

Thirteen patients (4 men and 9 women) were treated. The clinical diagnoses were probable Alzheimer's disease ($n = 11$) and probable vascular dementia ($n = 2$). The mean age was 77.2, the mean Folstein Mini-Mental Examination score was 9.75, and the mean Blessed-Roth Dementia Scale score was 9.3. All patients received an initial daily dose of 25 mg sertraline, which was increased to 50 mg in six patients when there was no apparent clinical response after two weeks. Differences in BEHAVE-AD scores before and after sertraline treatment were analyzed by conventional statistical analyses.

Global clinical improvement in 10 patients (77%) after sertraline treatment was documented by decreased mean total BEHAVE-AD scores. Global clinical improvement was further indicated by significant decreases in the mean Part I (symptomatology) and Part II (global rating) scores. More specific clinical improvement after treatment with sertraline was shown by significant post-treatment decreases in the mean scores for BEHAVE-AD subparts C (activity disturbances) and D (aggressiveness). These changes in BEHAVE-AD scores were not associated with age or severity of dementia.

These results of a preliminary study suggest that sertraline has a role in the management of noncognitive behavioral disturbances in demented elderly patients and point to the need for a double-blind, placebo-controlled, multicenter study.

NR679 Thursday, May 22, 12 noon - 2:00 p.m.

Caregiver Status in Late-Life Depression

Nancy Turret, M.S.W., Clinical Psychopharm, NYS Psychiatric Institute, 722 West 168th Street, New York NY 10032; Steven P. Roose, M.D., Davangere P. Devanand, M.D., Harold A. Sackeim, Ph.D.

Summary:

It has been documented that chronic, severe, and/or debilitating illness contributes to depression in late life. What has not been sufficiently studied is whether caring for a loved one with severe illness may also be a frequent stressor that provokes depression. A caregiver is defined as a person who is the primary provider of emotional and/or physical assistance to someone incapacitated due to illness. The purpose of this study was to evaluate the caregiver status among depressed patients enrolled in the Late Life Depression Research Center.

Caregiver status was evaluated in 68 consecutive patients who met DSM-III-R criteria for major depressive disorder; 32% (22 of 68) of the depressed patients were caregivers, a strikingly high rate compared with to a general population over 60. The caregiver group included 18 females and four males with mean age of 69 $\pm$ 8 and baseline HDRS of 21 $\pm$ 3. Seventy-eight percent were caring for their spouse or other first-degree relative, and the most frequent conditions involved were stroke, Alzheimer's, and cancer. In 64% of the group the caregiving began within one year prior to the onset of the depression.

The 22 caregivers were not different than the 46 noncaregiving depressed patients with respect to age or baseline HDRS, but there were significantly more females in the caregiving group ($X^2 = 8.28$, $p < .01$). Most importantly, the depressed caregivers responded to antidepressant treatment; 63% achieved remission (final HDRS ≤ 8). The results of this study suggest the need for systematic research in the diagnosis and treatment of depression in caregivers.

NR680 Thursday, May 22, 12 noon - 2:00 p.m.

Principle Component Analysis of Positive and Negative Syndrome Scale in Dementia

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Summary:

Objective: Negative symptoms (NS) have been noted in patients with dementia and stroke but the relationship between NS in these disorders and NS in schizophrenia has not been established. The purpose of this study was to assess the NS in these patients using principal component analysis of the Positive and Negative Syndrome Scale (PANSS) item ratings.

Method: PANSS was administered to 75 patients with dementia or stroke and no axis I diagnosis; principal component analysis of PANSS item ratings was subsequently performed.

Results: After Varimax rotation of factors with eigenvalue not less than 1, seven factors emerged. Factor I was interpreted as negative symptom complex. It explained 28.5% of variance and was indistinguishable from negative factor, described for patients with schizophrenia and schizoaffective disorders (S/SA). Factor II, cognition/insight, which was able to explain 19.2% of variance, was also not different from the similar factor, described in S/SA. Factor III with high loadings of poor impulse control and excitement was interpreted as compromised self-regulation. Factor IV with high loadings of guilt feelings, suspiciousness, and disturbance of volition, was considered as a relational attitude/indirect hostility. Anxious/depressive factor V explained 11.0% of total variance, and except for the absence of guilt item, was similar to the one described in S/SA. Factor VI, agitation/disinhibition was close in

content with manic-expansive factor in S/SA. Factor VII, prominent for high loadings of active social avoidance and hostility, constituted a (direct) hostility factor.

Conclusion: PANSS appears to be a comprehensive instrument for the assessment of diversity of psychopathological and cognitive symptoms in patients with dementia or stroke. The structure of negative symptom complex in these disorders was similar to S/SA. This might constitute a relative independence of NS from the nosologic entities.

NR681 Thursday, May 22, 12 noon - 2:00 p.m.

The Cognitive Effect of Risperidone in Elderly Schizophrenic Patients: A Pilot Double-Blind Comparison Study with Haloperidol

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Summary:

The purpose of this double-blind controlled study is to determine whether risperidone has a superior beneficial effect on cognitive performance in a group of stable elderly schizophrenic patients compared with haloperidol.

Method: Twenty stable geriatric schizophrenic patients entered the study. The patients were randomly assigned into two groups: one received risperidone (2–6 mg/day) and the other haloperidol (5–10 mg/day). The patients were assessed using the Positive and Negative Symptom Scale (PANSS) and a series of cognitive tests that included Mini-Mental Status Examination (MMSE), measures of verbal fluency, and tests of attention and memory. The baseline assessments were done while patients were maintained on their ongoing psychiatric medication and at least two weeks after the study medication dose was stabilized. All the psychiatric adjunctive medication (i.e., antiparkinsonian medication, benzodiazepines, or lithium) was kept constant throughout the study.

Results: Using analysis of covariance with baseline scores as covariates, we found no statistically significant differences in psychiatric and cognitive assessments between the two groups. Paired t-test in the same group suggested that negative symptoms improved significantly only in the patients treated with risperidone. The MMSE improved with risperidone and showed no change with haloperidol.

Conclusions: Although there were no significant group differences, risperidone improved the negative symptoms and the MMSE scores compared with baseline but not other aspects of cognition. Larger controlled studies that account for changes in schizophrenic symptoms are necessary to determine whether risperidone indeed has beneficial effect on cognitive function in schizophrenia.

NR682 Thursday, May 22, 12 noon - 2:00 p.m.

Geropsychiatric Day Hospital: Successful Utilizers Versus Inpatient Recidivists

David Klahr, M.D., Department of Psychiatry, Hillside Hospital, 75-59 263rd St/Lowenstein Bldg, Glen Oaks NY 11004; Eileen Rosendahl, Ph.D., Suzanne Paolucci, A.C.S.W., Blaine S. Greenwald, M.D.

Summary:

Objective: Market-driven reductions in lengths of stay in inpatient geriatric psychiatry units necessitate acute/subacute outpatient services to accomodate still-symptomatic patients. Geriatric psychiatry day/partial hospitalization programs serve as an important alternative to inpatient care. However, limited data are available on elderly patients successfully treated in this setting and those who decompensate and require inpatient hospitalization or rehospitalization. The objective of this exploratory study was to compare demographic and clinical variables in these two populations.

Methods: In order to control for variability in clinician treatment approaches, day/partial hospital charts of consecutive patients (n = 28) completing treatment under the care of one representative psychiatrist during a discrete period were systematically reviewed. The following information was collected: age, sex, marital status, referral source, living situation, diagnosis, and depression (Hamilton Depression Inventory) and cognitive (Folstein Mini-Mental State Exam [MMSE]), Mattis Dementia Rating Scale [DRS] ratings.

Results: 68% (n = 19) of enrollees were successfully treated in the day/partial hospital program and 32% (n = 9) required hospitalization or rehospitalization. Age, sex distribution, marital status, referral source, living situation, and diagnosis did not significantly distinguish groups. Inpatient recidivists had significantly worse Hamilton inventories (29.1 vs. 15.1; $p < 0.05$) than successful utilizers, and nonsignificantly worse performance on the Mattis DRS (124.4 vs. 133.1).

Conclusions: Findings suggest that greater severity of depression, and possibly poorer cognitive performance in geropsychiatric patients may be associated with unsuccessful day/partial hospital utilization with consequent inpatient hospitalization. To prevent recidivism, older patients with this profile may require special strategies (e.g. longer initial inpatient lengths of stay, more vigilant outpatient case management, more intensive outpatient treatment, adjunctive psychiatric home care).

NR683 Thursday, May 22, 12 noon - 2:00 p.m.

Pupil Dilation Test: A Potential Marker for Alzheimer's Disease?

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Summary:

Objectives: To determine whether there were significant differences in pupillary response between subjects with Alzheimer's disease and normal controls, and whether pupillary dilatation test could be used as a diagnostic tool for AD.

Methods: Changes in pupil size of 11 Chinese patients with probable AD, and 16 normal controls were recorded by a video pupillometry for two minutes after three-minute dark adaptation. Then, after instillation of 0.01% tropicamide to one eye, changes were recorded for another 40 minutes in a silent, dark room under calm atmosphere, without any physiological or psychological interference. The pupil diameters were measured at one-minute intervals for the whole course by computerized method. All the AD cases met DSM-IV diagnostic criteria, and were strictly excluded from other dementia by their clinical manifestations and CT scans. All the normal controls have normal intellectual capacity, attention, memory, language, and a normal CT scan (without any evidence of degeneration, ischemia, or infarcts).

Results: There was a faster maximum dilatation in the AD group. At minute 19, there was a 17.9% change in pupil diameter of patients with AD compared with a 2.94% change for normal controls; while at minute 20, there was a 19.1% change compared with 5.62% ($p = 0.01$). There was no significant difference at minute 29 or more between the groups.

Conclusion: There are significant differences in pupillary responses to dilute tropicamide between patients with AD and normal subjects. Further studies are needed to determine whether the test has enough sensitivity and specificity as a diagnostic tool for clinical use.

NR684 Thursday, May 22, 12 noon - 2:00 p.m.

Career Soldiers' Attitudes Toward Homosexuals

Elizabeth E. Correnti, M.D., Department of Psychiatry, Eisenhower Army MC, Bldg 300, East Hospital Road, Fort Gordon GA 30905; Laura Davidson, Ph.D., Mary B. Cruser, M.D.

Summary:

Objective: This study of career soldiers stationed at two major Army bases assessed how service members who have served at least ten years on active duty feel about homosexuals serving in the military.

Method: Questionnaires were distributed to 400 subjects who agreed to participate in a comprehensive survey of attitudes and military experiences. Equal numbers of men and women were enrolled and a total of 248 returned the questionnaires. Subjects responded, on a Likert scale, to questions regarding whether homosexuals should be permitted to serve in the military. They completed the Bem Sex Role Inventory and a representative subgroup of participants were interviewed by the researchers.

Results: Forty-eight percent disapproved of homosexuals serving in the military, 40% approved, and 12% were neutral or undecided. There were no differences in attitudes toward homosexuals based on rank, race, education, time in service, or occupational satisfaction, but women expressed more tolerance than did the men. Soldiers with more egalitarian attitudes were more likely to support homosexuals serving in the military.

