NEW RESEARCH

AMERICAN PSYCHIATRIC ASSOCIATION

2000 ANNUAL MEETING

The Doctor-Patient Relationship

APA2000
chicago

MAY 13 - 18, 2000 ■ CHICAGO, ILLINOIS

ABSTRACTS

American Psychiatric Association

1400 K Street, N.W.
Washington, DC 20005
Telephone 202.682.6237
Fax 202.682.6345
E-mail: apa@psych.org
Internet: www.psych.org

May 13, 2000

Dear Fellow APA Attendees:

On behalf of the members and staff of the Scientific Program Committee, I would like to welcome you to the 2000 New Research Program. This year's program reflects the 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 15, at 9:00 a.m. with the first of two Young Investigators' Poster Sessions. It continues at 10:30 a.m. with "Research Advances in Psychiatry: An Update for the Clinician," with special emphasis on the genetics of alcoholism, schizophrenia and the impact of depression on cardiovascular disease. The Young Investigators' Oral/Slide Sessions will begin at 1:00 p.m. on Monday afternoon, followed by the second 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 schizophrenia and severe mental illness and anxiety disorders (Tuesday); mood disorders(Wednesday); and substance abuse and psychopharmacology(Thursday). Poster Sessions will be held Tuesday and Wednesday from 12 noon-2:00 p.m. and 3:00 p.m.-5:00 p.m. and on Thursday from 12 noon-2:00 p.m. These sessions will be devoted to schizophrenia, anxiety, geriatrics, health services, biology, treatment techniques, cognitive personality and premenstrual disorders (Tuesday); mood, child and adolescent psychiatry, violence, HIV, addiction, alcohol and drug abuse, brain imaging, consultation-liaison, epidemiology, somatoform, dissociative behavior and other disorders (Wednesday); and psychopharmacology, combined pharmacotherapy and psychotherapy, professional issues, political issues, group and individual therapy(Thursday).

The 48 oral/slide papers (including 12 Young Investigators) and 690 poster presentations (including 203 Young Investigators) are a diverse and, we believe, representative sampling of that which is new and significant in psychiatric research. We hope that you will find them informative and provocative.

Sincerely,

Carol Tamminga

Carol A. Tamminga, M.D.
Chairperson, New Research Subcommittee of the
Scientific Program Committee

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NEW RESEARCH ABSTRACTS

Realizing that not all attendees wish to receive the individual abstracts, and in an effort to save paper, we have printed them in a separate book this year. You may receive a free copy of either the Abstracts on Disk (IBM or Mac) or the printed book (see instructions below).

Printed Book:
Please tear out the section below and present the coupon at any booth in the APA Resource Center in exchange for the abstract book.

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The American Psychiatric Association requires disclosure of the existence of any and all significant financial interest(s) or other affiliation(s) a presenter has with any commercial supporter(s) of these educational activities, and/or with the manufacturer(s) of any and all commercial product(s) and/or provider(s) of any and all commercial service(s) discussed in the scientific program. 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 every commercial supporter by an acknowledgment in the printed program and verbal or visual disclosure to participants at the session (disclosure by slide or overhead is required if AV equipment is used for the presentation). This policy is intended to openly identify any potential conflict(s) so that members of the audience in an educational activity are able to form their own judgements about the presentation. The APA also requires verbal disclosure of discussion of unlabeled uses of a commercial product or investigational use of a product not yet approved for this purpose.

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 #
Donald E. Addington, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Eli Lilly and Company; AstraZeneca Pharmaceuticals; Abbott Laboratories; Janssen Pharmaceutica and Research Foundation	NR279
Hagop S. Akiskal, M.D.	Lilly Research Laboratories, a division of Eli Lilly and Company; Abbott Laboratories; SmithKline Beecham Pharmaceuticals; Synthélabo; BW	NR 662
Ralph S. Albertini, M.D.	Eli Lilly and Company; Solvay Pharmaceuticals, Inc.	NR 264
George S. Alexopoulos, M.D.	National Institute of Mental Health	NR 292
Ahmad M. Almai, M.D.	Glaxo Wellcome Inc.	NR 17
Bjorn G. Appelberg	Bristol-Myers Squibb	NR 470
Ralph Aquila, M.D.	Eli Lilly and Company	NR 638
Monica Arora, M.D.	Janssen Pharmaceutica and Research Foundation	NR 99
Adam K. Ashton, M.D.	Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; Glaxo Wellcome Inc.; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; Pharmacia & Upjohn Company, Inc.; Solvay Pharmaceuticals, Inc.; Bristol-Myers Squibb; Janssen Pharmaceutica and Research Foundation; Abbott Laboratories; Organon Inc.; Parke-Davis, Division of Warner-Lambert Company; Forest Laboratories, Inc.	NR 684
Abraham Bakker, M.D.	SmithKline Beecham Pharmaceuticals	NR 43
Albert N. Bayer, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 435
Jeffrey L. Berlant, M.D.	Robert Wood Johnson Pharmaceutical Research Institute	NR 491
Christopher R. Bowie, M.A.	U.S. Pharmaceuticals, Pfizer Inc.	NR 303
Kathleen T. Brady, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Abbott Laboratories; Parke-Davis, Division of Warner-Lambert Company	NR 234
Peter F. Buckley, M.D.	Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation; AstraZeneca Pharmaceuticals; Novartis Pharmaceuticals Corporation	NR 375
Marian I. Butterfield, M.D.	Glaxo Wellcome Inc.; Organon Inc.; Wyeth-Ayerst Laboratories; Eli Lilly and Company	NR 572
Daniel E. Casey, M.D.	Abbott Laboratories; Hoechst Marion Roussel; Janssen Pharmaceutica and Research Foundation; Lilly Research Laboratories, a division of Eli Lilly and Company; Novartis Pharmaceuticals Corporation; U.S. Pharmaceuticals, Pfizer Inc.; AstraZeneca Pharmaceuticals	NR 337
K.N. Roy Chengappa, M.D.	Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation; AstraZeneca Pharmaceuticals; Novartis Pharmaceuticals Corporation	NR 522
Robert R. Conley, M.D.	Janssen Pharmaceutica and Research Foundation; AstraZeneca Pharmaceuticals; Zenith Goldline Pharmaceuticals; Novartis Pharmaceuticals Corporation; Aventis	NR 1
Ian A. Cook, M.D.	Eli Lilly and Company; Wyeth-Ayerst Laboratories; Pharmacia & Upjohn Company, Inc.; U.S. Pharmaceuticals, Pfizer Inc.	NR 439
Jean A. Cottraux, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 646
William Crumb, Ph.D.	Eli Lilly and Company	NR 338
Jeffrey L. Cummings, M.D.	Bayer Corporation, Pharmaceutical Division; U.S. Pharmaceuticals, Pfizer Inc.; Eisai Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation	NR 574
Glenn W. Currier, M.D.	Janssen Pharmaceutica and Research Foundation	NR 604
Sally J. Czaja, Ph.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 498
David G. Daniel, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Janssen Pharmaceutica and Research Foundation; Lilly Research Laboratories, a division of Eli Lilly and Company	NR 359

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Jonathan R.T. Davidson, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Parke-Davis, Division of Warner-Lambert Company; Bristol-Myers Squibb; Glaxo Wellcome Inc.; Eli Lilly and Company; Merck & Co., Inc.; Pharmacia & Upjohn Company, Inc.; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; Organon Inc.; Hoffman-LaRoche; Warner-Lambert; Ancile	NR 722
Pedro L. Delgado, M.D.	National Institute of Mental Health; Solvay Pharmaceuticals, Inc.; Organon Inc.; Eli Lilly and Company; Wyeth-Ayerst Laboratories; Bristol-Myers Squibb; Pharmacia & Upjohn Company, Inc.; Otsuka Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Boehringer Ingelheim; U.S. Pharmaceuticals, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Novartis Pharmaceuticals Corporation; Forest Laboratories, Inc.; AstraZeneca Pharmaceuticals	NR 487
Eric W. Dieperink, M.D.	Schering-Plough	NR 603
Douglas R. Dolnak, D.O.	Lilly Research Laboratories, a division of Eli Lilly and Company; Novartis Pharmaceuticals Corporation; Glaxo Wellcome Inc.; R.W. Johnson; U.S. Pharmaceuticals, Pfizer Inc.; Parke-Davis, Division of Warner-Lambert Company; Pharmacia & Upjohn Company, Inc.	NR 217
P. Murali Doraiswamy, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Novartis Pharmaceuticals Corporation; SmithKline Beecham Pharmaceuticals; Forest Laboratories, Inc.	NR 494
Martin K. Farlow, M.D.	Novartis Pharmaceuticals Corporation	NR 274
Maurizio Fava, M.D.	Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; U.S. Pharmaceuticals, Pfizer Inc.; Wyeth-Ayerst Laboratories; Organon Inc.; Bristol-Myers Squibb; Pharmacia & Upjohn Company, Inc.; Glaxo Wellcome Inc.; Solvay Pharmaceuticals, Inc.; Roche Laboratories, a member of the Roche Group; Novartis Pharmaceuticals Corporation; Synthélabo; Lorex Pharmaceuticals; Sanofi Pharmaceuticals, Inc.; Lichtwer Pharma; Forest Laboratories, Inc.; Janssen Pharmaceutica and Research Foundation; Lundbeck; Knoll Pharmaceuticals; Parke-Davis, Division of Warner-Lambert Company; Somerset Pharmaceuticals	NR 440, NR 441
Annette M. Fehr, M.B.A.	Eli Lilly and Company	NR 724
Benjamin Fischler, M.D.	U.S. Pharmaceuticals, Pfizer Inc. (Belgium)	NR 601, NR 602
Molly Fortner, B.S.	Glaxo Wellcome Inc.	NR 41
Jean A. Frazier, M.D.	Eli Lilly and Company	NR 482
Ellen W. Freeman, Ph.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 317
Ernest H. Friedman, M.D.	Speech Phase Time Monitor *(owner)*	NR 515
Matthew J. Friedman, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 238
Serge Gauthier, M.D.	Eisai Inc.; U.S. Pharmaceuticals, Pfizer Inc.	NR 647
Michael J. Gitlin, M.D.	Glaxo Wellcome Inc.	NR 616, NR 617
Andrew W. Goddard, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 659
Linda S. Godleski, M.D.	Eli Lilly and Company	NR 726
Joseph F. Goldberg, M.D.	Abbott Laboratories; Glaxo Wellcome Inc.; Eli Lilly and Company; Bristol-Myers Squibb; Pharmacia & Upjohn Company, Inc.; Robert Wood Johnson, Inc.; Shire Richwood Pharmaceuticals;	NR 504, NR 505
Stephen Grcevich, M.D.	AstraZeneca Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company	NR 566
David J. Greenblatt, M.D.	Forest Laboratories, Inc.	NR 739
Laurence L. Greenhill, M.D.	Alza Pharmaceuticals; Glaxo Wellcome Inc.; Shire Richwood Pharmaceuticals; Novum Pharmaceuticals; Gliatech; National Institutes of Health; Wyeth-Ayerst Laboratories; Eli Lilly and Company; Medeva Pharmaceuticals	NR 667
Sanjay Gupta, M.D.	Eli Lilly and Company; Forest Laboratories, Inc.	NR 62
Tanya Hair, M.S.C.	SmithKline Beecham Pharmaceuticals	NR 656
Uriel Halbreich, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 506
Mark B. Hamner, M.D.	Parke-Davis, Division of Warner-Lambert Company; Abbott Laboratories; Janssen Pharmaceutica and Research Foundation; U.S. Pharmaceuticals, Pfizer Inc.; AstraZeneca Pharmaceuticals	NR 266
Elie G. Hantouche, M.D.	Sanofi Pharmaceuticals, Inc.; Synthélabo	NR 475
Philip D. Harvey, Ph.D.	Janssen Pharmaceutica and Research Foundation; U.S. Pharmaceuticals, Pfizer Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company	NR 342, NR 343, NR 344
Peter Hauser, M.D.	Schering-Plough; Forest Laboratories, Inc.	NR 650
Angela M. Hegarty, M.D.	Abbott Laboratories	NR 518
David J. Hellerstein, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Glaxo Wellcome Inc.; Bristol-Myers Squibb; Wyeth-Ayerst Laboratories; Eli Lilly and Company; Dista Products	NR 702
David C. Henderson, M.D.	Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.	NR 372
Robert M.A. Hirschfeld, M.D.	Abbott Laboratories; Bristol-Myers Squibb; Organon Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Glaxo Wellcome Inc.; Forest Laboratories, Inc.; Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Parke-Davis, Division of Warner-Lambert Company; Pharmacia & Upjohn Company, Inc.	NR 461

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James J. Hudziak, M.D.	Glaxo Wellcome Inc.	NR 737
Enid M. Hunkeler, M.A.	Eli Lilly and Company; Wyeth-Ayerst Laboratories; SmithKline Beecham Pharmaceuticals	NR 402, NR 448
Naveed Iqbal, M.D.	Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company; AstraZeneca Pharmaceuticals; Novartis Pharmaceuticals Corporation	NR 390
Philip G. Janicak, M.D.	Abbott Laboratories; Janssen Pharmaceutica and Research Foundation; Lilly Research Laboratories, a division of Eli Lilly and Company; Bristol-Myers Squibb; Genentech; U.S. Pharmaceuticals, Pfizer Inc.; SmithKline Beecham Pharmaceuticals	NR 546
Hadine Joffe, M.D.	Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.	NR 2
Jorge L. Juncos, M.D.	AstraZeneca Pharmaceuticals; Hoechst Marion Roussel; Rhone-Poulenc Rorer Pharmaceuticals; Dupont Pharma	NR 687
John M. Kane, M.D.	Abbott Laboratories; Janssen Pharmaceutica and Research Foundation; U.S. Pharmaceuticals, Pfizer Inc.; Novartis Pharmaceuticals Corporation; AstraZeneca Pharmaceuticals; Lilly Research Laboratories, a division of Eli Lilly and Company	NR 345
Paul E. Keck, Jr., M.D.	Abbott Laboratories; Lilly Research Laboratories, a division of Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; Wyeth-Ayerst Laboratories; Parke-Davis, Division of Warner-Lambert Company; Janssen Pharmaceutica and Research Foundation; Merck & Co., Inc.	NR 224
Terence A. Ketter, M.D.	Abbott Laboratories; Glaxo Wellcome Inc.; Parke-Davis, Division of Warner-Lambert Company; Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company	NR 447
Sumant Khanna, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Glaxo Wellcome Inc.	NR 595
Suck Won Kim, M.D.	SmithKline Beecham Pharmaceuticals	NR 661, NR 668
Brian Kirkpatrick, M.D.	Novartis Pharmaceuticals Corporation	NR 353
Julie A. Kreyenbuhl, Ph.D.	Merck & Co., Inc.	NR 68
Helen H. Kyomen, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Wyeth-Ayerst Laboratories; AstraZeneca Pharmaceuticals; Glaxo Wellcome Inc.; Bayer Corporation, Pharmaceutical Division	NR 297
Lawrence A. Labbate, M.D.	Glaxo Wellcome Inc.	NR 477
Y.W. Francis Lam, Pharm.D.	Eli Lilly and Company; Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Company, Inc.; Wyeth-Ayerst Laboratories; U.S. Pharmaceuticals, Pfizer Inc.	NR 689
J. Steven Lamberti , M.D.	Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation	NR 221
Kimberly H. Littrell, N.P.	Eli Lilly and Company	NR 371
Jean Y. Liu, M.D.	Abbott Laboratories	NR 46
Anton J.M. Loonen, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Nourypharma; Bristol-Myers Squibb	NR 714
Jeffrey M. Lyness, M.D.	Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.	NR 291
Avram H. Mack, M.D.	Bristol-Myers Squibb	NR 177
Lauren B. Marangell, M.D.	Cyberonics; U.S. Pharmaceuticals, Pfizer Inc.; Eli Lilly and Company; Martek Biosciences; Parke-Davis, Division of Warner-Lambert Company; Forest Laboratories, Inc.; Bristol-Myers Squibb; Wyeth-Ayerst Laboratories; Abbott Laboratories; SmithKline Beecham Pharmaceuticals; Glaxo Wellcome Inc.	NR 460
John S. Markowitz, Ph.D.	Glaxo Wellcome Inc.	NR 674
John D. Matthews, M.D.	Eli Lilly and Company	NR 466
Brian J. McConville, M.D.	AstraZeneca Pharmaceuticals	NR 559
William M. McDonald, M.D.	Lilly Research Laboratories, a division of Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; Wyeth-Ayerst Laboratories; Searle; Janssen Pharmaceutica and Research Foundation; Glaxo Wellcome Inc.; SmithKline Beecham Pharmaceuticals; Novartis Pharmaceuticals Corporation; Solvay Pharmaceuticals, Inc.	NR 550
Patrick J. McGrath, M.D.	Pharmacia & Upjohn Company, Inc.; Glaxo Wellcome Inc.; Somerset Pharmaceuticals	NR 707
Joseph Menzin, Ph.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 420
Paolo Meoni, Ph.D.	Wyeth-Ayerst Laboratories *(employer)*	NR 257
Jonathan M. Meyer, M.D.	Janssen Pharmaceutica and Research Foundation	NR 681
Michael R. Miller, M.D.	Abbott Laboratories	NR 396
Jacobo E. Mintzer, M.D.	AstraZeneca Pharmaceuticals; Janssen Pharmaceutica and Research Foundation	NR 663
David Mischoulon, M.D.	Bristol-Myers Squibb	NR 145
Richard C. Mohs, Ph.D.	Eisai Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Novartis Pharmaceuticals Corporation; Searle; Ortho-Biotech Pharmaceuticals; Janssen Pharmaceutica and Research Foundation	NR 275
Angel L. Montejo, M.D.	Bristol-Myers Squibb; Lilly Research Laboratories, a division of Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.	NR 696, NR 697
Patrick J. Moriarty, M.A.	U.S. Pharmaceuticals, Pfizer Inc.; Eli Lilly and Company	NR 123
Robert O. Morton, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 50
Henry A. Nasrallah, M.D.	AstraZeneca Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Lilly Research Laboratories, a division of Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.	NR 354
Charles B. Nemeroff, M.D.	Janssen Pharmaceutica and Research Foundation	NR 451

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John W. Newcomer, M.D.	Janssen Pharmaceutica and Research Foundation; U.S. Pharmaceuticals, Pfizer Inc.; Eli Lilly and Company; AstraZeneca Pharmaceuticals	NR 660
Andrew A. Nierenberg, M.D.	Bristol-Myers Squibb; Forest Laboratories, Inc.; Glaxo Wellcome Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Lichtwer Pharma; Organon Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Sanofi Pharmaceuticals, Inc.; Wyeth-Ayerst Laboratories	NR 456
Philip T. Ninan, M.D.	Wyeth-Ayerst Laboratories; U.S. Pharmaceuticals, Pfizer Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; Bristol-Myers Squibb; Organon Inc.; Solvay Pharmaceuticals, Inc.; Pharmacia & Upjohn Company, Inc.; Janssen Pharmaceutica and Research Foundation	NR 465
Eric A. Nofzinger, M.D.	Glaxo Wellcome Inc.	NR 705
H. George Nurnberg, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 679
Michael J. Owens, Ph.D.	Forest Laboratories, Inc.	NR 324, NR 325
Phillippe M.J. Persoons, M.D.	U.S. Pharmaceuticals, Pfizer Inc. (Belgium)	NR 191
Katharine A. Phillips, M.D.	Eli Lilly and Company; Gate Pharmaceuticals; Solvay Pharmaceuticals, Inc.	NR 242
Bruce G. Pollock, M.D.	National Institute of Mental Health; Solvay Pharmaceuticals, Inc.; Forest Laboratories, Inc.; SmithKline Beecham Pharmaceuticals; Pharmacia & Upjohn Company, Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Janssen Pharmaceutica and Research Foundation; Glaxo Wellcome Inc.; Parke-Davis, Division of Warner-Lambert Company; Lundbeck	NR 280, NR 281
Leticia T. Postrado, Ph.D.	University of Maryland, Baltimore, Department of Psychiatry *(employer)*	NR 129
Paul M. Ramirez, Ph.D.	Multi-Health Systems Inc.	NR 664
Mark H. Rapaport, M.D.	Forest Laboratories, Inc.; Parke-Davis, Division of Warner-Lambert Company; Solvay Pharmaceuticals, Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Novartis Pharmaceuticals Corporation; Janssen Pharmaceutica and Research Foundation; Glaxo Wellcome Inc.; SmithKline Beecham Pharmaceuticals; U.S. Pharmaceuticals, Pfizer Inc.; Pharmacia & Upjohn Company, Inc.	NR 258
Michael J. Reinstein, M.D.	AstraZeneca Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company; Novartis Pharmaceuticals Corporation	NR 690
Margaret A. Richter, M.D.	SmithKline Beecham Pharmaceuticals	NR 627
Samuel C. Risch, M.D.	Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; Janssen Pharmaceutica and Research Foundation	NR 364
Thomas Roth, Ph.D.	Searle	NR 529
Peter P. Roy-Byrne, M.D.	SmithKline Beecham Pharmaceuticals; U.S. Pharmaceuticals, Pfizer Inc.; Bristol-Myers Squibb; Janssen Pharmaceutica and Research Foundation	NR 599, NR 600
A. John Rush, M.D.	Abbott Laboratories; Bristol-Myers Squibb; Eli Lilly and Company; Forest Laboratories, Inc.; Glaxo Wellcome Inc.; Janssen Pharmaceutica and Research Foundation; Novartis Pharmaceuticals Corporation; Organon Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Parke-Davis, Division of Warner-Lambert Company; Pharmacia & Upjohn Company, Inc.; SmithKline Beecham Pharmaceuticals	NR 508
James M. Russell, M.D.	Bristol-Myers Squibb; U.S. Pharmaceuticals, Pfizer Inc.	NR 384, NR 501
Gary S. Sachs, M.D.	Abbott Laboratories; Glaxo Wellcome Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Janssen Pharmaceutica and Research Foundation; Scios Nova Pharmaceuticals; Forest Laboratories, Inc.; Solvay Pharmaceuticals, Inc.; Bristol-Myers Squibb; U.S. Pharmaceuticals, Pfizer Inc.; SmithKline Beecham Pharmaceuticals	NR 492, NR 493
Martha Sajatovic, M.D.	Janssen Pharmaceutica and Research Foundation; AstraZeneca Pharmaceuticals; Eli Lilly and Company; Bristol-Myers Squibb; Otsuka Pharmaceuticals	NR 442
Hildebrando Salinas, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 124
Floyd R. Sallee, M.D.	Eli Lilly and Company; Bristol-Myers Squibb; Parke-Davis, Division of Warner-Lambert Company	NR 563
Lon S. Schneider, M.D.	Bayer Corporation, Pharmaceutical Division; Eisai Inc.; Novartis Pharmaceuticals Corporation; Parke-Davis, Division of Warner-Lambert Company; Somerset; SmithKline Beecham Pharmaceuticals; American Association for Geriatric Psychiatry; Wyeth-Ayerst Laboratories; Eli Lilly and Company; Abbott Laboratories; U.S. Pharmaceuticals, Pfizer Inc.	NR 290
Nina R. Schooler, Ph.D.	Janssen Pharmaceutica and Research Foundation; Novartis Pharmaceuticals Corporation; U.S. Pharmaceuticals, Pfizer Inc.; AstraZeneca Pharmaceuticals	NR 348
S. Charles Schulz, M.D.	AstraZeneca Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Eli Lilly and Company	NR 312
Albert J. Schutte, M.D.	Organon, The Netherlands	NR 704
Thomas L. Schwartz, M.D.	AstraZeneca Pharmaceuticals; Janssen Pharmaceutica and Research Foundation; Glaxo Wellcome Inc.; Bristol-Myers Squibb; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories; U.S. Pharmaceuticals, Pfizer Inc.	NR 193
R. Taylor Segraves, M.D.	Glaxo Wellcome Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Abbott Laboratories	NR 665
M. Katherine Shear, M.D.	Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; SmithKline Beecham Pharmaceuticals;	

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	Glaxo Wellcome Inc.; Hoffman-LaRoche; Pharmacia & Upjohn Company, Inc.	NR 727
Reinee E. Sheffield, Pharm.D.	Eli Lilly and Company	NR 418
Javaid I. Sheikh, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Bristol-Myers Squibb; Eli Lilly and Company	NR 255
Elizabeth B. Simpson, M.D.	Eli Lilly and Company	NR 316
George M. Simpson, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Lilly Research Laboratories, a division of Eli Lilly and Company; Novartis Pharmaceuticals Corporation; AstraZeneca Pharmaceuticals	NR 358
David A. Smelson, Psy.D.	Janssen Pharmaceutica and Research Foundation	NR 666
Caroline M. Sonnenberg, M.D.	SmithKline Beecham Pharmaceuticals	NR 299
Christian Spadone, M.D.	UCB-Pharma	NR 252
Thomas J. Spencer, M.D.	Abbott Laboratories; Alza Pharmaceuticals; Bristol-Myers Squibb; Eisai Inc.; Glaxo Wellcome Inc.; Janssen Pharmaceutica and Research Foundation; Lilly Research Laboratories, a division of Eli Lilly and Company; National Institute on Drug Abuse; National Institute of Mental Health; Novartis Pharmaceuticals Corporation; U.S. Pharmaceuticals, Pfizer Inc.; Shire Richwood Pharmaceuticals; Solvay Pharmaceuticals, Inc.; Wyeth-Ayerst Laboratories	NR 567
Jeffrey P. Staab, M.D.	SmithKline Beecham Pharmaceuticals; Eli Lilly and Company; Abbott Laboratories	NR 596
Vered Stearns, M.D.	SmithKline Beecham Pharmaceuticals	NR 675
Meir Steiner, M.D.	Lilly Research Laboratories, a division of Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; SmithKline Beecham Pharmaceuticals; Hoechst Marion Roussel	NR 318
Rita A. Suri, M.D.	Eli Lilly and Company	NR 513
Robert A. Sweet, M.D.	Janssen Pharmaceutica and Research Foundation; Lilly Research Laboratories, a division of Eli Lilly and Company	NR 409
Pierre N. Tariot, M.D.	Abbott Laboratories;	NR 457
Michael E. Thase, M.D.	Bristol-Myers Squibb; Eli Lilly and Company; Forest Laboratories, Inc.; Glaxo Wellcome Inc.; Merck & Co., Inc.; Organon Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Pharmacia & Upjohn Company, Inc.; Wyeth-Ayerst Laboratories; Parke-Davis, Division of Warner-Lambert Company; SmithKline Beecham Pharmaceuticals; Solvay Pharmaceuticals, Inc.; Lipha Pharmaceuticals, Inc.	NR 676, NR 677, NR 678
Mauricio F. Tohen, M.D.	Eli Lilly and Company *(employer)*	NR 380
Gregory B. Toney, Pharm.D.	Novartis Pharmaceuticals Corporation; Pharmacia & Upjohn Company, Inc.	NR 711
Madhukar H. Trivedi, M.D.	Abbott Laboratories; Organon Inc.; Bayer Corporation, Pharmaceutical Division; Bristol-Myers Squibb; Forest Laboratories, Inc.; Glaxo Wellcome Inc.; Janssen Pharmaceutica and Research Foundation; Johnson and Johnson; Lilly Research Laboratories, a division of Eli Lilly and Company; National Institute of Mental Health; MeadJohnson; Parke-Davis, Division of Warner-Lambert Company; U.S. Pharmaceuticals, Pfizer Inc.; Pharmacia & Upjohn Company, Inc.; Solvay Pharmaceuticals, Inc.; Wyeth-Ayerst Laboratories	NR 400
Jurgen Unutzer, M.D.	Abbott Laboratories	NR 430
Hein P. van Hout, Ph.D.	Organon Inc.; SmithKline Beecham Pharmaceuticals	NR 78
John C. Voris, Pharm.D.	Janssen Pharmaceutica and Research Foundation	NR 717
Marcel D. Waldinger, M.D.	Lundbeck	NR 685
Po W. Wang, M.D.	Parke-Davis, Division of Warner-Lambert Company	NR 151
Xiao-Hong Wang, M.D.	Janssen Pharmaceutica and Research Foundation	NR 98
Julia K. Warnock, M.D.	U.S. Pharmaceuticals, Pfizer Inc.	NR 467, NR 468
Peter J. Weiden, M.D.	Lilly Research Laboratories, a division of Eli Lilly and Company; U.S. Pharmaceuticals, Pfizer Inc.; AstraZeneca Pharmaceuticals; Johnson and Johnson	NR 218
Anders Wimo, M.D.	U.S. Pharmaceuticals, Pfizer Inc.; Merck & Co., Inc.; Hoechst Marion Roussel	NR 270
Jesse H. Wright, M.D.	Mindstreet *(employer)*	NR 649
Kimberly A. Yonkers, M.D.	Eli Lilly and Company; SmithKline Beecham Pharmaceuticals; U.S. Pharmaceuticals, Pfizer Inc.	NR 652
John M. Zajecka, M.D.	Abbott Laboratories; Bristol-Myers Squibb; Eli Lilly and Company; Forest Laboratories, Inc.; Glaxo Wellcome Inc.; Organon Inc.; U.S. Pharmaceuticals, Pfizer Inc.; Pharmacia & Upjohn Company, Inc.; Sanofi Pharmaceuticals, Inc.; SmithKline Beecham Pharmaceuticals; Wyeth-Ayerst Laboratories	NR 443, NR 642

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

Paulo S. Belmonte de Abreu, M.D. ..... NR 573
Charles L. Bowden, M.D. ..... NR 512
Roberto A. Dominguez, M.D. ..... NR 680
Tamara D. Jackson, Ph.D. ..... NR 19
Hans O. Kalkman, Ph.D. ..... NR 356, NR 357
Anne Karow, M.D. ..... NR 349
Titiksha V. Kubal, M.D. ..... NR 198
Peter D. Londborg, M.D. ..... NR 237
Martha J. Morrell, M.D. ..... NR 536
Carla E. Ramacciottii, M.D. ..... NR 393
Takuya Saito, M.D. ..... NR 206
Mujeeb U. Shad, M.D. ..... NR 90
Richard C. Shelton, M.D. ..... NR 462
Craig Springer ..... NR 214
Dawson Wolfe, B.S. ..... NR 28

NOTES

NEW RESEARCH

Monday, May 15, 2000, 9:00 a.m.–10:30 a.m.

New Research 1 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Richard Balon, M.D.

NR1 Risperidone Versus Olanzapine in Patients with Schizophrenia and Schizoaffective Disorder
Robert R. Conley, M.D., Ramy A. Mahmoud, M.D.

NR2 An Open Trial of Mirtazapine in Menopausal Women with Depression Refractory to Estrogen-Replacement Therapy
Hadine Joffe, M.D., Heather L. Groninger, B.A., Claudio N. Soares, M.D., Lee S. Cohen, M.D.

NR3 The Use of Intravenous Burprenorphine in the Treatment of Opioid Withdrawal in Medically Ill, Hospitalized Heroin-Addicted Patients
Christopher J. Welsh, M.D., Meenakshi Suman, M.S., Art Cohen, B.S., Eric Weintraub, M.D., Lauren Matukaitis, R.N.

NR4 Substance Abuse Patterns in Pregnant Women
Anjali M. Gupta, M.D., Eric Weintraub, M.D., Janine C. Delahanty, M.A., Christopher J. Welsh, M.D., Lisa B. Dixon, M.D.

NR5 Rapid Opiate Withdrawal with Anesthesia Compared with Rapid Detoxification Using Buprenorphine: A Controlled Trial
Norbert Scherbaum, M.D., Johannes Nebe, M.D., Anne Heringhaus, M.D., Susanne Klein, M.D., Peter Kienbaum, M.D., Juergen Peters, M.D., Markus Gastpar, M.D.

NR6 Morbidity of Lung and Liver Pathology in Heroin-Addicted Patients
Dadane Hawari, Ph.D.

NR7 Effects of Fluoxetine in Alcohol Withdrawal and Allopregnanolone Plasma Levels
Flavia Di Michele, M.D., Elena Romeo, M.D., Rainer Rupprech, M.D., Veska Uzunova, Ph.D., Augusto Pasini, M.D.

NR8 Basal Ganglia Morphometry in OCD
Justin R. Covey, B.A., Benjamin D. Greenberg, M.D., Jay N. Giedd, M.D., Vit Herynek, M.D., Gabriela Cora-Locatelli, M.D., John C. Keel, B.A., Dennis L. Murphy, M.D.

NR9 Carbon-Dioxide-Induced Panic Disorders
Alexandre M. Valenca, M.D., Antonio E. Nardi, M.D., Isabella Nascimento, M.D., Walter A. Zin, M.D., Marco A. Mezzasalma, M.D., Fabiana L. Lopes, M.D.

NR10 Initial Symptom Manifestations After Severe Injury and Subsequent PTSD
Karin F. Esposito, M.D., Daniella David, M.D., Victoria Bustamante, Psy.D., Thomas A. Mellman, M.D.

NR11 Obsessional Slowness in OCD and Tourette's Syndrome
Karen Vemura, Ana G. Hounie, M.D., Cara Moretti, Raquel C. Valle, Michael A. Jenike, M.D., Euripedes C. Miguel, M.D.

NR12 Hyperventilation Test in Patients with Panic Disorder
Isabella Nascimento, M.D., Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Walter A. Zin, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D.

NR13 Cigarette Smoking and Anxiety
Isabella Nascimento, M.D., Alexandre M. Valenca, M.D., Antonio E. Nardi, M.D., Walter A. Zin, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Ivan L.V. Figueira, M.D.

NR14 Electroretinography (ERG) and Panic Treatment
Fulvio Pieraccini, M.D., Sonia Iapichnio, M.D., Claudia Pacchierotti, M.D., Lettzia Bossini, M.D., Elisabetta Truglia, M.D., Paolo Castrogiovanni, M.D.

NR15 Panic-Agoraphobic Spectrum in Bipolar Disorder
Fulvio Pieraccini, M.D., Sonia Iapichino, M.D., Lettzia Bossini, M.D., Claudia Pacchierotti, M.D., Florinda Morana, M.D., Paolo Castrogiovanni, M.D.

NR16 An Epidemic of Phobic Disorders in Brazil? Results from a Population-Based, Cross-Sectional Survey
Wanderlei R. Motta, M.D., Mauricio S. Lima, Ph.D., Bernardo G.O. Soares, M.D., Nina R.D. Paixao, M.P.H., Ellis D. Busnello, M.D.

NR17 Bupropion Treatment of Civilian PTSD
Ahmad M. Almai, M.D., Thomas E. Brouette, M.D., Andrew W. Goddard, M.D.

NR18 Dialectical Behavior Therapy Adapted for Bulimia Nervosa
Debra L. Safer, M.D., Christy F. Telch, Ph.D., W. Stewart Agras, M.D.

NR19 Teasing History in Women with Bulimia Nervosa and Binge Eating Disorder
Tamara D. Jackson, Ph.D., Carlos M. Grilo, Ph.D., Robin M. Masheb, Ph.D.

NR20 Eating Disorders and Comorbidity
Fabiana L. Lopes, M.D., Antonio E. Nardi, M.D., Jose C. Appolinario, M.D., Walmir Coutinho, M.D., L.C. Povoa, M.D.

NR21 Anorexia Nervosa in the Turkish Culture
Emine N. Iscan, M.D.

NR22 Neurophysiologic Prediction of ECT Response
William F. Stubbeman, M.D., Andrew F. Leuchter, M.D., Ibrahim Gunay, M.D., Ian A. Cook, M.D., Julie E. King, R.N., Brett Shurman, M.D., Sergio Gonzalez, B.S.

NR23 Onset of Bipolar Illness With and Without Psychosis
Aysegul Yildiz, M.D., Gary S. Sachs, M.D.

NR24 The Impact of Depression on Health-Related Quality of Life
Samir H. Mody, Pharm.D., William S. Edell, Ph.D., Michael B. Durkin, M.S., Bryan E. Adams, Ph.D., Ed A. Repp, M.B.A.

NR25 Pleiotropic Effect of the 5HT Transporter Gene on Seasonality and Neuroticism
Leo Sher, M.D., Dean H. Hamer, Ph.D., Benjamin D. Greenberg, M.D., Dennis L. Murphy, M.D., Norman E. Rosenthal, M.D.

NR26 Predictors of Depression in Geriatric Medically Ill Patients
Lana M. Borina, M.D., Paul E. Ruskin, M.D., Allen Raskin, Ph.D., Kumar Menon, M.D.

NR27 Assessment of Motor and Process Skills in Depression
Ni A. Khin, M.D., Frances Oakley, M.S., Rebecca Parks, M.S., Trey Sunderland, M.D.

NR28 Treatment Choices in Unipolar and Bipolar Disorder
Dawson Wolfe, B.S., Steven Kaptik, B.S., Richard C. Shelton, M.D.

NR29 Utility Scores of the Symptoms of Depression
Ayal Schaffer, M.D., Susan K. Hershkop, M.D., Anthony J. Levitt, M.D., Paul Oh, M.D.

NR30 Proton Magnetic Resonance Spectroscopy Study of Treatment-Resistant Depression
Shamsah B. Sonawalla, M.D., Constance M. Moore, M.D., Perry F. Renshaw, M.D., Lindy E. Graham, B.A., Nelson A. Vega, B.A., Maurizio Fava, M.D., Ben Lafer, M.D., Andrew A. Nierenberg, M.D.

NR31 True Drug Response Versus Placebo Pattern Response to Fluoxetine: Differences in Cognitive Factors
Shamsah B. Sonawalla, M.D., Amy Farabaugh, M.A., Vinita Lesley, M.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

NR32 Affective Temperaments in Panic Disorder and MDD
Paolo Castrogiovanni, M.D., Fulvio Pieraccini, M.D., Sara Calossi, M.D., Massimo Garbini, M.D., Elena Pappagallo, M.D., Antonio Mantovani, M.D.

NR33 Temperaments in Features of Mood Disorders
Paolo Castrogiovanni, M.D., Massimo Garbini, M.D., Fulvio Pieraccini, M.D., Sara Calossi, M.D., Antonio Mantovani, M.D. Elena Pappagallo, M.D.

NR34 Menstrual Irregularity in Women with Bipolar Disorder
Sara R. Gaughan, B.A., Gary S. Sachs, M.D., Robert Knauz, Ph.D., Christina M. Demopulos, M.D.

NR35 The Short-Term Course of Untreated Depression: A Meta-Analysis of Studies Utilizing Wait-List Control Groups
Michael A. Posternak, M.D., Ivan W. Miller, Ph.D.

NR36 Visual Mental Imagery and Major Depressive Episode: The Role of Dorsolateral Prefrontal Cortical Hypoactivation
Amir Zarrinpar, Patricia Deldin, Ph.D., Stephen M. Kosslyn, Ph.D.

NR37 Childhood History of Distress in Patients with Mood Disorders
Candace N. White, M.Ed., Maurizio Fava, M.D., Constance Guille, B.A., Jordan W. Smoller, M.D.

NR38 Depression in Physicians: Access to Treatment and Impact on Career
Jane M. DeVeau, M.D., Jill A. RachBeisel, M.D.

NR39 Why Are Older Bipolar Patients Underrepresented in a Bipolar Specialty Clinic?
Victoria E. Cosgrove, B.A., Courtney L. Koslow, B.A., Caroline M.J. Orsini, B.S., Gary S. Sachs, M.D.

NR40 The Relationship Between Bipolar Disorder and Month of Birth
Courtney L. Koslow, B.A., Caroline M.J. Orsini, B.S., Victoria E. Cosgrove, B.A., Gary S. Sachs, M.D.

NR41 Bupropion Suspended Release in Elderly Medically Ill Patients
Molly Fortner, B.S., Indu Varia, M.D., Kenneth R. Gersing, M.D., Christopher O'Connor, M.D., P. Murali Doraiswamy, M.D.

NR42 The Management of SSRI-Induced Side Effects: A Survey of Psychiatrists
Christina M. Dording, M.D., Timothy J. Petersen, Ph.D., David Mischoulon, M.D., Rebecca A. Kornbluh, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

NR43 Locus of Control Orientation in Panic Disorder and the Differential Effects of Treatment
Abraham Bakker, M.D., Philip Spinhoven, Ph.D., Willem Van Der Does, Ph.D., Anton J.L.M. Van Balkom, M.D., Richard Van Dyck, M.D.

NR44 Distinguishing Psychotic and Nonpsychotic Depression
Juan C. Gonzalez-Seijo, M.D., Yolanda M. Ramos-Vicente, M.D., Ismael Lastra-Martinez, M.D., Jose L. Ayuso, Ph.D.

NR45 Do Antidepressants Alter the Course of Bipolar Disorder?
Caroline M.J. Orsini, B.S., Victoria E. Cosgrove, B.A., Courtney L. Koslow, B.A., Gary S. Sachs, M.D.

NR46 Review of Bipolar Disorder in a Geriatric Psychiatry Unit
Jean Y. Liu, M.D.

NR47 BPD in Primary Care
Raz Gross, M.D., Myrna M. Weissman, Ph.D., Mark Olfson, M.D., Marc Gameroff, M.A.

NR48 Reliability and Validity of the Korean Temperament and Character Inventory (TCI)
Seung-Mo Sung, M.D., Jong-Heun Kim, M.D., In-Kyoon Lyoo, M.D.

NR49 Treatment of Two Groups of Depressed Patients: One With and One Without Personality Disorders
Jean-Pierre Lepine, M.D., Antoine Pelissolo, M.D., Sylvie Troy, M.D.

NR50 Apathetic Syndrome and Depression: Responsiveness to Donepezil
Robert O. Morton, M.D., Mark D. Fossey, M.D., William R. Yates, M.D.

NR51 Risk Factors for Personality Disorders in the Hospitalized Military Population
Judith K. Denton, M.D., Nancy A. Harpold, D.O., Paul C. Burney, M.D., Christopher Lange, M.D., William J. Evans

NR52 Psychiatrists' Opinions on Dissociative Disorders
Justine Lalonde, M.D., James I. Hudson, M.D., Robin A. Gigante, B.A., Harrison G. Pope, Jr., M.D.

NR53 Is a Gift Ever Just a Gift? A Critical Review of the Interaction Between Physicians and the Pharmaceutical Industry
Ashley D. Wazana, M.D.

NR54 Association Analysis of G-Protein B3 Subunit Gene with Altered Ca2+ Homeostasis in Bipolar Disorder
Timothy W. Corson, B.S.C., Peter P. Li, Ph.D., James L. Kennedy, M.D., Fabio Macciardi, M.D., Robert Cooke, M.D., Sagar V. Parikh, M.D., Jerry J. Warsh, M.D.

NR55 Lithium Carbonate-Induced Mitotic Anomalies in Vicia Fabal
Rashmi Rashmi, Ph.D., Vinita Vishwakarma, M.S.C., Z.A. Haider, Ph.D., Anil Kumar, M.D.