Conclusions: A significant percentage of career soldiers surveyed were supportive of the integration of homosexuals into the military. Issues discussed by these service members could be the focus of educational efforts of advocacy groups.

NR685 Thursday, May 22, 12 noon - 2:00 p.m.

Influence of Disease Severity on Self-Perceived Mental and Physical Health in Schizophrenic and Neurotic Patients

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Summary:

Background: Self-perceived health is an important component of the "lack of disease insight," contributing to course and prognosis of mental illness.

Objective: To evaluate the association between disease severity and the self-perceived mental and physical health in patients with schizophrenia and neurosis.

Method: Cross-sectional study of 115 schizophrenic and 48 neurotic hospital patients in Muenster, Germany, from 1995 to 1996. Standardized patient evaluation was done by physicians within 24 hours after admission. ICD-9, BPRS, and SF-36 were used to classify diseases, rate of psychiatric symptoms, and self-reported mental and physical health. Linear regression was used in the analysis.

Results: Increasing disease severity changed the contribution of BPRS subscales to their summary score only in schizophrenic patients. A significant reduction in physical health with advancing severity of illness was observed in all patients, but a reduction in mental health was only observed in neurosis. BPRS subscales analysis in schizophrenic patients revealed significant increases in mental health scores with advancing severity of "thought disturbance" and "activation."

Conclusions: Increasing disease severity in schizophrenia and neurosis is perceived in self-reported physical health, but only in neurotic patients in mental health. "Thought disturbance" and "activation" contribute considerably to the lack of mental health perception in schizophrenic patients.

NR686 Thursday, May 22, 12 noon - 2:00 p.m.

Enhanced Dexamethasone Responsivity in Female Veterans with PTSD

M. Michele Murburg, M.D., Department of Psychiatry, University of Washington, 4260 Shoreclub Drive, Mercer Island WA 98040; Susan Ballagh, M.D.

Summary:

Purpose: To determine the incidence of enhanced cortisol suppression in response to dexamethasone (DEX) in women veterans with PTSD.

Method: We did a retrospective pilot data analysis of cortisol levels following low and high DEX doses in a clinical population of female veterans at the National Center for PTSD. We compared results for 19 women with PTSD by SCID and CAPS, and two women who failed to meet PTSD criteria.

Results: Mean serum cortisol following DEX 0.25 mg was 5.0 $\pm$ 2.9 μg/dl for women with PTSD and 10.4 $\pm$ 6.2 μg/dl for women without ($p < .033$). Mean serum cortisol following DEX 0.50 mg was 3.3 $\pm$ 3.6 μg/dl for women with and 11.6 $\pm$ 0.3 g/dl for women without PTSD ($p < .004$). Following DEX 1.0 mg, cortisol levels were 1.6 $\pm$ 2.1 μg/dl for patients with, and 4.8 $\pm$ 5.5 μg/dl for patients without PTSD ($p < .08$). Forty-three percent of Vietnam veterans suppressed their cortisol levels to <5μg/dl following both doses, while 83% and 86% of ODS veterans suppressed cortisol after the .025 and 0.50 mg doses, respectively. Sixty percent and 80% of sexually assaulted veterans suppressed cortisol after these respective doses.

Conclusion: Women with PTSD appear to have a high incidence of enhanced cortisol suppression following low doses of DEX. Prospective studies of the clinical features, which may contribute to this phenomenon, are warranted.

NR687 Thursday, May 22, 12 noon - 2:00 p.m.

Social Support, Coping Style, Stress Perception and Depressive Symptoms in the Patients Whose Esophageal Manometry and Gastroesophagea Reflux Tests Were Normal

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Summary:

Objective: The sensation of dysphagia and heartburn or globus hystericus are common symptoms of esophageal disease, but symptoms occur in normal subjects who undergo esophageal manometry (EM) and gastroesophageal reflux tests (GERT). This study investigated social support, coping style, stress perception, and depressive symptoms in patients whose EM and GERT were normal but who complained of symptoms of esophageal motility and gastroesophageal reflux disorder.

Method: 38 patients who complained of symptoms had been tested with 24-hour ambulatory EM and conventional GERT in our university gastroenterologic clinic. Thirty patients whose tests had been normal (Negative Group) were assessed with the Symptom Checklist 90-Revision(SCL-90-R). Beck Depression Inventory(BDI), Spielberger Stait-Trait Anxiety Inventory(STAI), the Ways of Coping Checklist, and Interpersonal Support Evaluation List and compared with 30 patients (Control Group) who had complained of symptoms of Hepatobiliary disorder. The two groups were also assessed by their quantity of perceived stress during the last year through self-report.

Results: 78.9% of 38 subjects who had been tested were normal in the EM and GERT. These patients tended to be predominately females, older, and possessed a lower education than control group. Compared to the control group, the patients whose tests

had been normal had significantly higher mean scores on four subscales (somatization, depression, anxiety, and positive symptom distress index) and significantly lower mean scores on two subscales (interpersonal sensitivity and paranoia) of the SCL-90-R. The negative group had significantly higher levels of depression than the control group in the BDI (28.4 ± 8.2 versus 17.6 ± 6.4, $p < .001$), but there was not any significant difference in the STAI. Also, the negative group had significantly more perceived stress than the control group (10.6 ± 3.4 versus 8.1 ± 3.6, $p < .01$), and lower scores in the interpersonal support (20.0 ± 6.6 versus 29.8 ± 7.4, $p < .001$), problem-focused coping (19.2 ± 12.2 versus 33.9 ± 8.1 $p < .001$), and seeking social support (3.6 ± 2.9 versus 8.5 ± 3.0, $p < .001$). There were no differences in the emotion-focused coping and wishful thinking between the two groups.

Conclusion: These findings suggest that such patients might benefit from psychiatric evaluation and treatment with psychotherapeutic and psychopharmacological modalities.

NR688 Thursday, May 22, 12 noon - 2:00 p.m.

Gender Bias in Psychiatric Texts

Raphael J. Leo, M.D., 42 Danbury Drive, Cheektowaga NY 14225-2017; Maria T. Cartagena, M.D.

Summary:

Objective: To review case vignettes employed in introductory psychiatric texts for gender bias.

Method: Five texts containing illustrative vignettes were selected for their use by medical students. The frequencies of vignettes featuring male or female subjects, along with the frequencies of psychiatric disorders reflecting male or female subjects were obtained.

Results: The difference observed between the number of vignettes featuring males and females, across the five texts, differed significantly, $x2 = 20.66, df = 1, < .0001$. The frequency of male versus female subjects was significantly different in all but two texts examined. In only one text did the number of vignettes featuring female subjects exceed those featuring males. Female subjects were predominantly employed in vignettes illustrating the following disorders: somatoform (67.6%), dissociative (62.5%), eating (72.2%), depressive (50.9%), and factitious (71.4%). Vignettes illustrating all remaining diagnoses predominantly featured men.

Conclusions: The present study is consistent with previous research examining gender bias in other aspects of medical training. Gender bias in educational materials used by medical trainees may impact on subsequent patient care. Use of gender in illustrative examples should reflect known epidemiological trends of psychiatric disorders. When these trends are unknown, gender equity or neutrality should be employed.

NR689 Thursday, May 22, 12 noon - 2:00 p.m.

Investigation of Perimenstrual History Among Climateric Patients: Steiner's PMS Questionnaire, Test-Retest

Caludio de Novaes Soares, M.D., Department of Psychiatry, University S. Paulo, Rua Jose Maria Liboa 1060 AP21, Sao Paulo SP 01423001, Brazil; Osvaldo P. Almeida, Ph.D.

Summary:

Background: The term "climacteric syndrome" has been used extensively to refer to physical and psychological symptoms that arise around the menopause period. These clinical features are sometimes similar to those observed at other times during women's life cycle such as in postnatal and premenstrual depression.

Objective: To determine the reliability of assessing premenstrual complaints retrospectively and evaluate the association between previous premenstrual complaints and psychiatric symptoms at the time of the menopause.

Methods: Twenty women attending a specialized psychiatric outpatient clinic (Pró-Mulher, Instituto de Psiquiatria do HC - Univ. de São Paulo) were assessed at the time of the menopause to investigate their psychiatric morbidity (SRQ-20) and previous perimenstrual history. A Brazilian version of Steiner's PMS Questionnaire (modified to assess symptoms retrospectively) was used to determine the severity of premenstrual symptoms. The schedule's test-retest reliability was also evaluated (four to eight week intervals).

Results: All Steiner's questions showed moderate to very good test-retest reliability ($0.41 < kappa < 1.00$). The mean total Steiner's score was 22.60 (95%CI = 20.06 to 25.14) and the mean total SRQ score was 12.60 (95%CI = 12.60 to 13.77). There was no clear association between Steiner and SRQ scores (Spearman correlation coefficient = 0.03).

Conclusions: Previous perimenstrual complaints are highly prevalent among climacteric patients attending a specialized psychiatric unit. The retrospective assessment of premenstrual symptoms among these patients can be made reliably with the Steiner's schedule. The lack of association between Steiner and SRQ scores is likely to have been caused by the high prevalence of both psychiatric symptoms and premenstrual complaints among these patients. The evaluation of climateric subjects in a nonspecialized setting is necessary to clarity the possible association between previous premenstrual complaints and current psychopathology among women in the menopause.

NR690 Thursday, May 22, 12 noon - 2:00 p.m.

Assessment of Prevalence of Eating Disorders Among Rural Adolescents

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Summary:

This pilot study was designed to assess the frequency in which rural adolescents in East Tennessee display attitudes associated with high risk for developing eating disorders. There has been very limited study of rural populations previously, and it has been generally believed that these disorders occur primarily in larger metropolitan areas. The Eating Attitudes Test (EAT), a self-administered questionnaire, was given anonymously to 1,302 male and female adolescents in grades seven through 10 at five regional public schools. The schools varied somewhat in their degree of rurality. Results showed that 19.8% of females and 3.7% of males scored above 29, indicating high risk. There was a possible trend toward increased incidence in areas that were more rural, which was a surprising finding that merits further study.

NR691 Thursday, May 22, 12 noon - 2:00 p.m.

The Role of Temperamental Traits in Determining the Association of Heavy Drinking and Bulimia-Like Behavior in College

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Summary:

Objective: The mechanism of the comorbidity of alcohol abuse/dependence and bulimia is not known. In animals, food deprivation potently increases drug and alcohol self-administration. We hypothesized that food deprivation triggers not only binge eating but also increases substance use. However, severity of dieting (and

food deprivation) cannot entirely explain why bulimics use more alcohol than anorexics as each group restricts food severely. We hypothesized that temperament might determine which college women with subclinical bulimic symptoms also use alcohol heavily. Specifically, we hypothesized that college women with subclinical bulimic symptoms (measured by the Dieting and Bingeing Severity Scale) who drank heavily (measured by the Monitoring the Future questions) would also be neurotic extraverts (i.e., impulsive) on the Eysenck Personality Questionnaire. We studied over 600 college women using the three scales mentioned above. We divided subjects into six groups based on drinking and dieting. We calculated the percentage of each group that had temperaments consistent with stable extraversion, stable introversion, neurotic extraversion, or neurotic introversion.

Results: Distribution of temperament types differed from expected (Chi-square = 78.1; $p < 0.00000$). Neurotic extraversion was the most frequent among heavy drinker/severe or at-risk dieters and least frequent among the nondrinker/non- or casual dieters. Neuroticism increased with dieting severity, while extraversion increased with drinking.

Conclusion: As temperament is significantly genetically influenced, it is possible that young women born with impulsive temperaments are more vulnerable to disinhibiting effects of food deprivation and will lose control of eating as well as substance use.

NR692 Thursday, May 22, 12 noon - 2:00 p.m.

Individual Versus Group Formats for Symptom-Focused Therapy of Bulimia Nervosa: Comparative Efficacy

Philippe Lageix, Eating Disorders, Douglas Hospital, 6875 Lasalle Boulevard, Verdun QC H4H 1R3, Canada; Howard Steiger, Ph.D., Sheila Jabalpurwala, Ph.D.

Summary:

This study compared the relative efficacy of intensive individual and group-based therapy formats (10 patients in a group), in the treatment of specific and nonspecific symptoms of bulimia nervosa. Three- and six-month response of 38 patients with bulimic symptoms, treated in an intensive, symptom-focused, individual therapy (including psychoeducational, cognitive-behavioral, and brief dynamic components), were compared with those of 38 cases (matched for severity of bulimic symptoms) receiving a less labor-intensive psychoeducational/process group treatment, and with 15 cases whose progress was followed over three months while on a waiting list for treatment. We evaluated response on measures reflecting severity of bulimic symptoms and of generalized psychiatric symptoms. Both active treatments proved to have significant benefits in comparisons implicating the wait-list control group over the first three months. Individual therapy showed certain advantages over group therapy during the first three months of treatment (yielding somewhat more rapid reduction in frequency of binge-purge episodes and in depressive symptoms), but the individual and group treatments proved to have equal effects by the end of the sixth month of therapy. Our findings suggest that psychoeducational group approaches provide a valid form of intervention for bulimia nervosa, with obvious cost-effectiveness benefits.

NR693 Thursday, May 22, 12 noon - 2:00 p.m.

Clinical and Demographic Characteristics of Active Duty Inpatients with Eating Disorders: A Retrospective Study

Anita M. Nusbaum, M.D., Branch Clinic, Mental Health Unit, Naval Air Station North Island, San Diego CA 92135; Vicki A. Alberts, M.D.

Summary:

Eating disorders among active duty personnel are controversial administrative problems in Navy psychiatry. Frequently these service members are outstanding sailors with years of exemplary service who hide their illnesses, fearful of the potential career ramifications. This is understandable since, to date, eating disorders are not considered ratable diagnoses by the Central Physical Evaluation Board (CPEB); thus, medical retirements are not an option.

Objective: We examined five years of psychiatry admissions for active duty personnel with anorexia nervosa, bulimia nervosa, or eating disorder not otherwise specified, and evaluated the relationships between several specific variables.

Results: There were 44 admissions during the period reviewed. The findings included a significant association between disposition and duration of hospitalization, gender, marital status, and presence of a coexisting depressive or anxiety disorder. Also interesting was the spread of eating disorders among the various branches of service. African Americans and Protestants were significantly heavier at admission. Males were more likely to be alcohol dependent, and females were more likely to be nicotine dependent and alcohol abusing.

Conclusion: We found many complex associations regarding active duty inpatients with eating disorders. Furthermore, the results corroborated civilian research relating to the clinical characteristics of patients with eating disorders.

NR694 Thursday, May 22, 12 noon - 2:00 p.m.

Comorbidity of Eating Disorders and Personality Disorders in Japan

Ken Murakami, M.D., Nevada Stress Center, 1000 Locust Street VAMC/151C, Reno NV 89520; Tetsuro Tachi, M.D., Teruhisa Washizuka, M.D., Keizou Murotsu, Ph.D., Yuko Miyake, Ph.D., Norimasa Ikuta, M.D.

Summary:

Objective: This study investigated the comorbidity of personality disorders in four classifications of eating disorders in Japanese subjects.

Method: Subjects were 46 outpatients with an eating disorder presenting to Tokai University Hospital, Japan. Eating disorder and personality disorder diagnoses were made using SCID-1 and SCID-2, modified for DSM-IV. All subjects were also administered EDI-2, and EDE.

Results: Eating disorder groupings were: anorexia nervosa (n = 18), bulimia nervosa (n = 14), binge-eating disorder (n = 6), and eating disorder NOS (n = 8). On the personality disorder (PD) dimensions, subjects were no-PD (n = 27), one-PD (n = 13), and multiple-PDs (n = 6). Anorexia showed 39% comorbidity with at least one PD, and 22% comorbidity with multiple PD. Bulimia showed comorbidity rates with single and multiple PD of 57% and 11%, binge eating showed 16% and 0%, and eating disorders NOS showed 38% and 0%. When the three PD groupings were compared on EDI-2, six of 11 scales showed significant differences. No significant differences were found on EDE.

Conclusion: Anorexia and bulimia showed highest comorbidity and contained all patients with multiple PDs. These Japanese results closely resemble data from the United States and Sweden. Also results from EDI-2 suggested that eating disorder patients with personality disorders are characterized by psychological immaturity.

NR695 Thursday, May 22, 12 noon - 2:00 p.m.

Cortisol and Catecholamine in Childhood PTSD

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Pittsburgh PA 15213; Boris Birmaher, M.D., Andrew S. Baum, Ph.D., Frank J. Jenkins, Ph.D., Neal D. Ryan, M.D.

Summary:

Dysregulation of cortisol and catecholamines, epinephrine (EPI), norepinephrine (NE), and dopamine (DA), are implicated in the pathophysiology of adult post-traumatic stress disorder (PTSD). This investigation examines 24-hour urinary catecholamine and cortisol excretion in children with DSM-III-R PTSD secondary to maltreatment (n = 17, 10.3 ± 1.4 yrs), DSM-III-R overanxious disorder (OAD) without trauma histories (n = 9, 10.9 ± 1.3 yrs), and nontraumatized healthy controls (n = 16, 10.8 ± 1.0 yrs). As in adult PTSD, it was hypothesized that PTSD subjects would manifest increased urinary catecholamine but lower cortisol excretion. Urinary and psychological measures were compared using ANOVA. PTSD subjects excreted more DA than anxious and healthy controls ($F = 3.45$, $p < .05$) and more NE than OAD subjects ($F = 4.13$, $p < .05$). Urinary cortisol did not differ. Child Behavior Checklist scores showed that PTSD subjects had more symptoms of school problems, aggression, and delinquent behaviors than both controls ($p < .05$), while PTSD and OAD subjects had more symptoms of depression, somatic complaints, and inattention than controls ($p < .05$). PTSD subjects had higher Child Dissociative Checklist scores than both controls ($F = 12.01$, $p < .001$). These results support the hypothesis of hyperactivity of the catecholamine system in maltreated children with PTSD. Childhood PTSD was associated with greater comorbid psychopathology.

NR696 Thursday, May 22, 12 noon - 2:00 p.m.

Are Anxious Children Smaller than Others?

E. Steven Dummit III, M.D., Child Psychiatry, St. Luke's/Roosevelt Hospital, 411 West 114th Street, New York NY 10025; Raul R. Silva, M.D.

Summary:

Objective: To examine the hypothesis that anxiety disorders in children correlate with smaller size.

Methods: A chart review of systematically gathered clinical data (clinical interviews, Structured Clinical Interview for DSM-IV-Childhood Diagnoses, and Parent and Teacher Questionnaires) was conducted on 487 consecutive referrals to a hospital child psychiatry clinic. Height and weight measurements and best estimate diagnoses were compared using unpaired t-tests.

Results: When adjusted for age, anxious girls (any anxiety diagnosis, regardless of comorbidity) are smaller than nonanxious girls ($p = .01$ for weight, nonsignificant trend for height), but size shows no clear trend for boys. When examined by ethnic subgroups, which might reduce variance in the size data, only African-American girls ($p < .005$) demonstrate the hypothesized difference. When diagnostic subgroups are divided into "non-disruptive anxious" (lacking any comorbid disruptive diagnosis) and "other," Hispanic girls ($p < .008$) showed the hypothesized difference. These differences persist when 55 children with histories of medical problems that might affect size are excluded.

Conclusions: Smaller size appears to be related to anxiety disorders in girls. Based on adult studies of anxiety, this finding may be related to abnormalities in growth hormone regulation and warrants further investigation.

NR697 Thursday, May 22, 12 noon - 2:00 p.m.

Validation of a New Depression Scale for Adolescents

Fabien Durif, M.D., Department of Psychiatry, Hopital Purpan, Place Du Docteur-Baylac, Toulouse 31059, France; Veronique Gentil, M.D., Jean P. Raynaud, Ph.D., Laurent Schmitt, M.D.

Summary:

Objective: The Durif Depressive Disorders Scale for Adolescents (DDDSA) is a self-rating scale for preliminary screening with these aims: easy use, few cognitive efforts, little time required (mean time three minutes), and competitive criterion validity.

Method: The DDDSA investigates 10 major depressive disorder symptoms: appetite, sleep, tiredness, sadness, self-image, suicidal thoughts, anxiety, pessimism, guilt, and concentration. Each item contains two propositions connected by an 11-centimeter side divided into 11 spaces going from 0 (no symptom) to 10 (maximal symptom). The subject checks the point corresponding to his mood. The score varies from 0 to 100, with three cut-off points defining four states going from no to high depression. A total of 409 school children (mean age 16.5 years) from 15 to 18 years old completed the DDDSA and the Beck Depression Inventory.

Results: Concurrent validity measured by the correlation between BDI and DDDSA scores is high ($r = .83$, $p < 0.001$). Internal consistency measured by the Chronbach alpha-coefficient is elevated (.87, $p < 0.001$). Internal homogeneity is good: correlations among items vary from .16 to .66 ($p < 0.01$), and correlations between each item and total score vary from .57 to .80 ($p < 0.001$). Factor analysis isolates two factors referring to emotional feelings and somatic complaints.

Discussion: The initial validation of the DDDSA is satisfactory. The simplicity and the little time required indicate it specifically for screening. Further studies are needed to study other points like test-retest and specificity.

NR698 Thursday, May 22, 12 noon - 2:00 p.m.

Gender Differences in Adolescents' Coping Strategies

Fabien Durif, M.D., Department of Psychiatry, Hopital Purpan, Place Du Docteur-Baylac, Toulouse 31059, France; Veronique Gentil, M.D., Jean P. Raynaud, Ph.D., Laurent Schmitt, M.D.

Summary:

Objective: To analyze gender-coping strategy differences with the Coping Scale for Adolescents (CSA), which investigates three fields (behavior, cognition, emotion) and four strategies (social support, denial, withdrawal, control).

Method: A total of 566 adolescents (285 girls, 281 boys) 12 to 20 years old, recruited from a high school, completed the CSA.