NR56 Predictors of Two-Year Survival in Elderly Veterans with Comorbid Medical and Psychiatric Symptoms
Helen Lavretsky, M.D., Roshan Bastani, Ph.D., Robert Gould, Ph.D., David L. Huang, Ph.D., Lissy F. Jarvik, M.D., Annette Maxwell, Ph.D.

NR57 Strain and Reward Among Caregivers of Geriatric Patients
Joanne Fenton, M.D., Jill A. RachBeisel, M.D., Niamh M. Holohan, M.D., Lisa B. Dixon, M.D.

NR58 Testosterone Level in Late-Life Male Dysthymia
Stuart N. Seidman, M.D., Steven P. Roose, M.D., Davangere P. Devanand, M.D., Andre Araujo

NR59 Comparison of Valproic Acid Versus Carbamazepine in the Treatment of Agitation in Dementia
Pranav Dave, M.D., Paul A. Kettl, M.D.

NR60 Efficacy and Tolerability of Carbamazepine in Treating Agitation and Aggression Associated with Dementia
Pranav Dave, M.D., Paul A. Kettl, M.D.

NR61 How Knowledge of and Experience with Life-Saving Procedures Influences Willingness to Undergo These Procedures
Umar F. Rahman, M.D., Kumar Menon, M.D., Allen Raskin, Ph.D., Paul E. Ruskin, M.D.

NR62 Older Schizophrenic Patients: Nature of Dwelling Status and Symptom Severity
Sanjay Gupta, M.D., Charles Steinmeyer, Ph.D., Bradford L. Frank, M.D., Kari Lockwood, R.N., Kay Schultz, R.N., Peggy Keller, R.N.

NR63 Anxiety in Patients Assessed for Memory Complaints
Louis Lopez, M.D., Elizabeth Crocco, M.D., Ranjan Duara, M.D., Raymond L. Ownby, M.D.

NR64 Relationship Between Religion and End-of-Life Treatment Preferences Among Geriatric Patients
Oscar R. Heeren, M.D., Kumar Menon, M.D., Allen Raskin, Ph.D., Paul E. Ruskin, M.D.

NR65 Coping Strategies in Patients with Mitral Valve Prolapse
Jung-Chen Chang, Ph.C., Chau-Shoun Lee, M.D.

NR66 Work Stress and Emotional Health in the U.S. Air Force
Steven E. Pflanz, M.D.

NR67 The Relationship Between Serum Lipid Levels and Suicidality in Suicide Attempters
Heon-Jeong Lee, M.D., Yong-Ku Kim, M.D., Leen Kim, M.D., Min-Soo Lee, M.D.

NR68 Circumstances of Suicide Among Individuals with Schizophrenia
Julie A. Kreyenbuhl, Ph.D., Deanna L. Kelly, Pharm.D., Robert R. Conley, M.D.

NR69 Suicide in Travis County, Texas: 1994-1998
Siqing Li, M.D., Lawrence A. Hauser, M.D., Beilin Gao, M.D.

NR70 Suicidal Behavior in the Elderly
Yoshiko Nishimatsu, M.D., Minshuku Ko, M.D., Takuya Saito, M.D.

NR71 Firearms and Suicide in Travis County, Texas: 1994-1998
Beilin Gao, M.D., Siqing Li, M.D.

NR72 Comparative Trial of Dysthymia Treatment
Marcelo F. Mello, M.D., Luciana Myczkowicz, M.D., Paulo R. Menezes, M.D.

NR73 Comparative Hemodynamic Effects of Urapidil and Labetalol During ECT
Jordi Blanch, M.D., Graciela Martinez-Palli, M.D., Richard Navines, M.D., Jose-Manuel Arcega, M.D., Maria-Luisa Imaz, Miquel Bernardo, M.D., Carmen Gomar, M.D.

NR74 Light Therapy to 26 Bipolar Patients
Eduard M. van Gent, M.D., Harry J. Keegstra, M.D., Willem Barents, Ph.D.

NR75 A Case Series Using ECT for the Treatment of Psychiatric Illness in Patients with Mental Retardation
Daniel Acosta, Diana J. Antonacci, M.D., Christopher M. de Groot, M.D.

NR76 Use of ECT for Severe Episodic Aggression in Patients with Treatment-Refractory Psychosis
Manish K. Parikh, M.D., Angela M. Hegarty, M.D., Elda P. Sancho, M.D.

NR77 A Prospective Naturalistic Study of 326 Agoraphobic Panic Patients
Giulio Perugi, M.D., Cristina Toni, M.D., Franco Frare, M.D., Belen Mata, M.D., Barbara Vitale, M.D., Francesco Mengal, Ph.D., Hagop S. Akiskal, M.D.

NR78 Improving Adherence of Antidepressants by Pharmacies
Hein P. van Hout, Ph.D., Rob Heerdink, Ph.D., Guy Goodwin, M.D., Bram B. Bakker, Ph.D., Hugo Nieuwenhuyse, Ph.D.

NR79 Association Between QEEG Characteristics and BPRS Subscales in Bipolar Disorder and Schizophrenia
Alexandra L. Sporn, M.D., Dean F. Salisbury, Ph.D., Paola Massoni, Iris Fisher

NR80 The Influence of Acupuncture on the Treatment of Cocaine-Addicted Patients
Daniela C. Ceron, Susan M. Mondoni, Andre Malbergier, M.D., Guilherme R. Silva, M.D.

NR81 Cognitive Effects of Repetitive Transcranial Magnetic Stimulation in Depressed Patients
Brian Martis, M.D., Valorie Carson, Rajiv P. Sharma, M.D., Eileen M. Martin, Ph.D., Philip G. Janicak, M.D., Mauli Verma, M.D., Cherise Chase, R.N.

NR82 A Meta-Analysis of Acupuncture for Psychiatric Disorders
Andrei A. Pikalov, M.D., Elizabeth C. Penick, Ph.D.

NR83 Characteristics and One-Year Outcome of Anxiety and Depression Outpatients in Taiwan
Jor-Chi Song, M.D., Andrew P. Ho, M.D.

NR84 A Comparison of St. John's Wort and SSRI Users
Leonard Lev, M.D., JoAnne Sirey, Ph.D., Patrick J. Raue, Ph.D., Martha L. Bruce, Ph.D., Barnett S. Meyers, M.D.

NR85 Description of an Outpatient Sample of Patients Diagnosed with Depression in a Managed Care Environment
Alisa B. Busch, M.D., Vanessa Azzone, Ph.D., Shelly F. Greenfield, M.D.

NR86 Response to a Partial Hospitalization Treatment Program: A Comparison of Inpatient and Outpatient Referrals
Keri L. Lemmond, M.D., Jill I. Mattia, Ph.D., Tina Egan, M.S.W., Rendueles Villalba, M.D.

NR87 Treatment of Panic Disorder in an Office-Based Practice
Carlos Blanco, M.D., Imram Khan, M.D., Renee Goodwin, Ph.D.

NR88 Initial Experience with a Primary Care Depression Disease Management Program
Catherine J. Datto, M.D., James C. Coyne, Ph.D., Mark A. Miani, M.D., David A. Horowitz, M.D., Ira R. Katz, M.D.

NR89 Risperidone Treatment of Chronic Tic Disorder and Tourette's Syndrome
Eun Young Oh, M.D., Jung-Eun Lee, M.D., Yoon-Mi Shin, M.D.

NR90 Prevalence of Polypharmacy in Different Clinical Settings: It's Relation to Drug-Drug Interactions
Mujeeb U. Shad, M.D., Cheryl Carmichael, B.A., Sheldon H. Preskorn, M.D., Dale Horst, Ph.D.

NR91 Prevalence of Domestic Violence Against Women in San Juan Teitipac, Oaxaca, Mexico
Alejandra Postlethwaite, M.D.

NR92 Depression and Belief in Life After Death Among Geriatric Home-Care Patients
Glen Milstein, Ph.D., Martha L. Bruce, Ph.D.

NR93 Relationship Between Religiosity and Symptoms of Depression
Sarabjit Singh, M.D., Richard Balon, M.D.

NR94 Career Plans Among Psychiatrists in Training
Babak Mirin-Babazadeghan, M.D., Jiri J. Danczik, M.D., Zinat Sobhani, M.D.

NR95 Pharmaceutical Industry Impact on Psychiatry Residents' Prescribing Practices
Daniel J. Kuhles II, M.P.H., Thomas L. Schwartz, M.D., Robert J. Gregory, M.D., Alan R. Beeber, M.D.

NR96 Psychiatric Inpatients Are Not More Likely to Receive Restrictive Measures During Weekends and Holidays
Charles Jin, M.D., Leo Sher, M.D.

NR97 Unrecognized Comorbid Sexual Dysfunction
Sandra B. Lare, D.O., Lawrence A. Labbate, M.D.

NR98 Prescribing Conventional Antipsychotics in the Era of Novel Antipsychotics
Xiao-Hong Wang, M.D., Daniel J. Kuhles II, M.P.H., Thomas L. Schwartz, M.D., Sanjay Gupta, M.D., Bhushan S. Agharkar, Jacob Manjooran, M.D., William J. Hardoby, M.D.

NR99 Prescribing Conventional Antipsychotics at Two Veterans Hospitals: Are There Geographic Differences?
Monica Arora, M.D., Anil Sharma, M.D., Xiao-Hong Wang, M.D., Thomas L. Schwartz, M.D., Subhash C. Bhatia, M.D. Daniel J. Kuhles II, M.P.H., Bhushan S. Agharkar

NR100 Psychiatric Clinical Research and the Doctor-Patient Relationship
Flavia C. Campos, Antonio E. Nardi, M.D.

NR101 Lack of Psychoeducation in Argentina: Stigma Issues?
Adolfo Canovi, M.D., Ricardo L. Perez-Rivera, M.D., Adrian Trajterman, M.D., Gustavo Rozadilla, M.D., Eugenia Dabi, M.D., Eduardo R. Sanchez de Antonio, M.D., Marcela Bonano, M.D.

NR102 Stigma in Functional Somatic Syndromes and Comparable Medical Conditions
Karl J. Looper, M.D., Laurence J. Kirmayer, M.D.

NEW RESEARCH

Monday, May 15, 2000, 1:00 p.m. - 2:30 p.m.

New Research 2 – Oral/Slide Session – Room E255, Level 2, McCormick Place Lakeside

BRAIN IMAGING AND OTHER NEW TECHNOLOGIES

Chp.: Carol A. Tamminga, M.D.

NR103	Schizophrenia: Progressive Prefrontal Gray Changes Almos I. Nagy, M.D., Chang U. Lee, M.D., Martha E. Shenton, Ph.D., Dean F. Salisbury, Ph.D., Ashley A. Kricun, B.S., Chandlee C. Dickey, M.D., Robert W. McCarley, M.D.	1:00 p.m.
NR104	MRI Analysis of Cortical Gray and White Matter in Patients with Bipolar Disorder Melissa P. Lopez-Larson, B.S., Melissa P. DelBello, M.D., Mark Steed, M.A., Stephen M. Strakowski, M.D.	1:15 p.m.
NR105	Uncinate Fasciculus in Schizophrenia: A Diffusion Tensor Study Marek Kubicki, Ph.D., Stephan E. Maier, Ph.D., Robert W. McCarley, M.D., Hatsuho Mamata, M.D., Enkeat Teh, M.A., Christopher Allen, B.A., Martha E. Shenton, Ph.D.	1:30 p.m.
NR106	White Matter Abnormalities in Schizophrenia As Measured by Magnetic Resonance Diffusion Imaging Melissa Frumin, M.D., Carl F. Westin, Ph.D., Robert W. McCarley, M.D., Stephan E. Maier, Ph.D., Hatsuho Mamata, M.D., Marek Kubicki, Ph.D., Martha E. Shenton, Ph.D.	1:45 p.m.
NR107	Cerebellar Function in Children at Risk for Bipolar Disorder Melissa P. Del Bello, M.D., Patricia McDonough-Ryan, M.A., Sarah M. Graman, B.A., Cesar A. Soutullo, M.D., Molly E. Zimmerman, B.A., H. Lee Rosenberg, B.A., Stephen M. Strakowski,	2:00 p.m.
NR108	Age-Related Decline of 5HT-1A Receptor Binding Johannes Tauscher, M.D., Nicolaas P.L.G. Verhoeff, M.D., Doug Hussey, B.S.C., Jeffrey H. Meyer, M.D., Alex Kecojevic, Professor Siegfried Kasper, Shitij Kapur, M.D.	2:15 p.m.

NEW RESEARCH

Monday, May 15, 2000, 1:00 p.m. - 2:30 p.m.

New Research 3 – Oral/Slide Session – Room E256, Level 2, McCormick Place Lakeside

ANXIETY AND MOOD DISORDERS

Chp.: James W. Thompson, M.D.

NR109	A Prospective Study of PTSD and Nonadherence in Survivors of a Myocardial Infarction Eyal Shemesh, M.D., Abraham Rudnick, M.D., Daniela Alon, R.N., Edo Kaluski, M.D., Olga Milovanov, M.D., Zui Verd, M.D., Gad Cotter, M.D.	1:00 p.m.
NR110	Cardiovascular and Metabolic Correlates of PTSD Sonia P. Yovtcheva, M.D., Martha M. Kato, M.D., Robert D. Cox, Ph.D., Rezhan Hussein, M.D., Ali Iranmanesh, M.D.	1:15 p.m.
NR111	Testosterone Replacement for Male Depression: Randomized Clinical Trial Steven P. Roose, M.D., Stuart N. Seidman, M.D.	1:30 p.m.
NR112	Survey of Clinicians' Long-Term Antidepressant Prescribing Practices Steffany J. Fredman, B.A., Maurizio Fava, M.D., Allison S. Kienke, B.A., Candace N. White, M.Ed., Jerrold F. Rosenbaum, M.D.	1:45 p.m.
NR113	Elevated 5HT-2A Binding Potential in SSRI-Responsive Depression Jeffrey H. Meyer, M.D., Shitij Kapur, M.D., Beata Eisfeld, B.S.C., Gregory M. Brown, M.D., Sylvain Houle, M.D., Helen S. Mayberg, M.D., Sidney H. Kennedy, M.D.	2:00 p.m.
NR114	An Analysis of Recent Valproate Prescribing Trends Neil B. Sandson, M.D., Narayanan Ramesh, M.D.	2:15 p.m.

NEW RESEARCH

Monday, May 15, 2000, 3:00 p.m.–5:00 p.m.

New Research 4 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

YOUNG INVESTIGATORS' POSTER SESSION

Moderator: Javier I. Escobar, M.D.

NR115 Premenstrual Symptom Changes in Women with Schizophrenia: A Prospective Study
So-Hyun Choi, M.D., Sang-Bum Kang, M.D., Sook-Haeng Joe, M.D.

NR116 Changes in Cortical Excitability in Women with PMS
Mark J. Smith, M.D., John C. Keel, B.A., Peter J. Schmidt, M.D., Linda F. Adams, B.A., David R. Rubinow, M.D., Margaret Nguyen, B.A., Eric M. Wassermann, M.D.

NR117 Topiramate in Premenstrual Dysphoric Disorder
Seema Hussain, M.D., Zubaida A. Chaudhry, M.B., Mohammad Z. Hussain, M.D.

NR118 Use of Complementary Medicine in Mental Disorders
Benjamin G. Druss, M.D., Robert A. Rosenheck, M.D.

NR119 Neuromotor Signs in Schizophrenia: Their Impact on Social Functioning
Stefanie Berns, Ph.D., Rosemarie Basile-Szulc, Ph.D., Rashmi Rastogi, Ph.D., Judith Jaeger, Ph.D., Pal Czobor, Ph.D., Christina Gomes, B.A.

NR120 Insight, Cognition and Disability in Schizophrenia
Stefanie Berns, Ph.D., Bonnie Creech, Ph.D., Judith Jaeger, Ph.D., Mark Ast, Ph.D., Pal Czobor, Ph.D.

NR121 A Five-Year Follow-Up Study of Deficit and Nondeficit Schizophrenia
Cenk Tek, M.D., Brian Kirkpatrick, M.D., Robert W. Buchanan, M.D.

NR122 Akathisia, Suicidality and Depersonalization
Cem Atbasoglu, M.D., Susan K. Schultz, M.D., Nancy C. Andreasen, M.D.

NR123 Neurocognitive Predictors of Functional Decline in Poor-Outcome Schizophrenia
Patrick J. Moriarty, M.A., Thomas Coleman, M.A., Joseph I. Friedman, M.D., Philip D. Harvey, Ph.D., Christopher R. Bowie, M.A., Len White, Ph.D., Michael Parella, Ph.D., Kenneth L. Davis,

NR124 Impact of Early Intervention with Intramuscular Antipsychotic Medication in an Acute-Care Setting
Hildebrando Salinas, M.D., James M. Russell, M.D., James M. Martinez, M.D., Joan A. Mackell, Ph.D.

NR125 Increased S100-Beta Protein in Schizophrenia
Clarissa S. Gama, M.D., Diogo R. Lara, M.D., Luis V. Portela, Ph.D., Carlos A. Goncalves, Ph.D., Diogo O. Souza, Ph.D., Paulo B. Abreu, Ph.D.

NR126 Schizophrenia With and Without a Comorbid Anxiety Disorder
Sanjay M. Vaswani, M.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Ekkehard Othmer, M.D., Cherilyn M. De Souza, M.D., Marsha R. Read, Ph.D., Edward E. Hunter, Ph.D.

NR127 Evidence of Heterogeneity in Cognitive Performances
Stacey D. Espinet, R. W. Heinrichs, Ph.D.

NR128 Metabolic and Cardiovascular Consequences of Prolonged Clozapine Treatment: A Retrospective Study
Martha M. Kato, M.D., Sonia P. Yovtcheva, M.D., Carolyn A. Stanley-Tilt, R.N., Rezhan Hussein, M.D., Ali Iranmanesh, M.D.

NR129 Medication Compliance and Quality of Life in Persons with Schizophrenia
Leticia T. Postrado, Ph.D.

NR130 Depression Is Not Associated with Short-Term Outcome in Acute Schizophrenia
Thomas Szafranski, M.D., Zuzanna Konieczynska, Ph.D.

NR131 Methylphenidate Treatment of Psychiatric Symptoms from Central Pontine Myelinolysis
Denise C. Bridgeford, M.D., David B. Arciniegas, M.D., Marcelo Fernando Batkis, M.D., Brandon K. Martin, B.A., Thomas P. Beresford, M.D.

NR132 Semantic Retrieval in Older Schizophrenia Patients
Angela O. Udebiuwa, M.D., Richard B. Rosse, M.D., Stephen I. Deutsch, M.D., Jill A. RachBeisel, M.D.

NR133 Neuropsychological Correlates of Schizophrenic Syndrome
Steffen Moritz, Ph.D., Burghard Andresen, Ph.D., Dieter Naber, M.D., Martin Lambert, M.D., Michael Krausz, Ph.D., Anne Karow, M.D.

NR134 Gender, Gamma Activity and Schizophrenia
Shameran Slewa-Younan, B.A., Evian Gordon, Ph.D., Leanne Williams, Ph.D., Elkwonon Goldberg, Ph.D.

NR135 Trends in the Treatment of Schizoaffective Disorder
Julianne Flynn, M.D., Thomas A. Grieger, M.D., David M. Benedek, M.D.

NR136 Factors Predicting Compliance with Appointments in Women Discharged from a Psychiatric Hospital in Turkey
Aykut Ozden, M.D., Huseyin H. Ozsan, M.D., Bedriye Oncu, M.D., Handan Tugcu, Ph.D.

NR137 Suspiciousness As a Specific Risk Factor for Major Depressive Episodes in Schizophrenia
Erick L. Messias, M.D., Brian Kirkpatrick, M.D., Ranganathan Ram, M.D., Allen Y. Tien, M.D.

NR138 Old Schizophrenics: Gender, Symptoms, Course and Outcome
Uma Naidoo, M.D., Carl Salzman, M.D., Omar Rahman, M.D., Emily Schwab, B.S., Kelly Czworka, A.B.

NR139 Morbidity from Catatonia in a Chronic Population
Chitra Malur, M.D., Andrew J. Francis, Jr., M.D.

NR140 SPECT Brain Imaging in Catatonia
Chitra Malur, M.D., Corazon Cabahug, M.D., Andrew J. Francis, Jr., M.D.

NR141 Catatonia in Post-ECT Delirium
Chitra Malur, M.D., Andrew J. Francis, Jr., M.D.

NR142 A Follow-Up Study Comparing Clinical and Endocrine Effects of Clozapine and Risperidone
Norberto M. Zelaschi, M.D., Juana L. Rodriguez, M.D., Sergio Gaitan, M.D., Sergio Panizzo, B.A., Azucena Sobrera, B.A. Angelica Lopez, B.A., Ferando Archuby, B.A.

NR143 Vlaproic Acid Increases Gene Expression of Superoxide Dismutase (SOD1)
Xin-Min Li, M.D., Ou Bai, Augusto Juorio, Vern Bennett, M.D., Rudy Bowen, M.D.

NR144 Venlafaxine Extended Release in Bipolar Depression
Jose M. Artadi, M.D., Manuela Georgescu, M.D., Paul J. Goodnick, M.D., Blanche Freund, Ph.D., C. Lindsay DeVane, Ph.D., Charles L. Bowden, M.D., Peyton White

NR145 Onset of Response to Fluoxetine As Assessed by the Symptom Questionnaire
David Mischoulon, M.D., Shamsah B. Sonawalla, M.D., Andrea C. Hutchins, B.A., Margarita L. Delgado, B.A., Mary J. Johnson, M.A., John J. Worthington III, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

NR146 Effects of Mirtazapine on Sleep Polygraphic Variables
Michel Schittecatte, M.D., Francoise Dumont, M.D., Robert Machowski, Ph.D., Catherine Cornil, Francis Lavergne, M.D. Jean Wilmotte, M.D.

NR147 Alpha2-Adrenoreceptor Sensitivity As a Marker of Depression
Michel Schittecatte, M.D., Francoise Dumont, M.D., Robert Machowski, Ph.D., Eric Fontaine, Catherine Cornil, Julien Mendlewicz, M.D., Jean Wilmotte, M.D.

NR148 Characteristics of Individuals Seeking Treatment for Gambling Problems and Reporting Excessive Tobacco Use
Marc N. Potenza, M.D., Marvin A. Steinberg, Ph.D., Susan McLaughlin, Dawn Hemstock, Ran Wu, M.S., Bruce J. Rounsaville, M.D., Stephanie S. O'Malley, Ph.D.

NR149 Switching Versus Augmentation: A Prospective, Naturalistic Comparison in Depressed, Treatment-Resistant Patients
Michael A. Posternak, M.D., Mark Zimmerman, M.D.

NR150 Therapeutic Drug Monitoring of Olanzapine
Matthias Dobmeier, M.D., Ekkehard Haen, M.D., Juergen Mueller, M.D., Helmfried E. Klein, M.D.

NR151 Gabapentin in Bipolar Depression
Po W. Wang, M.D., Claudia M. Santosa, M.A., Connie M. Strong, M.S., Debbie L. Tate, Terence A. Ketter, M.D.

NR152 Effect of SSRI on 5HT
Charl Els, W. E. Nel, M.D., J.M.C. Oosthuizen, M.D., E. H. de Wet, M.D., P. H. du Preez, B.S., P.T. Austin, B.S.

NR153 Adjunctive Gabapentin in Treatment-Resistant Depression
Sarah Yasmin, M.D., Linda L. Carpenter, M.D., Zelko Leon, M.D., Jason M. Siniscalchi, M.S., Lawrence H. Price, M.D.

NR154 Medication Outcomes in a Veterans Administration Domiciliary Program
Christopher P. Camilleri, M.D., David N. Osser, M.D., Paul Block, Ph.D., Eviline T. Meleka, M.D., Jagdish Ragade, M.D.

NR155 Efficacy of Mirtazapine in Panic Disorder
Joseph Berger, M.D., Philip T. Ninan, M.D., Bettina Knight, B.S.N., Amy Selvig, B.S., Charles B. Nemeroff, M.D.

NR156 Antipsychotic Tolerance, Rebound and Supersensitivity Psychosis with Quetiapine
Howard C. Margolese, M.D., Guy Chouinard, M.D., Linda Beauclair, M.D., Marie-Claire Belanger, R.N.

NR157 Olanzapine Treatment of Adult Stuttering: An Open-Label Prospective Analysis
Nathan E. Lavid, M.D., David L. Franklin, M.S., Gerald A. Maguire, M.D.

NR158 Citalopram Treatment of Social Phobia
Charles A. Cloutier, Indu Varia, M.D., P. Murali Doraiswamy, M.D.

NR159 Mirtazapine Versus Fluoxetine in Panic Disorder
Flavio Kapczinski, Ph.D., Luciana Ribeiro, M.D., Joao V. Busnello, Marcia K. Sant'Anna, Marcelo Madruga, Joao Quevedo, M.D., Ellis D. Busnello, M.D.

NR160 5HT Syndrome: A Review of Cases
Jimmy O. Ibikunle, M.D.

NR161 Overdose: A Review of 100 Cases
Jimmy O. Ibikunle, M.D., Suzi R. Levens, M.D.

NR162 Fluoxetine in the Treatment of Huntington's Disease
Nicola de Marchi, M.D., Alfredo Dama, M.D., M. Antonietta Ragone, M.D., Fabiana Daniele, M.D., Maria G. Ariano, M.D.

NR163 Risperidone and Clozapine: A Five Add-On APD in Acute Psychosis
Amresh K. Shrivastava, M.D., Meghana Thakar, M.A., Supriya Ghalsasi, D.P.M.

NR164 Use of Topiramate as a Mood Stabilizer
Lou Ann Eads, M.D., R. Greg Wooten, M.D., Thomas A.M. Kramer, M.D.

NR165 Head Trauma: Litigants Versus Nonlitigants
Reed Goldstein, Ph.D., Howard S. Sudak, M.D., Gary S. Bruss, Ph.D.

NR166 A Novel Functional MRI Memory Test for the Assessment of Early Alzheimer's Disease
Lauretta Baucher, Gene Chen, B.S., Jeffery Petrella, M.D., Amishi Jha, Ph.D., Gregory McCarthy, Ph.D., Halla Husn, P. Murali Doraiswamy, M.D.

NR167 Delirium Predisposal Factors
Adolfo Canovi, M.D., Ricardo L. Perez-Rivera, M.D., Cecilia J. De Simone, M.D., Gustavo Rozadilla, M.D.

NR168 Irritable Bowel Syndrome Treated with Amitriptyline: An Open Trial with 19 Patients
Hildeberto J. Tavares, M.D., Hyong-Jin Cho, M.D., Carlos R. Silva, M.D., Aytan M. Sipahy, M.D., Aderson D. Moreira, M.D., Wagner F. Gattaz, Ph.D.

NR169 Malingering in the Military
Nancy A. Harpold, D.O., Judith K. Denton, M.D., Paul C. Burney, M.D., Christopher Lange, M.D., William J. Evans

NR170 Dopamine and Electroretinogram in Cocaine-Dependent Patients
Jeffrey A. Berman, M.D., Abir Marcus, M.D., Benito Gonzalez, PA-C, Alec Roy, M.D., Monique Roy, M.D.

NR171 Testosterone and Pathological Gambling
Carlos Blanco, M.D., Angela Ibanez, M.D., Enrique Baca-Garcia, M.D., Carmen Blanco-Jerez, B.S., Jeronimo Saiz-Ruiz, M.D., Luis Orensanz, Ph.D.

NR172 Deep Brain Stimulation in OCD: A Reversible Last-Resort Therapeutic Option?
Loes Gabriels, M.D., Paul Cosyns, M.D., Bart Nuttin, M.D.

NR173 Cyclooxygenase and Brain Development: Implications in Rett's Syndrome
Carolina Stamu, M.D., Giulio M. Pasinetti, Ph.D., Lap Ho, Ph.D., Fitzroy Willis, Ph.D.

NR174 Olanzapine Augmentation for SSRI-Apathy Symptoms
Christopher R. Johnson, M.D., Michael Barber, Ph.D., Barbara Kertz, M.A., Kimberly K. Cress, M.D., Paul J. Carlson, M.D., Leanne Vogelson, B.A., Lauren B. Marangell, M.D.

NR175 fMRI to Assess Chinese Schizophrenia
Dein-Wen Lee, Chen-Hong Yang, M.D., Tung-Ping T. Su, M.D., Jen-Chuen Hsieh, M.D.

NR176 M-CPP/PET in Impulsive/Aggressive Personality Disorders
Diedre A. Reynolds, M.D., Antonia S. New, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Vivian Mitropoulou, M.A. Marianne Goodman, M.D., Larry J. Siever, M.D.

NR177 NPSLE, Age and the Neurodevelopmental Model
Avram H. Mack, M.D., Gregory L. Fricchione, M.D., Malcolm Rogers, M.D.

NR178 Neuroendocrine Response to Intravenous Clomipramine in Treatment-Resistant OCD
Sanjay J. Mathew, M.D., Brian A. Fallon, M.D., Kathryn Perko, Jeremy D. Coplan, M.D.

NR179 Valproate Increases the mRNA Levels of Bcl-2
Shumin Zhao, M.D., Husseini K. Manji, M.D., Guang Chen, M.D.

NR180 Visuospatial Memory Dysfunction in OCD: A Neuropsychological and PET Study
Kyung-Heup Ahn, M.D., Jae-Seung Lee, M.D., Myung-Chul Lee, M.D., Dong-Woo Lee, M.D., In-Kyoon Lyoo, M.D., Dong-Soo Lee, M.D., Jun-Soo Kwon, M.D.

NR181 Treatment-Resistant Schizophrenia: Predictive Factors
Jorge Henna, M.D., Helio Elkis, M.D.

NR182 Topographic Analysis of the Regional Brain Atrophy in Alzheimer Patients Using an Area-Based Radial Transformation Study
Ju-Han Kim, Jung-Hie Lee, M.D., Jong-Inn Woo, M.D.

NR183 99 Tc-ECD Brain SPECT in Alzheimer's Disease: Mexican Experience
Jose A. Santos, Juan C. Garcia, M.D., Oscar Ugalde, M.D., Gabriela Galindo, David E. Saucedo, M.D.

NR184 Decreased Repetitive Behaviors in Response to Oxytocin Challenge in Adult Autistic Disorders
Sherie L. Novotny, M.D., Eric Hollander, M.D., Andrea Allen, Ph.D., Bonnie A. Aronowitz, Ph.D., Concetta DeCaria, Ph.D. Charles Cartwright, M.D., Rona Yaffe

NR185 Is St. John's Wort a Mood Stabilizer in Bipolar Children and Adolescents?
Frederic J. Kochman, M.D., Ginette Hamm, M.D., Daniel Bavart, M.D.

NR186 Trauma, PTSD and Personality in Adolescents
Siham Muntasser, M.D., James W. Lowe, M.D., Jamet Rice, Ph.D., Lee Matthews, Ph.D.

NR187 A Systematic Open-Label Trial of Mirtazapine in Autism and Related Pervasive Developmental Disorders
David J. Posey, M.D., Krista D. Guenin, B.A., Arlene Kohburn, B.A., Naomi B. Swiezy, Ph.D., Christopher J. McDougle, M.D.

NR188 A Psychoeducational Group for Bipolar Adolescents
Kiki D. Chang, M.D., Joyce Dorado, Ph.D., Jacqueline Martin, Ph.D.

NR189 Autosomal Dominant Macrocephaly and Autism
Syed S. A. Naqvi, M.D., John M. Graham, Jr., M.D.

NR190 Gender Differences in the Relevance and Effect of Depression Post-Unstable Ischemic Syndrome
Syed S. A. Naqvi, M.D., Peter J. Panzarino, Jr., M.D., Yulius Mustafa, M.D., Haidar Sadeghi-Razlighi, M.D., Russell M. Poland, M.D., Tasneem Z. Naqvi, M.D.

NR191 Recognition of Mental Disorders by Residents in a Gastroenterology Unit
Phillippe M.J. Persoons, M.D., Benjamin Fischler, M.D., Koen Luyckx, M.A., Lukas Van Oudenhove

NR192 Panic Disorder in Mitral Valve Prolapse
Chau-Shoun Lee, M.D., Jung-Chen Chang, Ph.C.

NR193 Quetiapine Fumarate Treatment of Delirium
Thomas L. Schwartz, M.D., Prakash S. Masand, M.D.

NR194 Psychological Structure of Patients with Diabetic Polyneuropathy
Vladimir M. Diligenski, M.D., Natasa M. Sikanic, M.D., Svetlana F. Jelic, Zorica M. Caparevic, M.D., Gradimir V. Bojkovic, Nada P. Kostic, M.D.

NR195 A Pilot Study of Psychiatric Disorders in Adults with Irritable Bowel Syndrome
Catharine J. Munn, M.D., Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Peter Farvolden, Ph.D., Gervais Tougas, M.D.

NR196 The Quality of Life in Cancer Patients in Korea
Kwangil Kim, M.D., Sung-Kil Min, M.D., Youngchul Jung, M.D.

NR197 Healer Choice in a Multi-Ethnic Adolescent Population
Cathy K. Bell, M.D., Deborah A. Goebert, M.S., Naleen N. Andrade, M.D., Ronald C. Johnson, Ph.D., John F. McDermott, Jr., M.D., Earl S. Hishinuma, Ph.D., Barry S. Carlton, M.D.

NR198 The Relationship Between Irritable Bowel Syndrome and Panic Disorder in Mumbai, India
Titiksha V. Kubal, M.D., Charles Pinto, M.D., Sumeet Sharma, M.D., Subhdeep Virk, M.D., Sarah Vandervoort, Sanjay Gupta, M.D., Prakash S. Masand, M.D.

NR199 Outcome of Recognizing Major Depression Among Chinese Patients in Primary Care
Albert Yeung, M.D., Shauna Howarth, B.A., Andrew A. Nierenberg, M.D., Raymond Chan, B.S., Jonathan E. Alpert, M.D. David Mishoulon, M.D., Maurizio Fava, M.D.

NR200 The Association Between Schizophrenia and Cancer: A Population-Based Study
Mary E. Cohen, M.D., Bruce Dembling, John B. Schorling, M.D.

NR201 Characteristics of Depressive Symptoms in Koreans
Jin-Yeong Kim, M.D., Sung-Mi Choi, M.A., Guk-Hee Seo, M.D., Seong-Jin Cho, M.D., Maeng-Je Cho, M.D.

NR202 Effects of Perceived Health on Psychiatric Outcome
Richard Thompson, Ph.D., Tina L. Harralson, Ph.D., Alan C. Regenberg, B.A., Tiffany Purnell, B.A., Ira R. Katz, M.D., James C. Coyne, Ph.D., Trevor Hadley, Ph.D.

NR203 Odontological Problems in Patients Exposed to Lithium Therapy
Mariana F. Tatsch, M.D., Renata Kkrelling, M.D., Valentim Gentil, M.D.

NR204 The Role of Preinjury IQ in the Assessment of Intelligence Impairment Due to Traumatic Head Injury
Beilin Gao, M.D., Siqing Li, M.D.

NR205 Gender Role in Fitness-to-Stand-Trial Exams
Gary R. Collins, M.D., Stephen B. Billick, M.D.

NR206 An Association Between Bipolar Disorder and Synaptobrevin-Like 1 Gene (SYBL1)
Takuya Saito, M.D., Sam Parsia, M.D., Demitri F. Papolos, M.D., Herbert M. Lachman, M.D.

NR207 The Role of Gender in Determining Neuropsychiatric Outcome Following Mild or Moderate Head Injury
Ariel K. Dalfen, M.D., Alison Jardine, O.T., Donna Ouchterlony, M.D., Scott R. McCullagh, M.D., Andrea Protzner, M.A., Anthony Feinstein, M.D.

NR208 Attention and Eye Movement Control in OCD
Chiang-Shan R. Li, M.D., Yong-yi Yang, M.D., Hsuen-ling Chang, M.D., Sho-fen Lin, M.S.

NR209 Facial Expression Analysis of Psychiatric Patients
Georg Fuckel, M.D., Annuschua Praessl, Birgit Graf, Paraskevi Mavrogiorguv, M.D., Hans F. Moeller, M.D., Ulrich Hegerl, M.D.

NR210 The Merger of Two Psychiatry Residency Training Programs
Anjali M. Gupta, M.D., Lisa B. Dixon, M.D., Laura R. Gaffney, M.D., Patricia N. Nnadi, M.D.

NR211 Stress, Psychopathology and Cytokines in In Vitro Fertilization Patients
Florina Haimovici, M.D., Raina Fichorova, M.D., Janis Anderson, Ph.D., Wright Bates, M.D., Vincent Carey, Ph.D., Randy S. Glassman, M.D., Deborah J. Anderson, Ph.D.

NR212 Quality of Life Among Schizophrenics: Is Age a Contributing Factor?
Joanne Fenton, M.D., Lisa B. Dixon, M.D., Janine C. Delahanty, M.A.

NR213 On-Site Geropsychiatric Services in Senior Housing: Preliminary Findings
Nancy C. Maruyama, M.D., Blaine S. Greenwald, M.D., Phyllis Tobin, Grace S. Nierenberg, Donna Del Cielo, M.S.W. Barbara Vogel, M.S.W., Arlene Feuerman

NR214 Subtypes of OCD and Symptom Severity
Craig Springer, Francine J. Spinowitz, M.A., Juliana R. Lachenmeyer, Ph.D., Yoav Cohen, Regina Uccello, B.A.

NR215 Violence in Inner-City, State Psychiatric Patients
Denise De Guzman, M.D., Anthony F. Lehman, M.D., Lisa B. Dixon, M.D., Corey B. Smith, M.A., Patricia W. Kendall, Ph.D.

NEW RESEARCH

Tuesday, May 16, 2000, 9:00 a.m. - 10:30 a.m.

New Research 5 – Oral/Slide Session – Room E255, Level 2, McCormick Place Lakeside

SCHIZOPHRENIA AND SEVERE MENTAL ILLNESS

Chp: Richard Balon, M.D.

NR216	Diffusion Tensor MRI in the Schizophrenia Spectrum Lina S. Shihabuddin, M.D., Monte S. Buschsbaum, M.D., Cheuk Tang, Ph.D., Adam M. Brickman, B.A., Michael B. Fleischman, B.A., Antonia S. New, M.D., Larry J. Siever, M.D.	9:00 a.m.
NR217	Motor Dysfunction in Schizophrenia Douglas R. Dolnak, D.O., Mark H. Rapaport, M.D., Caligiuri Michael, M.D., Golshan Shahrokh, Ph.D.	9:15 a.m.
NR218	Obesity As a Risk Factor for Antipsychotic Noncompliance Peter J. Weiden, M.D., David B. Allison, Ph.D., Joan A. Mackell, Ph.D., Diana McDonnell, A.B.D.	9:30 a.m.
NR219	Cognitive Therapy of Schizophrenia: Toronto Trial Neil A. Rector, Ph.D., Mary V. Seeman, M.D., Zindel V. Segal, Ph.D.	9:45 a.m.
NR220	The Effectiveness of the Family to Family Education Program Lisa B. Dixon, M.D., Betty Stewart, B.A., Joyce Burland, Ph.D., Alicia Lucksted, Ph.D., Janine C. Delahanty, M.A., Marcia Hoffman, M.A., Leticia T. Postrado, Ph.D.	10:00 a.m.
NR221	Preventing Jail and Hospital Recidivism Among Adults with Severe Mental Illness J. Steven Lamberti, M.D., Robert L. Weisman, D.O., Rudo Mundondo-Ashton, M.S., Nancy Price, R.N.	10:15 a.m.

NEW RESEARCH

Tuesday, May 16, 2000, 9:00 a.m. - 10:30 a.m.

New Research 6 – Oral/Slide Session – Room E256, Level 2, McCormick Place Lakeside

ANXIETY DISORDERS

Chp: Andrew J. Cutler, M.D.

NR222	Fluoxetine in Adolescents with Major Depression Jack R. Cornelius, M.D., Oscar G. Bukstein, M.D., Kevin G. Lynch, Ph.D., Boris Birmaher, M.D., Samuel Gershon, M.D., Ihsan M. Salloum, M.D., Duncan B. Clark, Ph.D.	9:00 a.m.
NR223	Decreased Benzodiazepine Binding in PTSD J. Douglas Bremner, M.D., Robert B. Innis, M.D., Steven M. Southwick, M.D., Lawerence Staib, Ph.D., Sami Zoghbi, Ph.D., Dennis S. Charney, M.D.	9:15 a.m.
NR224	A Three-Week, Double-Blind, Randomized Trial of Ziprasidone in the Acute Treatment of Mania Paul E. Keck, Jr., M.D., Kathleen Ice, Ph.D.	9:30 a.m.
NR225	Affect in Salivary Cortisol in Bosnian Refugees Suffering from PTSD Aida Spahic-Mihajlovic, M.D., Edward J. Neafsey, Ph.D., John W. Crayton, M.D.	9:45 a.m.
NR226	Heavy Drinking: Alcohol Disorders in Social Phobia Rosa M. Crum, M.D., Laura Pratt, Ph.D.	10:00 a.m.
NR227	The Quality of Care for Depressive and Anxiety Disorders in the United States Alexander S. Young, M.D., Ruth Klap, Ph.D., Cathy D. Sherbourne, Ph.D., Kenneth B. Wells, M.D.	10:15 a.m.

NEW RESEARCH

Tuesday, May 16, 2000, 12 noon - 2:00 p.m.

New Research 7 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

ANXIETY, COGNITIVE, PERSONALITY AND PREMENSTRUAL DYSPHORIC DISORDERS; GERIATRIC AND BIOLOGICAL PSYCHIATRY; AND NEUROSCIENCE

Moderator: Daniel P. Chapman, Ph.D.

NR228 Panic Disorder Patients at the Time of Air Strikes
Vladan Starcevic, M.D., Goran Bogojevic, M.D., Katarina Kelin, M.D.

NR229 Combined Treatments in Panic Disorder with Agoraphobia Revisited
Vladan Starcevic, M.D., Goran Bogojevic, M.D., Dusan Kolar, M.D., Eberhard H. Uhlenhuth, M.D.

NR230 Modulation of 5HT-2C and 5HT-1A Receptor Responsiveness by Clomipramine Treatment or Aerobic Exercise in Patients with Panic Disorder
Andreas Broocks, M.D., Eckart Ruether, M.D., Ullrich Munzel, Ph.D., Goeran Majak, M.D., Borwin Bandelow, M.D.