Results: Boys use more total control strategies ($p < 0.01$) than girls, but there are no differences for internal control referring to cognition and emotion. Use of control increases with age for both groups, particularly for boys ($p < 0.05$). Boys use more denial ($p < 0.001$) especially alexithymie (referring to emotional denial) ($p < 0.0001$). During late adolescence, they tend to use less denial whereas girls use more ($p < 0.05$).

Girls use more social support ($p < 0.001$) during the entire adolescence, especially the emotional social support ($p < 0.0001$). They also use more withdrawal ($p < 0.001$), which indicates some depression and more emotional invasion (= addiction) ($p < 0.001$). For both groups withdrawal increases during early adolescence, and decreases later.

Discussion: Gender coping strategy differences appear during adolescence. Boys express both abilities to control (positive side), and denial of reality and refusal of emotion (negative side). On the contrary girls express both social support strategies (positive side) and social and behavioral withdrawal (negative side) due to emotional invasion (addiction) and alexythymie.

NR699 Thursday, May 22, 12 noon - 2:00 p.m.

Treatment of Primary Premature Ejaculation: A Model for Investigation of SSRI-Induced Sexual Side Effects

Marcel D. Waldinger, M.D., Psychiatry and Neurosexol, Leyenburg Hospital, Leyweg 275, 2545 Ch The Hague, The Netherlands

Summary:

Objectives: To assess the ejaculation retardation of four SSRs in equivalent dosages in males with primary premature ejaculation (PPE).

Methods: From May 1995 until December 1996, of 112 outpatients with PPE evaluated, 71 couples entered the study. Over a four-week period, baseline Intravaginal Ejaculation Latency Time (IELT) was evaluated by stopwatch. Sixty men with an IELT < 1 minute were randomized: 12 each to placebo, fluoxetine 20 mg/day, fluvoxamine 100 mg/day, paroxetine 20 mg/day, and sertraline 50 mg/day in a six-week trial.

Results: Patients' mean age was 42 years (SD 8). The mean IELT at baseline was 16 seconds (SD 13) varying from 1 to 52 seconds. There were nine dropouts (15%). During six weeks according to intention-to-treat, the geometric mean IELT in the placebo group was 20 seconds. In the paroxetine, fluoxetine, and sertraline groups there was an increase to 110 seconds, and to about 60 seconds in the fluvoxamine group ($p = 0.0004$). Post-hoc testing showed no significant difference between paroxatine, fluoxatine, and sertratine groups with respect to pattern over time ($p = 0.58$), but all three differed significantly from placebo and fluovaxamine ($p = 0.0038$). Compared with placebo, the fluvoxamine group also showed some increase of the geometric mean IELT ($p = 0.0061$). Paroxatine provided the strongest delay of ejaculation (7.8 fold increase), followed by fluxetine (6.6 f.i), sertraline (4.4 f.i), fluvoxemine (1.9 f.i), and placebo (1.5 f.i).

Conclusions: In males with PPE fluvoxamine has the least effect on ejaculation delay, compared with the other SSRs in equivalent dosages.

NR700 Thursday, May 22, 12 noon - 2:00 p.m.

Continuous Treatment with Long-Acting Gonadotropin-Releasing Analog Triptorelin for Males with Severe Paraphilias

Eliezer Witztum, M.D., Endocrinology, Hadassah University Hospital, 4 Revadim Street, Jerusalem, Israel; Ariel Rosler, M.D.

Summary:

Background: The increase of male pedophilia and exhibitionism has become an increasingly acute problem over the last decades. Psychotherapy, behavior therapy, and pharmacotherapy (antidepressants, progestins, and antiandrogens) have all been used, usually in various combinations. None has yielded very high success rates, and pharmacotherapy may cause severe side effects. Selective suppression of the hypothalamic-pituitary-gonadal axis with a long-acting gonadotropin-releasing hormone (GnRH) analog may eliminate the devious sexual behavior by reducing testosterone to undetectable concentrations.

Methods: Twenty-eight males (mean age 32.3 ± 7.7 SD years) with severe and intractable paraphilias (DSM-IV; 20 pedophilia; five exhibitionism, or voyeurism and frotteurism; and three both) of 16.3 ± 9.3 SD years duration were treated with monthly injections of 3.75 mg GnRH analog triptorelin and psychotherapy, for eight to 38 months.

Results: A significant decrease in deviant fantasies, urges, and sexual behavior, which resulted in termination of all paraphilic activities ($P < 0.00001$), was evident after two to six months of triptorelin administration, an effect that persisted in all 22 patients who complied with therapy (78.6%). Triptorelin therapy reduced testosterone to castration levels ($P < 0.00001$), but did not change the concentrations of androstenedione and DHEA-sulfate. Although eight patients had some residual normal sexual activity, the main side effects were impotence, hot flushes, and a progressive but inconsistent decrease in bone mineral density. No changes were found in parathyroid hormone and vitamin D concentrations.

Conclusions: Continuous administration of long-acting GnRH analog triptorelin, together with psychotherapy, may be a very effective treatment for males with severe paraphilias, particularly for those resistant to other modes of therapy.

NR701 Thursday, May 22, 12 noon - 2:00 p.m.

The Use of a 5HT 2a/2c and a2 Antagonist (Mianserin) in the Treatment of Sexual Dysfunction Induced by SSRIs

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Summary:

Objective: Sexual dysfunction is commonly encountered in patients treated with antidepressants. The mechanism for the impairment is as yet unclear, although, activation of the serotonergic system has been implicated. We examined the effect of the 5-HT 2a/2c and α 2 antagonist, mianserin, in the treatment of patients with sexual dysfunction induced by serotonin reuptake inhibitors (SRIs).

Method: Mianserin 15 mg was coadministrated to 15 male subjects with new-onset sexual dysfunction, who were under treatment with SRIs. Four major domains of sexual activity—desire, erection, orgasm and satisfaction—were assessed once weekly for four weeks.

Results: At the end of the study, 9 of the 15 subjects reported a marked improvement in their sexual functioning, two reported partial improvement and only four subjects showed no improvement at all. The beneficial effects were prominent in the areas of orgasm and satisfaction and were usually noted within the first and second week of mianserin treatment. The addition of mianserin to the treatment regimen was not associated with either improvement or worsening of the basic psychiatric clinical status.

Conclusion: The coadministration of low-dose mianserin may be an additional option in the treatment of sexual dysfunction induced by SRIs and merits further investigation.

NR702 Thursday, May 22, 12 noon - 2:00 p.m.

The Prevalence of Sexual Disorders in Tourette's Syndrome

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Summary:

Clinicians have long suspected that individuals diagnosed with Tourette's syndrome (TS) exhibit an increased number of sexually related behavioral disorders. Similar changes have been found in patients with Huntington's disease, which, like TS, involves abnormal functioning of the basal ganglia. The present study was designed to investigate the prevalence of sexual disorders in TS patients. Individuals with TS ($N = 21$) were interviewed using a standarized sexual disorder questionnaire. Where possible sexual partners were also interviewed to provide a matched control group and validation of the Tourette's patients' responses. Following the acquisition of informed consent all subjects were asked the same 78 questions, which covered a wide range of behavior related to normal and abnormal sexual activity. The main finding of this study

was that TS patients do display a marked increase in the frequency of paraphilias over matched controls and established population norms. The second major finding was that the sexual disorder "inhibited orgasm" was highly predictive of the number and severity of paraphilias. TS subjects with inhibited orgasm were 36% more likely to report paraphilic activity than TS patients without inhibited orgasm. Since this finding was also true of Huntington's patients, it is possible that inhibited orgasm is one of the basal ganglia mediated causes of increased paraphilic activity in these patients.

NR703 Thursday, May 22, 12 noon - 2:00 p.m.

Psychiatric Syndromes in Persian Gulf War Veterans: An Association of Handling Dead Bodies with Somatoform Disorders

Lawrence A. Labbate, M.D., Department of Psychiatry, Medical University of SC, VA Med Ctr/109 Bee Street #116, Charleston SC 29401; Etzel Cardena, Ph.D., Michael Roy, M.D., Charles C. Engel, Jr., M.D.

Summary:

Objective: To determine psychiatric diagnoses among referred Persian Gulf War (PGW) veterans.

Method: Outpatient (n = 131, 113 men, mean age 36 ± 8) veterans referred for a second evaluation of medical complaints temporally related to service in the PGW underwent thorough medical and psychiatric evaluation, including the SCID-P and the clinical assessment of PTSD scale. Consensus diagnoses were made by a team including internal medicine and psychiatry. Veterans also completed questionnaires regarding war experience. Logistic regressions were carried out on the following criterion variables: 1) PTSD diagnosis, 2) somatoform diagnosis, 3) any psychiatric diagnosis other than PTSD or somatofom disorder.

Results: Ninety (69%) patients received at least one DSM-III-R Axis I diagnosis. The most common diagnoses were major depression (28%), somatoform disorders (26%), and PTSD (18%). The most common medical diagnoses were headache (n = 31, 23%) and gastrointestinal diseases (n = 18, 14%). Of the veterans with headache, 81% (25/31) also received psychiatric diagnoses; veterans with gastrointestinal diagnoses received psychiatric diagnoses 71% (10/14) of the time. Logistic regression analysis revealed that receiving an injury increased the odds of PTSD more than five fold (p = 0.03), and each of five listed war experiences increased the odds of receiving a PTSD diagnosis by 1.65 (p = 0.02). Handling dead bodies increased the odds of obtaining a somatoform diagnosis by more than three fold (p = 0.02). Younger age also predicted a somatoform or other psychiatric diagnosis, with the odds of getting these diagnoses decreasing to less than half every ten years.

Conclusion: Somatizing, major depression, and readily explainable medical disorders accounted for many of the veterans' symptoms. Patients may have parallel physical and psychological distress. We did not find evidence of a PGW syndrome, though experience in the war, especially handling dead bodies, may have contributed to the development of symptoms.

NR704 Thursday, May 22, 12 noon - 2:00 p.m.

Application of DSM-IV to Patients with Pain

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Summary:

Objective: DSM-IV introduced a new category for the classification of pain—pain disorder. This category was developed in order to avoid the problems encountered with the infrequently employed pain-related diagnoses included in the previous DSMs. This study examined the use of the new category to determine if it is more applicable than its predecessors in the clinical setting.

Method: One hundred patients referred to a psychiatric consultation-liaison service were studied. At the time of the initial consultation, patients were asked if they had pain. For patients with pain it was determined whether they fit the diagnostic criteria for pain disorder (PD) and for the DSM-III-R diagnosis of somatoform pain disorder (SPD). Demographic information and medical diagnoses were obtained.

Results: Fifty-nine patients reported having pain at the time of evaluation. Thirty of these patients (51%) fit the diagnostic criteria for PD, while only one fit the criteria for SPD. The primary reasons patients fulfilled criteria for the diagnosis of PD but not for SPD were the pain being present for less than six months and general medical conditions playing a major role in the pain in addition to psychological factors.

Conclusions: This study demonstrates that the DSM-IV category of pain disorder is more clinically applicable than its predecessor. The most important changes that improved applicability appear to be the inclusion of pain of less than six months duration and providing for the diagnosis of patients whose pains have both physical and psychological components.

NR705 Thursday, May 22, 12 noon - 2:00 p.m.

Quantitative Morphology of the Caudate Nucleus in Boys with ADHD

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Summary:

Objectives: Because the caudate nuclei receive input from the dorsolateral prefrontal and orbitofrontal cortices, it is the area of interest in much research with ADHD patients. To identify the lack of normal asymmetry in the caudate nuclei, one slice of brain MRIs were selected, and the planimetric method was applied and analyzed.

Method: The Brain MRIs of 14 ADHD boys (mean age 11.1, SD 3.0) and 16 headache control group (mean age 10.6, SD 2.5) were collected retrospectively. Single best view axial slice of anterior horn of the lateral ventricle (TR 3000, TE 100, Thickness 6mm, Gap 2mm) was selected for analysis. MRI images were scanned with flat-bed scanner and data were analyzed with brain image pascal 2.3.3.1 software using the dual threshold method. Pixel counting and area measurement was done. Interrater reliabilities were 0.90 or greater.

Results: In both the ADHD and control group, right caudate area is slightly greater than left side, and this difference was more significant in the control group. Percent asymmetry defined as (R-L)/[(R + L)/2] were calculated and statistically analyzed. The results showed no differences between the ADHD and control group. As in previous works by Castellanos, et al., the normal pattern of slight but significantly greater right caudate volume across all ages was not seen in ADHD.

NR706 Thursday, May 22, 12 noon - 2:00 p.m.

Personality Functioning in Adolescent Psychopathology

Susan R. Borgaro, M.A., Department of Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; David L. Pogge, Ph.D., John M. Stokes, Ph.D., Joel Lord, Ph.D.

Summary:

Objective: Adolescents often present for psychiatric care with symptoms of both depression and conduct disorder, many meeting

criteria for both of these diagnoses. However, little is known about the personality traits associated with these disorders, either individually or together. Furthermore, it is unknown if specific personality traits differentiate these groups from one another.

Method: This study compared adolescent inpatients with depression (n = 65), conduct disorder (n = 48), and both diagnoses (i.e., mixed; n = 34) on personality traits using the Personality Style scales of the Millon Adolescent Personality Inventory. Diagnoses were obtained from a structured diagnostic interview and an independent chart review procedure based on DSM-III-R criteria.

Results: One-way ANOVAs, followed by Bonferonni corrections, revealed distinct differences in personality functioning between these groups. The depressed group was distinguished by avoidant, dependent, and compulsive traits, ($p < .05$), while the conduct disorder group was differentiated by histrionic, narcissistic, and antisocial traits ($p < .01$). The mixed group was not at all similar to the depressed group, but most similar to the conduct disordered group on histrionic, antisocial, and dependent traits.

Conclusions: These data suggest that specific personality traits may differentiate patients with conduct disorder from those with depression. In addition, they suggest that personality traits in patients with concurrent depression and conduct disorder are most similar to those with conduct disorder.

NR707 Thursday, May 22, 12 noon - 2:00 p.m.

Valproate Response Versus Blood Levels in Autistic and Pervasive Developmental Disorder Not Otherwise Specified Adolescents

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Summary:

Objectives: This study compares institutionalized adolescents with autistic disorder (AD) and with pervasive developmental disorder not otherwise specified (PDDNOS) according to the following parameters: 1) presenting psychiatric symptoms, 2) psychiatric history, and 3) valproate response as a function of blood levels in an open trial that targeted aggression, overactivity, and manic-like symptoms.

Methods: Subjects were ten white males aged 10 to 20 years (M = 15.3), institutionalized an average of six years (mean age at placement 9.8). All had received numerous previous medications (M = 5.3). Valproate was prescribed as add-on medication for aggression, overactivity, and manic-like symptoms at a dose of 20-30mg/kg/day in divided doses. Blood levels of valproate were measured and recorded at least five days after the last dosage adjustment. Changes in Clinical Global Impressions (CGI) scores were independently evaluated as a function of valproate blood levels after seven to 37 weeks of treatment (mean 18 weeks). Comorbid diagnoses were made using DSM-IV criteria as closely as possible.

Results: 1) Nearly all patients in both groups were rated as having symptoms of overactivity, intrusiveness, hypersexuality, and compulsiveness. Other symptoms reviewed were aggression, insomnia, euphoria, mood cycling, and irritability. 2) While the AD and PDDNOS groups did not differ in current age, AD subjects were hospitalized at a significantly earlier age (7.5 vs 12.3, $p < .057$), were more likely to have received neuroleptics (83.3% vs 25%, $p < .06$), and had received significantly more types of medications (6.5 vs 3.5, $p < .058$). Change scores on the CGI were correlated with valproate blood levels in the expected direction ($r = .49$, $p < .07$, Spearman's rank order test; $r = .613$; $z = -1.887$, $p < .06$, Person correlation coefficient), that is, higher blood levels were associated with greater improvement.

Conclusions: Valproate appears as efficacious in treating aggression and overactivity in adolescents with AD as it is in adolescents with PDDNOS, especially at higher therapeutic blood levels. Larger, double-blind studies are warranted.

NR708 Thursday, May 22, 12 noon - 2:00 p.m.

PTSD Symptoms in Adolescent Survivors of Ethnic Cleansing: Results from a One-Year Follow-Up Study

Daniel F. Becker, M.D., Menninger-SFBA, 1783 El Camino Real, Burlingame CA 94010; Stevan M. Weine, M.D., Dolores Vojvoda, M.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To describe the psychiatric sequelae of "ethnic cleansing" in adolescent Bosnian refugees, via a one-year follow-up study.

Method: Subjects were 10 Bosnian adolescents who had been exposed to the traumas of the recent war in Bosnia-Herzegovina and who had been resettled with their families in Connecticut. All received a baseline psychiatric assessment within the first year after their resettlement and a follow-up assessment one year later. Assessments were conducted by clinicians in the Traumatic Stress Clinic at the Yale Psychiatric Institute. At baseline and at follow-up, subjects participated in systematic, trauma-focused, clinical interviews that included an assessment scale for post-traumatic stress disorder (PTSD) symptom severity.

Results: At baseline three subjects met diagnostic criteria for PTSD. At follow-up, the PTSD diagnosis persisted in none of these subjects—though one subject met criteria for PTSD at follow-up only. For the group, mean PTSD severity scores at baseline and at follow-up were 8.9 and 4.0, respectively. At baseline, reexperiencing cluster symptoms were present in seven subjects, avoidance cluster symptoms were present in all 10 subjects, and hyperarousal cluster symptoms were present in seven subjects; at follow-up, the number of subjects who had symptoms in these three clusters were seven, six, and four, respectively.

Conclusions: Overall, rates of PTSD symptoms diminished during the one-year follow-up interval—suggesting that they may be transient and not representative of enduring psychopathology. The frequencies of the PTSD diagnosis in our group of adolescent Bosnian refugees are lower than those found in adult Bosnian refugees, and also lower than those found in adolescent refugees from Cambodia. This finding may reflect the relative resiliency of adolescents, as well as a variety of factors that facilitated adaptation in our refugee group.

NR709 Thursday, May 22, 12 noon - 2:00 p.m.

Personality Traits in Adolescent Conduct Disorder

Ashley Bennett, B.A., Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; Susan R. Borgaro, M.A., David L. Pogge, Ph.D., John M. Stokes, Ph.D., Joel Lord, Ph.D.

Summary:

Objective: Conduct disorder (CD) is a common diagnosis of adolescents in psychiatric inpatient settings. While conduct disorder is characterized by a number of delinquent behaviors, few studies have examined personality traits associated with this disorder. The focus of this study is to determine if specific personality traits differentiate seriously conduct-disordered adolescents from other inpatients who are not displaying significant conduct problems.

Method: This study compared adolescents who meet DSM-III-R criteria for a diagnosis of CD (n = 51) with a group of nonconduct-disordered adolescents (n = 68) on personality characteristics using the Millon Adolescent Personality Inventory (MAPI). The eight clinical scales of the MAPI that measure enduring aspects

of personality functioning (i.e., personality styles) were examined. Diagnoses were obtained from a structured diagnostic interview (i.e., SCID) and an independent chart review procedure.

Results: Independent t-tests with Bonferonni corrections were performed (alpha = .006). The CD group differed significantly from the nonconduct-disordered group on scales measuring histrionic ($t = 4.29$, $p < .001$) and antisocial ($t = 4.35$, $p < .001$) personality traits.

Conclusions: These data suggest that adolescents with conduct disorder are more similar in personality functioning to those eventually diagnosed with an axis II antisocial personality disorder than are other seriously disturbed but not conduct-disordered adolescents.

NR710 Thursday, May 22, 12 noon - 2:00 p.m.

Lateralization of Cognitive Impairment in Adolescent Psychopathology

David L. Pogge, Ph.D., Department of Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 11704; Susan R. Borgaro, M.A., Anne Lloyd, M.A., John M. Stokes, Ph.D., Philip D. Harvey, Ph.D.

Summary:

Objective: Although many neuropsychological tests have shown promise for detecting focal or lateralized deficits in patients with brain disease or brain injury, these tests are also often used with psychiatric patients. Deficits in psychiatric patients on these tests are often interpreted as reflecting hemispherically lateralized deficits. The purpose of this study was to test the validity of these inferences in neurologically intact psychiatric populations.

Method: Tests using verbal and visuo-spatial stimuli were used to measure three constructs: immediate memory span (WMS-R Digit and Spatial Span), serial learning and recall (CVLT and BFLT), and vigilance (Visual and Auditory CPT), in 145 adolescent psychiatric inpatients.

Results: Confirmatory factor analysis was used to identify the best of three models: lateralized (verbal vs. spatial factors), cognitive process (memory span, learning and recall, vigilance), and independent (all six tests). The lateralized and cognitive process models fit the data poorly (CFI's = .50 and .80), while the independent model fit the data best ($X^2 = 47$; CFI = .99).

Conclusions: These data suggest that in neurologically intact populations tests sharing common stimulus characteristics are very poorly intercorrelated in contrast to the pattern of results that would be expected if they were actually being performed by persons with lateralized functional deficits.

NR711 Thursday, May 22, 12 noon - 2:00 p.m.

Effectiveness of Day Treatment for Children with Severe Behavior Problems: Five-Year Follow-Up

Natalie Grizenko, M.D., Department of Psychiatry, Douglas Hospital, 6875 Lasalle Boulevard, Verdun Montreal QC H4H 1R3, Canada

Summary:

Objective: The purpose of this study was to evaluate the long-term effectiveness of a multimodal day treatment program for children with severe behavior problems and to identify factors that may predict a positive outcome.

Method: Thirty-three children who completed a day treatment program were assessed using a prospective single cohort design tested at intake, discharge, and five-year follow-up. The child's functioning was assessed using the Revised Child Behavior Profile (RCBP), Hare Self-Esteem Scale, Depression Self-Rating Scale, Hopelessness Scale for Children, Index of Peer Relations, and a five-point ordinal scale for scholastic reintegration.