NR231 Prevalence and Correlates of Panic in Postmenopause
Jordan W. Smoller, M.D., Albert Oberman, M.D., Robert P. MacMahon, Ph.D., Judith Hsia, M.D., Mark H. Pollack, M.D., Sylvia Wassertheil-Smoller, Ph.D., David S. Sheps, M.D., Bruce A. Barton, Ph.D., Susan Hendrix, Sandra Daugherty, Rebecca Jackson, M.D., Donna Keams, Tammy Dicken

NR232 TDT Analysis of Behavior Inhibition Using Candida
Jordan W. Smoller, M.D., Jerrold F. Rosenbaum, M.D., Joseph Biederman, M.D., Jerome Kagan, Ph.D., Nancy Snidman, Ph.D., Stephen V. Faraone, Ph.D., John Kennedy, B.S., Alyssandra Schwarz, B.A., Susan Slaugenhaupt, Ph.D.

NR233 Follow-Up Results of Treatment of Social Phobia
Tone T. Haug, M.D., Svein Blomhoff, M.D., Kerstin Hellstrom, Ph.D., Ingar Holme, Ph.D., Hans P. Madsbu, Jan E. Wold, M.D.

NR234 Affective and Anxiety Comorbidity in PTSD Treatment Trials of Sertraline
Kathleen T. Brady, M.D., Matthew J. Friedman, M.D., Gail M. Farfel, Ph.D.

NR235 Improvement of CCK-4-Induced Panic by Vigabatrin
Peter Zwanzger, M.D., Thomas C. Baghai, M.D., Cornelius Schuele, M.D., R. J. Boerner, M.D., Hans J. Moeller, Rainer Rupprech, M.D.

NR236 Sexual Dysfunctions: A Neglected Complication of Social Phobia and Panic Disorder
Ivan L.V. Figueira, M.D., Elizabete G.M. Possidente, M.D.

NR237 Results of a 24-Week Extension Study of Sertraline in PTSD
Peter D. Londborg, M.D., William Patterson, M.D., Mark Hegel, Ph.D., Carolyn R. Sikes, Ph.D., Gail M. Farfel, Ph.D.

NR238 Effects of Sertraline and Placebo in Men with PTSD
Matthew J. Friedman, M.D., Charles R. Marmar, M.D., Gail M. Farfel, Ph.D.

NR239 Survival Analysis of Discontinuation from Clinical Trials As a Measure of Effectiveness in GAD: Comparison of Venlafaxine Extended Release with Placebo
Stuart A. Montgomery, M.D., Vincent Hahe, M.D., Vincent Haudiquet, David Hackett, M.S.C.

NR240 The SSRI Citalopram Is Effective in the Treatment of OCD: Results from a Double-Blind, Fixed-Dose, Placebo-Controlled Trial
Stuart A. Montgomery, M.D., Professor Siegfried Kasper, K. Bang

NR241 Mirtazapine and Onset of Action of Antidepressant Activity
Stuart A. Montgomery, M.D., Albert J. Schotte, Paul D. Reimitz, Ph.D.

NR242 Depression, Anxiety, Anger and Somatic Symptoms in BDD
Katharine A. Phillips, M.D., Susan L. McElroy, M.D., Jason M. Siniscalchi, M.S.

NR243 Sensory Phenomena and Treatment Response in OCD
Roseli G. Shavitt, M.D., Maria C.R. Rosario-Campos, M.D., Raquel C. Valle, Eurípedes C. Miguel, M.D.

NR244 Pregabalin Treatment of GAD
Atul C. Pande, M.D., Jerri G. Crockatt, M.A., Carol Janney, M.S., Douglas E. Feltner, M.D.

NR245 Ages of Onset for Anxiety Disorders
Jill I. Mattia, Ph.D., Mark Zimmerman, M.D.

NR246 Combined Effects of Pharmacotherapy and Cognitive-Behavior Therapy in Treating OCD
David M. Direnfeld, M.A., Michele T. Pato, M.D.

NR247 Subthreshold PTSD: Impairment and Comorbidity
Randall D. Marshall, M.D., Mark Olfson, M.D., Fred Hellman, B.S., Carlos Blanco, M.D., Mary T. Guardino, B.A., Elmer Struening, Ph.D.

NR248 Controlled Trial of Paroxetine in Chronic PTSD
Randall D. Marshall, M.D., Franklin R. Schneier, M.D., Blair Simpson, M.D., Carlos Blanco, M.D., Katherine L. Beebe, Ph.D., Michael R. Liebowitz, M.D.

NR249 Fluoxetine in Panic Disorder: A Randomized, Placebo Controlled Study
David Michelson, M.D., Neena Sarka, Ph.D., Craig Pemberton, B.S.

NR250 Valproic Acid in Panic Disorder: A Study in Fluvoxamine Refractory Patients
Antonio E. Nardi, M.D.

NR251 OCD and Comorbid Disorders in Rheumatic Fever Patients
Pedro G. Alvarenga, Lisia G. Prado, Marcos T. Mercadante, M.D., Max Grimberg, Ana G. Hounie, M.D., Juliana B. Diniz, Eurípedes C. Miguel, M.D.

NR252 Evaluation of Hydroxyzine in the Treatment of GAD
Christian Spadone, M.D., Pierre M. Llorca, M.D., Olivier Sol, M.D., Emmanuelle Corruble, M.D., Dominique Servant, M.D. Thierry Bougerol, M.D., Jean-Paul Macher, M.D.

NR253 Paroxetine Treatment of GAD: A Double-Blind, Placebo-Controlled Trial
Kevin M. Bellew, B.S., James P. McCafferty, B.S., Malini Iyengar, M.D., Rocco M. Zaninelli, M.D.

NR254 OCD with History of Rheumatic Fever: A Different Subtype?
Juliana B. Diniz, Priscila Chacon, Maria C.R. Rosario-Campos, M.D., Helena Prado, Ana G. Hounie, M.D., Roseli G. Shavitt, M.D., Eurípedes C. Miguel, M.D.

NR255 The Efficacy of Sertraline in Panic Disorder: A Combined Fixed-Dose Analysis
Javaid I. Sheikh, M.D., Peter D. Londborg, M.D., Cathryn M. Clary, M.D.

NR256 Pregabalin Treatment of Social Phobia
Douglas E. Feltner, M.D., Mark H. Pollack, M.D., Jonathan R.T. Davidson, M.D., Murray B. Stein, M.D., Rise A. Futterer, M.D., James W. Jefferson, M.D., R. Bruce Lydiard, M.D.

NR257 Effect Size As a Measure of Specific Activity of Venlafaxine Extended Release in the Treatment of GAD
Paolo Meoni, Ph.D., David Hackett, M.S.C., Yves Brault, Eliseo Salinas, M.D.

NR258 Quality-of-Life Improvement in PTSD with Sertraline Treatment: Results of a Multicenter, Placebo-Controlled Trial
Mark H. Rapaport, M.D., Phebe M. Tucker, M.D., Gail M. Farfel, Ph.D., Cathryn M. Clary, M.D.

NR259 A 24-Week Prevention of Relapse of Generalized Social Phobia Study in Responders to 20-Weeks of Sertraline Treatment
John R. Walker, Ph.D., Michael A. Van Ameringen, M.D., Richard P. Swinson, M.D., Roger M. Lane, M.D.

NR260 Is the DSM-IV Criteria of 13 Panic Symptoms Valid for Japanese Patients?
Hisanobu Kaiya, M.D., Natsuko Kaiya, Shin Yasuda, M.D., Seiji Harata, M.D., Noriya Ishida, M.D., Isao Kitayama, M.D.

NR261 A Comparison of the Activity of Central and Peripheral Chemoreceptors in Panic Disorder Patients and Healthy Volunteers
Martin A. Katzman, M.D., Lukasz M. Struzik, B.S.C., Nishka Vijay, Aimee M. Coonerty-Femiano, B.A., Safraaz Mahamed, B.S.C., James Duffin, Ph.D.

NR262 A Dose-Finding and Discontinuation Study of Clomipramine in Panic Disorder
Francisco Lotufo-Neto, M.D., Marcio A. Bernik, M.D., Renato Ramos, M.D., Laura Andrade, M.D., Clarice Gorenstein, Ph.D., Taki Cordas, M.D., Valentim Gentil, M.D.

NR263 Dimensional Personality Models and the Anxiety and Depression Interface
Francisco Paez, M.D., Rebeca Robles, M.Psy.

NR264 Pharmacotherapy of BDD: A Chart-Review Study
Ralph S. Albertini, M.D., Katharine A. Phillips, M.D., Ajaz Khan, M.D., Marshall Robinson, M.A.

NR265 Personality and Mood Characteristics of Female Athletes
Karyn E. Hood, M.Ed., Martin A. Katzman, M.D.

NR266 Gabapentin in PTSD: Effects on Sleep Disturbances
Mark B. Hamner, M.D., Lawrence A. Labbate, M.D., Jeffrey P. Lorberbaum, M.D., Helen G. Ulmer, M.S.N., Clare Tyson, B.S., Charlotte C. Teneback, B.S.

NR267 The Cognitive Burden of Lewy Bodies
Michael J. Serby, M.D., Adam M. Brickman, B.A., Vahram Haroutunian, Ph.D., Dushvant P. Purohir, M.D., Kenneth L. Davis, M.D.

NR268 Serum Melanotranferrin, P97 in Alzheimer's Disease
Min-Kyung Seo, M.S.W., Doh-Kwan Kim, Sang-Sun Kang, Shin-Won Lim, Seonwoo Kim, Jong-Won Kim, Bernard J. Carroll, M.D.

NR269 Reduction of Psychotic Symptoms by Olanzapine in Patients with Possible Lewy Body Dementia
Todd M. Sanger, Ph.D., W. Scott Clark, Ph.D., Jamie S. Street, M.D., Alan F. Breier, M.D.

NR270 An Economic Evaluation of Donepezil in Mild to Moderate Alzheimer's Disease Patients: Results of a One-Year, Double-Blind, Randomized Trial
Anders Wimo, M.D., Bengt Winblad, M.D., Vera Mastey, Anders Haglund, Peter Hertzman, Robert Miceli, Lena Jacobson Ponni Subbiah, M.D.

NR271 Effects of a Novel M-1 Selective Agonist on Behavioral Symptoms in Patients with Mild to Moderate Alzheimer's Disease
Katherine L. Beebe, Ph.D., James P. McCafferty, B.S., Rajinder Kumar, M.B., Julia Loudon, Ph.D., Matthew Truman, M.S.C., Eve Cedar, M.S.C., Kevin M. Bellew, B.S.

NR272 Validation of the Delirium Rating Scale Revised-98 (DRS-R-98)
Paula T. Trzepacz, M.D., Dinesh Mittal, M.D., Rafael A. Torres, M.D., Kim Kanary, B.S., John Norton, M.D., Nita Jimerson, M.S.N.

NR273 Long-Term Efficacy of Olanzapine in the Control of Psychotic and Behavioral Symptoms in Patients with Alzheimer's Dementia
Jamie S. Street, M.D., W. Scott Clark, Ph.D., Beth E. Juliar, M.S.C., Peter D. Feldman, Ph.D., Deborah L. Kadam, M.A., Alan F. Breier, M.D.

NR274 Attentuation in the Progression of Cognitive Deterioration in Alzheimer's Disease with Rivastigmine: A Dose Dependent Effect
Martin K. Farlow, M.D., John Messina, Pharm.D., Ravi Anand, M.D., Richard Hartman, Ph.D., Jeffrey Veach, M.S.

NR275 Donepezil Preserves Functional Status in Alzheimer's Disease
Richard C. Mohs, Ph.D., Rachelle S. Doody, M.D., John C. Morris, M.D., John R. Leni, Ph.D., Sharon L. Rogers, Ph.D., Carlos A. Perdomo, M.S., Raymond D. Pratt, M.D.

NR276 Motoric Subtypes of Delirium: Relationship to Symptom Profile, Etiology and Management
David J. Meagher, M.D., Paula T. Trzepacz, M.D., Donal T. O'Hanlon, M.D., Edmond O'Mahony, Patricia R. Casey, M.D.

NR277 Intravenous Dopamine Increases the Risk for Delirium
Barbara R. Sommer, M.D., Lowell Wise, D.Sc., Helena C. Kraemer, Ph.D.

NR278 Trial of a Geriatric Delirium Service
Martin G. Cole, M.D., Jane McCusker, M.D., Francois Bellavance, Ph.D., Francois J. Primeau, M.D., Robert F. Bailey, M.D., Michael V. Bonnycastle, M.D.

NR279 Sertraline for Depression in Remitted Schizophrenia
Donald E. Addington, M.D., Jean M. Addington, Ph.D., Scott B. Patten, M.D., Gary J. Remington, M.D., Javad Moamai, M.D., Alain Labelle, M.D., Linda Beauclair, M.D.

NR280 5HT Transporter Polymorphism and SSRI Response
Bruce G. Pollock, M.D., Robert E. Ferrell, M.D., Benoit H. Mulsant, M.D., Mark D. Miller, M.D., Robert A. Sweet, M.D., Stephanie Davis, M.Ed., Margaret A. Kirshner, B.A.

NR281 Treatment of Behaviors in Dementia with Citalopram
Bruce G. Pollock, M.D., Jules Rosen, M.D., Benoit H. Mulsant, M.D., Robert A. Sweet, M.D., Robert S. Marin, M.D., N.J. Jacob, M.D., Kimberly A. Huber, B.A.

NR282 A Chronic Disease Model for Disease Management of Depression in the Primary Care Elderly
James C. Coyne, Ph.D., Gregory Brown, Ph.D., Ira R. Katz, M.D., Herbert C. Schulberg, Ph.D., Ellen Brown, Ed.D.

NR283 Effects of Cognitive and Affective Status on the Recovery Trajectory of Geriatric Patients After Discharge from Medical Rehabilitation
Joel E. Streim, M.D., Thomas R. Ten Have, Ph.D., Lan Zhou, Ph.D., Ira R. Katz, M.D.

NR284 Reliability of a Telephone Screen for Depression Among Elderly Primary Care Patients
Tina L. Harralson, Ph.D., Thomas R. Ten Have, Ph.D., Alan C. Regenberg, B.A., Margaret M. Rider, B.A., Michael J. Kallan, M.S., Joel E. Streim, M.D., Mary Ann Foreciea, M.D.

NR285 Depression and General Medical Comorbidity in a Behavioral Health Management Care Setting
Tina L. Harralson, Ph.D., Pamela E. Brody, Ph.D., James C. Coyne, Ph.D., Alan C. Regenberg, B.A., Ira R. Katz, M.D., Richard Thompson, Ph.D., Trevor Hadley, Ph.D.

NR286 Recognition of Depression in Elderly Homecare Patients: An Educational Intervention for Homecare Nurses
Ellen Brown, Ed.D., Martha L. Bruce, Ph.D., Barnett S. Meyers, M.D., Patrick J. Raue, Ph.D.

NR287 Anterior Cingulate Dysfunction and Treatment Response in Geriatric Depression
Balu Kalayam, M.D., George S. Alexopoulos, M.D., Joe Deasis, M.D., Alfredo Toro, B.A., Robert C. Young, M.D.

NR288 Five-Year Dementia Outcome of Elderly Depressives With and Without MRI Signal Hyperintensities
Blaine S. Greenwald, M.D., Elisse Kramer-Ginsberg, Ph.D., K. Ranga R. Krishnan, M.D., Manzar Ashtari, Ph.D., Jian Hu, M.D., Neil J. Kremen, M.D., Mahendra C. Patel, M.D.

NR289 Managing Behavioral Symptoms in Alzheimer's Disease
Thomas D. McRae, M.D., Teresa Griesing, Ph.D., Ed Whalen, Ph.D.

NR290 Sertraline in the Treatment of Elderly Depression: Results of a Large, Multicenter, Placebo-Controlled Trial
Lon S. Schneider, M.D., Cathryn M. Clary, M.D., Sanford I. Finkel, M.D., K. Ranga R. Krishnan, M.D., P. Murali Doraiswamy, M.D.

NR291 Depression and Self-Reported Functional Status in Older Primary Care Patients
Jeffrey M. Lyness, M.D., Paula A. Sinclair, B.A., Deborah A. King, Ph.D., Christopher Cox, Ph.D., Eric D. Caine, M.D.

NR292 Clinical Significance of Depression in Primary Care
George S. Alexopoulos, M.D., Martha L. Bruce, Ph.D., Thomas R. Ten Have, Ph.D., Ellen Brown, Ed.D., Herbert C. Schulberg, Ph.D.

NR293 Socioeconomic Status Differences in Screening for Depression
Martha L. Bruce, Ph.D., George S. Alexopoulos, M.D., Thomas R. Ten Have, Ph.D., Gail J. McAvay, M.S., Herbert C. Schulberg, Ph.D.

NR294 Signal Hyperintensities in Geriatric Mania
Jose M. De Asis, M.D., Robert C. Young, M.D., George S. Alexopoulos, M.D., Blaine S. Greenwald, M.D., Tatsu Kakuma, Ph.D., Manzar Ashtari, Ph.D.

NR295 Compliance with Medical Treatment in Patients with Alzheimer's Disease
Elizabeth Crocco, M.D., Ruben Bravo, M.D., Ranjan Duara, M.D., Raymond L. Ownby, M.D.

NR296 Neuropsychological Impairment in the Elderly with Mild to Moderate Depression
Armin von Gunten, M.D., Rene Duc

NR297 Estrogen Therapy and Cognitive Function in Postmenopausal Women with Dementia
Helen H. Kyomen, M.D., John Hennen, Ph.D., Jeanne Y. Wei, M.D.

NR298 Olanzapine in the Prevention of Psychosis Among Nursing Home Patients with Behavioral Disturbances Associated with Alzheimer's Disease
W. Scott Clark, Ph.D., Jamie S. Street, M.D., Todd M. Sanger, Ph.D., Peter D. Feldman, Ph.D., Alan F. Breier, M.D.

NR299 Drug Treatment in Depressed Elderly in the Dutch Community
Caroline M. Sonnenberg, M.D., Aartjaw T.F. Beekman, Ph.D., Dorly H. Deeg, Ph.D., Willem V. Tilburg, Ph.D.

NR300 Poorer Social Networks Increase Rehospitalization Risk in Older Veterans
Joan Rosansky, M.S.W., Ritesh Mistry, M.P.H., James McGuire, Ph.D., Charles McDermott, M.S.W., Lissy F. Jarvik, M.D.

NR301 Late-Onset Schizophrenia
Luis Aguera-Ortiz, M.D., Juan F. Artaloytia, Ainhua Garibi, Jose A. Perez, Ana Pascual, Tomas Palomo

NR302 Clinical Patterns of Spousal Homicide or Suicide in Older Persons
Donna Cohen, Ph.D., Carl Eisdorfer, M.D.

NR303 Verbal and Physical Aggression in Poor Outcome: Geriatric Schizophrenia
Christopher R. Bowie, M.A., Patrick J. Moriarty, M.A., Philip D. Harvey, Ph.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Kenneth L. Davis, M.D.

NR304 A Successful Regional Memory Screening Day for Community Dwelling Elders
Janet M. Lawrence, M.D., Donald A. Davidoff, Ph.D., Debra Katt-Lloyd, B.S., Michelle D. Auerbach, M.S.

NR305 Somatic Distress of the Mentally Ill and Its Relationship to Personality Disorders
Peter Manu, M.D., Norert Schmitz, M.D., Norbert Hartkamp, M.D., Wolfgang Tress, M.D., Matthias Franz, M.D.

NR306 Fatigue and Personality Pathology in the Mentally Ill
Peter Manu, M.D., Norert Schmitz, M.D., Norbert Hartkamp, M.D., Wolfgang Tress, M.D., Matthias Franz, M.D.

NR307 Traumatic Events and BPD
Julia A. Golier, M.D., Rachel Yehuda, Ph.D., Eres Bar-Tal, B.A., Vivian Mitropoulou, M.A., Antonia S. New, M.D., Larry J. Siever, M.D.

NR308 Memory Function in Holocaust Survivors with PTSD
Julia A. Golier, M.D., Rachel Yehuda, Ph.D., Sonia Lupien, Ph.D., Robert A. Grossman, M.D., Philip D. Harvey, Ph.D.

NR309 Factor Analysis of DSM-IV BPD Criteria
Charles A. Sanislow, Ph.D., Carlos M. Grilo, Ph.D., Thomas H. McGlashan, M.D.

NR310 Pathological Dissociation in BPD
Marianne Goodman, M.D., Harold W. Koenigsberg, M.D., Lawrence Sprung, B.A., Antonia S. New, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

NR311 Caudate and Ventricular Volume in Neuroleptic-Naïve Schizotypal Personality Disorder
James J. Levitt, M.D., Robert W. McCarley, M.D., Aleksandra Ciszewski, B.A., Chandlee C. Dickey, M.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Martha E. Shenton, Ph.D.

NR312 Efficacy of Quetiapine Versus Haloperidol and Placebo in the Short-Term Treatment of Acute Schizophrenia
S. Charles Schulz, M.D., Martin Jones, M.S., Emma Westhead, M.S., Paul P. Yeung, M.D.

NR313 Cannabis Use and Schizotypy in Healthy Students
Patrick Dumas, M.D., Sebastien Bouafia, M.D., Mohamed Saoud, Ph.D., Christel Gutknecht, Jean Dalery, M.D., Thierry D'Amato, Ph.D.

NR314 Three-Factor Structure of Self-Report Schizotypy
Patrick Dumas, M.D., Mohamed Saoud, Ph.D., Sebastien Bouafia, M.D., Christel Gutknecht, Jean Dalery, M.D., Thierry D'Amato, Ph.D.

NR315 Use of Paroxetine in Aggressive Personalities
Giampaolo La Malfa, M.D., Marco Bertelli, Michele Conte, Pierluigi Cabras, M.D.

NR316 Combined Dialectical-Behavior Therapy and Fluoxetine Pharmacotherapy in Patients with BPD: Is There an Addictive Effect?
Elizabeth B. Simpson, M.D., Karen J. Rosen, M.D., Teri B. Pearlstein, M.D., Ellen Costello, Ph.D., Shirley Yen, Ph.D., Ann Begin, Ph.D.

NR317 Sertraline in Premenstrual Dysphoric Disorder Patients on Oral Contraceptives
Ellen W. Freeman, Ph.D., Stephen J. Sondheimer, M.D., Beatriz Garcia-Espana, M.A.

NR318 Fluoxetine Improves Social Functioning in Women with Premenstrual Dysphoric Disorder
Meir Steiner, M.D., Rajinder A. Judge, M.D., Eileen Brown, Ph.D., Julia Dillon, Pharm.D.

NR319 A Two-Year Follow-Up Study of Personality Dysfunction in High School Students
Yueqin Huang, M.D., Lihong Shi, M.D., Guizhi Zhang, Shumei Yun, M.D.

NR320 Assessing Premenstrual Symptom Severity
Rebecca Robinson, M.S., Ralph W. Swindle, M.D.

NR321 Plasma Tryptophan Availability and Pathological Gambling
Rita Prieto, M.D., Angela Ibanez, M.D., Carlos Blanco, M.D., Jeronimo Saiz-Ruiz, M.D.

NR322 Elevated Peripheral Mu Opioid Receptor Densities Among Heroin Abusers
Ashwin A. Patkar, M.D., Allen R. Zeiger, Ph.D., Allan Lundy, Ph.D., Stephen P. Weinstein, Ph.D., Kenneth M. Certa, M.D.

NR323 Recognizing and Processing of Facial Expression in Acute First-Episode Psychosis
Minna K. Valkonen-Korhonen, M.D., Ina Tarkka, Ph.D., Jan Kremlacek, M.S.C., Ari Paakkonen, Ph.D., Johannes Lehtonen, M.D., Jari Karhu, Ph.D.

NR324 The Next Generation SSRIs: A Comparison of the Transporter Binding Profile of R-Fluoxetine and S-Citalopram (LU 26-054)
Michael J. Owens, Ph.D., David L. Knight, B.S.

NR325 Human Monoamine Transporter Binding Profile of the SSRIs
Michael J. Owens, Ph.D., David L. Knight, B.S.

NR326 Cortisol Secretion in Women with Temporomandibular Disorder and Depression
Ania Korszun, M.D., Elizabeth A. Young, M.D., Emily Dawson, B.S., Christine Brucksch, B.S., N. Cary Engelberg, M.D., Leslie Crofford, M.D.

NR327 Phospholipid Metabolism in Frontal Lobe of Schizophrenia Patients
Juliana Yacubian, M.D., Claudio C. Campi, M.D., Candida C. Pires, M.A., Mariella Ometto, M.A., Giovanni G. Cerri, M.D., Wagner F. Gattaz, Ph.D.

NR328 QEEG Effects of Maintenance Clozapine Therapy in Chronic Schizophrenia Patients
Duncan J. Macrimmon, Susan J. Adams, M.D., Donald W. Brunet, M.D., Margarita Criollo, M.D., Howard Galin, Ph.D., James S. Lawson, Ph.D.

NR329 Dopamine Depletion in Schizophrenia: A SPECT Imaging Study
Lakshmi N.P. Voruganti, M.D., Piotr Slomka, Ph.D., Pamela Zabel, M.S.C., Adel Mattar, M.D., A. George Awad, M.D., Giuseppe Costa, B.S.C.

NR330 Clozapine-Induced Obsessive-Compulsive Symptoms in Schizophrenia
Lakshmi N.P. Voruganti, M.D., Chris Tremblay, R.N., Mustaq Khan, Ph.D.

NR331 Selective Modulation of Long-Term Plasticity by 5HT
Claus Normann, M.D., Joerg Walden, M.D., Joseph Bischofberger, Ph.D.

NR332 Testing the Valeance Theory of Emotions Using Direct Noninvasive Brain Stimulation in Patients with GAD
Naresh P. Emmanuel, M.D., Mark S. George, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D., George W. Arana, M.D., Jeffrey P. Loberbaum, M.D., Olga Mintzer, M.D., Rebecca Kapp, R.N., Marsha Crawford, R.N., Alex Morton, Pharm.D., Michael R. Johnson, M.D., Sarah W. Book, M.D., Mark B. Hamner, M.D., Ziad H. Nahas, M.D.

NR333 B-Casomorphin, Schizophrenia and Autism
Zhongjie Sun, M.D., Robert Cade, M.D.

NR334 Sertraline and Fluoxetine Treatment of OCD
Arun V. Ravindran, M.D., Richard Bergeron, M.D., Vratislav Hadrava, M.D., Yves Choput, M.D., Elliot M. Goldner, M.D., Richard P. Swinson, M.D., Michael A. Van Ameringen, M.D.

NEW RESEARCH

Tuesday, May 16, 2000, 3:00 p.m. - 5:00 p.m.

New Research 8 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

SCHIZOPHRENIA, EATING AND GENDER IDENTITY DISORDERS, HEALTH SERVICES RESEARCH, AND TREATMENT TECHNIQUES AND OUTCOME STUDIES

Moderator: Richard Balon, M.D.

NR335 Fluvoxamine in OCD Schizophrenia
Pinkhas Sirota, M.D., Ilya Reznik, M.D.

NR336 Do Classic and Mixed Manic Episodes Run True?
Scott W. Woods, M.D., C. Bruce Baker, M.D.

NR337 Weight and Metabolic Changes with Clozapine and Olanzapine
Daniel E. Casey, M.D.

NR338 Effect of Olanzapine and Other Antipsychotics on Human Cardiac Ion Channel Blocking
William Crumb, Ph.D., Charles M. Beasley, Jr., M.D., Alan F. Breier, M.D., Anna Thornton, Pharm.D.

NR339 The Study of First-Episode Psychosis As an Early Intervention Strategy in Mexico
Ana Fresan, M.D., Rogelio Apiquian, M.D., Rosa E. Ulloa, M.D., Humberto Nicolini, Ph.D., Christina Loyzaga, M.D.

NR340 Alpha-2 Agonists Enhance Cognition of Schizophrenia Patients in Combination with Atypical But Not Typical Neuroleptics
Joseph I. Friedman, M.D., David Adler, M.D., Humberto D. Temporini, M.D., Philip D. Harvey, Ph.D., Eileen M. Kemether, M.D., Kenneth L. Davis, M.D.

NR341 The PERSIST-Study: A Clinical Comparative Study of Atypical Neuroleptics in the Treatment of Schizophrenia
Christian Perro, M.D., Martin Lambert, M.D., Steffen Moritz, Ph.D., Michael Krausz, Ph.D., Dieter Naber, M.D.

NR342 Cognitive Effects of Risperidone and Olanzapine in Patients with Schizophrenia or Schizoaffective Disorder
Philip D. Harvey, Ph.D.

NR343 Long-Term Cognitive Effects of Risperidone Treatment in Schizophrenia
Philip D. Harvey, Ph.D.

NR344 Improvement in Cognition Following a Switch to Open-Label Ziprasidone in Outpatients with Schizophrenia Treated with Conventional Antipsychotics, Olanzapine or Risperidone
Philip D. Harvey, Ph.D., Herbert Y. Meltzer, M.D., Steven J. Romano, M.D.

NR345 Efficacy of Aripiprazole in Psychotic Disorders: Comparison with Haloperidol and Placebo
John M. Kane, M.D., Gary Ingenito, M.D., Mirza Ali, M.D.

NR346 Tardive Dyskinesia in Chinese and Malays
Siow A. Chong, M.B., Rathi Mahendran, M.B., David Machin, Ph.D., Hong-Choon Chua, M.B., Gordon Parker, Ph.D., John M. Kane, M.D.

NR347 Rapid Reduction in Hyperprolactinemia
Bruce J. Kinon, M.D., Bruce R. Basson, M.S., Jeff Wang, M.S., Sandra K. Malcolm, B.S., Virginia L. Stauffer, Pharm.D.

NR348 Ziprasidone's Effect on Anxiety in a Group of Outpatients with Stable Schizophrenia
Nina R. Schooler, Ph.D., Cynthia O. Siu, Ph.D.

NR349 Quality of Life and Well-Being of Schizophrenia Patients Under New Drug Treatment
Anne Karow, M.D., Steffen Moritz, Ph.D., Michael Krausz, Ph.D., Martin Lambert, M.D., Dieter Naber, M.D.

NR350 Negative Symptoms, Cognitive Dysfunction and Disability in Schizophrenia: Evidence of an Interaction
Mark Ast, Ph.D., Stefanie Berns, Ph.D., Judith Jaeger, Ph.D., Pal Czobor, Ph.D., Stephen Panopoulos, M.A.

NR351 Gender Differences in the Disability of Schizophrenia
Mark Ast, Ph.D., Judith Jaeger, Ph.D., Stefanie Berns, Ph.D.

NR352 Gender, Cognition and Disability in Schizophrenia: Evidence of an Interaction
Judith Jaeger, Ph.D., Mark Ast, Ph.D., Stefanie Berns, Ph.D., Pal Czobor, Ph.D., Ann-Marie Donovan, M.A.

NR353 Summer Birth and the Deficit Syndrome of Schizophrenia
Brian Kirkpatrick, M.D., Erick L. Messias, M.D.

NR354 High Diabetes Frequency in Schizophrenia and Bipolar Disorder
Henry A. Nasrallah, M.D., Thantween S. White, Mary Robbins

NR355 Button Pressing Distorts P300 Topography
Dean F. Salisbury, Ph.D., Martha E. Shenton, Ph.D., Robert W. McCarley, M.D.

NR356 Iloperidone: Atypicality Through the Alpha2C-Adrenoceptor Blockade? A Comparative Analysis
Hans O. Kalkman, Ph.D., E. Loetscher, Ph.D.

NR357 Receptor Profile of Two Metabolites of Iloperidone
Hans O. Kalkman, Ph.D., N. Subramanian, Ph.D.

NR358 Benefits of Ziprasidone in Stable Outpatients with Schizophrenia Switched from Conventional Antipsychotics, Olanzapine or Risperidone
George M. Simpson, M.D., Steven G. Potkin, M.D., Peter J. Weiden, M.D., Richard L. O'Sullivan, M.D.

NR359 Improvement in Indices of Health Status in Outpatients with Schizophrenia Following a Switch to Ziprasidone from Conventional Antipsychotics, Olanzapine and Risperidone
David G. Daniel, M.D., Petter Weiden, M.D., Richard L. O'Sullivan, M.D.

NR360 The Factor Structure for Positive and Negative Symptoms in South-African Xhosa Patients with Schizophrenia
Robin A. Emsley, M.D., Dana J. Niehaus, M.B., N. Irene Mbanga, R.N., Dan J. Stein, M.B., Claudine Laurent, M.D., Piet P. Oosthuizen, M.D., Stephan J. Maritz, Ph.D.

NR361 Effects of Nicotine Smoking on Brain Stem Auditory Evoked Potentials in Positive and Negative Symptoms of Schizophrenia
Ahmed A.R. Mubarak, M.D., Adel A. Badawy, M.S.C.

NR362 Homicide and T102C of 5HT-2A Receptor Gene Polymorphism in Male Schizophrenia
Chee Ik-Sueng, M.D., Shin Suk-Chui, M.D., Wang Seong-Keun, M.D., Shin Yun-O, M.D., Lee Sun-Woo, M.D., Shin Yong-Jae, M.D., Kim Young-Lan, M.D.

NR363 Substance Abuse in Schizophrenia and Impulsivity
Alain Dervaux, M.D., Franck J. Bayle, M.D., Xavier Laqueille, M.D., Marie C. Bourdel, M.D., Michele Leborgne, M.D., Jean-Pierre Olie, M.D., Marie O. Krebs, Ph.D.

NR364 Donepezil Augmentation in Psychosis: fMRI Effects and Cognition
Samuel C. Risch, M.D., Mark S. George, M.D., John S. Markowitz, Ph.D., John S. Mintzer, Ph.D., Ziad H. Nahas, M.D., Juliet Goldman, M.D., Michael D. Horner, Ph.D., Simmy Palecko, R.N., Susan R. McGurk, Ph.D., Cynthia Gilliard, B.S., Susan Owens, B.S., C. Lindsay DeVane, Ph.D., Scott D. Christie, M.D.

NR365 An Overview of the Efficacy and Safety of Rapid-Acting Intramuscular Ziprasidone
Dan L. Zimbroff, M.D., David G. Daniel, M.D., Shlomo Brook, M.D., Karen R. Reeves, M.D.

NR366 5HT Receptor Dysfunction in Schizophrenia
Myung A. Lee, M.D., Herbert Y. Meltzer, M.D.

NR367 Subcortical Dopamine Activity in Schizotypal Personality Disorder
Harold W. Koenigsberg, M.D., Marianne Goodman, M.D., Vivian Mitropoulou, M.A., Antonia S. New, M.D., Larry J. Siever, M.D.

NR368 Risperidone in the Treatment of Schizotypal Personality
Harold W. Koenigsberg, M.D., Marianne Goodman, M.D., Vivian Mitropoulou, M.A., Antonia S. New, M.D., Larry J. Siever, M.D.

NR369 The Impact of Schizophrenia on Health-Related Quality of Life
Michael B. Durkin, M.S., William S. Edell, Ph.D., Samir H. Mody, Pharm.D., Bryan E. Adams, Ph.D., Ed A. Repp, M.B.A.

NR370 Relative Risk Estimates of Eye Tracking Dysfunction in Siblings of Patients with Schizophrenia
Christopher J. Case, B.A., Jonathan B. Strauss, B.S., Robert J. Nicolson, M.D., Daniel W. Hommer, M.D., Daniel R. Weinberger, M.D., Michael F. Egan, M.D.

NR371 Olanzapine Treatment of Patients with Schizophrenia and Comorbid Substance Abuse
Kimberly H. Littrell, N.P., Craig G. Johnson, M.D., Carol D. Peabody, M.S., Nicole M. Hilligoss, M.S.

NR372 Clozapine, Diabetes, Weight Gain and Lipid Abnormalities
David C. Henderson, M.D., Enrico Cagliero, M.D., Colin Gray, Rima A. Nasrallah, B.S., Doug L. Hayden, M.A., David A. Schoenfeld, Ph.D., Donald C. Goff, M.D.

NR373 The Impact of Untreated Psychosis in Mexican Patients with First-Episode Psychosis
Rogelio Apiquian, M.D., Rosa E. Ulloa, M.D., Ana Fresan, M.D., Humberto Nicolini, Ph.D., Christina Loyzaga, M.D.

NR374 The Role of Cognitive Functioning in Vocational Outcome in Schizophrenia
Susan R. McGurk, Ph.D., Christopher R. Bowie, M.A., Joseph I. Friedman, M.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Philip D. Harvey, Ph.D., Kenneth L. Davis, M.D.

NR375 Atypical Antipsychotics: Evolving Therapeutic Indications
Peter F. Buckley, M.D., Del D. Miller, M.D., Beth Singer, B.A., Karl Donenwirth, M.S.

NR376 The Neuroscience Sweepstakes in Schizophrenia Research
R. W. Heinrichs, Ph.D., Stephanie McDermid, B.A., Lara Davidson, M.A.

NR377 Neurocognitive Subtype in Schizophrenia
Stephanie McDermid, B.A., R. W. Heinrichs, Ph.D.

NR378 A Six-Year Follow-Up Study of Cognitive and Functional Decline Across the Life Span of Patients with Chronic Schizophrenia
Thomas Coleman, M.A., Joseph I. Friedman, M.D., Philip D. Harvey, Ph.D., Christopher R. Bowie, M.A., Patrick J. Moriarty, M.A., Michael Parrella, Ph.D., Leonard White, Ph.D., David Adler, M.D., Kenneth L. Davis, M.D.

NR379 Dissolution Profile and Safety of Olanzapine Orally-Disintergrating Tablet in Patients with Schizophrenia
Cindy C. Taylor, Ph.D., Barry Jones, M.D., P. Chue

NR380 Efficacy of Olanzapine Combined with Mood Stabilizers in the Treatment of Bipolar Disorder
Mauricio F. Tohen, M.D., Thomas G. Jacobs, M.A., Tricia M. Meyers, M.S., Richard C. Risser, M.S., Elizabeth L. Keeter, R.N., Peter D. Feldman, Ph.D., Alan F. Breier, M.D.

NR381 Olanzapine Versus Clozapine in Patients Nonresponsive or Intolerant to Standard Acceptable Treatment of Schizophrenia
Martin Dossenbach, I. Bitter, M. Slabber, J. Pretorius, G.Y. Bartko, Z. Banics, F. Martenyi

NR382 Predictive Value of Early Anti-Anxiety Effect on the Acute-Antipsychotic Outcome: A Comparison of Fluphenazine and Olanzapine
Martenyi Ferenc, Martin Dossenbach, M. Jakovljevic, S. Metcalfe

NR383 Mirtazepine Treatment of Negative Schizophrenia
Michael Berk, M.D., Camelia Ichim, M.D., Shlomo Brook, M.D.

NR384 Relationship Between Inadequate Physical Healthcare and Poor Mental Health Among Individuals with Schizophrenia
James M. Russell, M.D., Joan A. Mackell, Ph.D.

NR385 Early Psychosis: Duration of Untreated Psychosis Predicts Outcome
Katherine A. Black, M.D., Lynn Peters, M.D., Qing Rui, David Whitehorn, Ph.D., Lili C. Kopala, M.D.

NR386 Auditory P3 and Personality Traits in Schizophrenia
Ronald J. Gurrera, M.D., Margaret Niznikiewicz, Ph.D., Ileana Berman, M.D., Paul G. Nestor, Ph.D., Christopher Allen, B.A., Martha E. Shenton, Ph.D., Christopher Dodd

NR387 EEG Abnormalities and Antipsychotics
Franca Centorrino, M.D., Margaret Tuttle, B.A., Won-Myong Bahk, M.D., Matthew J. Albert, B.A., Bruce Price, M.D., Ross J. Baldessarini, M.D.

NR388 Weight, Cholesterol and Glucose in the Treatment of Patients with the Newer Antipsychotics
Franca Centorrino, M.D., Edward Rivera, M.D., Matthew J. Albert, B.A., Giuseppa Drago-Ferrante, M.D., Ross J. Baldessarini, M.D.

NR389 The Implications of Antipsychotic Treatment Patterns on Health Outcomes in Schizophrenia
Luella M. Engelhart, M.A., Carmela Janagap, Richard E. White, Ph.D., Margaret Rothman, Ph.D.

NR390 Atypical Antipsychotic-Induced Diabetes Mellitus
Naveed Iqbal, M.D., Raquel L. Oldan, M.D., Gordon Baird, M.D., Bruce J. Schwartz, M.D., Leyla Baloy, Bharat Bhagoji, M.D., Mohammad S. Simjee, M.D.

NR391 Evaluating the Cognitive Deficits in Schizophrenia
Shin-Min Lee, M.D., Shay-Yun Kuo, M.S., Mei-Chun Wang, M.S., Yue-Cune Chang, M.D., Hsin-Jung Lo, B.S., Ming Chang, M.D.

NR392 Are Clinical Ratings of Cognitive Dysfunction in Schizophrenia Valid?
Nehal Vadhan, M.A., Brett R. Goldberg, B.A., James C.Y. Chou, M.D., Philip D. Harvey, Ph.D., Mark R. Serper, Ph.D.

NR393 Cardiac Performance and Abnormalities in Anorexia Nervosa Patients
Carla E. Ramacciottii, M.D., Ombretta Biadi, M.D., Elisabetta Coli, M.D., Roberta Rossini, M.D., Lucia Polese, M.D., Mario Mariani, M.D., Giovanni B. Cassano, M.D.

NR394 Survey of Epidemiological Factors Associated with Adolescent Obesity
Sandra L. Straffen, R.N., Gabrielle Taylor, M.D., Kathleen S. Franco-Bronson, M.D., Rebecka Peebles, M.D., Ellen Rome, M.D.

NR395 Self-Destructiveness and 5HT Function in Bulimia Nervosa
WITHDRAWN

NR396 New Intravenous Pharmacology for Refractory Agitation
Michael R. Miller, M.D., Margaret Bennington-Davis, M.D.

NR397 Eating Behavior Items in Young Adult Twins
Carol A. Beresford, M.D., John K. Hewitt, Ph.D., Thomas P. Beresford, M.D.

NR398 Prevalence of Eating Disorders in Navarra, Spain: Epidemiological Survey of 4,962 Adolescents
Pilar Gual, M.D., Miguel A. Martinez-Gonzlez, M.D., Francisca Lahortiga, Ph.D., Marta Perez-Gaspar, M.D., Cesar A. Soutullo, M.D., Salvador Cervera-Enguix, M.D.

NR399 Interpersonal Psychotherapy in Resistant Obese Patients
Virginie Rouch, M.D., Laurent J. Schmitt, M.D., Henri Sztulman, M.D., Frederic Sanguignol, M.D., Stephanie Ruffie, M.D.

NR400 Patterns of Symptom Change for Three Types of Treatment Responses to Nefazodone
Madhukar H. Trivedi, M.D., Bruce D. Grannemann, M.A., Susan F. Mahadi, M.Ed.

NR401 Effect of Venlafaxine Extended Release on Diabetic Neuropathic Pain
Nadia R. Kunz, Pharm.D., Richard Entsuah, Ph.D., Veeraindar Goli, M.D., Richard L. Rudolph, M.D., Marc Cantillon, M.D.

NR402 Comorbid Mental Health Symptoms, Impaired Role Functioning and Nonpsychiatric Health Care Costs in an HMO
Enid M. Hunkeler, M.A., William D. Spector, Ph.D.

NR403 Clinical and Economic Outcomes with Olanzapine
Douglas Del Paggio, Pharm.D., Jeanette Logan, Pharm.D., Patrick Finley, Pharm.D.

NR404 New Approaches for Rating Belief About Depression
Larry G. Onate, M.D., Pedro L. Delgado, M.D., Rachel E. Manber, Ph.D., John J.B. Allen, Ph.D., Sabrina Hitt, Cynthia A. McGahuey, B.S., Mona Mort, Ph.D.

NR405 Retrospective One-Year Review of the Outcomes of Atypical Antipsychotics Use at Central Texas Veterans Health Care System
William R. Clark, Pharm.D., Jennifer L. Defilippi, Pharm.D.

NR406 Seizure Threshold in ECT: Differences Between Instruments
Worrawat Chanpattana, M.D., Wanchai Buppanharun, M.D., Somchai Chakrabhand, M.D.

NR407 Drugs and Post-ECT Course in Catatonic Depression
Conrad M. Swartz, M.D., Vicki Morrow, M.D., Lara Surles, M.D., J Frank James, M.D.

NR408 The Impact of Victimization on Inpatient Treatment
Robert M. Vidaver, M.D., Michelle P. Salyers, Ph.D., Kim T. Mueser, Ph.D., Stanley D. Rosenberg, Ph.D.

NR409 Risperidone and 9-Hydroxy Risperidone Concentrations Are Not Dependent on Age or Creatinine Clearance Among Elderly Subjects
Robert A. Sweet, M.D., RaeAnn Maxwell, Ph.D., Benoit H. Mulsant, M.D., Jules Rosen, M.D., Margaret A. Kirshner, B.A., Kari B. Kastango, M.S., Bruce G. Pollock, M.D.

NR410 Reducing the Use of Restraint and Seclusion in the Acute Inpatient Psychiatric Setting
Ilana Iacobovici, M.D., Jill A. RachBeisel, M.D.

NR411 Long-Term Impact of an Intensive Subunit on Acuity
Eric S. Cole, Ph.D., Cheryl K. Cantrell, M.D., Deborah E. Boyer, B.A.

NR412 Reasons for Discontinuation and Switching of SSRIs
Scott Bull, Pharm.D., Francois Collin, Enid M. Hunkeler, M.A.

NR413 Care of Persons with Schizophrenia on Medicare
Lisa B. Dixon, M.D., Alan Lyles, Sc.D., Corey B. Smith, M.A., Jeffrey S. Hoch, Mavreen Fahey, M.L.A., Leticia T. Postrado, Ph.D., Anthony F. Lehman, M.D.

NR414 Determinants of Psychotherapy Among Antidepressant Recipients
Thomas W. Croghan, M.D., Regina L.H. Powers, Ph.D., Thomas J. Kniesner, Ph.D.

NR415 Predictors of Use of Atypical Antipsychotic Medications in a Veterans Population
Teresa J. Hudson, Pharm.D., Weiwei Feng, Ph.D., Mark Austen, M.S., Richard R. Owen, M.D.

NR416 The Lifetime Cost of Bipolar Disorder in the U.S.: An Estimate Based on Incidence and Course of Illness
Charles E. Begley, Ph.D., John F. Annegers, Ph.D., Alan C. Swann, M.D., Christopher Lewis, B.S., Sharon Coan, M.S., William B. Schnapp, Ph.D., Lynda Bryant-Comstock, M.P.H.

NR417 Effect of Provider Choice on Treatment and Treatment Adequacy Among Depressed Patients
Thomas J. Kniesner, Ph.D., Regina L.H. Powers, Ph.D., Thomas W. Croghan, M.D.

NR418 SSRI Usage Patterns As Risk Factors for Hospitalization
Reinee E. Sheffield, Pharm.D., Anthony T. Losasso, Ph.D., Chistopher Young, Ph.D., Karen D. Way, Ph.D.

NR419 Concordance with Dose Recommendations of Schizophrenia Guidelines in Veterans Administration Hospitals
Weiwei Feng, Ph.D., Teresa J. Hudson, Pharm.D., Mark Austen, M.S., Richard R. Owen, M.D.

NR420 Differences in Medication Adherence Between Users of Conventional and Atypical Antipsychotics in a Large State Medicaid Program
Joseph Menzin, Ph.D., Luke Boulanger, M.A., Mark Friedman, M.D., Joan A. Mackell, Ph.D., John Lloyd

NR421 Factors Affecting Supply of Mental Care Services
Jong I. Park, M.D., Jin Pyo Hong, M.D., Yoon Kim, M.D., Tong W. Suh, M.D., Chang J. Suh, Ph.D.

NR422 Antidepressant Use Patterns in a Naturalistic Setting
Brent Hale, R.Ph., Ryan Tierney, B.S., Catherine A. Melfi, Ph.D., William Signa, M.S., Thomas W. Croghan, M.D.

NR423 Dosing of Conventional Antipsychotics in Severely Ill Veterans with Schizophrenia: Opportunities for Improvement
Marcia T. Valenstein, M.D., Frederic C. Blow, Ph.D., Richard R. Owen, Jr., M.D., Laurel A. Copeland, M.P.H., Stephanie Visnic, M.S.

NR424 Should We Screen for Depression in Primary Care Settings? A Decision Analysis
Marcia T. Valenstein, M.D., Sandeep Vijan, M.D., John Zeber, M.H.A., Kathryn Boehm, M.D., Amna Buttar, M.D.

NR425 Program Leaders' Attitudes and Beliefs About Clinical Practice Guidelines for Addiction Treatment
Mark L. Willenbring, M.D., Dan Kivlahan, Ph.D., Michael Grillo

NR426 The Generalizability of Antidepressant Efficacy Trials: Results from an Outpatient Practice
Mark Zimmerman, M.D., Michael A. Posternak, M.D.

NR427 An Outcomes Measure: The Multidimensional Assessment of Symptoms and Psychosocial Functioning (MASP)
Mark Zimmerman, M.D., Jill I. Mattia, Ph.D.

NR428 Pathological Gambling in Psychiatric Outpatients: Prevalence, Comorbidity, Demographics and Clinical Correlates
Mark Zimmerman, M.D., Jill I. Mattia, Ph.D.

NR429 Depression in a Diabetes Disease Management Program
Alan C. Regenberg, B.A., Tina L. Harralson, Ph.D., Maureen Disbot, R.N., Catherine J. Datto, M.D., Ira R. Katz, M.D., Joseph J. Gallo, M.D.

NR430 The Use of Administrative Data to Assess Quality of Care for Bipolar Disorder in a Large Staff Model HMO
Jurgen Unutzer, M.D., Gregory E. Simon, M.D., Wayne J. Katon, M.D.

NR431 Deviant Sexual Arousal in Pedophilia: A PET Study
Igor I. Galynker, M.D., Yelena Itskovich, M.D., Konstantin Nikiforov, M.D., Erik Klein, B.A., Sara Acker, B.A., John Matochik, Ph.D., Edyth London, Ph.D.

NR432 SPECT in the Diagnosis of Catatonia
Igor I. Galynker, M.D., Richard Goldfarb, M.D., Milica Stefanovic, M.D., Shelevaya Tamara, M.D., Lilia Katsovich, M.D., Thomas Moesse, B.A.

NR433 Is Pedophilia an Impulsive Aggressive Disorder?
Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D., Yelena Itskovich, M.D., Erik Klein, B.A., Sara Acker, B.A., Sean Murphy, B.A., Ken Cullen, M.S.W.

NR434 Personality in Pedophiles and Two Control Groups
Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D., Sara Acker, B.A., Yelena Itskovich, M.D., Erik Klein, B.A., Mandy Rosenfeld, Ken Cullen, M.S.W.

NR435 An Open-Label Trial of Sildenafil to Reverse Antidepressant-Induced Sexual Dysfunction in Women
Albert N. Bayer, M.D.

NR436 Risperidone in the Treatment of Behavioral and Psychological Symptoms in Institutionalized and Noninstitutionalized Demented Subjects
Adrian Sapetti, M.D., Marcos D. Sehinkman, M.D.

NR437 Response to Sildenafil by Patients with Erectile Dysfunction Related with the Presence of Major Risk Factors
Adrian Sapetti, M.D., Enrique Comesana-Diaz, M.D.

NR438 Treatment of Paraphilia and Sexual Aggressive Impulsiveness with the Luteinizing Hormone Releasing Hormone (LHRH-Agonist) Eeuprolide Acetate
Peer Briken, M.D., Evangelia Nika, M.D., Professor Wolfgang Berner

NR439 Frontal Changes Predict Response Durability/Speed
Ian A. Cook, M.D., Andrew F. Leuchter, M.D., Elise Witte, Ph.D., William F. Stubbeman, M.D.

NR440 Switching Fluoxetine to Reboxetine: An Efficacy and Safety Study in Depressed Patients Resistant to Fluoxetine
Maurizio Fava, M.D., Patrick J. McGrath, M.D., Wang-Pui Sheu, M.A., Monica Froeschke, R.N., Saeeduddin Ahmed, M.D.

NR441 A Validation Study of a Computerized Management System for the Diagnosis and Treatment of Depression
Maurizio Fava, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., James M. Russell, M.D., Michael O'Boyle, M.D., Angela Camilleri, M.P.H., Wilma M. Harrison, M.D.

NR442 Efficacy of Quetiapine and Risperidone Against Depressive Symptoms in Outpatients with Psychotic Disorders
Martha Sajatovic, M.D., Jamie A. Mullen, M.D., Dennis Sweitzer, Ph.D.

NR443 Sexual Function and Satisfaction in the Treatment of Chronic Depression with Nefazodone, Psychotherapy and Their Combination
John M. Zajecka, M.D., David L. Dunner, M.D., Robert M.A. Hirschfeld, M.D., Susan G. Kornstein, M.D., Philip T. Ninan, M.D., A. John Rush, M.D., Michael E. Thase, M.D.

NR444 Change in Health-Related Quality of Life in Patients with Schizophrenia Taking Antipsychotic Agents
William S. Edell, Ph.D., Michael B. Durkin, M.S., Samir H. Mody, Pharm.D., Bryan E. Adams, Ph.D., Richard E. White, Ph.D., Alec Z. Qiu, M.S.

NEW RESEARCH

Wednesday, May 17, 2000, 9:00 a.m. - 10:30 a.m.

New Research 9 – Oral/Slide Session – Room E255, Level 2, McCormick Place Lakeside

MOOD DISORDERS I

Chp.: Javier I. Escobar, M.D.

NR445	Depression and Methamphetamine and Cocaine Dependence Steven L. Batki, M.D., Julia D. Moon, Mark V. Bradley, Kevin Delucchi, Ph.D., David F. Hersh, M.D., Scott B. Smolar, D.O., Matilda M. Mengis, M.D.	9:00 a.m.
NR446	Genome Wide Scan of BPD: Parent of Origin Effect Melvin G. McInnis, M.D., Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., Dean F. MacKinnon, M.D., Tsuo H. Lan, M.D., James B. Potash, M.D., J. Raymond DePaulo, Jr., M.D.	9:15 a.m.
NR447	Baseline Cerebral Glucose Metabolism Compared to Other Potential Divalproex Response Markers Terence A. Ketter, M.D., Po W. Wang, M.D., Claudia M. Santosa, M.A., Debbie L. Tate, Connie M. Strong, M.S., Nadia Sachs, M.Eng.	9:30 a.m.
NR448	Efficacy of Nurse Tele-Health Care As an Augmentation to SSRI Treatment of Depression in Primary Care Enid M. Hunkeler, M.A., William A. Hargreaves, Ph.D., Joel Meresman, Ph.D.	9:45 a.m.
NR449	Rapid Antidepressant Response with ECT Mustafa M. Husain, M.D., Hilary Berstein, L.C.S.W., Melanie Biggs, Ph.D., Keith Rasmussen, M.D., Thomas J. Carmody, Ph.D., A. John Rush, M.D., Rebecca S. Knapp, M.D., Max Fink, M.D., Charles H. Kellner, M.D., Teresa A. Rummans, M.D., Kevin A. O'Connor, M.D., Georgios Petrides, M.D., Mark D. Beale, M.D.	10:00 a.m.
NR450	Mania Improvement During Olanzapine Treatment Is Unaffected by Outcome of Previous Mood Stabilizer Therapy Robert W. Baker, M.D., Mauricio F. Tohen, M.D., Denai R. Milton, M.S., Virginia L. Stauffer, Pharm.D.	10:15 a.m.

NEW RESEARCH

Wednesday, May 17, 2000, 9:00 a.m. - 10:30 a.m.

New Research 10 – Oral/Slide Session – Room E256, Level 2, McCormick Place Lakeside

MOOD DISORDERS I

Chp.: Daniel P. Chapman, Ph.D.

NR451	Excellent Response Frequency of Venlafaxine Charles B. Nemeroff, M.D., Marc Cantillon, M.D.	9:00 a.m.
NR452	Predictors of Response to Treatment Among Outpatients Resistant to Fluoxetine 20 mg/Day Jonathan E. Alpert, M.D., Jerrold F. Rosenbaum, M.D., Andrew A. Nierenberg, M.D., Johanna A. Gordon, B.A., Karen E. Kelly, B.A., Andrea C. Hutchins, B.A., Maurizio Fava, M.D.	9:15 a.m.
NR453	Transcranial Magnetic Stimulation in Major Depression: High Frequency Repetitive Transcranial Magnetic Stimulation Increases Cortical Excitability Fumiko Maeda, M.D., Julian P. Keenan, Ph.D., Robert J. Birnbaum, M.D., Stefanie Freund, M.D., Alvaro Pascual-Leone, M.D.	9:30 a.m.
NR454	Cortisol Concentrations in Breast Milk of Women with Major Depression Mary T. Cox, Ph.D., Zachary N. Stowe, M.D., Amy L. Hostetter, B.A., Clayton Ramsey, B.A., Kevan Sternberg, B.S., Jim Ritchie, Ph.D.	9:45 a.m.
NR455	Toward a Molecular Anatomy of Bipolar Affective Disorder Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., J. Raymond DePaulo, Jr., M.D., Melvin G. McInnis, M.D., Dean F. MacKinnon, M.D.	10:00 a.m.
NR456	Mirtazapine Relapse and Pattern of Acute Response Andrew A. Nierenberg, M.D., Charlotte Kremer, M.D., Megan M. Smith, B.A., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.	10:15 a.m.

NEW RESEARCH

Wednesday, May 17, 2000, 12 noon - 2:00 p.m.

New Research 11 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

MOOD, DISSOCIATIVE, SLEEP, SOMATOFORM AND OTHER DISORDERS; VIOLENCE, TRAUMA AND VICTIMIZATION; SUICIDE; AND OTHER SOMATIC THERAPIES

Moderator: Andrew J. Cutler, M.D.

NR457 Divalproex Treatment of Mania with Dementia
Pierre N. Tariot, M.D., Lon S. Schneider, M.D., Jacobo E. Mintzer, M.D., Andrew J. Cutler, M.D., Muriel R. Cunningham, M.Ed., James W. Thomas, M.S., Kenneth W. Sommerville, M.D.

NR458 Thyroid Axis Dysfunction Is Related to Longitudinal Course of Depression
Fabrice Duval, M.D., M. Claude Mokrani, Ph.D., Paul Bailey, M.D., Marc-Antoine Crocq, M.D., Thanh S. Diep, M.D., Jean-Paul Macher, M.D.

NR459 Dopamine Function in Men with Bipolar Depression
Fabrice Duval, M.D., M. Claude Mokrani, Ph.D., Paul Bailey, M.D., Thanh S. Diep, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

NR460 Vagal Nerve Stimulation in Depression
Lauren B. Marangell, M.D., A. John Rush, M.D., Mark S. George, M.D., Harold A. Sackeim, Ph.D.

NR461 Treatment of Psychosocial Impairments in Major Depression
Robert M.A. Hirschfeld, M.D., David L. Dunner, M.D., Gabor I. Keitner, M.D., Daniel N. Klein, Ph.D., Lorrin M. Koran, M.D. Susan G. Kornstein, M.D., John C. Markowitz, M.D.

NR462 A Placebo-Controlled Trial of St. John's Wort in Major Depression
Richard C. Shelton, M.D., David L. Dunner, M.D., Uriel Halbreich, M.D., Michael E. Thase, M.D., Robert M.A. Hirschfeld, M.D., Alan J. Gelenberg, M.D., Martin B. Keller, M.D.

NR463 Thyroid Hypofunction in Rapid-Cycling Bipolar Disorders
Laszlo Gyulai, M.D., Michael Bauer, M.D., Mark S. Bauer, M.D., Avital Cnaan, Ph.D., Peter C. Wybrow, M.D.

NR464 Efficacy of Divaproex for Bipolar Depression
Laszlo Gyulai, M.D., Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Susan L. McElroy, M.D., Frederick Petty, M.D., Samuel C. Risch, M.D., Alan C. Swann, M.D.

NR465 Anxiety Symptoms in the Treatment of Chronic Depression
Philip T. Ninan, M.D., A. John Rush, M.D., Frances E. Borian, M.B.A., Susan G. Kornstein, M.D., John M. Zajecka, M.D., Michael E. Thase, M.D., Barbara O. Rothbaum, Ph.D.

NR466 Psychotic Versus Nonpsychotic Major Depression: Distinct Clinical Features
John D. Matthews, M.D., Christina M. Dording, M.D., Robert W. Irvin, M.D., Andrew A. Nierenberg, M.D., Kathryn A. Bottonari, B.A., Margarita L. Delgado, B.A., Megan M. Smith, B.A., Maurizio Fava, M.D.

NR467 Sexual Energy Scale (SES): A Simple Valid Screening Tool for Measuring Sexual Dysfunction
Julia K. Warnock, M.D., Anita L.H. Clayton, M.D., William R. Yates, M.D., J. Clark Bundren, M.D.

NR468 Depressive Mood Symptoms Associated with Ovarian Suppression
Julia K. Warnock, M.D., J. Clark Bundren, M.D., David W. Morris, M.A.

NR469 Effects of Paroxetine and Mirtazapine on Driving
Ian Hindmarch, Ph.D., Fran M. Ridout, B.S.C.

NR470 Patients with Severe Depression May Benefit from Buspirone Augmentation of Selective SSRIs
Bjorn G. Appelberg, Erkka Syvalahti, Timo Muhonen, Teuvo Koskinen, Hannu Naukkarinen, Olli-Pekka Mehtonen

NR471 Dysphoric Mania and Suicide Risk
Jose de Leon, M.D., Berta Lalaguna, M.D., Fernando Mosquera, M.D., Miguel Gutierrez, M.D., Blanca Fernandez de Corres, M.D., Jose L. Perez de Heredia, M.D., Ana Gonzalez-Pinto,

NR472 The Effectiveness of Citalopram in the Prevention of Depression Recurrence in Elderly Patients
Rene Kylsner, E. Pleidrup, M.D., H. L. Hansen, M.D., J. Bent-Hansen, M.D., D. Loldrup Poulsen, M.D., M. Lunde, H.E. Hopfner Petersen, M.S.C.

NR473 Childhood Emotional Trauma and Chronic PTSD in Adult Outpatients with Treatment-Resistant Depression
Marcia J. Kaplan, M.D., Nadya Klinetob, Ph.D.

NR474 Incongruent Psychotic Symptoms and Age of Onset in Bipolar Disorder
Jose L. Perez de Heredia, M.D., Juan L. Figuerido, M.D., Miguel Gutierrez, M.D., Berta Lalaguna, M.D., Jesus Ezcurra, M.D., Jose de Leon, M.D., Ana Gonzalez-Pinto, M.D.

NR475 What Can We Learn from Self-Assessment of Mania?
Elie G. Hantouche, M.D., Hagop S. Akiskal, M.D., Jean-Francois Allilaire, M.D., Jean-Michel Azorin, M.D., Marc L. Bourgeois, M.D., Daniel Sechter, Sylvie Lancrenon, Ph.D., Liliane Chatenet-Duchene, M.D.

NR476 Long-Term Mirtazapine Versus Citalopram in Major Depression
Esa Leinonen, M.D., Jon Skarstein, M.D., Kirsten Behnke, Hans Agren, Ph.D., Albert J. Schutte, M.D.

NR477 Effects of Bupropion Sustained Release on Sexual Functioning
Lawrence A. Labbate, M.D., Peter S. Brodrick, M.D., Robert P. Nelson, M.D., George W. Arana, M.D., R. Bruce Lydiard, M.D.

NR478 Changes of Personality Traits During SSRI Treatment
Antoine Pelissolo, M.D., Sylvie Troy, M.D., Jean-Pierre Lepine, M.D.

NR479 Personality and Temperament in Bipolar Disorders
Courtney M. Rennicke, B.A., Connie M. Strong, M.S., Claudia M. Santosa, M.A., Nadia Sachs, M.Eng., Po W. Wang, M.D., Mirene E. Winsberg, M.D., Terence A. Ketter, M.D.

NR480 Clinical Depression and the Dissociation Between Conscious and Unconscious Memory
Mustaq Khan, Ph.D., Verinder Sharma, M.D., Shahe Kazarian, Ph.D.

NR481 Is Olanzapine a Mood Stabilizer?
Peter D. Feldman, Ph.D., Mauricio F. Tohen, M.D., Thomas G. Jacobs, M.A., Verna Toma, B.S.C., Fan Zhang, Ph.D., Todd M. Sanger, Ph.D., Alan F. Breier, M.D.

NR482 Olanzapine in the Treatment of Juvenile Bipolar Disorder
Jean A. Frazier, M.D., Joseph Biederman, M.D., Thomas G. Jacobs, M.A., Mauricio F. Tohen, M.D., Verna Toma, B.S.C., Peter D. Feldman, Ph.D., Michael A. Rater, M.D.

NR483 The Safety and Efficacy of Lamotrigine for the Long-Term Treatment of Bipolar Depression
Russell Huffman, Ph.D., David Rudd, Pharm.D., Eileen Monaghan, John A. Ascher, M.D., Gilda Womble, M.S., Charles L. Bowden, M.D., R. Bruce Lydiard, M.D.

NR484 Frontal Tests in Unipolar and Bipolar Depression
Janusz K. Rybakowski, M.D., Alina Borkowska, Ph.D.

NR485 Response and Remission Rates in Different Subpopulations with Major Depression Administered Venlafaxine, SSRIs, or Placebo
Richard Entsuah, Ph.D.

NR486 Lack of Gender Effects in Mood Response to Alpha-Methyl-Para-Tyrosine (AMPT)
Francisco A. Moreno, M.D., Cynthia A. McGahuey, B.S., Karen Bridges, Pedro L. Delgado, M.D.

NR487 Emotional Blunting with SSRIs
Pedro L. Delgado, M.D., Adam Opbroek, M.D., Cindy Laukes, M.A., Cynthia A. McGahuey, B.S., Alan J. Gelenberg, M.D., Francisco A. Moreno, M.D., Joanna Katsanis, Ph.D., Richard D. Lane, M.D., Mona Mort, Ph.D.

NR488 Mood Stabilization with Lamotrigine in Rapid-Cycling Bipolar Disorder: A Double-Blind, Placebo-Controlled Study
Paul Greene, Nancy L. Earl, M.D., John A. Ascher, M.D., Eileen Monaghan, Patricia Suppes, M.D., Charles L. Bowden, M.D., Joseph R. Calabrese, M.D.

NR489 Controlled Studies of Lamotrigine in Unipolar Depression
John A. Ascher, M.D., Sharyn R. Batey, Pharm.D., Margaret Beaman, Kathleen Mitchell, Eileen Monaghan, Arifulla Khan, M.D., Peter D. Londborg, M.D.

NR490 Mortality in Psychotic Depression
Meena Narayan, M.D., Joyce Chen, J. Douglas Bremner, M.D., J. Craig Nelson, M.D.

NR491 Topiramate in Chronic Civilian PTSD: An Open-Label Study of a Novel Treatment
Jeffrey L. Berlant, M.D.

NR492 Safety and Efficacy of Risperidone Versus Placebo As Add-On Therapy to Mood Stabilizers in the Treatment of the Manic Phase of Bipolar Disorder
Gary S. Sachs, M.D.

NR493 The Systematic Treatment Enhancement Program for Bipolar Disorder
Gary S. Sachs, M.D., Michael E. Thase, M.D., Leslie Leahy, Ph.D., Sara R. Gaughan, B.A., Phillip Lavori, Ph.D., Jennifer Conley, M.A., David J. Kupfer, M.D.

NR494 Does Antidepressant Therapy Improve Cognition?
P. Murali Doraiswamy, M.D., K. Ranga R. Krishnan, M.D., Cathryn M. Clary, M.D.

NR495 Interpersonal Sensitivity in Bipolar II: A 557-Case Study
Franco Benazzi, M.D.

NR496 Female Depression and Menopause
Franco Benazzi, M.D.

NR497 A Comparison of Three Self-Rating Scales for Acute Mania
Edward G. Altman, Psy.D., Donald Hedeker, Ph.D., James L. Peterson, B.S., John M. Davis, M.D.

NR498 Comorbidity of Headache and Depression in a Cohort of Patients with Mood Disorders
Sally J. Czaja, Ph.D., Donald S. Ciccone, Ph.D., Gerald S. Leventhal, Ph.D., Myron L. Pulier, M.D., Eric Anderson, Ph.D., Rhonda Matlack, M.A., Steven J. Schleifer, M.D.

NR499 Treatment Effects of Medical Comorbidity on Late-Life Depression
David W. Oslin, M.D., Thomas R. Ten Have, Ph.D., Michael J. Kallan, M.S., William S. Edell, Ph.D.

NR500 Clinical, Humanistic and Economic Outcomes Associated with Long-Term Olanzapine Treatment of Mania
Madhan Namjoshi, Ph.D., Gopalan Rajamannar, Ph.D., Thomas G. Jacobs, M.A., Peter D. Feldman, Ph.D., Todd M. Sanger, Ph.D., Mauricio F. Tohen, M.D., Alan F. Breier, M.D.

NR501 Economic Aspects of Nefazodone, Cognitive Behavioral Analysis System of Psychotherapy and Their Combination for the Treatment of Chronic Depression
James M. Russell, M.D., William H. Crown, Ph.D., Madhukar H. Trivedi, M.D., John C. Markowitz, M.D., Rachel E. Manber, Ph.D., Bruce A. Arnow, Ph.D., Frances E. Borian, M.B.A.

NR502 The Impact of Depression and Perceived Stress on Obstetrical Complications
Claudia L. Baugh, B.A., Kelley A. Calhoun, B.S., Kevan Sternberg, B.S., Donald J. Newport, M.D., Zachary N. Stowe, M.D.

NR503 A Survey of Prescribing in the Treatment of Depression
Timothy J. Petersen, Ph.D., Christina M. Dording, M.D., Rebecca A. Kornbluh, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava,

NR504 Medication Noncompliance in Bipolar Disorders
Joseph F. Goldberg, M.D.

NR505 The Evolution of Polypharmacy in Bipolar Disorders
Joseph F. Goldberg, M.D.

NR506 Intermittent Luteal Phase Dosing of Sertraline Is Effective in Premenstrual Dysphoric Disorder
Uriel Halbreich, M.D., Richard Bergeron, M.D., Anna Stout, Ph.D., Ellen W. Freeman, Ph.D., Kimberly A. Yonkers, M.D., Teri B. Pearlstein, M.D., Wilma M. Harrison, M.D.

NR507 Long-Term Treatment of Depression with Bupropion Sustained Release
Karen L. Weihs, M.D., Trisha Houser, B.A., Sharyn R. Batey, Pharm.D., John A. Ascher, M.D., Carolym Bolden-Watson, Ph.D., Rafe M.J. Donahue, Ph.D., Alan Metz, M.D.

NR508 Anxiety and Response to Bupropion Sustained Release or Sertraline
A. John Rush, M.D., Madhukar H. Trivedi, M.D., Sharyn R. Batey, Pharm.D., Rafe M.J. Donahue, Ph.D., Thomas J. Carmody, Ph.D., Trisha Houser, B.A., John A. Ascher, M.D.

NR509 Mood Stabilization with Lamotrigine in Rapid-Cycling Bipolar Disorder
Nancy L. Earl, M.D., Paul Greene, John A. Ascher, M.D., Chai-Ni Chang, Gary S. Sachs, M.D., Terence A. Ketter, M.D., Alan C. Swann, M.D.

NR510 A Comparison of Atypical Antipsychotic Agents As an Adjunct to Mood Stabilizers in Rapid-Cycling Bipolar Disorder
Christina M. Demopulos, M.D., S. Nassir Ghaemi, M.D., Aysegul Yildiz, M.D., Gabriele Sachs, M.D.

NR511 The Solar Eclipse Induces Rapid Mood Changes
Belso Nora, M.D., Szili Ilona, Rihmer Zoltan, M.D., Mirnics Zsuzsa

NR512 Risperidone for Acute Mania: Focus on Safety
Charles L. Bowden, M.D., Gary S. Sachs, M.D.

NR513 A Single-Blind Trial Assessing the Effectiveness/Efficacy of Fluoxetine Versus Sertraline for the Treatment of Major Depression
Rita A. Suri, M.D., Lori L. Altshuler, M.D., Natasha Rasgon, M.D., Jeffrey Calcagno, M.D., Mark A. Frye, M.D., Michael J. Gitlin, M.D., Sun Hwang, M.D.

NR514 A Naturalistic Study of Mirtazapine in Mexican Psychiatric Practice
Herben J. Harmsen, M.D., Ilse Van Hensbeek, M.D.

NR515 Primary Prevention of Schizophrenia
Ernest H. Friedman, M.D., Gary G. Sanders, B.S., Diane A. Sedlak, B.A.

NR516 Treatment of Bipolar Depression: Clinical and Economic Outcomes
Lynda Bryant-Comstock, M.P.H., Dell B. Mather, Todd A. Lee, Paul E. Keck, Jr., M.D., Hong Li, Ph.D., Sean D. sullivan, Ph.D.

NR517 Predictive Factors of Chronic PTSD in a One-Year Follow-Up Study of Rape Victims
Jean-Michel Darves-Bornoz, M.D., Jean-Pierre Lepine, M.D., Marie Choquet, M.D., Andree Degiovanni, M.D., Philippe Gaillard, M.D.

NR518 Treatment of Impulsive Aggression with Divalproex
Angela M. Hegarty, M.D.

NR519 Childhood Trauma Relates to Adult Inpatient Assault
Martha L. Crowner, M.D., A. Jonathan Porteus, Ph.D., Konstantina Myrianthopolos, B.A.

NR520 Risk Factors for PTSD Following Severe Injury
Daniella David, M.D., Karin F. Esposito, M.D., Victoria Bustamante, Psy.D., Thomas A. Mellman, M.D.

NR521 The Use of Different Typologies in Sexual Homicide
Evangelia Nika, M.D., Peer Briken, M.D., Professor Wolfgang Berner

NR522 Impact of Risperidone on Seclusion and Restraint at a State Psychiatric Hospital
K.N. Roy Chengappa, M.D., Joseph Levine, M.D., Richard Ulrich, M.S., Haranath Parepally, M.D., Jaspreet Brar, M.D., Rebecca Atzert, R.N.

NR523 Psychological Correlates of Assaultive Adolescents
Dwain C. Fehon, Psy.D., Carlos M. Grilo, Ph.D., Deborah Lipschitz, M.D.

NR524 Partner and Nonpartner Violence and Victimization Among Individuals in Substance Abuse Treatment: General and Gender-Specific Markers of Violence Involvement
Stephen T. Chermack, Ph.D., Maureen A. Walton, Ph.D., Bret E. Fuller, Ph.D., Frederic C. Blow, Ph.D.

NR525 Previous Exposure to Trauma and the Psychological Effects of Air Disasters
Philippe J.R. Birmes, M.D., Barbara A. Warner, M.D., Laurent J. Schmitt, M.D.

NR526 HPA Axis Dysfunction in Depersonalization Disorder
Daphne Simeon, M.D., Orna Guralnik, Psy.D.

NR527 Dissociative Style and Directed Forgetting
Bernet M. Elzinga, M.S.C.

NR528 Dissociative Proneness and Alexithymia
Bernet M. Elzinga, M.S.C., Bob Bermono, Ph.D., Richard Van Dyck, M.D.

NR529 Use of a Screening Questionnaire to Detect Sleep Disorders
Thomas Roth, Ph.D., Gary Zammit, Ph.D., Clete Kushida, M.D., Karl Dogharamji, M.D., Susan D. Mathias, M.P.H., Daniel J. Buysee, M.D.

NR530 Differential Diagnosis Between Primary Insomnia and Insomnia Comorbid with Mood Disorders
Tung-Ping T. Su, M.D., Wei-Chung Mao, M.D., Ian-Kai Shan, Liling Lin, Ann-Wen Lynn

NR531 Pregabalin Improves Sleep in Neuropathic Pain Patients
Uma Sharma, Ph.D., Don Iacobellis, Pharm.D., Coleen Glessner, B.S., MaryKay Hes, B.S., Linda Lamoreaux, M.P.H., Robert Allen, M.D., R. Michael Poole, M.D.

NR532 Alexithymia in DSM-IV Disorder: Comparative Evaluation in Somatoform Disorders, Panic Disorder, OCD and Depression
Bettina Bankier, M.D., Martin Aigner, M.D., Ulrike Demal, MAG, Michael Bach, M.D.

NR533 Clinical Validity of ICD-10 Neurasthenia
Bettina Bankier, M.D., Martin Aigner, M.D., Anna Spacek, M.D., Sandra Krones, Ph.D., Michael Bach, M.D.

NR534 The Somatoform Disorders Symptom Checklist (SDSC): Validation of a German Version in Chronic Pain Patients
Michael Bach, M.D., Alexandra Peternell, Ph.D., Martin Aigner, M.D., Bettina Bankier, M.D.

NR535 The Relation of Alexithymia, Somatic Complaint, Emotion and Vocabulary
Kuy-Haeng Lee, M.D., Hyun-Tae Jeon, M.D., Yong-Jin Yoo, M.D., Jae-Hyun Kim, M.D., Kwang So, M.D., Han-Joo Kim, M.D.

NR536 Gonadal and Adrenal Androgens in Women with Epilepsy
Martha J. Morrell, M.D., Mark V. Sauer, M.D., Linda C. Giudice, M.D., Silvia Done, B.A., Amelia J. Paulson, B.A., Cairn G. Seale, M.S.

NR537 Health Status and Pathological Gambling
Angela Ibanez, M.D., Rita Prieto, M.D., Carlos Blanco, M.D., Jeronimo Saiz-Ruiz, M.D.

NR538 Psychiatric Sequelae of Amputation: Immediate Effects
Rajaram Mohan, M.D., Rajes M. Wari, M.D.

NR539 Association Between Piracetam and Nefazodone in Patients with Cognitive Disorder and Depression
Julio C. Zarra, M.D.

NR540 Correlated of Suicidal Behavior in an Arctic Community
John M. Haggarty, M.D., Zachias Cernovsky, Ph.D., Harold Merskey, M.D., Mariwan Husni, M.D.

NR541 Analysis of Catechol-O-Methyltransferase and 5-Hydroxytryptamine Transporter Polymorphism in Patients at Risk for Suicide
Mark J. Russ, M.D., Herbert M. Lachman, M.D., Todd Kashdan, B.A., Takuya Saito, M.D., Senada Bajmakovic-Kalila, M.D.

NR542 Association Study with the Tryptophan Hydroxylase Gene in Suicide Attempters
Philippe Courtet, M.D., Mocrance Abbar, M.D., Marion Leboyer, M.D., Jean-Philippe Boulenger, M.D., DiDier Castelnau, M.D., Catherine Buresi, M.D., Alain Malafosse, M.D.

NR543 Suicide Prevention: Determining the Best Settings for Prevention Interventions
Peter L. Forster, M.D., Patricia A. Arean, Ph.D., Carol J. Peng, B.A.

NR544 Medical Contacts of Suicide Attempters Prior to the Event
Francoise Chastang, M.D., Patrice Rioux, M.D., Laurent Leclerc, M.D., Viviane Kovess, M.D., Edouard Zarifian, M.D.

NR545 Adolescent Suicidal Behavior in Buenos Aires and Mendoza
Guillermo J. Tortora, M.D., Miguel Marquez, M.D., Benigno Gutierrez, M.D., Liliana Florio, Ph.D., Edith M. Serfaty, M.D., Ignacio Brusco, M.D., Alicia Sotelo-Lago, M.D.

NR546 Repetitive Transcranial Magnetic Stimulation Versus ECT for Major Depressive Episode
Philip G. Janicak, M.D., Brian Martis, M.D., Jack S. Krasuski, M.D., Dennis D. Beedle, M.D., Rajiv P. Sharma, M.D., Cherise Chase, R.N., Mauli Verma, M.D.

NR547 Burst-Suppression Anesthesia As Alternative to ECT
Mauro Garcia-Toro, M.D., Antonio Garcia, M.D., Lorenzo Socias, M.D., Pedro Ibanez, M.D., Catalina Rubert, M.D., Joan Salva-Coll, M.D., Gemma Rialp, M.D.

NR548 Patient Expectations About ECT
Shoshana Peyser, Ph.D., Bruce Luber, Ph.D., Joan Prudic, M.D., Harold A. Sackeim, Ph.D.

NR549 Patients with SAD Report a More Complete Improvement in Summer than with Light Treatment in Winter
Teodor T. Postolache, M.D., Thomas A. Wehr, M.D., Ludy Y. Yi, Norman E. Rosenthal, M.D.

NR550 Maintenance Repetitive Magnetic Stimulation in the Treatment of Resistant Major Depression
William M. McDonald, M.D., Eve H. Byrd, Yvonne M. Greene, M.D., Leslie E. Smith, B.A., Autumn L. Clark, B.S. Charles M. Epstein, M.D.

NR551 Is It Possible to Predict Cerebal Dysrhythmias by Measuring Pulse and Blood Pressure Before and After ECT?
Mustafa K. Saadani, M.D.

NEW RESEARCH

Wednesday, May 17, 2000, 3:00 p.m. - 5:00 p.m.

New Research 12 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

CHILD AND ADOLESCENT DISORDERS; ADDICTION PSYCHIATRY; BRAIN IMAGING; CONSULTATION-LIAISON AND EMERGENCY PSYCHIATRY; CROSS-CULTURAL, DIAGNOSTIC AND OTHER PSYCHIATRIC ISSUES AND DISORDERS

Moderator: William B. Lawson, M.D.

NR552 Weight Gain in Pediatric Patients on Typical and Atypical Antipsychotics
Ann W. Mulqueen, M.S.N., Marianne Wudarsky, M.D., Robert J. Nicolson, M.D., Pete Gochman, M.A., Susan Hamburger, M.A., Marge Lenane, M.S.W., Judith H.L. Rapoport, M.D.

NR553 Regional Brain Functioning During Verbal Fluency Tasks in Subjects with Asperger's Disorder
Joanna T. Szelazek, Peter C. Williamson, M.D., Sandra Fisman, M.D., Margaret M. Steele, M.D., Joseph Gati, M.S.C., Maria Densmore, B.S.C., Ravi Menon, Ph.D.

NR554 Assessing Children at Risk for Bipolar Disorder
Sarah M. Graman, B.A., Kathleen A. Lake, M.S.W., Melissa P. Del Bello, M.D., Patricia McDonough-Ryan, M.A., Cesar A. Soutullo, M.D., Susan L. McElroy, M.D., Stephen M. Strakowski,

NR555 Familial Psychopathology of Children with School Refusal
Corinne Martin, M.D., Stephane Cabrol, M.D., Jean-Pierre Lepine, M.D., M. Christine Mouren-Simeoni, M.D., Manuel P. Bouvard, M.D.

NR556 Safety and Efficacy of Paroxetine in the Treatment of Children and Adolescents with OCD
David J. Carpenter, M.S., Graham J. Emslie, M.D., Karen Dineen-Wagner, M.D., Mark A. Riddle, M.D., Susan Lawrinson, B.S.C.

NR557 The Other Half of Teen Pregnancy: Characteristics of Male Partners and Opportunities for Physician Intervention
Daniel P. Chapman, Ph.D., Robert F. Anda, M.D., Vicent J. Feliti, M.D., Dale Nordenberg, M.D., Janet Croft, Ph.D., John Santelli, M.D., James S. Marks, M.D.

NR558 Personal Health and Preventive Counseling Characteristics of Women Psychiatrists: Results from the Women Physicians' Health Study
Daniel P. Chapman, Ph.D., Erica Frank, M.D.

NR559 Lack of Prolactin Elevations with Quetiapine
Brian J. McConville, M.D.

NR560 The Characteristics of Executive Dysfunctions and Change During Methylphenidate Treatment in Children with ADHD
Hyung-Bae Park, M.D., Jong-Bum Lee, Ph.D., Hyun-Seok Sea, Hyung-Mo Sung

NR561 The Comparison of the Executive Function Between Children with Tic Disorder and ADHD
Hyung-Mo Sung, Hyung-Bae Park, M.D., Sung-Duk Jung, Jin-Sung Kim

NR562 Comorbid ADHD and Disruptive Behavior Disorders
Boris Birmaher, M.D., James P. McCafferty, B.S., Kevin M. Bellew, B.S., Katherine L. Beebe, Ph.D.

NR563 Pharmacokenetics of Ziprasidone in Children and Adolescents with Tourette's Syndrome
Floyd R. Sallee, M.D., Jeffrey J. Miceli, Ph.D., Keith D. Wilner, Ph.D., Lisa Robarge, Ph.D.

NR564 ADHD and Treatment of Adolescent Dysphoric Mania
Rosanne C. State, M.D., Mark A. Frye, M.D., Lori L. Altshuler, M.D.

NR565 Metformin Leads to Weight Loss in Adolescents Who Gained Weight on Psychotropic Drugs
Elizabeth M. Cottingham, M.D., John A. Morrison, Ph.D., Bruce A. Barton, Ph.D.

NR566 Comparative Side Effects of Atypical Neuroleptics in Children and Adolescents
Stephen Grcevich, M.D., Connie McBurney, R.N.C., Constance Ray, R.N.C., Rosemary Richards, R.N.C., Meredith Shotschar, R.N.C.

NR567 Pharmacodynamic and Pharmacokinetic Profiles of a New Modified Release Formulation of Ritalin in Children with ADHD
Thomas J. Spencer, M.D., James M. Swanson, Ph.D., Sabri Markabi, M.D., Meredith Weidenman, B.A., Herbert Faleck, D.O.

NR568 Bupropion Sustained Release Versus Methylphenidate Versus Placebo in the Treatment of Adult ADHD
Paul J. Perry, Ph.D., Samuel Kuperman, M.D., Gary R. Gaffney, M.D., Kristine Bever-Stille, Pharm.D., Brian Lund, Pharm.D., Timothy Holman, M.A., Jane Paulsen, Ph.D.