Results: Repeated measures ANOVAS showed that improvement was maintained on all measures between intake and five-year follow-up. A stepwise multiple regression showed that 92% of the adjusted variance in behavioral functioning of the children at five year follow-up as assessed by the RCBP was explained by parental cooperation with treatment, initial RCBP total, and externalizing scores and history of problem pregnancy.

Conclusions: Day treatment appears to be effective in improving the global functioning of children five years after discharge. Parental cooperation was the most important variable in predicting a positive outcome.

NR712 Thursday, May 22, 12 noon - 2:00 p.m.

Diagnostic Validity in Childhood Depression

Michele Zaccario, M.A., Department of Psychology, Four Winds Hospital, 800 Cross River Road, Katonah NY 10536; Susan R. Borgaro, M.A., Julie Krauss, B.A., John M. Stokes, Ph.D., David L. Pogge, Ph.D.

Summary:

Objective: Depression in children is thought to be best assessed via multiple measures and informants. However, studies of measures of childhood depression have yielded inconsistent results. The goal of this study is to examine the concurrent validity of parallel assessments of depression in a clinical population.

Methods: Forty-nine child patients (ages 7–11 years) in a private psychiatric hospital were evaluated for depression in four ways: through self-report using the Kovak's Childhood Depression inventory (CDI), via parent ratings using a symptom rating scale (Devereaux Scale of Mental Disorders; DSMD) and a more complex psychometric instrument (Personality Inventory for Children; PIC), and through chart diagnoses generated by a psychiatrist on the basis of clinical evaluation.

Results: A significant correlation was observed between the two parent ratings (PIC & DSMD; $r = 55$, $p < .001$), but neither correlated with the child's self-report (CDI), and none was significantly correlated with chart diagnoses.

Discussion: These data indicate poor agreement between different measures of childhood depression; the only significant correlation occurred between measures that rely upon the same source of information (i.e., parent ratings). Given that these are all common sources of diagnostic information used in research on childhood depression, this finding calls into question all of these sources of information, raises questions about the validity of findings generalized from studies that classify subjects on the basis of any single source of information, and suggests that diagnoses of depression in children may reflect more about the source of information than about the presence of significant mood disorder.

NR713 Thursday, May 22, 12 noon - 2:00 p.m.

Effects of Targeted Assertive Outreach in Patients with Schizophrenia and Substance Use Disorders

Richard N. Rosenthal, M.D., Department of Psychiatry, Beth Israel Medical Center, First Ave at 16th Street, New York NY 10003; Christian Miner, Ph.D., David J. Hellerstein, M.D.

Summary:

Objective: To assess the effect on symptom severity of adding assertive community treatment (ACT) to integrated psychiatric and substance abuse services for outpatients with SCID/DSM-IV schizophrenia and comorbid substance use disorders.

Method: As part of an ongoing, randomized outcome study, we compared a manualized control treatment intergrating psychiatric and substance abuse services (COPAD) to integrated treatment plus targeted assertive outreach (COPAD + TAO). We used re-

peated measures ANOVA to evaluate short-term efficacy for 42 subjects, assessed via SANS and SAPS at 0 and 4 months.

Results: Subjects were 81% male, 86% minority. Age (M ± SD) = 35.7 ± 6.9 years. Two-thirds had been homeless; most had history of multiple psychiatric hospitalizations. At four months, two subjects were deceased (one suicide, one MI); seven (five control) dropped out. For 33 remaining subjects, repeated measures ANOVA using aggregate SANS scores yielded no significant effects. However, using aggregate SAPS scores, we obtained a significant within-subjects effect for time ($F_{1,31} = 20.84$, $p < .001$) and a significant between-groups effect ($F_{1,31} = 4.89$, $P < .05$) in favor of COPAD + TAO. On average, control subjects showed 27% diminution in positive symptom severity compared with 51% for those receiving ACT-style services.

Conclusions: This is preliminary evidence for strong differential efficacy of TAO over and above the gains of integrated treatment.

NR714 Thursday, May 22, 12 noon - 2:00 p.m.

Autobiographical Memory and Mood Disorders in Heroin Addicts

Renate Eiber, M.D., Department of Psychiatry, Hospital Purpan, Casselardit, Toulouse 31400, France; Laurent Schmitt, M.D., Philippe Cadilhal, M.D.

Summary:

Background: Early psychiatric interviews with opiate addicts show a very factual and objective conversation, and a difficulty in evaluation of autobiographical memory.

Objectives: Our aims were to compare episodic and semantic autobiographical memory in primary opiate addicts and healthy controls and to estimate the impact of depression and anxiety on the ability to produce autobiographical recollection.

Methods: Participants were 21 consecutive attenders of a methadone outpatient clinic who were polydrug-dependent patients consuming mainly heroine. The first investigation took place at entry, the second after two months. Mean duration of intoxication was 11 years. Ten of these patients were investigated again after two months; eight of them were included in a methadone maintenance program. We investigated autobiographical memory, only at intake, with a autobiographical fluency test and the semistructured memory interview of Kopelman; the psychiatric assessment included self- and observer-rating questionnaires.

Results: In the fluency test, opiate addicts, compared with controls, showed a significant decrease in episodic autobiographical memory ($p = .009$), an increase in semantic memory ($p = .05$), but no difference in total number of items produced. Kopelman's interview displayed a significant memory impairment in addicts ($p = .0074$). Episodic memory of both tests was affected by educational levels. Memory impairment occurred independently of concomitant depression.

Conclusion: The implication of drugs in the origin of memory deficits and mental functioning is discussed. With improvement of depressive symptomatology occurring after two-months without psychotropic drugs, it suggests transient features of depression and emphasizes nonpharmacological aspects of treatment.

NR715 Thursday, May 22, 12 noon - 2:00 p.m.

Growth Hormone Treatment in Anorexia Nervosa

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Summary:

Objective: In anorexia nervosa (AN), renourishment is essential for physical and psychological recovery. Recombinant human growth hormone (rhGH) promotes metabolic stabilization in undernourished patients during refeeding. We hypothesize that rhGH treatment will hasten medical stabilization in AN patients.

Methods: Twelve patients (11 females/one male) with AN, ages 12 to 17 years, were enrolled in a 28-day randomized, double-blind, placebo-controlled study. Patients received rhGH (0.05 mg/kg sq qd) or an equivalent volume of placebo. The primary outcome measure was time to reach functional stability. We defined functional stability as two consecutive days in which the patient did not have an increase in pulse of greater than 20 bpm with change from a supine to standing position. All patients received a standard refeeding protocol.

Results: Admission body mass index (BMI) was 14.3 kg/m^2. The rhGH and placebo groups did not differ significantly in admission weight, BMI, or daily caloric intake. No adverse events occurred. Patients treated with rhGH reached functional stability more rapidly than those treated with placebo (22 ± 8 vs. 38 ± 17 days, $p < 0.01$).

Conclusion: AN patients treated with rhGH during nutritional repletion achieved functional stability more rapidly than those treated with placebo. This resulted in briefer hospitalizations for the rhGH group compared with the placebo controls.

NR716 Thursday, May 22, 12 noon - 2:00 p.m.

Suicidality and Eating Disorders: Epidemiology in a Canadian Community Sample

David S. Goldbloom, M.D., Department of Psychiatry, Clark Institute of Psychiatry, 250 College Street, Toronto ON M5T 1R8, Canada; Cathy Spegg, M.B.A., Paul E. Garfinkel, M.D., Elizabeth Lin, Ph.D., Paul N. Goering, Ph.D., Allan S. Kaplan, M.D.

Summary:

Objective: Long-term outcome studies of individuals with eating disorders reflect significant mortality—as high as 18% in some series. Suicide is typically the second most common cause of death but there is little reported on the nature or frequency of suicidality. We report relevant findings of an epidemiological study of a community sample in Ontario, Canada.

Method: A multi-stage stratified sampling design generated a sample of 4,285 females aged 15 to 64. DSM-III-R diagnoses were made using the Composite International Diagnostic Interview and additional data were obtained by interview and self-report questionnaires.

Results: Suicidal ideation was present in women meeting criteria for anorexia nervosa (full and partial syndrome) 33.3%, bulimia nervosa (full and partial syndrome) 42.4%, major depression (current or lifetime but no history of eating disorder) 42.7%, and women free of any psychiatric disorder 9.0% ($p < .00001$). Suicide attempts were similarly elevated for these diagnoses compared with healthy women. Risk factors for suicidality among eating disorders samples included histories of depression, anxiety disorders, alcohol dependence, sexual abuse, and family history of psychiatric disorder or parental conflict.

Conclusions: In a nonclinical sample, suicidality occurred as commonly in women with eating disorders as with major depression. It occurred in the context of psychiatric comorbidity, sexual abuse, and family psychopathology.

NR717 Thursday, May 22, 12 noon - 2:00 p.m.

5HT-1A Challenge Study: Test Meal Response

Barbara E. Wolfe, Ph.D., Department of Psychiatry, Beth Israel Hospital, 330 Brookline Avenue, Boston MA 02215; Eran D. Metzger, M.D., David C. Jimerson, M.D.

Summary:

Objective: Regulation of CNS serotonin is a current focus in research on eating disorders and obesity. In preclinical studies, serotonin-1A agonists increase eating behavior through presynaptic inhibition of serotonin release. This placebo-controlled pilot study compared effects of ipsapirone on food intake and neuroendocrine/temperature responses in healthy volunteers.

Method: Initial results were assessed for seven medication-free, healthy, normal weight women, age 23.5 ± 3.5 years. Following overnight bed rest and fast, subjects received single dose ipsapirone or placebo on separate days in a double-blind, randomized design. Food intake was measured using a single-item, frozen yogurt test meal. Body temperature and blood samples for cortisol and ACTH measurements were collected at baseline and following drug/placebo.

Results: In comparison to placebo, ipsapirone resulted in decreased body temperature and increased cortisol and ACTH levels. Test meal food intake was highly correlated between the two study days (r_1 = .85, $p < .002$), but did not differ significantly on the active day (311 ± 107 grams) compared with the placebo day (336 ± 158 grams).

Conclusions: Ipsapirone administration produced expected responses in temperature and neuroendocrine hormones. Initial results from test meal studies suggest that the hypothesized increase in food intake may be more variable than other physiological responses as a measure of serotonin-1A receptor activation by ipsapirone.

NR718 Thursday, May 22, 12 noon - 2:00 p.m.

Treatment and Six-Year Course of Binge Eating Disorder

Manfred M. Fichter, M.D., Department of Psychiatry, Klinik Roseneck, Am Roseneck 6, Prien 83209, Germany; Norbert Quadflieg, Ph.D., Winfried Rief, Ph.D.