NR569 RCT Cognitive Group Therapy: Early Breast Cancer
David W. Kissane, M.D., Sydney Bloch, M.D., David M. Clarke, M.B., Graeme C. Smith, M.D., Patricia Miach, Ph.D., Anthony Love, Ph.D.

NR570 Atypical Antipsychotics, Weight Gain and Hyperlipidemia in Hospitalized Preadolescents
Michael P. Duran, M.D., Jonathan M. Meyer, M.D.

NR571 Divalproex Effectiveness in a Pediatric Inpatient Psychiatric Unit
Gahan J. Pandina, Ph.D., Karen Senese, M.D., Julie Lewerenz, M.D., Robert L. Hendren, D.O.

NR572 Gender Differences in HIV, HBV, HCV and Associated Risks in Severely Mentally Ill Persons
Marian I. Butterfield, M.D., Hayden Bosworth, Ph.D., Keith G. Meador, M.D., Karen M. Stechuchak, M.S., Marvin S. Swartz, M.D., Jeffery W. Swanson, Ph.D., Lori A. Bastian, M.D.

NR573 Early Cognitive Deficits in HIV-1 Patients
Paulo S. Belmonte de Abreu, M.D., Adriana C. Schoffel, M.D., Edino Parolo, M.D.

NR574 Behavioral Benefits in Alzheimer's Disease Patients Residing in a Nursing Home Following 52 Weeks of Rivastigmine Treatment
Jeffrey L. Cummings, M.D., Ravi Anand, M.D., Barbara Koumaras, Richard Hartman, Ph.D.

NR575 Risperidone Versus Placebo for Severe Conduct Disorder
Michael G. Aman, Ph.D., Robert L. Findling, M.D., Albert T. Derivan, M.D., Ursula Merriman

NR576 Stress, Depressive Symptomatology and Craving in Nontreatment-Seeking Individuals with Cocaine Dependence
Katherine Karlsgodt, B.A., David R. Gastfriend, M.D., Sara Krause, B.A., Igor Elman, M.D.

NR577 The Effects of MAOA CA Repeat Polymorphism on Behavioral Personality Trait and Clinical Characteristic in Alcoholic Korean Male
Jung-Sik Lee, M.D., Byung-Hwan Yang, Ph.D.

NR578 Sociocultural Factors Associated with Binge Drinking Among College Athletes
Merry N. Miller, M.D., Barney E. Miller, Ph.D., Ruth Verhegge, Holly Linville, M.D., Andres J. Pumariega, M.D., Hubert B. Vance, Ph.D.

NR579 Two-Year Follow-Up of a Group of Heroin Addicts
Eduardo Gutierez, M.D., Pilar A. Saiz, Ph.D., Maria P. Gonzalez, Ph.D., Juan M. Fernandez, M.D., Celso Iglesias, Ph.D., Julio B. Bobes, Ph.D.

NR580 Dependence and Abuse in Schizophrenia Patients in Hawaii
F.M. Baker, M.D.

NR581 Anticonvulsant Treatment for Alcohol Dependence After Brain Injury
Thomas P. Beresford, M.D., Stephanie D. Morrison, B.A., Brandon K. Martin, B.A., David B. Arciniegas, M.D.

NR582 Multicenter Alcohol Use Data from Liver Transplant Candidates
Thomas P. Beresford, M.D., Brandon K. Martin, B.A., Stephen L. Snyder, M.D., Andrea F. DiMartini, M.D.

NR583 Compliance with Court Ordered Versus Voluntary Disulfiram Therapy
Brandon K. Martin, B.A., Lori Clapp, R.N., Denise C. Bridgeford, M.D., Akwasi Amponsah, M.D., Dianna Bialkowski, R.N. Levester Lyons, M.S.W., Thomas P. Beresford, M.D.

NR584 Stable Patients Tolerate Step-Down in Targeted Assertive Outreach (TAO) Services
Richard N. Rosenthal, M.D., David J. Hellerstein, M.D., Christian R. Miner, Ph.D.

NR585 Early Dropout of Mentally Ill Chemical Abusers in a Therapeutic Community
Serge M. Sevy, M.D., Kyra Sposato

NR586 Prolactin Levels and SCH39166 in Cocaine PTS
Vasant P. Dhopesh, M.D., James W. Cornish, M.D., Elmer Yu, M.D., AnnaRose Childress, Ph.D., Sabrina A. Poole, M.D.

NR587 Striatal Size and Metabolism in Elderly Schizophrenia
Lina S. Shihabuddin, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Adam M. Brickman, B.A.

NR588 Cingulate Gyrus Volume in Drug Naïve Schizophrenia Patients
M. Mehmet Haznedar, M.D., Erin A. Hazlett, Ph.D., Jimcy Platholi, M.A., Monte S. Buchsbaum, M.D.

NR589 Follow-Up Study of Depression with Siemens-CTI Exact HR Plus PET in the Acute Stage and Clinical Remission
Vjera A. Holthoff, M.D., Bettina Beuthien-Baumann, M.D., Antje Triemer, Ph.D., Peter Winiecki, Ph.D., Franke Wolf-Gunter, M.D., Otto Bach, M.D.

NR590 Idal-Motor Symptoms Under Risperidone
Ulf Kuenstler, M.D., Ralf Regenthal, M.D., Hermann J. Gertz, M.D., Swen Hesse, M.D., Karin Hohdorf, M.D.

NR591 Morphine Is Effective in the Reduction of Phantom Limb Pain and Cortical Reorganization
Wolfgang Larbig, M.D., Ellena Huse, Ph.D., Herta Flor, Ph.D., Niels Birbaumer, Ph.D.

NR592 Striatal Size and Metabolic Rate in Normal Aging
Adam M. Brickman, B.A., Lina S. Shihabuddin, M.D., Erin A. Hazlett, Ph.D., Olga G. Berwid, B.A., Li Zhang, M.A., Monte S. Buchsbaum, M.D.

NR593 Basal Ganglia Activation in Schizophrenia Patients Under Haloperidol and Olanzapine and in Healthy Controls Revealed by fMRI
Juergen Mueller, M.D., Matthias Dobmeier, M.D., Helmfried E. Klein, M.D.

NR594 Contradictory Findings of Brain MRI Abnormalities in Treatment-Resistant Schizophrenia
Helio Elkis, M.D., Jose R. Oliveira, M.D., Claudio C. Campi, M.D., Paulo C. Sallet, M.D., Erley Sassi, M.D.

NR595 Relationship of Irritable Bowel Syndrome with OCD in India
Sumant Khanna, M.D., V.M. Vidyaranya, M.D., Prakash S. Masand, M.D.

NR596 An Open Trial of SSRIs in Patients with Dizziness and Major or Minor Psychiatric Symptoms
Jeffrey P. Staab, M.D., Michael J. Ruckenstein, M.D., David A. Solomon, M.D., Neil T. Shepard, Ph.D.

NR597 Treatment of Depression Following Acute Coronary Syndrome Reduces the Risk for Recurrent Acute Cardiac Events
Peter J. Panzarino, Jr., M.D., Tasneem Z. Naqvi, M.D., Haidar Sadeghi-Razlighi, M.D., Yulius Mustafa, M.D., Russell M. Poland, M.D., Syed S. A. Naqvi, M.D.

NR598 Adverse Reactions to Antidepressants in Consultation-Liaison Psychiatry Inpatients
Graeme C. Smith, M.D., David M. Clarke, M.B., Dennis Handrinos, M.B., Thomas Trauer, Ph.D.

NR599 Primary Care Panic: ID by Doctor Versus Screening
Peter P. Roy-Byrne, M.D., Deborah S. Cowley, M.D., Joan Russo, Ph.D., Emily Cohen, B.A., Erin Michelson, B.A., Wayne J. Katon, M.D.

NR600 The Effect of SSRI Panic Disorder Treatment on Laboratory and Emergency Department Resource Utilization and Cost
Peter P. Roy-Byrne, M.D., Cathryn M. Clary, M.D., Amy N. Grundzinski, Pharm.D.

NR601 Prime-MD Patient Health Questionnaire (PHQ) in the Specialist Medical Setting: Validation for Anxiety and Mood Disorders
Benjamin Fischler, M.D., Phillippe M.J. Persoons, M.D., Koen Luyckx, M.A.

NR602 Epidemiology of Axis-I Disorders in Medical Inpatients
Benjamin Fischler, M.D., Phillippe M.J. Persoons, M.D., Koen Luyckx, M.A.

NR603 A Prospective Evaluation of Neuropsychiatric Symptoms in Patients with Hepatitis C Treated with Interferon-Alpha and Ribavirin
Eric W. Dieperink, M.D., Mark L. Willenbring, M.D., Paul D. Thuras, Ph.D., Lori Tetrick, Samuel B. Ho, M.D.

NR604 Risperidone Oral Solution Versus Intramuscular Haloperidol
Glenn W. Currier, M.D., George M. Simpson, M.D.

NR605 Parental Sedation in 385 Psychiatric Emergency Room Patients
Murat Pakurek, M.D., Fahim Kazi, M.D., Horacio Preval, M.D., Laura J. Fochtmann, M.D., Andrew J. Francis, Jr., M.D.

NR606 An Open-Label Trial of Citalopram for Major Depression in Hepatitis C
Ondria C. Gleason, M.D., William R. Yates, M.D.

NR607 Ethnic Variations in Psychiatric Treatment
Wendy L. Colquitt, Ph.D., Diane Herbeck, M.A., Harold Alan Pincus, M.D.

NR608 The Interpersonal Support Evaluation List in American Indians
Brett Koplin, M.D., Gary Leonardson, Ph.D., Thomas Welty, M.D.

NR609 Anxiety in Individuals with Self-Reported Coronary Heart Disease
Nils H. Dahl, M.D., Alv A. Dahl, M.D., Oystein Kruger, M.D.

NR610 Stress Among Kenyans Exposed to the 1998 Bombing of the U.S.Embassy in Nairobi
Victoria E. Wells, M.D., Margaret Ma'Kanyengo, M.D., Pius A. Kigamwa, M.D., Josephine Omondi, M.D., Lawson R. Wulsin, M.D.

NR611 Depression Among Kenyans Exposed to the 1998 Bombing of theU.S.Embassy
Victoria E. Wells, M.D., Josephine Omondi, M.D., Pius A. Kigamwa, M.D., Margaret Ma'Kanyengo, M.D., Lawson R. Wulsin, M.D.

NR612 Mother Tongue and Psychopathology: A Representative Study Among Migrants with Schizophrenia
Oktay Yagdiran, M.D.

NR613 Navajo Religious Healing: Patient-Healer Profiles
Michael G. Storck, M.D., Thomas Csordas, Ph.D.

NR614 Race Differences in Diagnosis of Comorbid Disorders in Schizophrenia
Lisa D. Green-Paden, M.D., Alicia Lucksted, Ph.D., Janine C. Delahanty, M.A., Leticia T. Postrado, Ph.D., Lisa B. Dixon, M.D.

NR615 Evaluating Changes in Sexual Dysfunction in Depressed Patients: Sensitivity to Change of the Changes in Sexual Functioning Questionnaire (CFSQ)
Maria P. Gonzalez, Ph.D., Julio B. Bobes, Ph.D., Maria T. Bascaran, M.D., Fernando Rico-Villademoros, M.D., Sebastian Banus, M.D., Margarita Garcia, M.D.

NR616 Changes in Peripheral Thyroid Function with Antidepressant Treatment
Michael J. Gitlin, M.D., Lori L. Altshuler, M.D., Mark A. Frye, M.D., Rita A. Suri, M.D., Lynn Fairbanks, Ph.D., Emily K. Lee, M.D.

NR617 Bupropion As a Treatment for SSRI-Induced Sexual Side Effects
Michael J. Gitlin, M.D., Rita A. Suri, M.D., Lori L. Altshuler, M.D., Joni Zuckerbrow-Miller, B.A., Lynn Fairbanks, Ph.D.

NR618 Antidepressant Treatment Received by Depressed Subjects in the Finnish General Population
Tanja I. Laukkala, Ph.D., Erkki T. Isometsa, Ph.D., Juha Hamalainen, M.D., Martti E. Heikkinen, Ph.D., Hillevi Aro, Ph.D.

NR619 Marital Dissatisfaction and Psychiatric Disorder
Tess Sheldon, M.S.C., Mark A. Whisman, Ph.D., Paula N. Goering, Ph.D.

NR620 Chronic Therapy of Schizophrenic Relapse
Thomas R. Ten Have, Ph.D., Alfredo Morabia, Philippe Huguelet, Francois P. Ferrero, M.D.

NR621 Longitudinal Study of the Association Between Alcohol Dependents and Major Depression in the General Population
Stephen E. Gilman, S.M., Henry D. Abraham, M.D.

NR622 Illicit Drug Consumption and Personality in Teenagers
Pilar A. Saiz, Ph.D., Juan L. Lopez, M.D., Jesus M. Delgado, M.D., Maria P. Gonzalez, Ph.D., Sara Martinez, M.D., Luis Jimenez, M.D., Julio B. Bobes, Ph.D.

NR623 Risk Factors for Completed and Attempted Suicides
Halise Ozgeven, M.D., Isik Sayil, M.D., Oguz Berksun, M.D.

NR624 Disability and Mental Disorders Among Primary Care Patients: A French Perspective
Patrick Martin, M.D., Catherine Richard-Berthe, M.D., Jean-Pierre Lepine, M.D.

NR625 Prediction of Treatment Response in OCD Via Functional Brain Imaging
Yehuda Sasson, M.D., Talma Hendler, M.D., Elinor Goshen, M.D., Zila Zwas, M.D., Joseph Zohar, M.D.

NR626 Exaggeration of Post-Concussive Symptoms in Mild Head Injury Litigants
Jim Andrikopoulos, Ph.D.

NR627 The 5HT Transporter Protein Gene and OCD: Application of the Transmission Disequilibrium Test for Quantitative Traits
Margaret A. Richter, M.D., Emanuela Mundo, M.D., Sam Fariba, B.S.C., James L. Kennedy, M.D.

NR628 A Novel Nonsense Mutation of MECP2 in a Patient with Rett Syndrome
Soo-Jeong Kim, M.D., Edwin H. Cook, Jr., M.D.

NR629 Gender Differences in the 5HT Transporter Link Polymorphic Region in Geriatric Depression
David C. Steffens, M.D., Ingrid Svenson, B.S., Douglas A. Marchuk, Ph.D., Bobby Levy, B.S., Judith C. Hays, Ph.D., Elizabeth P. Flint, Ph.D., K. Ranga R. Krishnan, M.D.

NR630 Quantitative TDT on the 5HT-1D Beta-Receptor in OCD
Emanuela Mundo, M.D., Margaret A. Richter, M.D., Sam Fariba, B.S.C., James L. Kennedy, M.D.

NR631 Childhood-Onset Neuropsychiatric Disorders in Adult Forensic Psychiatric Patients
Henrik Soderstrom, M.D., Anders Forsman, M.D., Agneta Nilsson, M.D.

NR632 The Goteborg Forensic Neuropsychiatry Project: Results from Two Pilot Groups
Henrik Soderstrom, M.D., Anders Forsman, M.D.

NR633 A Follow-Up Study of Neuropsychiatric Sequelae in Patients with Varying Degrees of Mild Traumatic Brain Injury
Scott R. McCullagh, M.D., Donna Ouchterlony, M.D., Alison Jardine, O.T., Andrea Protzner, M.A., Nancy Blair, M.A., Anthony Feinstein, M.D.

NR634 Tourette's Syndrome and Psychiatric Comorbidity
Miguel Marquez, M.D., Guillermo J. Tortora, M.D., Beatriz Moyano, M.D., Silvia Figiacone, M.D., Ignacio Brusco, M.D.

NR635 Metalloproteinases and Neurological Disorders
Marion E. Wolf, M.D., Maria A. Valenzuela, Ph.D., Luis Cartier, M.D., Lucia Collados, Ph.D., Ana M. Kettlun, Ph.D., Aron D. Mosnaim, Ph.D.

NR636 Training General Practitioners in the Management of Depression
Clare Dixon, B.S.C., Linda Gask, M.D., Christopher F. Dowrick, M.D., Rachel Perry, M.A., Tim Usherwood, M.D., David Torgerson, Ph.D., Christopher Sutton, Ph.D.

NR637 Assessing Psychiatry Residents Cultural and Religious Beliefs Before and After a Related Course
Roubini Kambolis, M.D., Essam-Eldin Ellabbad, M.D., William M. Greenberg, M.D., Farah Farooq, M.D.

NR638 Effectiveness of Olanzapine Upon Psychiatric and Vocational Rehabiliation Outcomes
Ralph Aquila, M.D., Peter J. Weiden, M.D., Bruce J. Kinon, M.D., Denai R. Milton, M.S., Annette Zygmunt, Ph.D., Ralph W. Swindle, M.D., Virginia L. Stauffer, Pharm.D.

NR639 Low Levels of Antibodies to Cardiolipin in First-Episode and Chronic Schizophrenia
Pinkhas Sirota, M.D., Irene Bogdanov, M.D., Aviva Katzav, M.D., Ruth Hershko, M.D., Joab Chapman, M.D.

NR640 Neuroleptic Effects on Cytokines in Schizophrenia
Pinkhas Sirota, M.D., Meital Meiman, Bella Epstein, M.D., Irene Bogdanov, M.D., Ruth Hershko, M.D., Ruben Benatov, Ph.D.

NR641 Monocyte Activation in Depressed Patients
Javier Schlatter, M.D., Felipe Ortuno, M.D., Maria L. Subira, M.D., Salvador Cervera-Enguix, M.D.

NR642 Psychometric Analyses of the Modified Rush Sexual Inventory
John M. Zajecka, M.D., Deepa Rao, M.A., Taisa Skubiak, B.A.

NR643 Depression and Family Functioning in the Caregivers of Patients with Chronic Mental Illness
Alison M. Heru, M.D., Kim Vlastos, M.H.A., Maria Bassi, M.H.A., Dorota Gawlas, M.D., Christine E. Ryan, Ph.D.

NR644 Race and Age Differences in Illness Knowledge and Empowerment in Schizophrenia
LeaAnn Moricle, M.D., Janine C. Delahanty, M.A., Leticia T. Postrado, Ph.D., Lisa D. Green-Paden, M.D., Alicia Lucksted, Ph.D., Lisa B. Dixon, M.D.

NR645 Stress and Emotional Response in Patients with Mood Disorder
Min-Cheol Park, M.D., Jung-In Koh, M.D., Sang-Woo Oh, Ph.D., Sang-Yeol Lee, M.D.

NR646 Cognitive Therapy Versus Intensive-Behavior Therapy
Jean A. Cottraux, M.D., Ivan Note, M.D., Sainan Yao, M.D., Alain Sauteraud, M.D., Brigitte Note, M.A., Sylviane Lafont, M.A., Jean-Francois Dartigues, M.D.

NR647 Donepezil Improves Neuropsychiatric Symptoms in Moderate to Severe Alzheimer's Disease
Serge Gauthier, M.D., Howard Feldman, M.D., Jane Hecker, M.D., Bruno Vellas, M.D., Ponni Subbiah, M.D., Ed Whalen, Ph.D.

NR648 Paroxetine Versus Behavior Therapy in Triotillomania: Interim Results of a Pilot Study
Annett Neudecker, Iver E. Hand, M.D.

NR649 Computer-Assisted Cognitive Therapy for Depression
Jesse H. Wright, M.D., Andrew S. Wright, M.D., Aaron T. Beck, M.D., Paul Salmon, Ph.D., L. Jane Goldsmith, Ph.D. Jeffrey Kuykendall

NEW RESEARCH

Thursday, May 18, 2000, 9:00 a.m. - 10:30 a.m.

New Research 13 – Oral/Slide Session – Room E255, Level 2, McCormick Place Lakeside

SUBSTANCE ABUSE

Chp: William B. Lawson, M.D.

NR650	Point Prevalence of Hepatitis-C and Comorbid Psychiatric Diagnosis in the Baltimore VA Medical Center Peter Hauser, M.D., Jaswinder S. Khosla, M.D., Richard Calabria, M.A., Susan Reed, R.N., Naomi Tomoyasd, Ph.D.	9:00 a.m.
NR651	Outcomes of Experimental Cocaine Administration Igor Elman, M.D., Sara Krause, B.A., Katherine Karlsgodt, B.A., David R. Gastfriend, M.D.	9:15 a.m.
NR652	The Influence of Prior Major Depressive Episode on Sertraline Treatment Response in Premenstrual Dysphoric Disorder Kimberly A. Yonkers, M.D., Anna Stout, Ph.D., Grady Tanna, M.D., Teri B. Pearlstein, M.D., Andrea B. Stone, M.D., Jean Endicott, Ph.D., Ellen W. Freeman, Ph.D.	9:30 a.m.
NR653	Dually-Diagnosed Schizophrenia Patients Display More Craving Than Individuals with Cocaine Dependence Genata Carol, Ph.D., David A. Smelson, Psy.D., Claudia Gerigk, B.S., Miklos F. Losonczy, M.D., Douglas M. Ziedonis, M.D.	9:45 a.m.
NR654	Association of OPRMI +118A Allele with Alcoholism Patricia I. Ordorica, M.D., Terrance Town, M.S., Laila Abullah, B.S., John A. Schinka, Ph.D., James A. Mortimer, Ph.D., Amy B. Graves, Ph.D., Michael Mullan, M.D.	10:00 a.m.
NR655	Risk Factors for Substance Abuse in First-Episode Schizophrenia Patients Serge M. Sevy, M.D., Jose Alvir, D.Phil., Delbert G. Robinson, M.D., Margaret Woerner, Ph.D., Robert Goldman, Ph.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.	10:15 a.m.

NEW RESEARCH

Thursday, May 18, 2000, 9:00 a.m. - 10:30 a.m.

New Research 14 – Oral/Slide Session – Room E256, Level 2, McCormick Place Lakeside

PSYCHOPHARMACOLOGY

Chp: Carol A. Tamminga, M.D.

NR656	Maintained Efficacy of Paroxetine in the Treatment of Social Anxiety Disorder Tanya Hair, M.S.C., Rajinder Kumar, M.B., Timothy E. Rolfe	9:00 a.m.
NR657	Comparing Modafinil to Dextroamphetamine in the Treatment of Adult ADHD Fletcher B. Taylor III, M.D.	9:15 a.m.
NR658	Comparing Guanfacine and Dextroamphetamine for Adult ADHD: Efficacy and Implications Fletcher B. Taylor III, M.D., Joan Russo, Ph.D.	9:30 a.m.
NR659	SSRI and Benzodiazepine Treatment for Panic Andrew W. Goddard, M.D., Ahmad M. Almai, M.D., Praveen Jetty, M.D., Kathleen A. Morrissey, B.A., Katherine K. Shobe, Ph.D., Cathryn M. Clary, M.D., Dennis S. Charney, M.D.	9:45 a.m.
NR660	Antipsychotic-Related Change in Glucose Regulation John W. Newcomer, M.D., Angela K. Melson, M.A., Gregg Selke, B.A., Robert Fucetola, Ph.D., Julie A. Schweiger	10:00 a.m.
NR661	A Double-Blind, Placebo-Controlled Study of Naltrexone in the Treatment of Pathological Gambling Disorder Suck Won Kim, M.D., Jon E. Grant, M.D., David E. Adson, M.D., Young Chul Shin, M.D., Julie A. Toth, B.A.	10:15 a.m.

NEW RESEARCH

Thursday, May 18, 2000, 12 noon - 2:00 p.m.

New Research 15 – Poster Session – Hall E, Level 2, McCormick Place Lakeside

PSYCHOPHARMACOLOGY AND OTHER PSYCHIATRIC ISSUES

Moderator: Carol A. Tamminga, M.D.

NR662 BP-II With and Without Cyclothymic Temperament
Hagop S. Akiskal, M.D., Elie G. Hantouche, M.D., Jean-Francois Allilaire, M.D., Sylvie Lancrenon, Ph.D., Jean-Michel Azorin, M.D., Marc L. Bourgeois, M.D., Daniel Sechter, Liliane Chatenet-Duchene, M.D.

NR663 EPS Variations in the Elderly
Jacobo E. Mintzer, M.D., Paul P. Yeung, M.D., Jamie A. Mullen, M.D., Dennis Sweitzer, Ph.D.

NR664 The Influence of Personality Variables on Psychophysiological Responsivity Within a Startle Reflex Paradigm
Paul M. Ramirez, Ph.D., Vivian M. Mougios, M.A.

NR665 Bupropion Sustained Release for the Treatment of Hypoactive Sexual Desire Disorder in Nondepressed Women
R. Taylor Segraves, M.D., Harry A. Croft, M.D., Richard J. Kavoussi, M.D., John A. Ascher, M.D., Sharyn R. Batey, Pharm.D., Vicki J. foster, M.S., Carolym Bolden-Watson, Ph.D.

NR666 Reduced Cue-Elicited Cocaine Craving and Relapses
David A. Smelson, Psy.D., Jill Williams, M.D., Maureen Kaune, M.D., Jacqueline Constantino, M.D., Miklos F. Losonczy, M.D., Mathew Menzza, M.D., Douglas M. Ziedonis, M.D.

NR667 Efficacy and Safety of Once-Daily Methylpheniadate HCL, Standard Methylphenidate and Placebo in Children with ADHD
Laurence L. Greenhill, M.D.

NR668 A Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Paroxetine in the Treatment of Pathological Gambling Disorder
Suck Won Kim, M.D., Jon E. Grant, M.D., Young Chul Shin, M.D., Julie A. Toth, B.A., David E. Adson, M.D., Rocco M. Zaninelli, M.D.

NR669 Kinetics and Safety of a Novel Risperidone Depot
Marielle Eerdekens, M.D., Merete Rasmussen, M.S.C., An Vermeuzen, Ph.D., Richard Lowenthal, M.S.C., Achiel Vanpeer, Ph.D.

NR670 Adherence to Atypical Versus Typical Antipsychotic
Esperanza Diaz, M.D., Michelle C. Sullivan, B.S.N., Elizabeth Neuse, M.A., H. Rowland Pearsall, M.D., Keith A. Hawkins, Psy.D., Scott W. Woods, M.D.

NR671 Quetiapine Regulates Neuroprotective Genes
Ou Bai, Augusto Juorio, Rudy Bowen, M.D., David L. Keegan, M.D., Vern Bennett, M.D., Satish Shrinkhande, Xin-Min Li, M.D.

NR672 Modafinil Augmentation of Antidepressant Treatment in Depression
Matthew A. Menza, M.D., Kenneth R. Kaufman, M.D.

NR673 Cognitive Impairment Associated with Antidepressant Treatment
Stefano Pini, M.D., Isa Corradi, Ph.D., Concettina Mastrocinque, M.D., Ciro Conversano, Ph.D., Patrizia Panicucci, M.D. Liliana Dell'Osso, M.D., Giovanni B. Cassano, M.D.

NR674 Intranasal Sumatriptan for Post-ECT Headache
John S. Markowitz, Ph.D., Charles H. Kellner, M.D., C. Lindsay DeVane, Ph.D., Mark D. Beale, M.D., Jeffery W. Folk, M.D., Carol Burns, M.S.N.

NR675 Paroxetine: Preliminary Data on Breast Cancer Survivors
Vered Stearns, M.D., Claudine Isaacs, M.D., Julia Rowland, Ph.D., Jeanette Crawford, R.N., Matthew Ellis, Ph.D., Daniel P. Hayes, M.D., Katherine L. Beebe, Ph.D.

NR676 Effects of Nefazodone and Psychotherapy on Sleep Disturbance in Chronic Depression
Michael E. Thase, M.D., A. John Rush, M.D., Rachel E. Manber, Ph.D.

NR677 Mirtazapine in Relapse Prevention
Michael E. Thase, M.D., Andrew A. Nierenberg, M.D., Martin B. Keller, M.D., John Panagides, Ph.D.

NR678 Citalopram Treatment of Depressed Patients Discontinued from Fluoxetine Because of Adverse Events
Michael E. Thase, M.D., Peter D. Londborg, M.D., Joseph R. Calabrese, M.D.

NR679 Sidenafil for SRI-Associated Sexual Dysfunction: A Three-Center, Six-Week, Double-Blind, Placebo-Controlled Study in 90 Men
H. George Nurnberg, M.D., Alan J. Gelenberg, M.D., Maurizio Fava, M.D., Paula L. Hensley, M.D., John Lauriello, M.D., Wilma M. Harrison, M.D., Richard Siegel, M.D.

NR680 The Schizo-Obsessive Subtype of Schizophrenia
Roberto A. Dominguez, M.D., Karl E. Backman, M.D., Susana C. Lugo, M.D.

NR681 Novel Antipsychotics and Severe Hyperlipidemia
Jonathan M. Meyer, M.D.

NR682 Fluvoxamine for Obsessive-Compulsive Symptoms in Schizophrenia Patients
Michael Poyurovsky, M.D., Victoria Isakov, M.D., Sofia Hromnikov, M.D., Ilan I. Modai, M.D., Boris Rauchverger, M.D., Michael Schneidman, M.D., Abraham Weizman, M.D.

NR683 Fluvoxamine Treatment of Hypochondriasis
Altamash I. Qureshi, M.D., Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., J. Arturo Sanchez-Lacay, M.D.

NR684 Bupropion Sustained Release for SSRI-Induced Sexual Dysfunction: A Randomized Double-Blind, Placebo-Controlled, Parallel Group Study
Adam K. Ashton, M.D., Prakash S. Masand, M.D., Sanjay Gupta, M.D., Bradford L. Frank, M.D.

NR685 SSRIs and Ejaculation: A Double-Blind, Randomized, Comparative Fixed-Dose Study with Paroxetine and Citalopram
Marcel D. Waldinger, M.D., Aeilko Zwinderman, Ph.D., B. Olivier, Ph.D.

NR686 Duration of Side Effects and Changes in Brain Levels with Fluoxetine Discontinuation
Michael E. Henry, M.D., Constance M. Moore, M.D., Christina M. Demopulos, M.D., Janis Breeze, Gary S. Sachs, M.D., Eve P. Stoddard, B.A., Perry F. Renshaw, M.D.

NR687 Quetiapine in Psychotic Patients with Parkinson's Disease
Jorge L. Juncos, M.D., Matian L. Evatt, M.D., Rita D. Jewart, Ph.D., Vivki J. Roberts, Ph.D., Larry S. Potter, M.S., Hann-Chang Jou, Ph.D., Paul P. Yeung, M.D.

NR688 5HT Response to Quetiapine
Hugh M. Jones, M.R.C., Michael J. Travis, M.R.C., Rachel Mulligan, M.S.C., Ridrigo Bressan, M.D., Peter J. Ell, Ph.D., Robert W. Kerwin, D.Sc., Lyn S. Pilowsky, Ph.D.

NR689 The Effects of Reboxetine or Nafazodone on the Pharmacokinetics and Pharmacodynamics of Alprazolam
Y.W. Francis Lam, Pharm.D., Larry Ereshefsky, Pharm.D., Gregory B. Toney, Pharm.D., John P. Houston, M.D., Joseph C. Fleishaker, Ph.D., L. Haley Burgess, Pharm.D.

NR690 Incidence and Treatment of Side Effects with Clozapine Treatment: A Retrospective Study of 1,000 Patients After One Year of Clozapine Therapy
Michael J. Reinstein, M.D., Larissa A. Sirotovskaya, M.D., Maxim A. Chasanov, M.D., Lynne E. Jones, R.N., Shephali A. Patel, M.D., Sangarapillai C. Mohan, M.D.

NR691 The Impact of Dosing Regimen on Medication Compliance
Ami J. Claxton, Ph.D., Joyce Cramer, B.S., Courtney Pierce, B.A.

NR692 Risperidone Dosing Pattern Effectiveness: Indian Survey
Amresh K. Shrivastava, M.D., Sanjay Gupta, M.D., M. Srinivasa, M.D., Rajesh C. Maniar, M.D., Gpd Rao, M.D., Nilesh Shah, M.D.

NR693 A Naturalistic Study of Mirtazapine in the Chilean Psychiatric Practice
Sandra Kroeze, C. Fuenzalida, L. Plaza, J. Hernandez

NR694 Antipsychotic Treatment and Menstrual Irregularity
Ruta M. Nonacs, M.D., Mary H. Collins, M.D., Suzanne M. Bouffard, B.A., Lee S. Cohen, M.D.

NR695 Risperidone Treatment of Tourette's Syndrome: A Double-Blind, Placebo-Controlled Trial
Yves Dion, M.D., Lawrence Annable, Paul Sandor, M.D., Guy Chouinard, M.D.

NR696 Switching to Olanzapine in Patients with Antipsychotic-Induced Sexual Dysfunction: A Prospective and Naturalistic Study
Angel L. Montejo, M.D., Gines Llorca, M.D., Juan A. Izquierdo, M.D.

NR697 Switching to Nefazodone in Patients with Anitdepressant-Induced Sexual Dysfunction: A Six Month Prospective and Naturalistic Study
Angel L. Montejo, M.D., Gines Llorca, M.D., Juan A. Izquierdo, M.D., Fernando Rico-Villademoros, M.D., Margarita Garcia, M.D.

NR698 Early Reduction of Anxiety and Insomnia Symptoms in the Therapy of Depression
Thomas E. Schlaepfer, M.D., Lorenzo Hess, Ph.D., Hans U. Fisch, M.D.

NR699 Patterns of Antidepressant and Anxiolytic Usage
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NR700 The Effect of Risperidone on Serum Prolactin Concentrations
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NR701 Long-Term Treatment Outcomes of Depression/Anxiety
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NR702 Bupropion Sustained Release in the Treatment of Dysthymic Disorder
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NR703 Onset of Action of Mirtazapine on Anxiety Symptoms Related to Depression
Ilse Van Hensbeek, M.D., Albert J. Schutte, M.D., Paul D. Reimitz, Ph.D.

NR704 Onset of Action of Mirtazapine on Depression Related Symptoms: Factor Analysis of Pooled Data Mirtazapine Versus SSRIs
Albert J. Schutte, M.D., Ilse Van Hensbeek, M.D., Paul D. Reimitz, Ph.D.

NR705 Bupropion Sustained Release and Sleep in Depression
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NR706 Methylphenidate-Ethanol Interaction to Form Ethylphenidate
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NR707 Bupropion Sustained Release for SSRI-Resistant Major Depression
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NR709 Topiramate As an Anti-Obesity Agent
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NR711 Interchangeability of Clozapine Formulations in Stabilized Patients
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NR713 Open Study of Lamotrigine in Mood Disorder with Substance Use Comorbidity
Simon S. Chiu, M.D.

NR714 Comparison of Costs and Effects of Risperidone Treatment Versus Olanzapine Treatment in Daily Practice
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NR715 Nefazodone Improves Subjective Sleep Measures and Decreases the Use of Sleep Aids in Depressed Patients
Jose L. Ayuso, Ph.D., Julio B. Bobes, Ph.D., Juan Gibert, Ph.D., Maria P. Gonzalez, Ph.D., Jeronimo Saiz-Ruiz, M.D., Julio Vallejo, M.D., Fernando Rico-Villademoros, M.D.

NR716 Sexual Functioning in Depressed Patients Under Treatment with Nefazodone, Fluoxetine, Paroxetine and Venlafaxine: A Prospective Naturalistic Study Using the Changes in Sexual Functioning Questionnaire (CSFQ)
Julio B. Bobes, Ph.D., Maria P. Gonzalez, Ph.D., Maria T. Bascaran, M.D., Fernando Rico-Villademoros, M.D., Sebastian Banus, M.D., Margarita Garcia, M.D.

NR717 Risperidone and Olanzapine: Patterns of Use in a Veterans Administration System
John C. Voris, Pharm.D.

NR718 Six-Week, Double-Blind, Placebo-Controlled Trial of Bupropion Sustained Release in the Treatment of Adults with ADHD
Frederick W. Reimherr, M.D., Robert E. Strong, D.O., Barrie Marchant, M.S., Dawson W. Hedges, M.D., Erika Williams, M.S.W., Paul H. Wender, M.D.

NR719 Use of Atypical Neuroleptics in Younger Adults
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NR720 Efficacy of Mirtazapine in Stimulant-Associated Insomnia in Patients with ADHD
Lenard A. Adler, M.D., Lauren M. Braverman, B.A., David L. Ginsberg, M.D.

NR721 New Neuroleptics: An Eight-Year Naturalistic Study
Cheryl K. Cantrell, M.D., Eric S. Cole, Ph.D.

NR722 Double-Blind, Randomized, 28-Week Continuation Study of Sertraline and Placebo in PTSD
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NR723 Citalopram Pharmacokinetic Profile Is Unaffected by the CY3A4 Inhibitor Ketoconazole
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NR724 Validation of Antidepressant Utilization Rates in the Pacific Northwest
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NR725 Effectiveness of Using Templates to Comply with Medicare Regulations and Impact on Revenue
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NR726 Depot Antipsychotic Versus Oral Olanzapine Treatment
Linda S. Godleski, M.D., L. Jane Goldsmith, Ph.D., Nancy C. Zettwoch, R.N., Dejzi C. Stikovac, M.D., Susan J. Lewis, Ph.D.

NR727 Emotion-Focused Psychotherapy for Panic Disorder: A Randomized Controlled Trial
M. Katherine Shear, M.D., Ellen Frank, Ph.D., Kim Weiner, Ph.D., Patricia Houck, M.S., Sphia Masters, B.S., Catherine Greeno, Ph.D.

NR728 Relationships Between Creativity and Temperament in Bipolar Disorder Patients and Healthy Controls
Connie M. Strong, M.S., Claudia M. Santosa, M.A., Nadia Sachs, M.Eng., Courtney M. Rennicke, B.A., Po W. Wang, M.D., Anne-Marie Hier, M.S.W., Terence A. Ketter, M.D.

NR729 Aging and Creativity in Bipolar Disorders
Claudia M. Santosa, M.A., Nadia Sachs, M.Eng., Connie M. Strong, M.S., Courtney M. Rennicke, B.A., Anne-Marie Hier, M.S.W., Po W. Wang, M.D., Terence A. Ketter, M.D.

NR730 Prevalence of Depressive Disorders Among Women with Disability
Vincent A. Campbell, Ph.D., Daniel P. Chapman, Ph.D.

NR731 Benzodiazepine Discontinuation Program: Two-Year Follow-Up
Jaap E. Couvee, M.S.C., Manuela A. Timmermans, M.A., Frans G. Zitman, Ph.D.

NR732 Minority Patient Response to Physician Race and Nonverbal Behavior in Analogue Medical Encounters
Mara S. Arguette, Ph.D., Kimberly M. Collins, Carlos A. Roberts

NR733 Psychological Barriers As Predictors of Antidepressant Adherence
JoAnne Sirey, Ph.D., Martha L. Bruce, Ph.D., Barnett S. Meyers, M.D., George S. Alexopoulos, M.D.

NR734 The Doctor-Patient Relationship and the Willingness to Use Psychiatric Medications
Molly E. Tomlin, M.S., Jack K. Martin, Ph.D., Bernice A. Pescosolido, Ph.D., Thomas W. Croghan, M.D., Keri Lubell, M.S. Ralph W. Swindle, M.D.

NR735 DSM-IV Diagnoses and Data Deficiencies
Paul R. Miller, M.D.

NR736 Data Deficiencies and Diagnostic Inaccuracies
Paul R. Miller, M.D.

NR737 Bupropion Sustained Release in the Treatment of Stimulant Responsive Adolescents
James J. Hudziak, M.D., Thor C. Bergersen, M.D., Larry Rudiger, Ph.D., Ben Marte, M.D., G. Scott Waterman, M.D., Joan Kemsley, B.S.

NR738 Gaps in the Maintenance Antipsychotic Treatment of First-Admission Schizophrenia
Ramin Mojtabai, Ph.D., Evelyn Bromet, Ph.D., P. Joseph Gibson, Ph.D., Janet Lavelle, M.S., Nancy Sohler, M.P.H.

NR739 The S-Enatiomer of Citalopram (Lu 26-054): Cytochromes P450 Mediating Metabolism and Cytochrome Inhibitory Effects
David J. Greenblatt, M.D., Lisa L.G. Von Moltke, Richard I. Shader, M.D.

NR1 Monday, May 15, 9:00 a.m.–10:30 a.m.

Risperidone Versus Olanzapine in Patients with Schizophrenia and Schizoaffective Disorder

Robert R. Conley, M.D., *Spring Grove Hospital Grounds, Maryland Psychiatric Research Center, Maple and Locust Streets, p o box 21247, Baltimore, MD 21228*; Ramy A. Mahmoud, M.D.

Summary:

Background: A large double-blind trial compared risperidone (RIS) and olanzapine (OLA) at doses most frequently used in clinical practice.

Methods: A total of 407 adults at 41 sites received flexible doses of RIS (2–6 mg/day) or OLA (5–20 mg/day) for eight weeks. Assessments included PANSS, ESRS. Statistical testing was two-tailed. Two sites were excluded due to data quality concerns, leaving 377 patients for analysis. Data quality was verified by audit of every patient file.

Results: Mean modal doses were 4.8 mg/day RIS and 12.4 mg/day OLA. Both drugs were associated with significant and similar symptom improvement (total PANSS). Among patients completing eight weeks, there was significantly greater symptom improvement with RIS than OLA on PANSS scores for anxiety/depression ($p < 0.02$) and positive symptoms ($p < 0.05$). A greater number of RIS patients had positive symptom improvement (significant improvement level, $p < 0.03$). There were no significant differences in the improvement of extrapyramidal symptoms (total ESRS scores). OLA patients had significantly greater increases in mean body weight and BMI.

Conclusions: Patients treated with RIS or OLA had significant clinical improvement. Both drugs were generally well tolerated. This study suggests efficacy advantages for RIS for anxiety/depression and positive symptoms. With the exception of substantial weight gain among OLA patients, tolerability profiles were similar.

NR2 Monday, May 15, 9:00 a.m.–10:30 a.m.

An Open Trial of Mirtazapine in Menopausal Women with Depression Refractory to Estrogen-Replacement Therapy

Hadine Joffe, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114*; Heather L. Groninger, B.A., Claudio N. Soares, M.D., Lee S. Cohen, M.D.

Summary:

Methods: Perimenopausal and postmenopausal women aged 40–60 years treated with ERT for ≥ 2 months were eligible if they met DSM-IV criteria for major depressive disorder (MDD) and had a baseline Hamilton Depression Rating Scale (HDRS) score ≥ 17. All subjects (n = 20) were treated with mirtazapine 30–45 mg/day in an eight-week, open-label trial. Mood was assessed every two weeks with the 17-item HDRS. Remission of MDD was defined as HDRS score ≤ 8 at the end of the study.

Results: The median age of the subjects was 51 years (range 43–56 years). A total of 50% were perimenopausal, 35% were naturally postmenopausal, and 15% were surgically postmenopausal. Median duration of ERT use was 3.5 years (range 0.25–14 years) and the median duration of the current depression episode was two years (range one month-five years). In 35% of subjects, depression developed before ERT was started and did not improve with ERT use. The median 17-item HDRS changed from 21.5 (range 12–37) at baseline to 2 (range 0–9) at end of treatment ($z = -3.63$, $p < 0.001$). By the fourth week, 82.4% of subjects had full remission of MDD (HDRS ≤ 8), a response rate that was sustained at the end of the study. Among those whose depression predated ERT use, 75% demonstrated full remission of MDD. No differences in response rates were noted in women whose depression started either before or after initiation of ERT, or in perimenopausal versus postmenopausal women. Mirtazapine was well tolerated and safely used in middle-aged women on ERT. The average weight gain was 4.3 ± 4.0 pounds. Five (25%) subjects discontinued treatment due to adverse events (three for sedation, one for appetite stimulation, and one for nausea).

Conclusion: This preliminary study suggests that mirtazapine is an effective antidepressant in menopausal women with depression refractory to treatment with ERT.

NR3 Monday, May 15, 9:00 a.m.–10:30 a.m.

The Use of Intravenous Burprenorphine in the Treatment of Opioid Withdrawal in Medically Ill, Hospitalized Heroin-Addicted Patients

Christopher J. Welsh, M.D., *Department of Psychiatry, University of Maryland, 22 South Green Street, P1H01 Box 349, Baltimore, MD 21201*; Meenakshi Suman, M.S., Art Cohen, B.S., Eric Weintraub, M.D., Lauren Matukaitis, R.N.

Summary:

Objective: Though buprenorphine is used sublingually and intramuscularly in the treatment of opioid withdrawal, there are no reports of its use intravenously. The purpose of this study was to assess the safety of buprenorphine administered intravenously for the treatment of opioid withdrawal in medically ill hospitalized patients.

Methods: A chart review was conducted on 30 patients who received buprenorphine intravenously (0.3–0.9 mg q 6–12 hours) during their hospitalization for an acute medical problem. Discharge summaries, addiction consultation notes, medication records, and vital sign flow sheets were reviewed for each patient.

Results: The 30 patients (14 males, 16 females) received a total of 228 doses (average 7.8/patient; range 1–21) of buprenorphine intravenously. No respiratory depression was observed. No patients reported feeling "high." Seventeen patients reported some sedation following some of their doses. All patients reported that buprenorphine helped withdrawal symptoms. One patient asked to be switched to intramuscular because she felt that the effects did not last as long following intravenous administration.

Conclusions: Intravenous administration of buprenorphine appears to be safe for the treatment of opioid withdrawal in medically ill hospitalized patients. Further research is needed to determine optimal dosing strategies, effect of patient pain on dosing, and efficacy compared with intramuscular administration.

NR4 Monday, May 15, 9:00 a.m.–10:30 a.m.

Substance Abuse Patterns in Pregnant Women

Anjali M. Gupta, M.D., *MHCC, VA Medical Center, 10 North Greene Street, Baltimore, MD 21201*; Eric Weintraub, M.D., Janine C. Delahanty, M.A., Christopher J. Welsh, M.D., Lisa B. Dixon, M.D.

Summary:

Objective: The purpose of this study was to examine the demographic characteristics and substance abuse patterns of pregnant women on an inpatient substance abuse consultation service.

Methods: A consult summary form was used to evaluate patients seen by the alcohol and drug consultation service between 1993 and 1998. Pregnant women (N = 1408) were compared on race, drugs used, and HIV status with a control group of nonpregnant women (N = 3311) on the consult service. The age of the nonpregnant women was restricted to 18–44 similar to the pregnant women, and age was controlled.

Results: Women using drugs during pregnancy were less likely to be Caucasian (10.9% vs. 20.4% P = .001), less likely to be HIV positive (13.5% vs. 49.2% P = .001), and less likely to be

injection drug users (13.5% vs. 49.0% P = .001). The percentage of women using alcohol, cocaine, heroin, or any combination of these was lower in the pregnant women (P = .001), whereas the percentage using marijuana was increased (P = .001).

Conclusion: This study suggests reduced severity of substance abuse among pregnant women. Perhaps pregnant women are in an earlier stage of addiction. If this is true, treatment may be beneficial in preventing the development of severe addictive problems in the future. More studies are needed to further explore the factors that may lead to these differences.

NR5 Monday, May 15, 9:00 a.m.–10:30 a.m.

Rapid Opiate Withdrawal with Anesthesia Compared with Rapid Detoxification Using Buprenorphine: A Controlled Trial

Norbert Scherbaum, M.D., *Department of Psychiatry, University of Essen, Virchowstr 174, Essen 45147, Germany*; Johannes Nebe, M.D., Anne Heringhaus, M.D., Susanne Klein, M.D., Peter Kienbaum, M.D., Juergen Peters, M.D., Markus Gastpar, M.D.

Summary:

Objective: Comparative evaluation of two methods for rapid opiate detoxification.

Methods: Open, randomized, controlled study in an inpatient setting of a university hospital.

Participants: 44 mono-opiate addicts in methadone substitution (16 female, 28 male; on average 28 years old with seven years of opiate dependence). Exclusion: Somatic diseases associated with an increased anesthetic risk or interfering with the measurement of withdrawal symptoms.

Interventions: (a) Rapid opiate detoxification with anesthesia (ROD): during a general anesthesia lasting approx. six hours, naloxone was administered in bolus doses, starting with 0.4 mg and doubling the dose every quarter of an hour up to a total dose of 12.4 mg within 60 minutes, followed by a naloxone infusion of 0.8 mg/h until next morning. Naltrexone (50 mg/d) treatment was initiated a few hours after anesthesia. (b) Rapid opiate detoxification using buprenorphine (BUP): abrupt discontinuation of methadone substitution was followed by induction of buprenorphine (daily dose 3 or 6 mg/d depending on previous methadone dosage). Buprenorphine was administered in a fixed dose for five days, and then abruptly discontinued. Both groups: In case of withdrawal symptoms, specific medication was added.

Main outcome criteria: Duration and intensity of withdrawal symptoms (pretreatment and for four weeks from detoxification, using established clinical scales).

Results: Intensity of withdrawal symptoms was significantly ($p < 0.05$) elevated in ROD group in comparison with the BUP group on days 1 to 5. Dropout during the first two weeks: five ROD patients vs. nine BUP patients. No serious medical complications in both groups.

Conclusion: Because of smaller efforts for coordination, lower costs, and fewer contraindications the BUP method seem to be more promising than ROD.

NR6 Monday, May 15, 9:00 a.m.–10:30 a.m.

Morbidity of Lung and Liver Pathology in Heroin-Addicted Patients

Dadane Hawari, Ph.D., *Department of Psychiatry, University of Indonesia—Medical School, 6 Salemba Raya, Jakarta 10430, Indonesia*

Summary:

Scope and Method: The study was done on 196 patients who were diagnosed as having heroin addiction. Sample was collected by *purposive*. Diagnosis was made by psychiatric clinical examination and supported by urine test. Every patient was re-examined by internist and completed with lung X-ray and liver function laboratory test.

Objectives: The purpose of the study was find out the morbidity of lung and liver pathology on heroin-addicted patients.

Result and Conclusions: From the examination of 196 patients, 105 cases had pathologies on their lung (53.57%), which included 66 cases bronchitis (33.67%), 38 cases bronchopneumonia (19.38%), and one case of lung fibrosis (0.51%); 108 cases had liver pathology based on increase of SGOT and SGPT (55.10%), which consisted of 72 cases categorized as mild (36.73%), 20 cases moderate (10.21%), right cases severe (4.08%), and eight cases very severe (4.08%); 110 cases hepatitis C (56.56%). From this study we concluded that on heroin-addicted patients there were pathology on lung (53.67%), liver (55.10%), and hepatitis C (55.56%).

NR7 Monday, May 15, 9:00 a.m.–10:30 a.m.

Effects of Fluoxetine in Alcohol Withdrawal and Allopregnanolone Plasma Levels

Flavia Di Michele, M.D., *Brain Research Department, NYU Medical Center, 550 First Avenue, New York, NY 10016*; Elena Romeo, M.D., Rainer Rupprech, M.D., Veska Uzunova, Ph.D., Augusto Pasini, M.D.

Summary:

Recently, it has been hypothesized that the potent $GABA_A$ receptors active neurosteroid allopregnanolone (ALLO) may contribute to behavioral effects of ethanol. The purpose of this study was to investigate the effect of fluoxetine (F) and indomethacin (I), two drugs that regulate the ALLO synthesis by acting on the rate-limiting enzyme 3α-HSOR, on ALLO plasma levels and on symptoms of anxiety and depression in alcoholics during withdrawal.

Method: Patients who met DSM-III-R criteria for alcohol abuse were randomly assigned to treatment with F (40mg/day) or I (100mg/day) or placebo (P), were evaluated with the Hamilton Anxiety and Depression Scales on days 1, 5, 7, 15, 28 of withdrawal, and with a Visual Analogue Scale for Anxiety/Depression on days 1, 2, 3, 4, 5, 7, 15, 28. On the same days a plasma sample collected to measure ALLO levels by means of a sensitive gas-chromatographic/mass-spectrometric method.

Results: In early withdrawal days (1–5) ALLO levels were lower and symptoms of anxiety and depression were higher compared with the late withdrawal phase (days 15, 28). In the F and I treatment, depression and anxiety scores decreased markedly at days 5–7, and contemporarily ALLO levels significantly increased compared to P condition.

Conclusion: Treatment of alcohol withdrawal with F or I significantly reduced the extent of symptomatology and speeded up the recovery of ALLO normal levels compared with P.

NR8 Monday, May 15, 9:00 a.m.–10:30 a.m.

Basal Ganglia Morphometry in OCD

Justin R. Covey, B.A., *NIMH/LCS, National Institute of Health, 10 Center Dr. MSC-1264 Rm-3D41, Bethesda, MD 20892-1264*; Benjamin D. Greenberg, M.D., Jay N. Giedd, M.D., Vit Herynek, M.D., Gabriela Cora-Locatelli, M.D., John C. Keel, B.A., Dennis L. Murphy, M.D.

Summary:

Obsessive-compulsive disorder may involve basal ganglia dysfunction. In a prior study (Greenberg et al., in preparation) we found basal ganglia abnormalities on MRI relaxometry, in a pattern most consistent with excess hemosiderin deposition, in 35 adult OCD patients and 36 matched volunteers. T2 values were most

abnormal in the right globus pallidus. In this subsequent study, we assessed basal ganglia volumes in the same sample of patients and volunteers. Volumes for the basal ganglia were determined interactively on coronal MRI images in which each structure was visible by a single-blind rater. Although volumes in all three structures tended to be lower in patients than in volunteers, the differences did not reach significance. Basal ganglia volumes also did not differ between never-medicated patients and those treated with antidepressants or neuroleptics, those with childhood or adult OCD onset, or those with or without tics. These findings may indicate that such techniques are relatively insensitive to focal abnormalities in the basal ganglia in OCD compared with other imaging techniques such as MRI relaxometry and spectroscopy. However, the sample size in our study may have obscured significant differences across subgroups tested. Exploratory analyses of possible volumetric differences in other brain regions are under way.

NR9 Monday, May 15, 9:00 a.m.–10:30 a.m.

Carbon-Dioxide-Induced Panic Disorders

Alexandre M. Valenca, M.D., *Department of Psychiatry, University Feder Rio Janeiro, Hadock Lobo 53, Apto1001, Rio de Janeiro, RJ 20260-130, Brazil*; Antonio E. Nardi, M.D., Isabella Nascimento, M.D., Walter A. Zin, M.D., Marco A. Mezzasalma, M.D., Fabiana L. Lopes, M.D.

Summary:

Objective: Determine if an acute dose of clonazepam-2mg-attenuates the panic attacks induced by an inhalacion of 35% carbon dioxide in panic disorder.

Method: We selected twenty-two panic disorder subjects, using the Structured Clinical interview for DSM-IV. All the subjects were randomly assigned to either pretreatment with a tablet of clonazepam (2 mg) or placebo, double blindly one hour prior to a carbon dioxide challenge test. Patients received both 35% CO2 and atmospheric compressed air 20 minutes apart under double-blind conditions. Two investigators should agree about the diagnosis of a panic attack.

Results: In the clonazepam group (n = 11) two patients (18.2%) had a mild panic attack in the CO2 challenge test. In the placebo group (n = 11) nine patients (81.8%) had a moderate to severe panic attack (McNemar's Test with Yates correction, chi-square = 7.111, df = 1, $p < 0.01$) also in the CO2 challenge test.

Conclusion: Although in a small sample, this study suggest the efficacy of an acute dose of clonazepam in attenuating panic attacks induced by carbon dioxide inhalation. Carbon dioxide panic-provoking challenges might be useful tools for screening antipanic properties of psychotropic drugs.

NR10 Monday, May 15, 9:00 a.m.–10:30 a.m.

Initial Symptom Manifestations After Severe Injury and Subsequent PTSD

Karin F. Esposito, M.D., *Psychiatry, University of Miami, 1400 NW 10th Avenue #304A, Miami, FL 33136*; Daniella David, M.D., Victoria Bustamante, Psy.D., Thomas A. Mellman, M.D.

Summary:

Background: The need to identify individuals at risk for PTSD early led to the designation of ASD with criteria based on observations relating early dissociative reactions and subsequent PTSD. We assessed ASD and PTSD symptoms following severe injury at baseline and six weeks and evaluated the relationship between early symptomatology and PTSD status.

Methods: Seventy subjects (ages 18–60) testing negative for substance use and having total recall of the trauma, no current psychiatric diagnosis, no loss of consciousness, and a Glasgow Coma Scale score of 15 on admission were recruited from a Level 1 trauma center. PTSD and ASD were assessed using the Clinician-Administered PTSD Scale for DSM-IV (CAPS-SX). Subjects completed measures of initial reactions to trauma. Baseline assessment was completed an average of 10.9 ± 12.8 days post-trauma. Forty-four subjects were available at six week follow-up.

Results: At baseline, seven subjects (10%) met criteria for ASD. However, 33 subjects (47%) exhibited PTSD symptoms; 14 met full symptom (not duration) criteria and 19 met subthreshold (two of three symptom clusters positive) criteria. At follow-up, 43% of subjects were symptomatic (n = 10) with full criteria and n = 9 with subthreshold criteria for PTSD). Five of those symptomatic at follow-up had not been symptomatic at baseline, and of those symptomatic at baseline, seven had recovered, including four of six who initially met criteria for ASD. Baseline CAPS score was significantly correlated with PTSD severity at six weeks ($r = 0.38$, $p = 0.01$). There was no significant relationship between peritraumatic dissociation and PTSD.

Conclusions: In our subjects ASD occurred at a low frequency. Initial severity of PTSD symptoms, not a diagnosis of ASD, was predictive of subsequent PTSD.

NR11 Monday, May 15, 9:00 a.m.–10:30 a.m.

Obsessional Slowness in OCD and Tourette's Syndrome

Karen Vemura, *Department of Psychiatry, Psychiatric Institute, R DK Ovideo Pires de Campos SN, Sao Paulo, SP 05403-010, Brazil*; Ana G. Hounie, M.D., Cara Moretti, Raquel C. Valle, Michael A. Jenike, M.D., Euripedes C. Miguel, M.D.

Summary:

Background: Rachman (1974) conceptualized "primary obsessional slowness" (POS) to describe 10 patients with OCD who exhibited handicapping slowness that was not related to OC symptoms. There is evidence that OCD and Tourette's syndrome (TS) are related. Hymas (1991) found 17 of 59 inpatients with significant slowness, two of them with TS.

Methods: Twenty outpatients with OCD and 20 with OCD + TS were studied. SCID-IV, Y-BOCS, Beck Depression Inventory, Hymas questionnaire, and the slowness component of the Maudsley Obsessional—Compulsive Inventory were used.

Results: None of the patients studied scored above 30 on the Hymas questionnaire, the established criterion for POS. Eighty percent of the patients reported their slowness as secondary to OC rituals. There was no statistically significant difference between the groups according to the scales used.

Conclusion: We found no case of slowness as a primary problem. In our sample, the presence of slowness was not related to TS. It's possible that our patients were less severe and therefore not included Rachman's POS, what seems to be a very rare syndrome. Slowness can be secondary to the severity of OC symptoms, constituting a covert ritual without repetitiveness.

NR12 Monday, May 15, 9:00 a.m.–10:30 a.m.

Hyperventilation Test in Patients with Panic Disorder

Isabella Nascimento, M.D., *Department of Psychiatry, Federal University Rio Janiero, Guimaraes Rosa 203, Apto 305, Rio De Janeiro, RJ 20260-130, Brazil*; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Walter A. Zin, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D.

Summary:

The aim was to observe the induction of panic attacks by hyperventilation in a group of panic disorder and social phobia patients (DSM-IV) in comparison with normal volunteers. We randomly

selected 26 panic disorder and 22 social phobic patients in the Laboratory of Panic & Respiration of Brazil. They were free of psychotropic drugs for one week. A comparison group consisted of 25 subjects. They were free of any lifetime history of psychiatric disorder. The subjects were induced to hyperventilate (30 breaths/min) for three minutes. They completed before and after hyperventilating the Subjective Units of Disturbance Scale (SUDS) and the Diagnostic Symptom Questionnaire (DSQ) adapted for DSM-IV. A total of 61.5% (n = 16) panic disorder patients, 22.7% (n = 5) social phobics, and 4.0% (n = 1) of control subjects had a panic attack after hyperventilating ($p < 0.01$, panic disorder vs control; $p < 0.05$, panic disorder vs social phobia; and p = ns, social phobia vs control). Both anxiety disorder group were more sensitive to hyperventilation than normal volunteers. The induction of panic attacks by hyperventilation may be an easy and useful test for validating the diagnosis in some specific panic patients.

NR13 Monday, May 15, 9:00 a.m.–10:30 a.m.

Cigarette Smoking and Anxiety

Isabella Nascimento, M.D., *Department of Psychiatry, Federal University Rio Janiero, Guimaraes Rosa 203, Apto 305, Rio De Janiero, RJ 20260-130, Brazil*; Alexandre M. Valenca, M.D., Antonio E. Nardi, M.D., Walter A. Zin,, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Ivan L. V. Figueira, M.D.

Summary:

The objectives were to observe the frequency of cigarette smoking, the attempts at cigarette quitting, and the rate of nicotine withdrawal symptoms in outpatients of an anxiety unit. A total of 251 subjects answered a questionnaire about smoking habits. The patients' diagnoses were: 31% (n = 78) depressive disorders; 22% (n = 54) panic disorder; 15% (n = 38) social phobia; 24% (n = 61) comorbidity disorders, and 8% (n = 20) other anxiety disorders. A total of 27.5% were smokers; 23.5% were former smokers, and 49% were nonsmokers; 15.7% (n = 17) of the sample reported nicotine-withdrawal symptoms. Social phobic patients (75%) were considered the heaviest smokers of the sample (more than 11 cigarette/day). The failure rate of cigarette quitting (88%) was also higher in social phobic patients, suggesting a higher nicotine dependence in this group.

NR14 Monday, May 15, 9:00 a.m.–10:30 a.m.

Electroretinography and Panic Treatment

Fulvio Pieraccini, M.D., *Department of Psychiatry, University of Siena, Viale Bracci #1, Siena 53100, Italy*; Sonia Iapichnio, M.D., Claudia Pacchierotti, M.D., Lettzia Bossini, M.D., Elisabetta Truglia, M.D., Paolo Castrogiovanni, M.D.

Summary:

In a recent study we have suggested that a deficient adaptation of light stimulation in panic patients is probably mediated by a dysfunction in dopaminergic system (Bassi & Powers, 1986), measured using the b-wave electroretinography (ERG): the panic patients showed a significantly lower b-wave ERG than control subjects (Pieraccini and Coll., 1998).

The present experiment was designed to examine the possible effects on the amplitude of b-wave-ERG induced in clinical sample after six mounths of therapy. We studied 30 patient with panic disorder (without lifetime and intraepisodic psychiatric comorbidity) with ERG pre- and post-panic treatment.

All patients showed a consistent improvement of a clinical feature after six months of antipanic treatment. There was no significant variability in amplitude b-wave ERG between the pre- and post- treatment. It will be important to determine whether the retinal activity in panic patients is state or trait dependent.

NR15 Monday, May 15, 9:00 a.m.–10:30 a.m.

Panic-Agoraphobic Spectrum in Bipolar Disorder

Fulvio Pieraccini, M.D., *Department of Psychiatry, University of Siena, Viale Bracci #1, Siena 53100, Italy*; Sonia Iapichino, M.D., Lettzia Bossini, M.D., Claudia Pacchierotti, M.D., Florinda Morana, M.D., Paolo Castrogiovanni, M.D.,

Summary:

In the literature there's evidence for a frequent comorbidity (20.8% to 36.8%) between panic disorder (DP) and bipolar disorder (DB) (Cassano and Coll., 1989). At present there are no studies about the presence of subthreshold symptoms of the panic-agoraphobic spectrum in patients with DB. Our study was undertaken to confirm the data in literature about comorbidity between DP and DB and to evaluate the dimensions of panic-agoraphobic spectrum in the bipolar patients.

Method: We recruited 50 bipolar outpatients and 50 healthy subjects for the study. The bipolar and the control subjects were assessed with the Italian version the of Structured Clinical Interview of Panic Agoraphobic Spectrum (SCI-PAS) (Cassano and Coll., 1997).

Results: The data analysis in bipolar patients show positivity for the dimensions "Panic's Symptoms" (80%), "Separation's Anxiety" (76%), and "Reassurance" than in control subjects. The high prevalence of subthreshold symptoms in the sample with DB is not surprising in the light of well-known comorbidity between the two disorders, not only between the form to expression full symptomatology.

NR16 Monday, May 15, 9:00 a.m.–10:30 a.m.

An Epidemic of Phobic Disorders in Brazil? Results from a Population-Based, Cross-Sectional Survey

Wanderlei R. Motta, M.D., *Department of Psychiatry, UFPEL, Goncalves Chaves 962-404, Pelotas, RS 96015-560, Brazil*; Mauricio S. Lima, Ph.D., Bernardo G.O. Soares, M.D., Nina R.D. Paixao, M.P.H., Ellis D. Busnello, M.D.

Summary:

Objectives: To discuss a high prevalence of phobic disorders found in a Brazilian population-based survey.

Methods: A representative sample of the urban population of Pelotas, Southern Brasil, was obtained using multistage random sampling. The survey was conducted in two stages. First, the Self-Reported Questionnaire (SRQ-20) was used. Subsequently, a subsample (2/3 of SRQ-20 positives and 10% of the negative ones) was interviewed through the DSM-III-R checklist. Weighted prevalences of mental disorders were obtained for lifetime, one-year, and one-month periods.

Results: 1277 subjects were interviewed in the first stage (9.3% of refusals); 273 subjects (63% females) were included in the subsample. For most of the mental disorders, the prevalences were similar to those reported in Brazilian and international surveys. However, a high prevalence of phobic disorders in the last month was found, particularly for simple phobia: 30.7%. The prevalences for agoraphobia (3.7%) and social phobia (11%) were also high.

Discussion: Information bias can explain these findings. The DSM-III-R checklist, used in this survey as gold standard, seems to be accurate for more specific diagnosis, like schizophrenia. However, it may lack a clear distinction between common and self-limited symptoms, which is essential for assessing the frequency of nonpsychotic disorders in the general population.

NR17 Monday, May 15, 9:00 a.m.–10:30 a.m.

Bupropion Treatment of Civilian PTSD

Ahmad M. Almai, M.D., *Department of Psychiatry, Yale University, 471 Goshen Road, Litchfield, CT 06759*; Thomas E. Brouette, M.D., Andrew W. Goddard, M.D.

Summary:

Pharmacotherapies for PTSD presently include antidepressants (tricyclics, MAOIs, and SSRIs), anxiolytics, and mood stabilizers. However, the use of these medications is limited due to side effects, dietary restrictions, and partial response especially by the core symptoms of PTSD. Therefore, finding more effective treatments for this condition remains a clinical challenge. Neurobiological studies of PTSD patients have implicated norepinephrine (NE) system hyperactivity in the pathophysiology of the disorder. Thus, treatments that modulate NE system function could theoretically contribute to clinical improvement of PTSD. The atypical antidepressant bupropion may decrease locus cerulus/NE neuronal activity with chronic administration, and via this mechanism, could alleviate PTSD symptomatology.

Methods: We are conducting a 10-week, open-label trial of bupropion (target dose = 300mg/d) for civilians with chronic PTSD. Clinical responses are assessed by serial administration of behavioral ratings including CAPS, PCL-C, HAM-A, HAM-D, and CGI-improvement. Patients are considered responders at end point if they have at least a 30% decrease in their CAPS score from baseline or have a CGI-improvement score of at least 2 (much improved).

Results: So far 8/9 patients have met responder criteria. The medication has been well tolerated.

Conclusion: Bupropion shows promise as a potential treatment of chronic civilian PTSD.

If more data confirm this early impression, controlled clinical trials of bupropion in chronic PTSD would be indicated.

NR18 Monday, May 15, 9:00 a.m.–10:30 a.m.

Dialectical Behavior Therapy Adapted for Bulimia Nervosa

Debra L. Safer, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5722*; Christy F. Telch, Ph.D., W. Stewart Agras, M.D.

Summary:

Objective: To describe the preliminary results of a 20-week randomized clinical trial comparing Linehan's dialectical behavior therapy (DBT) adapted for binge and purge behavior to a wait-list control group.

Method: 31 adult women who averaged one or more binge and purge episodes per week for the preceding three months were recruited from a behavior clinic or by advertisement. Subjects were randomly assigned to 20 weeks of DBT therapy or 20 weeks of a wait list (followed by 20 weeks of DBT therapy). The treatment, which followed a manual, focused on emotion regulation skills training. Outcome measures included: 1.) Eating Disorders Examination, 2.) Back Depression Inventory, 3.) Attitudes Toward Feelings Scale, 4.) Emotional Eating Scale, 5.) Minnesota Impulsivity Scale, 6.) Positive and Negative Affect Schedule, 7.) Rosenberg Self-Esteem Scale. Follow-up assessments at three, six, and 12 months are in progress.

Results: The major finding from the first 17 subjects was a highly significant decrease in binge/purge behavior with DBT ($p < .005$) compared with no significant change for wait-list controls ($p = .48$). By the end of the 20 weeks of therapy, 43% of the treatment subjects were abstinent from binge eating and 29% stopped purging.

Conclusion: A 20-week manualized treatment adapting DBT results in highly significant decreases in binge/purge behavior compared to wait-list controls.

NR19 Monday, May 15, 9:00 a.m.–10:30 a.m.

Teasing History in Women with Bulimia Nervosa and Binge Eating Disorder

Tamara D. Jackson, Ph.D., *Yale University, Department of Psychiatry, 184 Liberty Street, New Haven, CT 06519*; Carlos M. Grilo, Ph.D., Robin M. Masheb, Ph.D.

Summary:

Objective: To examine associations among teasing history and current eating-related psychopathology and psychological functioning in outpatients with bulimia nervosa (BN) and binge eating disorder (BED).

Method: Subjects were 79 female adults who met DSM-IV criteria for BN (n = 47) or BED (n = 32). The 32 BED patients were selected from a larger BED cohort and matched to BN patients on age and body mass index. A battery of psychometrically established self-report instruments was administered to assess physical-appearance related teasing history (general appearance (GAT) and weight and size (WST) teasing), current eating-related psychopathology (eating restraint, concerns regarding eating, shape and weight), and psychological functioning (depression and self-esteem).

Results: BN patients reported more WST than BED patients, but the groups did not differ significantly in GAT. For BN patients, GAT was negatively associated with self-esteem and positively associated with depression, whereas WST was positively associated with frequency of binge eating and vomiting and negatively associated with self-esteem. For BED patients, GAT was positively associated with depression and eating restraint, but WST was not significantly associated with any of the variables.

Discussion: The association of general appearance (GAT) and weight and size teasing (WST) to current eating-related psychopathology and associated psychological functioning differed for patients with BN and BED. The findings suggest that WST may serve as risk factor for binge eating and vomiting in women with BN. History of GAT may be a risk factor for depression in women with BN and BED.

NR20 Monday, May 15, 9:00 a.m.–10:30 a.m.

Eating Disorders and Comorbidity

Fabiana L. Lopes, M.D., *Institute of Psychiatry, University FED Rio de Janiro, Min Octavio Kelly 467, AP1204-B, Niteroi, RJ 24220-300, Brazil*; Antonio E. Nardi, M.D., Jose C. Appolinario, M.D., Walmir Coutinho, M.D., L.C. Povoa, M.D.

Summary:

Objective: Investigate the relationship between comorbidity of psychiatric disorders and pathological eating behavior among obese, depressive and Social phobic patients.

Method: We randomly selected patients from the Institute of Psychiatry, Rio de Janeiro, before drug treatment, who fulfilled the SCID-I (DSM-IV) diagnoses for depression and social phobia. In the same way we applied the SCID-I to obese subjects from a eating disorder unit. The diagnoses were compared with a group control without any psychiatric diagnoses. All the sample answered the Questionnaire of Eating and Weight Patterns-Revised (QEWP-R) as part of their assessment.

Results: 148 subjects were selected: 31 major depressive, 37 social phobic, 31 obese outpatients, and 49 healthy controls. There was a high prevalence of ginge eating disorder (BED) as a comorbidity in the group of obese (19, 4%). Depressive (12.8%) and social phobic patients (10.8%), compared with the control

group (2.0%). The abnormal eating pattern was considered in the spectrum concept of BED.

Conclusion: These data suggest that pathological eating patterns are very frequent in depressive and social phobic patients. Binge eating syndrome has an important role in the clinical picture and treatment of major depression, social phobia, and obesity disorders.

NR21 Monday, May 15, 9:00 a.m.–10:30 a.m.

Anorexia Nervosa in the Turkish Culture

Emine N. Iscan, M.D., *Department of Psychiatry, Boston University, 751 Lansdowne Way, #T2, Norwood, MA 02062*

Summary:

Objective: Considering the historical data and the original descriptions, it is possible to view eating disorders as originally Western illnesses, which in decades spread to non-Western cultures via acculturation and assimilation. This paper reports six Turkish in patients with anorexia nervosa in an attempt to demonstrate the differences in clinical presentations of anorexia nervosa and discuss these cases within the concept of culture-bound syndromes.

Method: The patients were referred to SSK Ankara Training Hospital between 1992–1996, for further psychiatric evaluation. The patients were evaluated initially in the outpatient clinic and then assigned to clinicians for treatment and management. All of them were diagnosed with anorexia nervosa according to DSM-III-R.

Results: Five of the patients were single girls aged 17 to 24. Only one was married. Four out of six were from low socioeconomic levels, and three of those had only completed 5th grade. Three of these cases were high school graduate and two of them were from middle class families, where both parents were educated and worked. They lived in rather small cities in Turkey with the exception of one case, who lived in a suburb in Ankara. All cases carried a diagnosis of anorexia nervosa, binge eating/purging type. Their body mass index ranged from 11.8 to 16.6. Although all of them came from traditional Turkish families, those from middle-class families showed adoption of Western values as well as disturbed body image and pursuit of thinness.

Conclusions: This paper demonstrates that anorexia nervosa exists in Turkish culture and most importantly these patients have different presentations when compared to their Western counterparts. It appears that each culture has a different threshold with regards to emergence of eating disorder symptomatology as well as eating patterns, body perception, and satisfaction. These are influenced by many factors including media, assimilation of Western values and globalization.

NR22 Monday, May 15, 9:00 a.m.–10:30 a.m.

Neurophysiologic Prediction of ECT Response

William F. Stubbeman, M.D., *Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Box 17, Los Angeles, CA 90024*; Andrew F. Leuchter, M.D., Ibrahim Gunay, M.D., Ian A. Cook, M.D., Julie E. King, R.N., Brett Shurman, M.D., Sergio Gonzales, B.S.

Summary:

Objective: Recent brain imaging studies have indicated that right dorsolateral prefrontal cortex (RDLPFC) and right inferior parietal cortex (RIPC), structures involved in attentional processing, may play a role in the pathophysiology of depression. This study tested the hypothesis that decreased neurophysiologic activity in these brain regions after an electroconvulsive therapy (ECT) treatment is necessary for therapeutic response.

Method: Ten patients with unipolar or bipolar depression had Hamilton Depression Rating Scales (HAM-D's) at baseline and at set intervals during and following ECT treatment. One day before and after their first treatment, patients received a resting, eyes-closed, 35-lead quantitative EEG (QEEG) recording. Data were analyzed using QEEG cordance, a measure of brain electrical activity correlated with cortical perfusion. Cordance is the sum of z-transformed absolute and relative power.

Results: Average decreased theta-band cordance of > .75 standard deviations over RDLPFC (F8 electrode) and RIPC (T6 electrode) correctly predicted all responders (defined by 50% decrease in HAM-D) and excluded all non-responders ($N = 10$, $p = .03$). Cordance change in these electrodes following the first treatment also predicted HAM-D score decrease over the first five (minimum number for all subjects) ECT treatments ($r = .73$, $N = 10$, $p = .01$).

Conclusion: After the first ECT treatment, decreased activity in RDLPFC and RIPC predicts final ECT response.

NR23 Monday, May 15, 9:00 a.m.–10:30 a.m.

Onset of Bipolar Illness With and Without Psychosis

Aysegul Yildiz, M.D., *Department of Psychiatry, Mass General Hospital/BipolRP, 50 Staniford Street, 5th floor, Boston, MA 02114*; Gary S. Sachs, M.D.

Summary:

Objective: To examine the association between psychotic symptoms and age onset of bipolar illness.

Method: The charts of bipolar patients treated at the MGH bipolar program were reviewed for age of the first affective episode, demographics, and history of psychotic symptoms.

Results: Data were obtained for 328 bipolar patients (56.7% females) of whom 42% had psychotic symptoms. Overall, there was no significant difference in age of onset between the psychotic and the nonpsychotic groups ($p < .42$). However, additional analysis carried out separately by gender found significant difference for males but not for females ($p < .03$ for males, $p > .65$ for females). Age of onset for psychotic males was significantly lower than for nonpsychotic males (18.4 years versus 21.8 years, $p < .03$). Psychosis was less common in males than females (34.5% versus 47.8%; $p < .02$). The mean age of onset for the psychotic males was significantly lower than psychotic females (18.4 years versus 22.3 years, $p < .01$).

Conclusion: This result implies that the physiology underlying development of psychosis in bipolar illness may be different for men than women. The confounding results in the literature for the age onset of the psychotic bipolar illness may be due to the different proportions of males and females in the study samples.

NR24 Monday, May 15, 9:00 a.m.–10:30 a.m.

The Impact of Depression on Health-Related Quality of Life

Samir H. Mody, Pharm.D., *Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200*; William S. Edell, Ph.D., Michael B. Durkin, M.S., Bryan E. Adams, Ph.D., Ed A. Repp, M.B.A.

Summary:

Objective: To describe the effect of depression on health-related quality of life (HRQL) utilizing the SF-36.

Methods: SF-36 scores were collected from a behavioral health database of patients admitted to an adult or geriatric psychiatric unit with a discharge diagnosis of depressive disorder. Admission SF-36 scores for each group were compared with age- and gender-matched U.S. population norms using independent sample t-tests. The findings were then placed in the context of SF-36 scores

for other psychiatric conditions including schizophrenia, bipolar disorder, and cognitive disorder.

Results: HRQL for both groups of depressed patients was significantly lower than the U.S. population sample for all eight domains of the SF-36 ($p < 0.001$). Adult inpatients with depression ($n = 600$) had similar scores on all domains as compared with patients with the other psychiatric diagnoses. However, geriatric patients with depression ($n = 4,439$) had lower scores on HRQL across all domains versus geriatric patients with other psychiatric illnesses.

Conclusion: Depression has a strong negative association with a patient's perceived HRQL. Depressed patients not only had the expected decreases on mental health domains, but also scored significantly lower on physical health domains. Finally, depression in geriatric patients is associated with greater decrements in HRQL than other psychiatric illnesses examined.

NR25 Monday, May 15, 9:00 a.m.–10:30 a.m.

Pleiotropic Effect of the 5HT Transporter Gene on Seasonality and Neuroticism

Leo Sher, M.D., *Biological Rhythms, NIMH/Building 10, Room 3S-231, 9000 Rockville Pike, Rockville, MD 20892*; Dean H. Hamer, Ph.D., Benjamin D. Greenberg, M.D., Dennis L. Murphy, M.D., Norman E. Rosenthal, M.D.

Summary:

Objective: Pleiotropy refers to the ability of one gene or group of genes to give rise to variation in multiple traits. The serotonin transporter gene (5-HTTLPR) has been associated with two personality traits—neuroticism and seasonality (the tendency to experience changes in mood and behavior with the changing seasons). One possible explanation for this association is that these two personality traits may both be associated with this gene because they are overlapping constructs. Alternatively, this may be a case of pleiotropy, with the gene in question coding for two different traits. We hypothesized this to be the case on the basis of other studies suggesting that neuroticism and seasonality are different traits. We tested this hypothesis by measuring both seasonality and neuroticism and looking for mediation.

Method: We administered the Seasonal Pattern Assessment Questionnaire, which measures severity of seasonality, and the Revised NEO Personality Inventory, which measures severity of neuroticism, to 236 healthy volunteers. DNA was extracted from peripheral blood of the subjects and the 5-HTTLPR was genotyped. Mediation was tested using regression analysis.

Results: The results indicated that the 5-HTTLPR contributions to variation in the two traits are independent. Sib-pair analysis confirmed that the effects of the 5-HTTLPR were due to genetic pleiotropy rather than population stratification.

Conclusion: The serotonin transporter gene influences seasonality independently of neuroticism.

NR26 Monday, May 15, 9:00 a.m.–10:30 a.m.

Predictors of Depression in Geriatric Medically Ill Patients

Lana M. Borin, M.D., *Department of Psychiatry, Baltimore VA Medical School, 10 North Green Street, Baltimore, MD 21201*; Paul E. Ruskin, M.D., Allen Raskin, Ph.D., Kumar Menon, M.D.

Summary:

The presence of depression is often overlooked in geriatric patients with medical illnesses. The purpose of the study was to identify the variables that would successfully predict depression in this population. The total sample consisted of 378 male, medically ill veterans, age 60 and older, who were admitted to the acute medical service at the Baltimore Veteran Administration Medical Center. Sixty of 378 patients met criteria for major depression and scored 11 or higher on the Geriatric Depression Scale. Eleven variables, such as age, race, psychological stressor, social support, severity of illness, and degree of functional disability, were included in a logistic regression analysis as predictors of depression. The chi-square to test this model was 114.175 ($p > 0.01$). The variables that significantly predicted depression were the total score for the Beck Hopelessness Scale, Life Satisfaction Total Score, and the Cumulative Illness Rating Score. Our results highlight the importance of hopelessness, satisfaction with life, and health status in the development of depression in older medically ill patients.

NR27 Monday, May 15, 9:00 a.m.–10:30 a.m.

Assessment of Motor and Process Skills in Depression

Ni A. Khin, M.D., *GPB, NIMH-NIH, 10 Center Drive Bldg 10/ 3N228, Bethesda, MD 20892-1275*; Frances Oakley, M.S., Rebecca Parks, M.S., Trey Sunderland, M.D.

Summary:

It is estimated that over 800,000 individuals become bereaved yearly in the United States. During the first year of spousal bereavement, one could present with major depression that can greatly limit the person's ability to function in everyday activities. Yet few bereaved persons receive pharmacotherapy for their depression. As part of a larger study examining the links among bereavement, depression, biology, and daily functioning, we evaluated the usefulness of the Assessment of Motor and Process Skills (AMPS) as an outcome measure for pharmacotherapy in post-bereavement depression. The AMPS simultaneously measures motor and process skills and their effect on a person's ability to perform activities of daily living.

To date, eight (3M, 5F) bereaved persons (aged 51 to 71) with major depression (pre-treatment mean Hamilton Depression Score "HAM-D" of 21.5, minimental score 29.4) are participating in randomized, parallel, double blind, antidepressant study (nortriptyline vs. sertraline). We found a significant difference in motor ($p < 0.02$) and process ($p < 0.005$) skill ability between pre-treatment and remission (mean "HAM-D" of 8.6). We have begun using the AMPS on a cohort of bereaved nondepressed subjects matched for age and gender with the same AMPS administration intervals. Preliminary results and their implications will be presented.

NR28 Monday, May 15, 9:00 a.m.–10:30 a.m.

Treatment Choices in Unipolar and Bipolar Disorder

Dawson Wolfe, B.S., *Department of Psychiatry, Vanderbilt University, 1500 21st Avenue, South, #2200, Nashville, TN 37212*; Steven Kaptik, B.S., Richard C. Shelton, M.D.

Summary:

Objective: This project was intended to evaluate the impact of prior treatment on initial treatment decisions for patients with unipolar and bipolar disorders.

Methods: Detailed chart reviews were performed on 200 subjects collected from university-affiliated clinics: 100 each with major depression and bipolar disorder. Demographic, prior treatment, and initial treatment (three months) were systematically collected and analyzed. Adequacy of prior treatment was estimated using a standard algorithm.

Results: In the unipolar depressed subjects, SSRIs were most commonly used both retrospectively and prospectively. Type or adequacy of prior treatment exposure had little to do with subsequent treatment choice; 68% of patients treated prospectively with SSRIs and 59% treated with NSRIs continued treatment for at least three months. In bipolar patients, there was a reduced frequency of

the use of all antidepressants and lithium, with an increase in use of anticonvulsants, especially divalproex (the most commonly used mood stabilizer). However, documentation of prior treatment was less complete in bipolars in contrast to unipolars. e.g., prior plasma levels of anticonvulsants and lithium were almost never documented. Prior psychotherapy was uncommon in both unipolar (25%) and bipolar (33%) groups. Psychotherapy was initiated in 66% and 45%, respectively.

Conclusions: Clinicians appear to follow an algorithmic approach that emphasizes standard therapies rather than depending on prior treatment as a principal guide to prospective treatment choices. Documentation of prior medication in bipolar subjects is less adequate than in unipolars.

NR29 Monday, May 15, 9:00 a.m.–10:30 a.m.

Utility Scores of the Symptoms of Depression

Ayal Schaffer, M.D., *Department of Psychiatry, Sunnybrook and WCHSC, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada*; Susan K. Hershkop, M.D., Anthony J. Levitt, M.D., Paul Oh, M.D.

Summary:

Objective: To determine utility ratings for the individual symptoms of major depression. We hypothesized that: (1) symptoms of depression would have different utility ratings, and (2) mean utility scores for the symptoms would differ between healthy controls and depressed subjects.