Summary:

Binge eating disorder (BED) has been provisionally defined in the appendix of DSM-IV as a disorder with recurrent episodes of bingeing larger amounts, a sense of lack of control over eating, and the absence of counterregulatory measures such as vomiting. Since the empirical basis of BED is limited and nothing is known about its longer-term cause, 68 consecutively treated females with BED were studied longitudinally. These patients (mean age 29.3 years) were assessed at four points of time: 1) beginning of therapy, 2) end of therapy, 3) three-year follow-up, and 4) six-year follow-up. Self-ratings as well as expert ratings were used to measure general psychopathology as well as symptoms specific for eating disorders. Results indicated a general pattern over time as follows: substantial improvement during therapy was followed by a slight (in most variables nonsignificant) decline during the first three years after the end of treatment; further improvement and stabilization was seen during the fourth, fifth, and sixth year after the end of treatment. At the six-year follow-up, the majority of patients showed no major DSM-IV eating disorder, 5.9% had BED, 7.4% had shifted to bulimia nervosa—purging type (DSM-IV), 7.4% were classified as ED-NOS, and one patient had died. Based on an operationalized six-year global outcome score for the complete sample, 57.4% had a good outcome, 35.3% an intermediate outcome, 5.9% a poor outcome, and one person (1.4%) was deceased. In comparison with a sample of 196 females treated for bulimia nervosa, the intermediate and long-term cause was very similar. Further data on course and outcome will be provided. Factors contributing to the cause were identified on the basis of linear causal relationship models (LISREL).

NR719 Thursday, May 22, 12 noon - 2:00 p.m.

Decreased Plasma Leptin Levels in Bulimia Nervosa

Timothy D. Brewerton, M.D., Department of Psychiatry, Medical University of SC, 171 Ashley Ave, Charleston SC 29425-0002; Michael D. Lesem, M.D., Adele Kennedy, M.D., W. Timothy Garvey, M.D.

Summary:

Background: Leptin is a protein produced by the *ob-ob* gene, which inhibits food intake in humans. Plasma levels are reported to be altered in obesity and anorexia nervosa (AN) but not bulimia nervosa (BN).

Method: We measured plasma leptin levels using radioimmunoassay (RIA) in 53 subjects studied at NIMH, including 37 subjects meeting DSM-III-R criteria for BN (10 with concurrent AN [body mass index (BMI)] = 14.1 ± 1.4), 27 without AN (BMI = 20.4 ± 1.6)] and 16 normal controls (NCs) (BMI = 21.1 ± 2.0). Patients were medication free and abstinent from bingeing and purging for three to four weeks prior to study.

Results: Plasma leptin levels were significantly correlated to BMI ($r = 0.41$, $p < 0.002$), weight (kg, $r = 0.43$, $p < 0.001$), and percent average body weight (%ABW, $r = 0.45$, $p < 0.001$) in the total group. Plasma leptin levels were lower in the BN subjects (3.4 ± 2.5 ng/ml) compared with the NCs (6.1 ± 2.6 ng/ml, $p < 0.001$, ANCOVA) even after controlling for BMI and weight. There was no significant difference between BN subjects with AN (n = 10, 2.6 ± 2.6 ng/ml) and those without AN (n = 27, 3.8 ± 2.4 ng/ml). Plasma leptin concentrations were negatively correlated with baseline plasma cortisol levels (n = 49, $r = -0.49$, $p < 0.001$) and positively correlated with prolactin responses following L-tryptophan (n = 49, $r = 0.37$, $p < 0.009$) and m-chlorophenylpiperazine (n = 52, $r = 0.24$, $p < 0.09$).

Conclusions: This is the first known report of decreased leptin levels in BN. The reasons for this are unclear but appear to be unrelated to BMI or weight. HPA axis activation as well as serotonin dysregulation may be related to decreased leptin levels, which may in turn contribute to disinhibited eating in BN. Although leptin levels were not correlated with self-reported weekly binge frequency, the role of leptin in the pathophysiology of BN deserves further study.

NR720 Thursday, May 22, 12 noon - 2:00 p.m.

Very Low Calorie Diet Combined with Cognitive-Behavioral Therapy in the Treatment of Obese Patients with Binge Eating Disorders

Martina de Zwaan, M.D., Department of Psychiatry, University of Vienna, Wahringer Gurtel 18-20, Vienna 1090, Austria; James E. Mitchell, M.D., Melissa P. Mussell, Ph.D., Ross Crosby, Ph.D.

Summary:

The study evaluates the efficacy of CBT, focusing on binge eating behavior coupled with a very-low-calorie diet (VLCD) in obese patients with binge eating disorder (BED). One hundred and fifty-four females (83 nonBED, 71 BED) completed the 26-week program. All subjects attended a behaviorally oriented group weekly. In addition, one half of our BED subjects also received 10 cognitive behavior therapy (CBT) group sessions for binge eating. The active treatment phase was followed by a one-year follow-up period. Adherence to the fast and the rate of attendance of the weekly group sessions were similar in all groups. The results do not indicate a significant difference in weight changes between binge eaters and nonbinge eaters or between binge eaters with and without CBT. On average, the patients lost 17% (± 7.8) of their initial body weight during the VLCD and maintained an average weight loss of 6.4% (± 9.8) during follow-up. On a short-term basis the VLCD with or without CBT appeared to be successful

in suppressing high frequency binge eating. At the one-year follow-up 41.7% of the BED + CBT patients and 37.1% of the BED-CBT patients continued to meet criteria for BED. In conclusion, the combination of a VLCD with a CBT component did not improve the short- and long-term results with regard to weight loss and binge eating frequency in obese BED subjects.

NR721 Thursday, May 22, 12 noon - 2:00 p.m.

Changes in Sympathetic Activity and Metabolic Rate in Patients with Anorexia Nervosa During Refeeding Treatment

Susan K. Schultz, M.D., Department of Psychiatry, University of Iowa, 200 Hawkins Drive, Iowa City IA 52242-1009; Philippe van de Borne, M.D., Erling Anderson, Ph.D., Tim Ruffin, R.C.P.T., Lou Ann Vogel, R.R.T., Virend K. Somers, M.D.

Summary:

Objectives: To examine the effect of refeeding on sympathetic activity and metabolic rate in patients with anorexia nervosa (AN). We tested the hypothesis that patients would have low baseline measures of metabolic and sympathetic activity, which would increase during treatment.

Methods: Microneurography of efferent muscle sympathetic nerve activity (MSNA), peroneal nerve, was utilized as well as measures of resting metabolic rate (RMR) via indirect calorimetry. Seven female patients were assessed shortly after inpatient admission. Follow-up measures of weight, RMR, and MSNA were obtained after three weeks of treatment comprised of approximately 3,500 kcal/day.

Results: Weight increased in all subjects from 37.3 (± 3.5 SEM) to 42.0 (± 4.2) kg. At intake, RMR averaged 15% below predicted values for current weight. After treatment, RMR increased significantly from 1,021 (± 44) to 1,211 (± 18) kcal/day ($p = 0.002$), such that follow-up RMR averaged only 2% less than predicted. Pre- and post-treatment MSNA measures were detectable in four subjects. MSNA was observed to increase from 5.9 (± 2.8) to 13.4 (± 6.6) bursts/minute in the resting baseline condition, but this change did not reach statistical significance.

Conclusions: Increased sympathetic activity related to an abrupt rise in caloric intake may have substantial clinical implications when one considers the occurrence of refeeding heart failure and arrhythmias associated with anorexia nervosa. This study reports a significant increase in metabolic rate during refeeding and a concomitant increase in sympathetic activity, though larger studies are needed to further examine sympathetic changes with treatment of anorexia nervosa.

NR722 Thursday, May 22, 12 noon - 2:00 p.m.

Sertindole Treatment in Elderly Patients with Dementia

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Summary:

Sertindole is a novel atypical antipsychotic discovered and patented by H. Lundbeck (Copenhagen) and under development by Abbott Laboratories in the United States, Latin America, and Canada. Sertindole demonstrates selective antagonistic activity at D_2, 5-HT_2 and ∞_t receptors with no affinity for histaminic, muscarinic, or ∞_2 receptors. The efficacy of sertindole in psychosis, without extrapyramidal symptoms (EPS), has been attributed to its 100-fold greater selectivity for limbic D_2 receptors as compared with nigrostriatal D_2 receptors.

This double-blind, placebo-controlled, single-center study, assessed the safety and tolerability of sertindole in elderly patients with dementia. Twenty patients, age 65 years or older and meeting DSM-IV criteria for dementia, were hospitalized and randomized to receive sertindole (n = 16) or placebo (n = 4). The initial dose of sertindole was 4 mg, which was titrated to a maximum of 16 mg in 4 mg increments every four days. All patients received 16 days of study medication. Assessments of safety and tolerability included movement rating scales, adverse events, laboratory tests, and ECGs.

Sertindole was generally well tolerated by these elderly patients. In this study, with a duration of 16 days, all parameters indicated that sertindole produced minimal extrapyramidal side effects, corroborated by the lack of use of anti-EPS medications.

NR723 Thursday, May 22, 12 noon - 2:00 p.m.

Amyloid Beta Protein Concentration in CSF Decreases with Advancing Severity of Alzheimer's Dementia

Steven C. Samuels, M.D., Department of Psychiatry, Mount Sinai, One Gustave Levy PI/Box 1230, New York NY 10029; Jeremy Silverman, Ph.D., Deborah B. Marin, M.D., Steven Younkin, M.D., Elaine Peskind, M.D., David Greenberg, M.D.

Summary:

Objective: This study examines the relationship between Alzheimer's disease (AD) severity and CSF beta-amyloid-protein (A-beta).

Methods: After informed consent, 31 probable AD patients (61% male, 87% white, age 73.39 ± 5.87 years, age at disease onset 67.23 ± 6.73 years, and illness duration of 6.16 ± 4.4 years) had CSF A-beta 1-40 and A-beta 1-42 concentration measured, APOE genotype determined, and dementia severity assessed.

Results: MMSE scores were 17.39 ± 6.80, APOE distribution was E4/E4, n = 8; E3/E3, n = 6; E3/E4, n = 15; E2/E3, n = 1; and E2/E4, n = 1. MMSE significantly correlated with A-beta 1-40 ($r = .45$, $p < .05$) and A-beta 1-42 ($r = .40$, $p < .05$) after controlling for age at onset and illness duration, reflecting an inverse relationship between CSF A-beta concentration and dementia severity. Neither CSF A-beta concentration nor APOE genotype significantly correlated with illness duration or age at onset. The CSF A-beta concentration and disease severity relationship disproportionately owed to the APOE3/3 genotype (A-beta 1-40: $r = .78$, $p < .05$, n = 6; A-beta I-42; $r = 94$, $p < .05$, n = 6) rather than the APOE3/4 (A-beta 1-40: $r = .40$, $p = .11$, n = 17; A-beta 1-42: $r = .38$, $p = .13$, n = 17) or APOE 4/4 genotype (A-beta 1-40: $r = .45$, $p = .26$, n = 8; A-beta 1-42: $r = .06$, $p = .88$, n = 17).

Conclusions: The findings may be related to increasing amyloid protein deposition into plaques as AD advances, resulting in decreased CSF A-beta. The APOE4 allele may modify this relationship.

NR724 Thursday, May 22, 12 noon - 2:00 p.m.

Use of Risperidone in the Elderly

Carlos A. Zarate, Jr., M.D., McLean Hospital, 115 Mill Street, Belmont MA 02178; Ross J. Baldessarini, M.D., Arthur J. Siegel, Ataru Nakamura, M.D., Jane McDonald, Lou Ann Muir-Hutchinson

Summary:

Objective: A retrospective study was conducted to evaluate the use of risperidone in psychogeriatric patients.

Methods: Medical records of 122 hospitalized elderly patients treated with risperidone were reviewed. The patients (83 women, 39 men; aged 65 to 95 years) received risperidone for agitation or psychosis associated with dementia (53%), a major mood disorder

(34%), or other disorders (13%). Most (77%) were also medically ill and were receiving other psychotropic (76%) or cardiovascular agents (70%). The mean daily dose of risperidone was 1.6 mg (78% received ≤2.0 mg/day).

Results: Risperidone appeared to be effective in 85% of the 108 patients who did not discontinue the drug because of adverse events. Adverse events, reported in 32% of the patients, included hypotension (29%) or symptomatic orthostasis (10%), extrapyramidal symptoms (11%), delirium (1.6%), and cardiac arrest (1.6%) with fatality (0.8%). Treatment was discontinued in 7% of patients because of insufficient response. Improvement was associated with younger age and male gender, but not risperidone dose. Adverse events were associated with cardiovascular disease and its treatment, cotreatment with an SRI antidepressant or valproate, and rapid risperidone dose increases.

Conclusion: Risperidone appeared to be effective and safe in many elderly psychiatric patients with comorbid medical conditions provided that doses were low and increased slowly. Particular caution is advised in patients with cardiovascular disease and those receiving other psychotropic agents.

NR725 Thursday, May 22, 12 noon - 2:00 p.m.

Decision-Making Capacity in the Elderly

Stephen L. Pinals, M.D., Department of Psychiatry, University Hospitals, 11100 Euclid Avenue, Cleveland OH 44106; Steven Steiner, M.D., Ashok J. Bharucha, M.D., Debra A. Pinals, M.D., Andrew Satlin, M.D.

Summary:

Objective: The objective of this study was to compare the capacity of depressed geriatric patients with healthy, elderly controls in their ability to understand diagnostic and treatment information as one component of informed consent.

Methods: Seven geriatric inpatients admitted to the McLean Hospital Geriatric Unit who met DSM-IV criteria for major depression participated in this study. A comparison group of seven healthy, age- and sex-matched control subjects also participated in the study. Patients were evaluated by Mini-Mental Status Exam, Yesavage Mood Assessment Scale, Brief Psychiatric Rating Scales, and the Shipley Institute of Living Scale. The assessment of decision-making capacity was determined by the Understanding Treatment Disclosures (UTD) instrument, designed by Grisso and Appelbaum (1992).

Results: Patients with major depression had significantly more difficulty with treatment decisions and understanding information regarding their illness when compared with healthy controls ($p < .05$). The extent of debility in understanding diagnostic or treatment information was directly correlated with the degree of cognitive impairment and severity of psychiatric symptoms.

Conclusion: This study suggests that elderly patients with depression have impaired decision-making capacity with regard to their ability to understand diagnostic and treatment information. Thus, it is critical that clinicians assess decisional capacity in elderly patients to support their functional independence and to protect those with compromised capacity by seeking appropriate medical guardianship.

NR726 Thursday, May 22, 12 noon - 2:00 p.m.

Effect of Alzheimer's Disease Severity on Functional Failure in Different Brain Regions: Assessed by Parametric Visual Stimulation During PET

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Summary:

Objective: We evaluated the effect of Alzheimer's disease (AD) severity on neural response capabilities of different brain regions as input stimulus was parametrically increased.

Method: Using goggles with a grid of red lights imbedded into each lens, we performed five positron emission tomography (PET) H2150 water scans on each subject at alternating (left to right eye) flash frequencies of 0, 1, 4, 7, and 14 Hz. Neural function, measured as change in regional cerebral blood flow above 0 Hz (drCBF), was measured in 19 control subjects, 10 mild AD (ADM, Mini-mental state [MMS] score greater than 19) and 11 moderately/severely demented (ADs) patients (MMS less than 20).

Results: drCBF in striate, extrastriate, and many anterior brain were affected by the stimulus. In ADm, neural function failed only when the stimulus required a large drCBF in the control group. ADs failed when large and intermediate responses were required. ADm and ADs responses were within normal limits for stimuli resulting in small responses.

Conclusions: Increasing AD severity progressively impaired response capabilities of neurons in primary and association visual areas; magnocellular more than parvocellular function in striate cortex; complex visual processing in extrastriate regions; and anterior brain inhibition, perhaps representing signal-to-noise gain.

NR727 Thursday, May 22, 12 noon - 2:00 p.m.

Serial Cognitive Testing of Chronic Psychiatric Patients

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Summary:

Objective: Over the past decade, clinical research psychiatrists have revisited the area of cognitive deficits associated with chronic mental illness. This investigation assessed the prevalence of cognitive deficits in subgroups of chronic psychiatric inpatients.

Method: Thirty chronic psychiatric inpatients were tested along four cognitive dimensions: 1) recognition of unit staff by photograph, 2) right-left orientation, 3) time-telling (analog and digital), and 4) directional orientation. They were retested after a two-year interval, during which the patients were exposed to both social and cognitive rehabilitation. Results were analyzed over time and across diagnostic subgroups using the appropriate t-test.

Results: All diagnostic groups displayed impairment in the four cognitive areas tested at both baseline and retest. Scores deteriorated over time in right-left orientation ($p = 0.009$) and directional sense ($p = 0.04$). At baseline, the axis I psychosis subgroup performed significantly better at staff recognition (16.1/30 vs 8.9/30, $p = 0.026$), directional sense ($p = 0.041$), and telling time in digital (7/7 vs 6.08/7, $p = 0.03$) and analogue (6.88/7 vs 4.93/7, $p = 0.009$) formats in comparison with groups with multiple diagnoses. This superiority had disappeared at retest.

Conclusions: Chronic psychiatric patients display profound, persisting cognitive deficits. The long-term effectiveness of cognitive rehabilitation with this population remains unclear.

NR728 Thursday, May 22, 12 noon - 2:00 p.m.

Cognitive-Behavior Therapy Versus Supportive Therapy in Social Phobia: A Controlled Study

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Summary:

Objective: This multicenter study evaluates the effectiveness and process of cognitive-behavior therapy (CBT) in social phobia.

Method: Sixty-seven DSM-IV social phobic patients were randomized into two groups. Group 1 received eight sessions of individual cognitive therapy (ICT) over six weeks followed with six weekly sessions of group behavior therapy (GBT). Group 2 received six sessions of supportive therapy (ST) over 12 weeks. Group 2 then had the same treatment as Group 1. The general criterion of improvement was a drop of 25% on the Fear Questionnaire (FQ) social phobia scale.

Results: At week 6, the FQ social phobia scale demonstrated a significantly higher improvement in ICT ($p = 0.03$) but there was no significant between-group difference in the rate of responders. At week 12, the FQ social phobia, the negative Social Interaction Self-Statement Test subscale, the Liebowitz scale (avoidance), and the quality of life, showed significantly higher improvements in CBT, in which the rate of responders was also higher ($p = 0.001$). At week 24 the positive effects of CBT were replicated in Group 2.

Conclusion: CBT was more effective than ST. Improvement started in ICT, but GBT significantly increased its effectiveness. (Grant from the French Ministry of Health : PHRC 94020.)

NR729 Thursday, May 22, 12 noon - 2:00 p.m.

Are Psychiatry Residents Biased Against Cognitive-Behavior Therapy?

Ari E. Zaretsky, M.D., Department of Psychiatry, Mount Sinai Hospital, 600 University Avenue, #941A, Toronto ON M5G 1X5, Canada

Summary:

Background: Although cognitive-behavior therapy (CBT) has demonstrated strong efficacy in the treatment of an array of different psychiatric problems, there has been a lag in its acceptance and full utilization by psychiatrists. Deficits in training and psychotherapy supervision are obvious culprits, but additional factors may also be interacting with lack of training to explain the relative failure of many psychiatrists to learn and utilize this new approach.

Objective: To investigate the training experiences and attitudes of psychiatry residents toward CBT.

Method: A self-report survey was mailed to all PGY2 to PGY5 psychiatry residents in the University of Toronto Department of Psychiatry. The survey assessed CBT training intensity, resident satisfaction with training, and also explored underlying negative beliefs and attitudes about CBT.

Results: 74/85(94%) psychiatry residents responded to the survey. In general, a minority of psychiatry residents (47%) had received case supervision of any length and only 16% had obtained supervision beyond six months duration. Although psychiatry residents appeared to be genuinely interested in CBT, a large percentage of them also endorsed a variety of negative attitudes and beliefs about CBT.

Conclusions: Ensuring that psychiatrists of the future utilize CBT in their practice may not be accomplished simply by providing additional supervision. Supervisors may also need to pay closer attention to underlying negative attitudes and beliefs about CBT that preclude its full acceptance.

NR730 Thursday, May 22, 12 noon - 2:00 p.m.

Are Dependency and Self-Criticism Risk Factors for MDD?

Ari E. Zaretsky, M.D., Department of Psychiatry, Mount Sinai Hospital, 600 University Avenue, #941A, Toronto ON M5G 1X5, Canada; Maurizio Fava, M.D., Katharine Davidson, B.A., Joel A. Pava, Ph.D., John D. Matthews, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Background: Beck (1983) has proposed that two personality traits, sociotropy and autonomy, are important in predicting the type of life events triggering depression and its symptom profile. Whereas sociotropic individuals derive most of their self-esteem from interpersonal interactions and are very sensitive to disapproval and rejection (dependent), autonomous individuals derive most of their self-esteem from achievement and are often discontented with themselves (self-critical).

Objective: To determine whether dependent and self-critical personality traits are associated with a) specific types of life events that occur during index episodes of major depression and b) certain subtypes of depression.

Method: Eligible subjects were depressed outpatients with a SCID-P-determined diagnosis of major depressive disorder who completed a) the Dysfunctional Attitude Scale (DAS), a 40-item questionnaire, which contains dependent and self-critical subscales and measures self-worth contingencies, and b) the Life Experiences Survey (LES), an inventory of 57 life events. The items of the LES were classified as congruent with dependency (loss events), congruent with self-criticism (failure events), or neither. Simple linear regressions were performed to determine the relationship between self-criticism and dependency and life events as well as depression subtypes. Depression severity was measured before and after eight weeks of fluoxetine treatment with the HAM-D-17.

Results: The DAS dependency subscale showed significant correlations with life events regardless of congruency, whereas the DAS self-criticism subscale was not associated with any type of life events. Dependency and self-criticism were not associated with either melancholia or atypical depression. The baseline HAM-D scores were positively correlated with both DAS subscales and the total DAS score.

Conclusions: These results confirm a growing body of research that has found an association between sociotropic/dependent personality traits and life events. Our results also supported earlier studies reporting a correlation between depression severity and dysfunctional cognitive style.

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