Methods: Seventy five subjects were included-19 with current major depression, 21 with past depression, and 35 healthy controls. Subjects were presented ten scenarios that reflected individual symptoms of depression. A utility rating from 0–1.0 (with 1.0 signifying "perfect health") was determined for each scenario using a "standard gamble" methodology.

Results: Mean utility scores varied greatly between symptoms. Psychological symptoms such as guilt, suicidal ideation, and anhedonia were ranked as the most undesirable, with mean utility scores of 0.73, 0.51, and 0.77, respectively. Somatic symptoms such as appetite and sleep were ranked as the least undesirable, with mean utility scores of 0.86 and 0.82, respectively. Mean utility scores for several symptoms were significantly higher in the currently depressed group, but not in the past depressed group.

Conclusions: Certain symptoms of depression are viewed as more undesirable than others. This may have important implications for how we currently assess severity of depression, treatment efficacy, and impact of depression on quality of life.

NR30 Monday, May 15, 9:00 a.m.–10:30 a.m.

Proton Magnetic Resonance Spectroscopy Study of Treatment-Resistant Depression

Shamsah B. Sonawalla, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WAC 812, Boston, MA 02114*; Constance M. Moore, M.D., Perry F. Renshaw, M.D., Lindy E. Graham, B.A., Nelson A. Vega, B.A., Maurizio Fava, M.D., Ben Lafer, M.D., Andrew A. Nierenberg, M.D.

Summary:

Objectives: Studies using proton magnetic resonance spectroscopy (1H-MRS) have identified basal ganglia choline/creatine ratio (Cho/Cr) changes in depressed patients compared to non-depressed subjects. The purpose of this study was to compare caudate nucleus choline/creatine (Cho/Cr) and N-acetyl-aspartate/creatine (NAA/Cr) ratios, as measured by in vivo 1H-MRS, in patients with treatment-resistant depression (TRD) and non-treatment-resistant depression (non-TRD).

Methods: We evaluated 26 depressed outpatients (TRD = 13; mean age 37.9 ± 12.1 years, 38.5% women; non-TRD = 13; mean age 40.8 ± 9.8 years, 38.5% women) meeting DSM-III-R or DSM-IV criteria for major depressive disorder, and 15 normal control subjects (mean age 40.4 ± 10.2 years, 60% women). All subjects underwent 1H-MRS using a 1.6 cm3 voxel centered on the head of the left caudate before they entered a clinical trial. The Mann-Whitney-U test was used for data analysis.

Results: We found a statistically significant gender difference in Cho/Cr ratios, with depressed women having significantly higher Cho/Cr ratios compared with depressed men (1.5 ± 0.3 and 1.2 ± 0.3 respectively; $Z = -2.1$; $p = 0.037$). We also found significantly higher Cho/Cr ratios in both TRD and non-TRD women compared with women in the control group (1.5 ± 0.4; 1.5 ± 0.2 and 1.0 ± 0.3, respectively; $p < 0.01$). There was no significant difference in the 1H-MRS Cho/Cr and NAA/Cr ratios of depressed patients with TRD, non-TRD, and control subjects.

Conclusions: Our preliminary findings suggest that treatment-resistant depression does not appear to be associated with significant caudate nucleus Cho/Cr and NAA/Cr ratio changes on 1H-MRS compared with non-TRD. However, depressed women have higher Cho/Cr ratios compared with depressed men.

NR31 Monday, May 15, 9:00 a.m.–10:30 a.m.

True Drug Response Versus Placebo Pattern Response to Fluoxetine: Differences in Cognitive Factors

Shamsah B. Sonawalla, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WAC 812, Boston, MA 02114*; Amy Farabaugh, M.A., Vinita Lesley, M.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Summary:

Introduction: Pattern analysis has identified two types of response patterns to antidepressants: true drug response (TDR) and placebo pattern response (PPR). TDR is characterized by a two-week delay in onset followed by persistent improvement and PPR is characterized by early, transient, or non-persistent improvement. This study examines the relationship between cognitive factors and TDR and PPR to fluoxetine.

Methods: We assessed 310 depressed outpatients meeting DSM-IV criteria for major depressive disorder (MDD), who were enrolled in an eight-week open trial of fluoxetine 20 mg/day. Response patterns were determined using the Clinical Global Impressions-Improvement (CGI-I) scale at weeks two, four, six, and eight. We administered the following self-rated scales to all patients at the screen visit and at endpoint: Perceived Stress Scale (PSS), Cognitions Questionnaire (CQ), Beck Hopelessness Scale (BHS), and Dysfunctional Attitudes Scale (DAS). The Mann Whitney-U test was used for data analysis.

Results: One hundred and thirty-four patients had TDR, 66 patients had PPR, and 110 patients were non-responders (NR). We compared cognitive factors across patients with TDR and PPR. Mean age of patients with TDR was 40.5 ± 9.6 years and that of PPR was 41.1 ± 9.6 years ($F = 0.1$; $df = 1, 198$; $p = 0.7$). There were 52% women ($n = 70$) in the TDR group, and 60% women ($n = 40$) in the PPR group (chi-square = 1.3; $p = 0.3$). There were no significant differences at baseline between TDR and PPR patients in CQ, PSS, BHS, and DAS scores. At endpoint, PPR patients had significantly lower scores on the PSS and BHS ($p < 0.001$ and $p < 0.05$, respectively).

Conclusions: Our preliminary data suggest that significant changes in cognitive/psychological factors accompany placebo pattern of response to antidepressant treatment and differentiate it from true drug response pattern. Further studies in a larger sample are required to confirm our findings.

NR32 Monday, May 15, 9:00 a.m.–10:30 a.m.

Affective Temperaments in Panic Disorder and MDD

Paolo Castrogiovanni, M.D., *Department of Psychiatry, University of Siena, Viale Bracci 10, Siena, I 53100, Italy*; Fulvio Pieraccini, M.D., Sara Calossi, M.D., Massimo Garbini, M.D., Elena Pappagallo, M.D., Antonio Mantovani, M.D.

Summary:

Objective: Aim of this study is to verify the presence and to evaluate the influence of affective temperaments on psychopathology, severity, and treatment response in panic disorder (PD) and major depressive disorder (MDD).

Methods: 112 outpatients affected by MDD and PD, according to DSM-IV criteria, have been evaluated by means of Akiskal and Mallya's semistructured affective temperament interview. Patients were assessed by SCL-90, BDI, SAD, and CGI at inclusion. CGI was repeated after six weeks of treatment.

Results: Depressive temperament in MDD and hyperthymic in PD are the most represented. In all scales, depressive patients with affective temperaments, compared with patients without them presented significantly higher scores. In PD there were no significative differences. The presence of temperaments in patients with MDD is correlated to pharmacological response. In PD treatment response is not correlated with the presence of affective temperaments.

Conclusions: These data confirm the different distribution and the role of affective temperaments in MDD and PD. Contrary to MDD, the affective temperaments wouldn't influence both symptom severity and treatment response in PD.

NR33 Monday, May 15, 9:00 a.m.–10:30 a.m.

Temperaments in Features of Mood Disorders

Paolo Castrogiovanni, M.D., *Department of Psychiatry, University of Siena, Viale Bracci 10, Siena, I 53100, Italy*; Massimo Garbini, M.D., Fulvio Pieraccini, M.D., Sara Calossi, M.D., Antonio Mantovani, M.D., Elena Pappagallo, M.D.

Summary:

Objective: Purpose of this study is to evaluate the distribution of affective temperaments and their correlation with the symptoms of mood disorders.

Methods: The sample is composed of 83 outpatients with diagnosis of major depressive disorder (MDD) and bipolar disorder (BD) according to DSM-IV criteria. The Akiskal and Mallya's semistructured interview is used to evaluate affective temperaments and three self-reported scales for psychopathological description.

Results: Depressive temperament is clearly prevalent in MDD, single episode, while in MDD, recurrent, there is a fairest distribution of all temperaments. On the contrary, cyclothymic temperament is the most frequent in bipolar I, while in bipolar II is also present the hyperthymic one. Analyzing our patients' mean scores with or without temperaments, we found statistically significant differences in specific symptoms.

Conclusions: The highest prevalence of affective temperaments in patients with mood disorders in relation to the general population confirms that the temperaments would represent the smooth phenotypic expression of a genetic substrate. Our data show that the affective temperaments would correlate with specific symptomatological features in both MDD and BD.

NR34 Monday, May 15, 9:00 a.m.–10:30 a.m.

Menstrual Irregularity in Women with Bipolar Disorder

Sara R. Gaughan, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Stanford Street, #580, Boston, MA 02114*; Gary S. Sachs, M.D., Robert Knauz, Ph.D., Christina M. Demopulos, M.D.

Summary:

Objective: (1) to determine if menstrual irregularity is more common among women with bipolar disorder than in the general population.

(2) to determine if menstrual irregularity is more common in rapid cyclers versus non rapid cyclers.

Methods: Charts of pre-menopausal women were harvested alphabetically from a bipolar clinic. Age, bipolar subtype, self-reported irregular menses, and antipsychotic use were examined. Women on oral contraceptives or with primary ammenhorea were excluded.

Results: Pilot data were harvested from 30 bipolar women (BPI = 27, BPII = 2, BP-NOS = 1). Overall, 17 of the 30 patients (57%) reported irregular menses. Seven of the 11 (64%) rapid cyclers and 10 of the 19 (53%) non-rapid cyclers ($p = 0.47$) had irregular menses.

Conclusions: A higher percentage of women with bipolar disorder reported irregular menses than in the general population (25% to 30%). We found a slight (nonsignificant) trend toward higher rates of menstrual irregularity among women with rapid cycling versus non-rapid cycling bipolar disorder. Because antipsychotics may be related to irregular menses, we further examined only those patients on antipsychotics (N = 10). For those individuals, irregular menses were more common in rapid cyclers (6/6) than non-rapid cyclers (2/4) ($p = 0.53$). In this study, sample size was small. Thus, we will harvest 150 charts for further analyses.

NR35 Monday, May 15, 9:00 a.m.–10:30 a.m.

The Short-Term Course of Untreated Depression: A Meta-Analysis of Studies Utilizing Wait-List Control Groups

Michael A. Posternak, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Ivan W. Miller, Ph.D.

Summary:

Introduction: While the short-term response rates to antidepressant medication and placebo are well established, very little is known about the short-term course of untreated depression. Knowing how much patients improve without treatment can serve as a benchmark in assessing the true benefit of active treatment.

Method: A meta-analysis was performed of all psychotherapy studies that randomized adult outpatients suffering from major depression to a wait-list control (WLC) group.

Results: The outcomes of 221 WLC subjects, from 19 studies lasting two to 20 weeks, were reviewed. The mean decrease in Hamilton Depression Rating Scale scores was 11.6%, while the mean decrease in Beck Depression Inventory (BDI) scores was 15.7%. We estimated that 15/77 (19.5%) improved to a degree comparable to what is considered a positive response in antidepressant trials. In seven separate studies that randomized subjects with mild depression to a WLC group, there was a 13.2% decrease in BDI scores.

Conclusions: In the short-term, depressive symptomatology can be expected to decrease by an average of 10% to 15% without treatment. As many as 20% of subjects in an antidepressant trial may experience a spontaneous remission.

NR36 Monday, May 15, 9:00 a.m.–10:30 a.m.

Visual Mental Imagery and Major Depressive Episode: The Role of Dorsolateral Prefrontal Cortical Hypoactivation

Amir Zarrinpar, *Department of Psychology, Harvard University, 3899 Nobel Drive, Suite 1230, San Diego, CA 92122*; Patricia Deldin, Ph.D., Stephen M. Kosslyn, Ph.D.

Summary:

Recent hemodynamic studies of participants in a major depressive episode (MDE) have shown a hypoactivation in the left dorso-lateral prefrontal cortex (DLPFC) that was hypothesized to be related to observed psychomotor retardation (PMR) and the global degradation of cognition observed in MDE patients. Since this region is vital to many top-down processing tasks, and since visual mental imagery tasks allow a segregation of the analysis of decision-making component from sensory and motor control components, imagery tasks would allow the investigation of the role of left DLPFC in PMR.

Three behavioral experiments were conducted: (1) an image generation/perception task, (2) a hand rotation task, and (3) a canonical/noncanonical task. Results showed that the decision-making component was unaffected by left DLPFC, yet the sensory and/or motor control components were affected across all three tasks. This provides evidence that the observed global deficit in cognition is a result of a deficit in one component. Furthermore, unexpected significant negative correlation was found between performance and self-reported measures of depression across all three tasks, suggesting that MDE participants could have a comorbidity for anxious apprehension and encounter some hyper-activation of DLPFC as well.

NR37 Monday, May 15, 9:00 a.m.–10:30 a.m.

Childhood History of Distress in Patients with Mood Disorders

Candace N. White, M.Ed., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Maurizio Fava, M.D., Constance Guille, B.A., Jordan W. Smoller, M.D.

Summary:

Background: Stressful life events, such as parental loss or divorce, have been postulated to be antecedents of mood disorders in childhood, in particular of unipolar depression. The aim of this analysis was to compare childhood history of anxiety, traumatic events, losses, and symptoms of child distress, such as enuresis, between unipolar and bipolar outpatients.

Methods: Forty-nine (26 bipolar and 23 unipolar) subjects in a genetic study were included in the analysis. Diagnoses were established with use of the SCID, while the childhood history of traumatic events, parental losses and divorce, and childhood enuresis were assessed using a self-rated questionnaire.

Results: We found a significant difference in rates of childhood enuresis (Fisher's exact $p < .05$) between unipolar (45%) and bipolar (16%) patients. Rates of parental divorce/separation before age 17 were also higher in unipolar (45%) than bipolar (23%) patients, although this difference did not reach statistical significance ($p = .13$). No significant differences were noted between unipolar and bipolar patients as far as parental death before age 17 (14% vs. 8%, respectively) and traumatic experiences during childhood (65% vs. 54%, respectively).

Conclusion: Because multiple items were tested, we cannot rule out the possibility of Type I error. These preliminary results suggest a trend towards higher rates of parental divorce/separation during childhood/adolescence and of childhood enuresis among patients with unipolar major depressive disorder compared to bipolar patients.

NR38 Monday, May 15, 9:00 a.m.–10:30 a.m.

Depression in Physicians: Access to Treatment and Impact on Career

Jane M. DeVeau, M.D., *Department of Psychiatry, UMMS, 701 West Pratt Street, 4th floor, Baltimore, MD 21201*; Jill A. RachBeisel, M.D.

Summary:

Objective: Studies have demonstrated increased rates of depression among physicians in training compared with the general population. This study further examines the prevalence of depression among physicians, factors influencing access to treatment among faculty, fellows, and housestaff within an urban medical center.

Method: A 12-question, self-report survey of depression was sent to attendings, fellows, and housestaff. Survey questions included experiences of depression, types of treatment, factors influencing access to treatment, and impact upon medical careers. Chi-square analysis was performed.

Results: 885 surveys were mailed with a 28% response rate. Of the responders 60% were male, 75% were ever married, 54% were attending faculty, 12% fellows, 32% residents, and 2% interns. Of the 106 (40%) reporting depression 63% ($n = 67$) reported that the depression had interfered with life activities, 61% ($n = 65$) sought treatment, 40% ($n = 44$) contemplated suicide, and 23% ($n = 24$) considered leaving the field of medicine. Access to treatment was most impeded by the stigma of counseling/psychiatric treatment (51%, $n = 54$) and lack of time (32%, $n = 34$).

Conclusion: This study suggests the rate of depression in physicians is more than twice the rate for the general population. These findings emphasize the importance of educating physicians about depression early in the medical education process to promote identification of symptoms and accessing treatment.

NR39 Monday, May 15, 9:00 a.m.–10:30 a.m.

Why Are Older Bipolar Patients Underrepresented in a Bipolar Specialty Clinic?

Victoria E. Cosgrove, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, #580, Boston, MA 02114*; Courtney L. Koslow, B.A., Caroline M. J. Orsini, B.S., Gary S. Sachs, M.D.

Summary:

Objective: To examine aging as a factor influencing the underrepresentation of older bipolar patients in a bipolar specialty clinic.

Methods: A sample of patients who discontinued clinical care was obtained by reviewing 100 charts of outpatients who began treatment at Massachusetts General Hospital between 1983 and 1999. Demographic and clinical data were harvested for subjects with complete charts. Statistical analyses were used to compare demographics of patients who discontinued care (DCC) with those who continued care (RIC). Duration of treatment in the clinic was compared for older versus younger patients. Reasons for discontinuation will be determined.

Results: Analyses reflect data from 63 patients (DCC = 15, RIC = 47). Median age was 40 years. Mean age for DCC was 38.80 ± 11.18 years, while that for RIC was 42.98 ± 13.15 ($p < 0.66$). Among DCC, duration of treatment for younger patients (<40 years of age, $n = 9$) was 66.67 ± 93.68 weeks compared with duration for older patients (≥40 years, $n = 6$), 136.67 ± 199.28 weeks for older patients ($p < 0.052$).

Conclusion: Preliminary analyses suggest that older patients were not more likely to discontinue treatment than younger patients. Difference in duration may indicate that younger and older patients discontinue for different reasons. Results will be presented for 50 patients who discontinued care.

NR40 Monday, May 15, 9:00 a.m.–10:30 a.m.

The Relationship Between Bipolar Disorder and Month of Birth

Courtney L. Koslow, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, 5th floor, Boston, MA 02114*; Caroline M.J. Orsini, B.S., Victoria E. Cosgrove, B.A., Gary S. Sachs, M.D.

Summary:

Objective: To examine the distribution of birth date for patients treated with bipolar disorder.

Methods: Demographics and lifetime diagnosis were harvested from charts of bipolar patients treated at the Massachusetts General Hospital Bipolar Clinic. Analyses using chi square were carried out to determine if the distribution of births across seasons varied from chance.

Results: Preliminary results were available for 100 bipolar patients (92% BPI, 54% female). The percentages of bipolar I patients born in the winter:spring:summer:fall were 28:27:25:20, respectively ($p > 0.05$). The relative percentages of bipolar II patients born during these seasons were 0:0:25:75 ($p = 0.007$). Percentages of bipolar season.

Conclusions: Unlike prior studies, which find a higher than expected percentage of schizophrenics are born in the winter months, our preliminary analysis found no significant differences in the distribution of birth across seasons for the sample overall or for patients with bipolar I disorder. The finding of significantly higher birthrates in the fall among bipolar II patients must be interpreted cautiously since the sample is very small. Additional data collection is planned to expand the sample to 400 bipolar patients.

NR41 Monday, May 15, 9:00 a.m.–10:30 a.m.

Bupropion Suspended Release in Elderly Medically Ill Patients

Molly Fortner, B.S., *102-A Mulberry Street, Carrboro, NC 27510*; Indu Varia, M.D., Kenneth R. Gersing, M.D., Christopher O'Connor, M.D., P. Murali Doraiswamy, M.D.

Summary:

The objective was to evaluate the effectiveness and costs of bupropion SR treatment of elderly medically ill patients with major depression. Eighteen elderly subjects with major depression and comorbid serious medical illnesses (e.g., heart failure, recurrent cancer, type I diabetes) were treated in an open trial for eight weeks with a week-12 follow up. Efficacy was evaluated by the CGI, Hamilton Rating Scale for Depression (HAM-D), and Medical Outcomes Study Short Form-36 (SF-36). Red Book and AWP data were used to evaluate the daily cost/price of treatment. Bupropion SR treatment was associated with reductions in the CGI ($p < 0.0001$) and HAM-D total score ($p < 0.0001$). The SF-36 quality of life domains, "mental health" ($p < 0.01$) and "social functioning" ($p < 0.0006$), improved significantly by week 4, and "vitality" ($p < 0.03$) improved significantly by week 12. Only two subjects dropped out owing to adverse events. No drug-drug interactions or significant changes in vital signs occurred. The mean dose of bupropion SR at endpoint was 222 mg/day. The average daily price was $2.26. These data suggest that bupropion SR is a cost-effective non-serotonergic antidepressant choice for this population.

NR42 Monday, May 15, 9:00 a.m.–10:30 a.m.

The Management of SSRI-Induced Side Effects: A Survey of Psychiatrists

Christina M. Dording, M.D., *Department of Psychiatry, Massachusetts General Hospital, WACC 812/15 Parkman Street, Boston, MA 02114*; Timothy J. Petersen, Ph.D., David Mischoulon, M.D., Rebecca A. Kornbluh, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Background: Despite the superior side-effect profile of the newer antidepressants over the tricyclics and monamine oxidase inhibitors, all newer antidepressants are associated with a wide array of side effects. Clinicians are constantly confronted with the challenge of managing these side effects in the context of minimal research to prove one management strategy is more effective than another.

Objective: The purpose of this study was to examine prescribing practices regarding the management of SSRI-associated side effects in a sample of psychiatrists attending a psychopharmacology review course.

Method: A total of 439 out of 800 clinicians (55%) attending a psychopharmacology review course responded to a 15-item questionnaire that was given prior to beginning the review course. Among these items were questions designed to assess clinician preference for the management of SSRI-induced side effects.

Results: As a treatment for SSRI induced sexual dysfunction, 43% (143/330) chose adding bupropion while 36% (120/330) opted to switch agents as their first choice; for SSRI-induced insomnia, 78% (264/326) chose adding trazodone. Switching agents was the first choice of 61% (214/353) of clinicians for managing SSRI-induced agitation 93% (339/363) for managing SSRI-associated weight gain, and 73% (245/337) for managing SSRI-associated sedation.

Discussion: In an effort to manage most SSRI-associated side effects (with the exception of sexual dysfunction and insomnia), the majority of the clinicians responding to our survey opted to switch agents rather than add a specific medication to the existing SSRI. In our opinion, this practice may reflect the relative lack of research studies on the role of adjunctive treatments in the management of SSRI-induced side effects and/or the tendency to favor monotherapy over polypharmacy.

NR43 Monday, May 15, 9:00 a.m.–10:30 a.m.

Locus of Control Orientation in Panic Disorder and the Differential Effects of Treatment

Abraham Bakker, M.D., *Department of Psychiatry, Vrye Universitei, Valeriusplein 9, Amsterdam 1075 BG, Netherlands*; Philip Spinhoven, Ph.D., Willem Van Der Does, Ph.D., Anton J.L.M. Van Balkom, M.D., Richard Van Dyck, M.D.

Summary:

In this study the effects of treatment with cognitive therapy, antidepressants, or pill-placebo on the locus of control orientation in panic disorder patients were analyzed as was the relation of this panic locus of control to panic frequency and cognitive measures of panic. A Multidimensional Anxiety Locus of Control scale (MALC) was developed and completed along with other measures (ACQ and BSQ) before and after treatment. Patients also kept a panic diary. Four subscales were derived from the MALC: one internal, and three external (a chance, a medication, and a therapist) locus of anxiety control orientation scales.

Cognitive therapy was superior over pill-placebo on most outcome measures. Antidepressants were only superior in reducing the number of panic attacks. Treatment with cognitive therapy resulted in an increase of "internal" anxiety control orientation and a decrease of "chance" and "medication" orientation in comparison with antidepressant therapy. The residualized gain scores on the MALC subscales only correlated with clinical improvement in subjects treated with cognitive therapy. Results suggest that the locus of control orientation is important in evaluating the differential

effects of treatments in panic disorder. A differential effect on panic locus of control in favor of cognitive therapy in comparison with medication was found.

NR44 Monday, May 15, 9:00 a.m.–10:30 a.m.

Distinguishing Psychotic and Nonpsychotic Depression

Juan C. Gonzalez-Seijo, M.D., *Salud Mental, S. E. S. P. A., Uria 34, #4, Gijon 33202, Spain*; Yolanda M. Ramos-Vicente, M.D., Ismael Lastra-Martinez, M.D., Jose L. Ayuso, Ph.D.

Summary:

Introduction: There is a renewed interest in the role of psychotic features in depression. The objective of the present study is to establish the significance of delusions and hallucinations in depressions.

Methods: The sample included 70 inpatients diagnosed with major depressive disorder using DSM-IV criteria, hospitalized in the psychiatric department of a university general hospital. Thirty-three of these patients met criteria for psychotic depression. The evaluation instruments were: Hamilton Depression Rating Scale, FH-RDC, Eysenck Personality Inventory, Brown and Harris life-events scale, Newcastle depression Index, and Salpetriere Retardation Rating Scale.

Results: There were not significant differences between psychotic and non-psychotic depressions in sociodemographic variables. Psychotic patients had higher scores using the Hamilton Depression Rating Scale (35.58 Vs. 28.65; $p = 0.000$). Salpetriere total score was also higher in the psychotic depressed patients (35.94 Vs. 26.54; $p = 0.000$). In respect to treatment, ECT was used more frequently in the group with psychotic depression (30%) than in the non-psychotic group (8%).

Conclusion: The presence of psychotic features in major depressive disorder indicates a more severe form of that disorder.

NR45 Monday, May 15, 9:00 a.m.–10:30 a.m.

Do Antidepressants Alter the Course of Bipolar Disorder?

Caroline M. J. Orsini, B.S., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, 5th floor, Boston, MA 02114*; Victoria E. Cosgrove, B.A., Courtney L. Koslow, B.A., Gary S. Sachs, M.D.

Summary:

Objective: To determine the impact of antidepressant treatment on the course of illness for patients subsequently diagnosed with bipolar disorder.

Methods: This pilot study reviewed charts of bipolar patients treated at a bipolar specialty clinic to identify those on which the semistructured Affective Disorders Evaluation completed at intake included the age of onset for both the first major depression episode (MDE) and the first episode of mania. For comparison, bipolar patients with a positive history of antidepressant treatment for an initial MDE (BPDA+) were age- and sex-matched with bipolar patients with an initial MDE for which no antidepressant (BPDA–) was prescribed. Time from onset of first MDE to onset of first mania will be compared for 20 BPDA+ and 20 BPDA– patients using paired t-test.

Results: Preliminary results found the mean time from first depression to first mania for BPDA+ ($n = 3$) and BPDA– ($n = 3$) was 2.0 ± 1.7 yrs and 11.3 ± 14.4 yrs, respectively ($p < 0.33$, NS).

Conclusion: Although the preliminary results are not statistically different, the magnitude of the difference in this small sample raises concern that antidepressant medication accelerates the course of bipolar illness. Results for the full sample are needed to address this important issue.

NR46 Monday, May 15, 9:00 a.m.–10:30 a.m.

Review of Bipolar Disorder in a Geriatric Psychiatry Unit

Jean Y. Liu, M.D., *Department of Psychiatry, Pennsylvania State-Hershey, p o box 850, Hershey, PA 17033-0850*

Summary:

Introduction: Few data are available concerning the treatment of bipolar disorder in the elderly. We surveyed all patients with bipolar disorder admitted to a university hospital geriatric psychiatry service over an 18-month period ($n = 15$).

Method: A retrospective chart review was conducted for all patients. They were analyzed for age, sex, education, cognitive ability (as measured by MMSE), presence of psychotic symptoms, family history of psychotic disorder, length of stay, and medications used. Global Assessment Score (GAS) was used to gauge improvement. Data were analyzed using T test.

Results: Six out of 15 were much improved with a GAS of 4; eight out of 15 were noticeably improved

(GAS) of 3; one out of 15 was not improved

(GAS) of 2. Divalproex sodium ($p = 0.098$) showed tendency to be more effective for this patient sample than lithium carbonate ($p = 0.312$). There were no significant difference in improvement compared with length of stay ($p = 0.72$). There was a tendency for late-onset bipolar disorder patients to do a bit better on discharge ($p = 0.087$). Late-onset bipolar disorder patients did not have different MMSE on discharge (both MMSE compared mean is 25).

Conclusion: Bipolar disorder in the elderly is quite treatable. Late-onset bipolar-disorder patients respond as well to treatment as early-onset patients. Divalproex sodium is at least as effective as lithium carbonate in the treatment of bipolar disorder in the elderly.

NR47 Monday, May 15, 9:00 a.m.–10:30 a.m.

BPD in Primary Care

Raz Gross, M.D., *Department of Epidmiology, Columbia University, 600 West 168th St. PH-18 RM303, New York, NY 10032*; Myrna M. Weissman, Ph.D., Mark Olfson, M.D., Marc Gameroff, M.A.

Summary:

Background: Borderline personality disorder (BPD) is a severe condition, characterized by instability of interpersonal relationships, self-image, and affect, and marked impulsivity, with high rates of comorbid Axis I disorders and suicidal behavior. Little data are available about the prevalence and clinical picture of BPD outside of psychiatric settings. Specifically, there have been no published studies on its prevalence in primary care.

Method: We used data from a survey conducted on a probability sample ($n = 205$, ages 18 to 70) from an urban primary care practice, with predominantly low income patients, to examine the prevalence, clinical features, associated impairment, and rate of treatment of DSM-IV BPD. Linkage to billing and clinical data were used to assess health care utilization.

Results: Lifetime prevalence of BPD was 6.8%. Patients had high rates of comorbid Axis I depressive and anxiety disorders, high suicidal ideation rate, and an increased frequency of current bipolar disorder, and were significantly impaired. Despite this, 50% of the BPD patients were not receiving mental health treatment in the past year, and 45.5% were not recognized by their primary care physicians as having an ongoing mental health problem. Rates of health care utilization will also be presented.

Conclusion: The prevalence of BPD in this primary care study (6.8%) was several-fold higher than the 0.2% to 1.8% reported in the few general community studies available. BPD patients had high rates of comorbid conditions and disability.

NR48 Monday, May 15, 9:00 a.m.–10:30 a.m.

Reliability and Validity of the Korean Temperament and Character Inventory (TCI)

Seung-Mo Sung, M.D., *Department of Psychiatry, Yongin Mental Hospital, 4 Sangha-Ri Kusung-Myun, Yongin-SiKyunggi-D 449-910, South Korea*; Jong-Heun Kim, M.D., In-Kyoon Lyoo, M.D.

Summary:

Objectives: The purpose of this study was to evaluate the reliability and validity of the Korean version of the Temperament and Character Inventory

(TCI), a self-report questionnaire based on Cloninger's psychobiological model of personality.

Methods: The TCI was translated into Korean and administered with the Social Desirability Scale

(SDS) and the General Health Questionnaire

(GHQ) to 851 university students. A test-retest study of the TCI was conducted after three months on 130 students.

Results: Cronbach α values for the TCI scales were .60 to .85 for the temperament scales

(NS, HA, RD, and PS) and .82 to .87 for the character scales

(SD, C, and ST). Test-retest correlation (r) were .52 to .72 for the temperament scales and .52 to .71 for the character scales. Three correlation coefficients between TCI scales were greater than .40 (HA with SD[r = –.56], C with SD[r = .44], C with RD[r = .43]). Correlations between the TCI scale score and GHQ and SDS scores were negligible. Confirmatory factor analysis showed similar factor structure to the American version except persistence

(PS).

Conclusion: The reliability and validity of the Korean version of TCI were supported by the results. The TCI seems to be suitable for use in Korean population. Cloninger's psychobiological model of personality seems to be successfully reflected in this questionnaire.

NR49 Monday, May 15, 9:00 a.m.–10:30 a.m.

Treatment of Two Groups of Depressed Patients: One With and One Without Personality Disorders

Jean-Pierre Lepine, M.D., *Hopital, Fernand-Vidal, Paris 72010, France*; Antoine Pelissolo, M.D., Sylvie Troy, M.D.

Summary:

Objectives: To compare the efficacy and safety of sertraline in two groups of patients with and without personnality disorders.

Methods: It was a six-month open study. Outpatients presenting a major depressive episode (MDE) according to the DSM-IV (simple or recurrent) with a score of at least 25 on the Montgomery Asberg Depression Rating Scale (MADRS) could be included. The presence or absence of personality disorders (PD+ and PD–) was determined on the basis of the PAS. Each investigator was asked to recruit the same number of patients in each group. Patients were evaluated at the inclusion and after 2,4,6,8,16, and 24 weeks. The scales rated by the physician were MADRS, CGI Clinical Global Impression, MINI, and the scales rated by the patient were HAD, TCI, and Disability Scale of Sheehan. Patients received flexible doses of sertraline from 50 to 200 mg/day.

Results: Of the 123 patients included, 58 presented a personnality disorder and 65 did not. The mean age was 40.41 years. It was the first episode for 32.5% of the patients. There was no difference at inclusion between the two groups. There was a decrease in the mean MADRS score in both groups PD+ (n = 53) from 31.15 +/– 5.77 to 10.79 +/– 9.81 and PD– (n = 62) from 30.60 +/– 4.07 to 9.81 +/– 8.12. Considering the responders rate MADRS as a reduction score of at least 50%, the efficacy of sertraline was similar within the two groups: 79.2% responders in the group with personality disorder and 75.8% in the group without. The CGI responders rate defined as a final severity score of 1- or 2 was similar within the groups 54.71% PD+ and 61.3% PD–. The mean final dosage was higher in the group of patients with personality disorder 92.7 mg/day compared with the group without 81.4 mg/day (56.9% of the patients completed the study with 50 mg). The treatment was well tolerated; 25% of the patients prematurely discontinued the study before the six months: the discontinuation for adverse events represents 9.75%.

Conclusion: The presence of personality disorders in patients with a major depressive episode doesn't influence the efficacy of sertraline

NR50 Monday, May 15, 9:00 a.m.–10:30 a.m.

Apathetic Syndrome and Depression: Responsiveness to Donepezil

Robert O. Morton, M.D., *Department of Psychiatry, University of Oklahoma-Tulsa, 2808 South Sheridan Road, Tulsa, OK 74129*; Mark D. Fossey, M.D., William R. Yates, M.D.

Summary:

Objective: (1) To evaluate apathy as a distinct neuropsychiatric syndrome in an adult outpatient mood disordered population. (2) Utilizing an open-label trial, determine the efficacy of donepezil in treating patients identified as having disproportionate levels of apathy relative to depression.

Method: Eighty-eight patients (mean age 38) were given a modified Apathy and Zung depression scale at zero and sixty days. Patients (N = 15) with a high ratio of apathy to depression were identified and received donepezil (5 mg daily) for 60 days as an augmentation to their medication program. The remainder of the non-treated patients were divided into five groups, matched for similarities in pretreatment scale scores and medication strategies.

Results: The donepezil treated patients showed a significant reduction in apathy scores (mean 59.8 pre vs. 45.2 post, t = 6.4, p = 0.0001, df = 14) but no change in depression scores. No statistically significant changes were seen in the other groups tested. Apathy scores reverted to pretreatments levels in five patients whose donepezil was discontinued at the end of the trial. Six patients refused to stop donepezil, as a result of perceived improvement in self-motivation and productivity.

Conclusions: Apathy appears to exist in a broader patient population than previously suspected. The effectiveness of donepezil in this condition would suggest a state of cholinergic dysregulation, expressed as impaired motivation and complacency.

The mechanism of this dysfunction does not appear to be attributable to diagnosis or to the type, dose, or length of psychotropic medication treatment.

NR51 Monday, May 15, 9:00 a.m.–10:30 a.m.

Risk Factors for Personality Disorders in the Hospitalized Military Population

Judith K. Denton, M.D., *Department of Mental Health, Eisenhower AMC, DDEAMC, Fort Gordon, GA 30905*; Nancy A. Harpold, D.O., Paul C. Burney, M.D., Christopher Lange, M.D., William J. Evans, M.D.

Summary:

Objective: To identify risk factors in soldiers presenting for acute psychiatric hospitalization that will assist the provider in screening for personality disorders.

Method: A comprehensive chart review was performed on 161 patients (aged 21–38) admitted to the psychiatric unit of an Army medical center between 1993–1997. Exclusion criteria include all Axis I DSM-IV diagnosis other than adjustment disorder.

Results: Of 161 charts reviewed, 96 patients met DSM-IV criteria for a personality disorder (PD); 65 were diagnosed with an adjustment disorder (AD) and no Axis II diagnosis. 92% of the PD's presented with thoughts of harm to themselves or a suicide gesture compared with 69% of the AD's. The PD's had increased current legal difficulties (40%). (AD's = 17%). The PD's had an increased percentage with family substance use problems (36%) and family psychiatric history (47%) compared with the AD's (21% and 25%).

Conclusion: In the military hospitalized population, personality disordered patients present more often with current legal difficulties and increased thoughts and gestures of harm towards themselves compared with the AD patient. Also, the PD's family history reveals an increase in family psychiatric history and family substance use problems. These risk factors may assist the provider with diagnosing a personality disorder. Personality disorders are crucial for the military mental health provider to detect, in order to estimate the patient's future adjustment to the military.

NR52 Monday, May 15, 9:00 a.m.–10:30 a.m.

Psychiatrists' Opinions on Dissociative Disorders

Justine Lalonde, M.D., *Harvard/McLean, 115 Mill Street, Belmont, MA 02478*; James I. Hudson, M.D., Robin A. Gigante, B.A., Harrison G. Pope, Jr., M.D.

Summary:

Objective: To compare opinions of American and Canadian psychiatrists regarding the diagnostic status and scientific validity of the DSM-IV categories dissociative amnesia (DA) and dissociative identity disorder (DID).

Method: We mailed a one-page questionnaire to a random national sample of 406 board-certified American and 550 certified Canadian psychiatrists.

Results: The response rate was 82% in the United States and 79% in Canada. Only about one-third of respondents replied that DA and DID "should be included without reservations in DSM-IV" (35% and 33% for DA, 35% and 23% for DID, for Americans and Canadians, respectively). The modal response was that these categories should be included as "proposed diagnoses." Also, only a small minority felt that the diagnoses of DA and DID were supported by "strong evidence of scientific validity" (23% and 13% for DA, 21% and 12% for DID). Overall, American psychiatrists were more likely to accept these diagnoses than Canadian psychiatrists, with psychodynamically oriented psychiatrists significantly more accepting than biologically oriented psychiatrists. We found no significant differences in attitudes between francophone and anglophone Canadian psychiatrists.

Conclusion: Among American and Canadian psychiatrists, there is little consensus regarding the diagnostic status or scientific validity of DA and DID.

NR53 Monday, May 15, 9:00 a.m.–10:30 a.m.

Is a Gift Ever Just a Gift? A Critical Review of the Interaction Between Physicians and the Pharmaceutical Industry

Ashley D. Wazana, M.D., *Department of Psychiatry, McGill University, 4169 Clarke Street, Montreal, PQ H2W 1X1, Canada*

Summary:

Context: Controversy exists over the fact that physicians have regular contact with the pharmaceutical industry and its sales representatives, who spend large sums of money each promoting to them by way of gifts, free meals, travel subsidies, sponsored teachings, and symposia.

Purpose: To identify the extent of and attitudes toward the relationship between physicians and the pharmaceutical industry and its impact on the knowledge, attitudes, and behavior of physicians.

Data Sources: A MEDLINE search was conducted from English-language articles published from 1994 to the present, with review of reference lists from retrieved articles; in addition, an Internet database was searched and five key informants were interviewed.

Study Selection: A total of 538 studies that provided data on any of the study questions were targeted for retrieval, 29 of which were included in the analysis.

Data Extraction: Data were extracted by one author. Articles using an analytical design were considered to be of higher methodological quality.

Data Synthesis: Physician interactions with the pharmaceutical industry were generally endorsed, began in medical school, and continued at a rate of about four times per month. There is good evidence for the effect of CME funding and conference travel funding on the prescription rate of the sponsor, as well as PR speakers on non-rational prescribing. There is also evidence, although less robust, of the impact of interactions with PRs.

Conclusions: The present extent of physician-industry interaction appears to affect prescribing and professional behavior and should be further assessed at the level of policy and education.

NR54 Monday, May 15, 9:00 a.m.–10:30 a.m.

Association Analysis of G-Protein B3 Subunit Gene with Altered Ca2+ Homeostasis in Bipolar Disorder

Timothy W. Corson, B.S.C., *Psychiatric Biochemistry Department, CAMH-Clarke Division, 250 College Street, Room R18, Toronto, ON M5T 1R8, Canada*; Peter P. Li, Ph.D., James L. Kennedy, M.D., Fabio Macciardi, M.D., Robert Cooke, M.D., Sagar V. Parikh, M.D., Jerry J. Warsh, M.D.

Summary:

Objective: Considerable evidence implicates disturbances in G-protein-mediated signal transduction in the pathophysiology of bipolar disorder (BD). We previously reported a trait-dependent elevation of basal intracellular B lymphoblast $[Ca^{2+}]_i$ in bipolar patients. The C825T variant of the G-protein β3 subunit (*GNB3*) gene is associated with altered Ca^{2+} dynamics in B lymphoblasts from a subgroup of essential hypertensive patients. Using a genetic association analysis, we sought to determine whether *GNB3* is involved in altered Ca^{2+} homeostasis in BD.

Method: Restriction-fragment genotyping of the C825T polymorphic locus of *GNB3* was performed for subjects with BD I (with "high" and "normal" $[Ca^{2+}]_i$ phenotypes), BD II, major depressive disorder, and for healthy controls.

Results: No significant association was found between genotype and $[Ca^{2+}]_i$ phenotype in BD I patients ($\chi^2 = 2.24$, 2 d.f., $P = 0.33$) or between genotype and psychiatric diagnosis in the entire cohort ($\chi^2 = 10.27$, 8 d.f., $P = 0.25$). Polymorphic allele frequencies were independent of diagnosis ($\chi^2 = 2.51$, 4 d.f., $P = 0.64$).

Conclusions: These results suggest that the high $[Ca^{2+}]_i$ BD phenotype is unrelated to expression of a *GNB3* variant, and imply that the mechanism underlying the elevated stimulated $[Ca^{2+}]_i$ phenotype in HT patients is distinct from the disturbances of Ca^{2+} homeostasis involved in the pathophysiology of BD.

NR55 Monday, May 15, 9:00 a.m.–10:30 a.m.

Lithium Carbonate-Induced Mitotic Anomalies in Vicia Faba L

Rashmi Rashmi, Ph.D., *Botany Department, Ranchi Women's College, 4 Crescent Tower/South Office, Ranchi, BI 834002, India*; Vinita Vishwakarma, M.S.C., Z.A. Haider, Ph.D., Anil Kumar, M.D.

Summary:

Lithium is commonly used by psychiatrists for manic patients. Evidence of its toxicity on central nervous system, thyroids, kidneys, gastrointestinal system, and metabolic system has been worked out in some detail. So far no report is available on its effect on chromosomes, the carriers of genetic material. To generate some information on cytotoxicity of lithium salt, an experiment was set up taking *Vicia faba* 2n = 12 as the text system because (a) genetic system in animals and plants are more or less the same, (b) easy availability for a wide range of study, (c) the cell division is fast. The result indicated a stimulatory effect on root length at 0.1%, while at 0.2% the root growth ceased after the second day on germination. The shoot primordia, on the other hand, suffered a setback at 0.125% and could show delayed growth as compared with the control. There was, however, no shoot growth at 0.15%. The cytological anomalies of the root tips chiefly induced stickiness, chromosome breakage, and unequal chromosome movement at anaphase at 0.125% and 0.15% treatments. The 0.1% treated roots, which had stimulatory effect, showed endomitotic divisions.

NR56 Monday, May 15, 9:00 a.m.–10:30 a.m.

Predictors of Two-Year Survival in Elderly Veterans with Comorbid Medical and Psychiatric Symptoms

Helen Lavretsky, M.D., *Department of Psychiatry, UCLA, 760 Westwood Plaza, #37-425, Los Angeles, CA 90095*; Roshan Bastani, Ph.D., Robert Gould, Ph.D., David L. Huang, Ph.D., Lissy F. Jarvik, M.D., Annette Maxwell, Ph.D.

Summary:

Objectives: The following report investigates predictors of mortality in patients with comorbid medical and psychiatric conditions.

Methods: Patients admitted to acute medical and surgical inpatient services of nine V.A. medical centers were screened for symptoms of depression, anxiety, and alcohol abuse, and re-examined six, 12, and 24 months later. Using T-tests, we compared survivors and deceased at 24 months with regard to severity of symptoms of anxiety and depression (Mental Health Index (MHI-38 Depression and Anxiety subscales), alcohol abuse (AUDIT), and eight scale and composite (MCS and PCS) scores derived from the Medical Outcomes Study Short Form 36- Item Health Survey (SF-36), which measures health-related quality-of-life (HRQOL). To assess predictors of survival, we used Cox proportional hazard model survival analysis.

Results: For the 2,639 patient enrolled at baseline, mortality was 11.3% at six months, 15.8% at 12 months, and 18.4%, at 24 months. Mortality at 24 months was predicted by poor HRQOL-PCS ($p = 0.0001$) and MCS ($p = 0.0003$); Physical functioning ($p = 0.0001$); general health ($p = 0.0001$), and bodily pain ($p = 0.0001$). The severity of symptoms of depression, anxiety, and alcohol abuse were not predictive of mortality. Among demographic characteristics, age ($p = 0.02$) and race ($p = 0.01$) predicted mortality.

Conclusions: Annual mortality rate in the first year was elevated in our patient sample compared with mortality in the age-matched general population (i.e., 9% or less). Poor HRQOL at baseline predicted mortality at 24 months. It remains to be seen to what extent, if any, reduction in psychiatric symptoms will reduce mortality.

NR57 Monday, May 15, 9:00 a.m.–10:30 a.m.

Strain and Reward Among Caregivers of Geriatric Patients

Joanne Fenton, M.D., *Department of Psychiatry, University of Maryland Medical School, 22 South Greene Street, box 351, Baltimore, MD 21201*; Jill A. RachBeisel, M.D., Niamh M. Holohan, M.D., Lisa B. Dixon, M.D.

Summary:

Objective: The importance of caregiver burden to caregiver and patient outcomes is recognized among adults with severe mental illness (SMI). This study assessed the degree of burden, stress, and gratification in those persons caring for elderly SMI patients about which less in known.

Method: A trained psychiatrist completed structured interviews with 41 caregivers of geriatric psychiatric inpatients. The interview included the Hamilton Depression Inventory, Caregiver Burden Scale, and Perceived Stress Scale, access to community resources and a rating of perceived benefits to the caregiver. Stepwise regression analysis was done to assess the significant variables influencing burden, stress and gratification.

Results: Caregivers reported relatively low stress (mean = 18.5, SD-10.4), depression (mean = 7.1, SD = 4.6) and burden (mean = 23.2, SD = 18.8). Burden, stress, and depression were highly intercorrelated ($p < .001$). Regression analysis showed that gender of the caregiver, relationship to the patient, difficult behaviors, access to support systems, and severity of psychiatric illness accounted for 40% of the variance in predicting burden in caregivers. Level of education, relationship to the patient, difficult behaviors, and race accounted for 30% of the variance in predicting stress and level of education, health of the caregiver, access to social services, severity of mental illness, and difficult behaviors accounted for 25% of the variance in predicting gratification.

Conclusion: This study demonstrates that while perceived burden appears to be relatively low, factors influencing burden and stress and gratification in geriatric caregivers are clearly identifiable. This allows focused targeting of caregiver interventions and supports.

NR58 Monday, May 15, 9:00 a.m.–10:30 a.m.

Testosterone Level in Late-Life Male Dysthymia

Stuart N. Seidman, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Steven P. Roose, M.D., Davangere P. Devanand, M.D., Andre Araujo

Summary:

Background: Hypothalamic-pituitary-gonadal (HPG) axis function declines in elderly men, and the prevalence of dysthymia increases. Symptoms of hypogonadism include low mood, energy, and libido.

Objective: To compare HPG functioning in dysthymic, depressed, and non-depressed elderly men.

Method: We compared total testosterone (T) levels in three groups of men aged 60–70: 22 depressed men, meeting DSM-IV criteria for major depressive disorder (MDD); 62 dysthymic men, meeting DSM-IV criteria for dysthymic disorder; and 310 non-depressed men who participated in a large, representative epidemiological study and scored below the median on the Center for Epidemiologic Studies Depression Scale (CES-D), a well-validated self-report depression symptom inventory.

Results: There were no between-group differences in demographic variables, including age and weight. In depressed men, the mean T level was 493 (SD ± 265) ng/dl, and mean baseline HRSD score 24 (SD ± 8); in dysthymic men, the mean T level was 262.5 (SD ± 198) ng/dl, and mean baseline HRSD score 17 (SD ± 6). In non-depressed men, the mean T level was 493 (SD ± 158) ng/dl.

Conclusion: Total T level was significantly lower among elderly men with dysthymia than among men with MDD or non-depressed men. Late-life dysthymia may be related to HPG hypofunction.

NR59 **Monday, May 15, 9:00 a.m.–10:30 a.m.**

Comparison of Valproic Acid Versus Carbamazepine in the Treatment of Agitation in Dementia

Pranav Dave, M.D., *Department of Psychiatry, Penn State University, 107 University Manor East, Hershey, PA 17033*; Paul A. Kettl, M.D.

Summary:

Objective: To compare the efficacy of valproic acid and carbamazepine in dementia-associated agitation.

Method: A retrospective chart review of 56 geriatric psychiatry inpatients diagnosed with Alzheimer's, vascular, or mixed dementia; 34 patients received carbamazepine and 22 patients received valproic acid. Drug dosages were individualized and given for a nonstandardized time—until the patient care team felt the patient was stabilized or worse. All patients had previously failed on one or more psychotropic medications. Both carbamazepine and valproic acid were given in the context of a full treatment program including activity, music, group therapy, and medicine consult. Physicians were nonblinded. Primary outcome measure in both groups was the Efficacy Index of the Clinical Global Impression (CGI) scale in controlling agitation and aggression.

Results: In the valproic acid study, 17 of 22 (77%) patients were either noticeably or much improved compared with 22 of 34 (65%) patients in the carbamzepine study. In general, both valproic acid and carbamazepine were well tolerated. There was no statistically significant difference in the two drugs with respect to Efficacy Index of the CGI scale.

Conclusion: Both valproic acid and carbamazepine are useful adjuncts in the treatment of dementia in the context a full treatment program.

NR60 **Monday, May 15, 9:00 a.m.–10:30 a.m.**

Efficacy and Tolerability of Carbamazepine in Treating Agitation and Aggression Associated with Dementia

Pranav Dave, M.D., *Department of Psychiatry, Penn State University, 107 University Manor East, Hershey, PA 17033*; Paul A. Kettl, M.D.

Summary:

Objective: To review the efficacy and tolerability of carbamazepine in treating agitation and aggression associated with dementia.

Method: In a retrospective chart review of 34 geriatric psychiatry inpatients diagnosed with Alzheimer's, vascular, or mixed dementia, individualized doses of carbamazepine were given for a nonstandarized time period. All patients had previously failed one or more psychotropic medications. Carbamazepine was given in the context of a full treatment program including activity, music, group therapy, and medicine consult. Physicians were nonblinded. Primary outcome measure was the Efficacy Index of the Clinical Global Impression (CGI) scale in controlling agitation and aggression.

Results: 22 of 34 (65%) patients showed noticeable or much improvement using the CGI scale. In general, carbamazepine was well tolerated. Of the six patients (18%) who did worse on carbamazepine, three were due to gait problems. There was no statistically significant difference in those who improved on carbamazepine and those who did not w.r.t. carbamazepine level on discharge, age, MMSE on admission, psychiatric history, focal CT brain scan, or number of days in the hospital.

Conclusion: Carbamazepine is useful in the treatment of dementia-associated agitation. Further systematic studies investigating this drug are justified.

NR61 **Monday, May 15, 9:00 a.m.–10:30 a.m.**

How Knowledge of and Experience with Life-Saving Procedures Influences Willingness to Undergo These Procedures

Umar F. Rahman, M.D., *Gero. Psych., VAMC, 10 North Greene Street, Baltimore, MD 21201*; Kumar Menon, M.D., Allen Raskin, Ph.D., Paul E. Ruskin, M.D.

Summary:

The purpose of this study was to determine if a patient's knowledge of and/or prior experience with four life-saving procedures, i.e., CPR, mechanical ventilation, IV fluids, and tube feeding, influences later decisions to undergo these procedures in six life-threatening scenarios. A total of 374 male veterans 60 years of age or older who were hospitalized on the acute medical service of the Baltimore Veterans Affairs Center served as subjects. Analyses of variance were performed with summation scores across the six scenarios of a willingness to undergo each of the four life-saving procedures serving as the dependent variables, and experiences with these procedures serving as the independent variables. Experience with two life-saving procedures, CPR and tube feeding, significantly predicted willingness to undergo these procedures in the life-threatening scenarios. For CPR, the significant item was a history of having suffered when administered CPR, which resulted in an unwillingness to undergo CPR again. Similarly, for tube feeding, a bad personal experience with this procedure or awareness of a bad experience by a family member or friend predisposed the patient not to want to undergo this procedure. A bad experience with a life-saving procedure rather than prior experience is the determining factor in willingness to undergo this procedure.

NR62 **Monday, May 15, 9:00 a.m.–10:30 a.m.**

Older Schizophrenic Patients: Nature of Dwelling Status and Symptom Severity

Sanjay Gupta, M.D., *Department of Psychiatry, Olean General Hospital-Psychiatric Net, 2221 West State Street, Olean, NY 14760*; Charles Steinmeyer, Ph.D., Bradford L. Frank, M.D., Kari Lockwood, R.N., Kay Schultz, R.N., Peggy Keller, R.N.

Summary:

Purpose: There is limited information available on older adults with schizophrenia spectrum disorder. This cross-sectional study enrolled patients from a community sample with a diagnosis of schizophrenia or schizoaffective disorder.

Methods: The sample consisted of 14 males and 37 females. The patients were dichotomized into two groups based on dwelling status, those living independently versus those in residential settings (group homes, family care, nursing home). The groups were compared with regard to Mini Mental Status Examination (MMSE), Brief Psychiatric Rating Scale (BPRS), Geriatric Depression Scale (GDS), and age.

Results: The two groups differed significantly only on the MMSE ($p = .041$) and age ($p = .042$). No significant differences were found with regard to symptomatology (BPRS and GDS).

Conclusion: These data reveal that the MMSE score and age are important discriminators with regard to residential status.

NR63 **Monday, May 15, 9:00 a.m.–10:30 a.m.**

Anxiety in Patients Assessed for Memory Complaints

Louis Lopez, M.D., *Department of Psychiatry, University of Miami/MSMC Psychiatry, 4300 Alton Road, Miami, FL 33140*; Elizabeth Crocco, M.D., Ranjan Duara, M.D., Raymond L. Ownby, M.D.

Summary:

Objective: Little is known about the correlates of anxiety in patients with complaints of memory impairments. This is important since anxiety might be expected to affect the extent to which such patients present for evaluation. The purpose of this study was to assess the prevalence of worries in patients presenting for evaluation of memory problems.

Method: Seventy-seven consecutively evaluated patients were seen for multidisciplinary evaluation in an outpatient memory disorders clinic. All were administered the Anxiety Symptoms Inventory, a checklist that assesses anxiety symptoms for DSM-IV diagnoses.

Results: Twenty-nine (38%) reported excessive worry over the last six months, and 22 (29%) of these reported difficulty in controlling the worry. Twelve patients (16%) fulfilled DSM-IV criteria for generalized anxiety disorder. The most common worry was about health; the most common physical symptoms were feeling "on edge" and "fatigued." Presence of excessive worry was not related to rated anxiety on rating scales.

Conclusion: These results show that excessive worry and GAD may be common in patients with complaints about memory functioning. Assessment should specifically assess this issue, as rated anxiety was not related to its presence.

NR64 Monday, May 15, 9:00 a.m.–10:30 a.m.

Relationship Between Religion and End-of-Life Treatment Preferences Among Geriatric Patients

Oscar R. Heeren, M.D., *Department of Psychiatry, Baltimore VAMC, 10 North Greene Street, Baltimore, MD 21201*; Kumar Menon, M.D., Allen Raskin, Ph.D., Paul E. Ruskin, M.D.

Summary:

The purpose of this study was to determine if religious preference and religiosity influenced choosing end-of-life treatments in medically ill geriatric patients. The sample consisted of 374 males 60 years of age or older, hospitalized on the acute medical service at the Baltimore Veterans Affairs Medical Center. Choices for end-of-life treatment preferences were CPR, mechanical ventilation, tube feeding and IV fluids within six different illness scenarios. Patients indicated how often they attended religious services, how much strength and comfort they got from religion, and how religious they would describe themselves. Analyses of variance were performed using as the dependent variables the summation scores across the six scenarios of a willingness to undergo each of the four life-saving procedures. The religious preference and religiosity scores served as the independent variables. Only tube feeding showed a significant ($p < 0.05$) relationship, with Catholics less willing to undergo this procedure than other Christians. This trend continued for the other life-saving procedures for the Scheffe range test.

NR65 Monday, May 15, 9:00 a.m.–10:30 a.m.

Coping Strategies in Patients with Mitral Valve Prolapse

Jung-Chen Chang, Ph.C., *Nursing Department, University of Washing, No. 83 Nan-Chang Street, Lo-Tung l-Lan 265, Taiwan*; Chau-Shoun Lee, M.D.

Summary:

Objective: The study investigated ways of stress coping and their relationship with demographic factors in patients with mitral valve prolapse (MVP).

Methods: A total of 32 MVP patients, ascertained by standard echocardiographic methods, completed Taiwannese Coping Strategies Inventory, including eight primary coping strategies. Their mean age was 29.25 ± 10.0, 14 (43.8%) male, 15 (46.9%) married, 22 (68.8%) having folk belief, and education years 12.5 ± 2.8.

Results: In face of stress, MVP patients were most likely to use Cognitive Restructuring and least likely to use Social Withdrawal ($t = 8.4$, $df = 31$, $p = .000$). Additionally, they used more Engagement than Disengagement strategies ($t = 5.1$, $df = 31$, $p = .000$). Age was positively related to the use of Problems Solving ($r = .37$, $p = .036$), Problem Avoidance ($r = .35$, $p = .047$), and Self-criticism ($r = .38$, $p = .034$). Wishful Thinking was more used in patients having folk belief than those having other religions ($t = 2.4$, $df = 30$, $p = .021$). Females were more likely to use Support Seeking than males ($t = 2.2$ $df = 30$, $p = .039$).

Conclusions: MVP patients tend to use Problem-focused Engagement as coping strategies. Elder patients might use Problem Solving at first, but change to Problem Avoidance and Self-criticism once stress resolved. The relationship between Taiwannese folk belief and Wishful Thinking strategy may be an interest for further study.

NR66 Monday, May 15, 9:00 a.m.–10:30 a.m.

Work Stress and Emotional Health in the U.S. Air Force

Steven E. Pflanz, M.D., *Department of Mental Health, FE Warren Air Force Base, 408 West First Avenue, Cheyenne, WY 82001*

Summary:

Objective: Almost 30% of American workers report exposure to mental stress at work and 14% believe that their experience of work stress could be deleterious to their mental health. This study examined the incidence of occupational stress and its relationship to mental illness in military personnel.

Methods: A total of 76 military personnel answered a 65-item survey that included items on the perception of occupational stress and reported life changes. It incorporated the 43-item Schedule of Recent Experiences (SRE). By adding the weighted values assigned to the 43 items, each respondent was given an SRE score, which is a measure of overall stress and has been shown to be predictive of future illnesses.

Results: Significantly fewer military personnel reported job stress than the general American working population ($p < .05$). A total of 23% reported suffering from significant work stress, 14% reported that work stress was causing them significant emotional distress, and 7% reported suffering from work stress that was so severe that it was considered to be damaging to their emotional health. The average SRE score for all respondents was 161, reflecting increased risk for future illnesses. Generic work stressors were endorsed more frequently than military specific stressors.

Conclusions: These results support previous research that suggests that work stress may be a significant occupational health hazard in the U.S. military. Using these data, interventions can be planned to mitigate the impact of stress caused by the military work environment on the mental health of military personnel.

NR67 Monday, May 15, 9:00 a.m.–10:30 a.m.

The Relationship Between Serum Lipid Levels and Suicidality in Suicide Attempters

Heon-Jeong Lee, M.D., *Department of Psychiatry, Korea Univ. Ansan Hospital, 516 Go-Jan Dong, Ansan, Kyunggi-Do 425-020, Korea*; Yong-Ku Kim, M.D., Leen Kim, M.D., Min-Soo Lee, M.D.

Summary:

Objectives: Many studies have demonstrated that suicide is related to low serum cholesterol level, whereas conflicting results have also been reported. The aims of the study are to determine whether suicidal attempters have low lipid concentration and to identify the relationship between suicidal attempt severity and serum lipid levels.

Methods: Subjects were 50 suicidal attempters who visited the emergency room at Korea University Medical Center between July 1998 and June 1999. All subjects had been interviewed by psychiatrist and evaluated with risk-rescue rating, HDRS, and BPRS. They were diagnosed as major depressive disorder (n = 29), personality problem (n = 19), and schizophrenia (n = 2). Serum lipid levels in 50 suicidal attempters were compared with those in 50 nonsuicidal hospitalized psychiatric patients corresponding to the age, sex, and diagnosis of the suicidal attempters. We also examined the Spearman's rank correlations between the serum lipid levels and risk-rescue score.

Results: The serum total cholesterol level
($t = -3.29$, $p = .001$), total lipid level
($t = -2.62$, $p = .01$), and LDL level
($t = -2.64$, $p = .011$) in suicidal attempters were significantly lower compared with nonsuicidal controls. In major depressive patients, total cholesterol level, total lipid level, and LDL level in suicidal attempters were significantly lower than those of nonsuicidal controls. In personality problem patients, however, only serum total cholesterol level was significantly lower. Risk-rescue score was negatively correlated with serum total cholesterol level ($p = -.293$, $p = .039$), and positively correlated with BPRS ($p = .544$, $p < .001$), and HDRS ($p = .488$, $p = .001$).

Conclusion: The lipid levels in suicidal attempter were significantly decreased. Suicidal attempt severity was also significantly correlated with serum total cholesterol level. These findings suggest that low serum cholesterol may be related with severe impulsive suicidal attempt.

NR68 Monday, May 15, 9:00 a.m.–10:30 a.m.

Circumstances of Suicide Among Individuals with Schizophrenia

Julie A. Kreyenbuhl, Ph.D., *MD Psychiatric Research Center, po box 21247, Baltimore, MD 21228*; Deanna L. Kelly, Pharm. D., Robert R. Conley, M.D.

Summary:

Objective: The goal of this report is to compare the circumstances of suicide between individuals with and without a diagnosis of schizophrenia.

Method: The psychological autopsy method was used to gather information on the circumstances of suicide of 15 victims with schizophrenia and 100 victims without schizophrenia whose families had donated brain tissue to the Maryland Brain Collection between September 1989 and August 1998.

Results: Suicide victims with schizophrenia exhibited more lifetime depressive symptoms than persons without schizophrenia ($p = 0.04$). Jumping from a height was the most frequently used method of suicide among persons with schizophrenia (40%), whereas gunshot wounds were most common among persons without schizophrenia (37%). Although the difference was not statistically significant, a smaller proportion of persons with schizophrenia (20%) planned the suicide, compared with 47% of those without the disorder ($p = 0.08$). A smaller, but noteworthy proportion of persons with schizophrenia (40%) made efforts to ensure the lethality of the suicide, compared with 79% without schizophrenia ($p = 0.003$).

Conclusions: Suicide in schizophrenia is a significant clinical problem, and opportunities to intervene prior to the act are often limited. Therefore, sustained efforts to reduce depressive symptoms may prove to be an effective suicide prevention strategy.

NR69 Monday, May 15, 9:00 a.m.–10:30 a.m.

Suicide in Travis County, Texas: 1994–1998

Siqing Li, M.D., *Austin Psychiatric Resident Program, Austin State Hospital, 4100 Guadalupe, Austin, TX 78751*; Lawrence A. Hauser, M.D., Beilin Gao, M.D.

Summary:

Suicide is the ninth leading cause of death in the United States. Suicide in Travis County, Texas, has not been adequately studied. To describe the occurrence of completed suicide in Travis County, a total of 426 cases of completed suicide were collected between 1994 and 1998, data analyzed with Chi-square test and T-test, Annual suicide rate in Travis County is 13.0 per 100,000. The suicide rate of Caucasian males has the highest annual rate among all races. The suicide rate in Hispanics is between those of Caucasians and blacks. The highest suicide rate is for those aged 75 and over. A second peak is between ages 45–54. Gunshot is the most common suicide method in both males and females (60.8% and 37.3%, respectively). The person with the characteristics of Caucasian, male, and age 75 and over is at the highest risk for suicide. Reducing the availability of firearms may have a significant impact on the suicide rates in Travis County.

NR70 Monday, May 15, 9:00 a.m.–10:30 a.m.

Suicidal Behavior in the Elderly

Yoshiko Nishimatsu, M.D., *Department of Psychiatry, Nippon Medical School, 1-1-5 Sendagi, Bunkyo, Tokyo 113-8603, Japan*; Minshuku Ko, M.D., Takuya Saito, M.D.

Summary:

Objective: In Japan the proportion of the population older than 65 year old reached 15% in 1996 and is still growing. The rate of suicide among the elderly is higher than in any other age group, and more than 25% of suicide is in the elderly. Also 85% of the elderly who commit suicide have psychiatric illness. Therefore, we investigated the rates and patterns of suicide among psychiatrically ill elderly patients in Japan.

Method: From 1990 to 1999, 1654 consecutively admitted patients older than 65 were followed after discharge for suicidal behavior. The diagnosis of the patients was dementia in 919 patients (55.6%), affective disorder in 424 patients (25.6%), schizophrenia in 68 patients (4.1%), anxiety disorder in 92 patients (5.6%), substance-related disorder in 68 patients (4.1%), and other diagnosis in 92 patients (5.6%) were assessed.

Result: Suicide attempts were found in 67 patients (4.1%). The diagnosis of patients with suicide attempt was anxiety disorder in three patients (3%), schizophrenia in two patients (3%), dementia in 30 patients (3%), and affective disorder in 32 patients (6%). Seven patients (0.4%) committed suicide. The diagnosis in suicide patients was affective disorder in six patients (1.4%) and anxiety disorder in one patient (1%). All seven patients had previous suicide attempts and hanging was chosen by all patients as the method.

Conclusion: The elderly patients with affective disorder have the highest risk for suicide attempts and completed suicide. Previous suicide attempt is an important predicting factor for completed suicide.

NR71 Monday, May 15, 9:00 a.m.–10:30 a.m.

Firearms and Suicide in Travis County, Texas: 1994–1998

Beilin Gao, M.D., *Shenzhen Kangnin Hospital, Guizhu Road #1080, Guang Zhou Shenzhe 518020, China*; Siqing Li, M.D.

Summary:

Objective: Texas has a high firearm suicide rate among states. The present study examines the association between demographic factors and the use of firearm vs non-firearm suicide methods using data covering the years 1994–1998.

Methods: 235 suicide completes by firearm and 191 by non-firearm were analyzed with Chi-square and T-test.

Results: (1) Average age of using firearm suicides is significantly higher than that of using non-firearm suicides. (2) Caucasians commit suicide by firearm significantly more often than that by non-firearm methods; Asians have significantly lower firearm suicides than that of non-firearm suicides. (3) Males age 65 and over and aged 45–54 have significantly higher firearm suicides than non-firearm suicides.

Conclusions: People who are male, Caucasian, and aged 65 and over were more likely to be associated eith the use of firearm as a suicide method. However, the methods of suicide are different with race, sex, and age. The prevention strategies of suicide should be explored in different ways.

NR72 Monday, May 15, 9:00 a.m.–10:30 a.m.

Comparative Trial of Dysthymia Treatment

Marcelo F. Mello, M.D., *Department of Psychiatry, Servidor Publico, R. Jorge Coelho 157, apt. 21, Sao Paulo 01451-020, Brazil*; Luciana Myczkowicz, M.D., Paulo R. Menezes, M.D.

Summary:

We compared the outcome of 35 outpatients with dysthymic disorder when treated with moclobemide associated with interpersonal therapy adapted and moclobemide associated with clinical follow-up. Psychiatrists performed the diagnostic evaluations using the ICD (International classification of Diseases) symptoms checklist according to the ICD-10 criteria. The treatment has an acute phase of eight weeks and a continuation phase of 48 weeks. The patients were evaluated by trained raters using the HAM-D-17, MADRS, Global Assessment Functioning Scale, and the Quality of Life and Satisfaction Questionnaire at baseline, 12, 24, and 48 weeks. The groups are comparable for demographic and clinical data. Although the IPT associated with moclobemide group has a better outcome with a continued improvement, these differences are not statistically significant (ANOVA). As the dropout late is very high (17 patients, 48%), the small sample size affected the results. More trials should be done in order to study the efficacy of the IPT plus medication combination treatment for dysthymic disorder.

NR73 Monday, May 15, 9:00 a.m.–10:30 a.m.

Comparative Hemodynamic Effects of Urapidil and Labetalol During ECT

Jordi Blanch, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Graciela Martinez-Palli, M.D., Richard Navines, M.D., Jose-Manuel Arcega, M.D., Maria-Luisa Imaz, Miquel Bernardo, M.D., Carmen Gomar, M.D.

Summary:

Introduction: Urapidil, a postsynaptic α_1-adrenergic antagonist, has been reported to attenuate the hypertensive response in some surgical procedures, but never in electroconvulsive therapy (ECT). This study evaluates the effectiveness of urapidil in preventing the hemodynamic response of ECT, comparing it with no-drug and labetalol pretreatments.

Methods: Twenty-seven patients undergoing a series of consecutive ECT treatments received pretreatment with: no-drug; labetalol, 0,2 mg/kg; or urapidil, 25 mg. Measurements of systolic, diastolic, and mean blood pressure (SBP, DBP, and MBP) and heart rate (HR) were recorded during awake state, before anesthetic induction, and 1, 2, 5, 10, and 30 minutes after convulsion ended. Duration of motor and electroencephalographic convulsion were also recorded.

Results: After anesthetic induction, HR similarly increased for no-drug and urapidil pretreatments, whereas it decreased when labelatol was given. After ECT, SBP, DBP, and MBP, increased reaching peak values for all three regimens at minute 1. However, labetalol and urapidil attenuated the peak increase of blood pressure by about 50%. Blood pressure returned to baseline values earlier when antihypertensive pretreatment was given. There were no differences either in motor or in electroencephalographic convulsion duration between the three pretreatments.

Conclusions: Labetalol and urapidil similarly attenuate the hemodynamic response to ECT without effects on the duration of convulsion.

NR74 Monday, May 15, 9:00 a.m.–10:30 a.m.

Light Therapy to 26 Bipolar Patients

Eduard M. van Gent, M.D., *Department of Psychiatry, Slingeland Hospital Paaz, po box 169, Doetinchem, NL 7000 AD, Netherlands*; Harry J. Keegstra, M.D., Willem Barents, Ph.D.

Summary:

Seasonal affective disorders (SADS) are not only an entity of depressive disorders but an also occur in the bipolar spectrum. Some authors have found a high percentage of bipolar patients in their sample. Others mentioned that lithium therapy decreases the success of light therapy.

In the present study 156 SADS patients were screened for bipolar disorder and the effect of light therapy with or without medication. The regular dose of 2500 lux bright white light for two hours on five successive days was given to all SADS patients.

Of the 26 bipolar patients, 17 were using lithium, one carbamazepine, three had no medication, and the five others only took antidepressants. Some patients used combinations of lithium, neuroleptics, and antidepressants. For measurements the Beck Depression Inventory with three items added for SADS and the Hamilton Depression Rating Scale for light (HDRSadd) were used. Of the patients on lithium, 59% percent had more than 50% reduction of the BDIadd and/or on the HDRSadd. Of the patients not on lithium, 89% had success. Two patients became manic and two hypomanic. The opinion in the literature that lithium decreases the effect of light therapy will be discussed.

NR75 Monday, May 15, 9:00 a.m.–10:30 a.m.

A Case Series Using ECT for the Treatment of Psychiatric Illness in Patients with Mental Retardation

Daniel Acosta, *Department of Psychiatry, ECU SOM, Doctor's Park #6, Greenville, NC 27858*; Diana J. Antonacci, M.D., Christopher M. de Groot, M.D.

Summary:

Objective: Electroconvulsive therapy (ECT) is a proven, safe, and effective treatment for patients with psychiatric conditions. However, significant conflict over the role of ECT in mentally retarded (MR) patients has limited investigations of the efficacy of ECT in this population. Nonetheless, both theoretical constructs and anecdotal case reports support further research in this arena.

Methods: A retrospective chart review of five patients with mental retardation and pharmacologically resistant psychiatric symptoms were treated with ECT. Post hoc examinations of demographic and other variables potentially predicative of improvement

were explored. The ECT treatment paradigm was consistent with that used for general adult patients in our tertiary care university hospital.

Results: The overall positive response rate was 60% (3/5) with no serious complications. One patient had a marked and robust response necessitating no further intervention. Two patients were found to require ongoing outpatient maintenance ECT. Finally, two patients who appeared to be initial responders had their treatment discontinued due to a plateau of improvement and increased cognitive impairment.

Conclusion: ECT is a safe and effective somatic therapy for psychiatric conditions in MR patients. Similar to their non-cognitively impaired peers, MR patients have affective disorders as an independent predictor of a positive response to ECT.

NR76 Monday, May 15, 9:00 a.m.–10:30 a.m.

Use of ECT for Severe Episodic Aggression in Patients with Treatment-Refractory Psychosis

Manish K. Parikh, M.D., *Department of Psychiatry, Maimonides, 675 McLean Avenue, Yonkers, NY 10704*; Angela M. Hegarty, M.D., Elda P. Sancho, M.D.

Summary:

Background: In spite of increased attention paid in recent years to the problem of aggression in patients with psychiatric disorders, review of the literature reveals that there has been little systematic or controlled study of treatment for patients not responsive to commonly used medications. The present study examines use of ECT for severe episodic aggression in patients with treatment-resistant psychosis.

Method: A retrospective review of the medical records of 12 patients who received ECT for treatment-resistant psychosis with severe episodic aggression at a maximum security forensic facility. The patients received at least 12 bilateral treatments with brief pulse stimuli given between two to three times weekly.

Results: Seven of the 12 patients were not included in the review-four because of insufficient follow-up, two because they were on medications concomitantly with ECT, and one because of confidentiality issues. None of the excluded patients presented an increase in aggression or side effects following treatment with ECT. All five of the patients reviewed showed overall behavioral improvement and a decreased number of violent episodes during the year following treatment.

Conclusion: ECT may be useful in reducing the frequency of violent episodes in patients with treatment resistant aggression and psychosis. Prospective controlled studies are needed to assess the significance of these findings.

NR77 Monday, May 15, 9:00 a.m.–10:30 a.m.

A Prospective Naturalistic Study of 326 Agoraphobic Panic Patients

Giulio Perugi, M.D., *Department of Psychiatry, Institute of Psychiatry, Via Roma 67, Pisa 56100, Italy*; Cristina Toni, M.D., Franco Frare, M.D., Belen Mata, M.D., Barbara Vitale, M.D., Francesco Mengal, Ph.D., Hagop S. Akiskal, M.D.

Summary:

Objective: How far the results of randomized controlled studies apply to everyday care cannot be judged without the regular measurements of outcomes in daily practice. We report systematic data on a three-year naturalistic prospective study on panic disorder-agoraphobic (PDA) patients treated with antidepressants in a setting of routine clinical practice. Our aim is to describe the evolution of PDA in relation to the treatments employed and to explore demographic and clinical characteristics that might be predictive of outcome.

Method: 326 DSM-III-R PDA patients treated with antidepressants in a setting of routine clinical practice were included in a three-year naturalistic prospective study. We utilized structured and semistructured instruments, including the Structured Clinical Interview for Diagnosis and the Longitudinal Interview Follow up Examination. The main antidepressants used were imipramine (39%), clomipramine (28.5%), and paroxetine (23.3%); only 9% of patients received other antidepressants.

Results: 147 patients (45.1%) stayed on medication throughout the entire period of the follow-up. Of those who interrupted the treatment, 38% stayed in remission. The probability of achieving at least one remission during the three year follow-up period was, respectively, 96.5% for PD and 95.9 for agoraphobia. Relapses after a period of at least two months of complete remission were also common, and the probability of presenting at least one relapse during the three-year follow-up period was, respectively, 67.1% for PD and 39% for agoraphobia. The longest period of remission of PD is associated with low severity, medium-lasting course in patients with an onset of the illness in young adulthood. Less severe agoraphobia associated with moderately severe panic attacks appears to confer a better control of phobic behavior. All three major drugs were reasonably well tolerated (only 9% dropped out because of side effects), with sexual dysfunction and increased appetite being the most common side effects at the last evaluation; in the first phase of the treatment anticholinergic effects and jitteriness were more common with TCAs.

Conclusion: Both classical antidepressants and paroxetine emerge as useful treatments in the long-term management of PDA; paroxetine appears particularly useful in PDA patients because it was significantly less likely to induce jitteriness, thereby reducing barriers to compliance.

NR78 Monday, May 15, 9:00 a.m.–10:30 a.m.

Improving Adherence of Antidepressants by Pharmacies

Hein P. van Hout, Ph.D., *Institute Health Foundation, Europalaan 506, Utrecht 352 6KS, Netherlands*; Rob Heerdink, Ph.D., Guy Goodwin, M.D., Bram B. Bakker, Ph.D., Hugo Nieuwenhuyse, Ph.D.

Summary:

Background: A pooled analysis was performed to assess the efficacy of mirtazapine in comparison with fluoxetine, paroxetine, and citalopram in the relief of anxiety symptoms related to depression.

Method: Data from three double-blind controlled studies of mirtazapine (MIR) vs fluoxetine (FLU), paroxetine (PAR) and citalopram (CIT) in depressed patients were analysed. The studies had similar in exclusion criteria. Statistical analyses were performed on the basis of the intention-To-treat group(s). To evaluate the onset of efficacy on anxiety symptoms related to depression, the absolute change from baseline on anxiety/somatization factor of the HAMD-17 scale, which was used in the FLU and PAR trials, and of the scores on the HAM-A scale, which was used in the CIT and PAR trials, were analysed. In addition, responder rates on HAM-A factors 1 ("Somatic anxiety") and 2 ("Psychic anxiety"), defined by a reduction of at least 50% and remitter rates on HAM-A, defined as a HAM-A total score ≤ 8, were analysed.

Results: In the pooled analysis on the absolute change from baseline on HAMD-17 anxiety/somatization factor, mirtazapine showed a statistically significantly greater reduction from week 1 onwards. On HAM-A, a statistically significant difference at week 1 was seen. Responder rates on HAM-A factors 1 and 2 were detected in favor of mirtazapine with a statistically significant difference at week 1 for both factors. More mirtazapine-treated patients were classified as remitters from week 1 onwards, reaching statistically significant levels at week 2, 3 and 4.

Conclusion: Mirtazapine proved to have a better efficacy on anxiety symptoms related to depression with a faster onset of anxiolytic effect compared with the SSRIs.

NR79 Monday, May 15, 9:00 a.m.–10:30 a.m.

Association Between QEEG Characteristics and BPRS Subscales in Bipolar Disorder and ????

Alexandra L. Sporn, M.D., *Department of Psychiatry, Harvard Medical School, 62 Pleasant, Brookline, MA 02446*; Dean F. Salisbury, Ph.D., Paola Massoni, Iris Fisher

Summary:

This study examines the spectral properties of brain electrical activity in schizophrenia and bipolar disorder in relation to clinical symptoms. Resting Q-EEGs of 25 schizophrenic patients, 16 bipolar patients, and 25 controls were obtained with eyes open and closed. Patients were rated on the BPRS scale. Several of BPRS scores were correlated with the Q-EEG measures using Pearson correlation analysis.

There was a strong positive correlation between BPRS-8 (grandiosity), a measure of manic state, and Theta2 power with eyes open across the frontal, central, and parietal areas ($r = 0.433$; 0.497; and 0.480 respectively, $p < 0.01$). This correlation was stronger for the bipolar group alone ($r = 0.636$; 0.679; and 0.693, $p < 0.01$). In the schizophrenic group there was a positive correlation of BPRS-12 (hallucinatory behavior) and Theta2 power with eyes open in frontal, central, and parietal areas ($r = 0.466$; 0.400; and 0.438, $p < 0.05$). In schizophrenic group there was also a positive correlation between BPRS-12 score and Alpha2 power with eyes open, particularly in the frontal area ($r = 0.537$, $p < 0.01$).

Lastly, there was a strong negative correlation of Alpha2 attenuation (normal suppression of Alpha2 rhythm with eye opening) and BPRS-8 in the bipolar group ($r = -0.583$, $p < 0.05$).

These data suggest that certain changes in the Theta2 and Alpha2 spectrum may be associated with specific symptoms.

NR80 Monday, May 15, 9:00 a.m.–10:30 a.m.

Schizophrenia
The Influence of Acupuncture on the Treatment of Cocaine-Addicted Patients

Daniela C. Ceron, *Department of Psychiatry, University of Sao Paulo, Joao Moura 942 AP21, Sao Paulo, SP 05412-002, Brazil*; Susan M. Mondoni, Andre Malbergier, M.D., Guilherme R. Silva, M.D.

Summary:

Objective: Acupuncture has been suggested as a potential clinical instrument to improve drug treatment outcome, though more rigorous clinical researches are still needed. This study intends evaluate the influence of acupuncture on cocaine abuse treatment in a specialized service in Brazil.

Method: Sixty-four cocaine-dependent patients who came for treatment were randomly assigned to two groups. The case group received psychiatric treatment, behavioral-oriented group psychotherapy, and auricular acupuncture (one-hour session once a week). The control group received the same treatment but a "placebo acupuncture" (the needles were introduced in auricular points that are considered "non-effective points" in the literature). The patients were evaluated by a five-item scale (drug use, employment status, family relationship, leisure, and medical complications) at baseline, and at weeks 4, 8, and 12. The study was double blind as neither the interviewer nor the patients were aware of the treatment status of each patient. ANOVA was used to compare the average scores between the two groups.

Results: Eight controls and 13 cases completed the treatment. The two groups did not differ in relation to sociodemographic characteristics. The outcome of the case group was significantly better than the control group ($p < .01$).

Conclusion: Acupuncture can be a useful coadjuvant in cocaine abusers' treatment.

NR81 Monday, May 15, 9:00 a.m.–10:30 a.m.

Cognitive Effects of Repetitive Transcranial Magnetic Stimulation in Depressed Patients

Brian Martis, M.D., *Psychiatric Institute, 1601 West Taylor, Chicago, IL 60612*; Valorie Carson, Rajiv P. Sharma, M.D., Eileen M. Martin, Ph.D., Philip G. Janicak, M.D., Mauli Verma, M.D., Cherise Chase, R.N.

Summary:

The objectives of this study are to determine the neurocognitive effects of (a) a course of daily repetitive transcranial magnetic stimulation (rTMS) and (b) a single rTMS treatment session, in subjects with major depression. Subjects randomized to rTMS in an ongoing study (rTMS vs. ECT for depression) are stimulated daily over the left prefrontal cortex. We are administering a battery of neurocognitive tests to assess prefrontal function (attention and executive) in these subjects at baseline and following the last rTMS treatment (two to four weeks). To examine the effects of a single rTMS session subjects receive a shorter test battery immediately before and one hour following a treatment on day 5. Preliminary analysis of the first seven patients indicate that following rTMS treatments, subjects demonstrate improvements in divided attention, verbal fluency, working memory, and verbal memory ($p < .05$ for all comparisons). Of note, we found no evidence of adverse cognitive effects in these patients. Significance of these findings in view of the existing literature will be discussed.

NR82 Monday, May 15, 9:00 a.m.–10:30 a.m.

A Meta-Analysis of Acupuncture for Psychiatric Disorders

Andrei A. Pikalov, M.D., *Department of Psychiatry, Kansas University Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160-7341*; Elizabeth C. Penick, Ph.D.

Summary:

Objective: This is a first ever attempt to statistically analyze the efficacy of acupuncture treatment for patients with different types of psychiatric disorders by applying meta-analysis to controlled outcome studies.

Method: A comprehensive search of MEDLINE (1967–1999), PsychINFO (1986–1999), and CINAHL (1985–1999) was performed in order to locate controlled studies of acupuncture with patients suffering from substance abuse disorders, mood disorders, anxiety disorders, psychotic disorders, or somatization disorders excluding pain associated with a specific cause. One hundred and thirty-five articles were located. Studies were grouped by design, statistical methods, and type of disorder studied. Further subgrouping included type of the publication, duration of treatment, duration of the follow up, utilization of a sham treatment as a control, and use of randomization to create the nontreated control groups. Duplicate publications were excluded. Data in subgroups, groups, and overall were tabled and analyzed using the SPSS package of statistical software.

Results: Very few publications met the rigorous methodological criteria associated with a randomized, double-blind, placebo-controlled clinical trial. The most sophisticated research designs focused on acupuncture with substance abuse. Preliminary results suggest that acupuncture is effective in the short-term treatment of substance abuse and probably effective in the short-term treatment of mood disorders. For other psychiatric conditions, the results were inclusive or negative.

Conclusion: The findings suggest a cautiously optimistic but conservative approach towards possible recommendations of the use of acupuncture with psychiatric disorder. Additional well-designed studies with adequate controls are necessary to clarify indications for the procedure and its effectiveness.

NR83 Monday, May 15, 9:00 a.m.–10:30 a.m.

Characteristics and One-Year Outcome of Anxiety and Depression Outpatients in Taiwan

Jor-Chi Song, M.D., *Department of Psychiatry, TYPC, Fl 12-2, No. 67, Ta-Hsing Wt. Road, Tao-Yuan City, TW 330, China*; Andrew P. Ho, M.D.

Summary:

Objective: The reasons for the underutilization of psychiatric services by nonpsychotic patients are unknown.

Method: 1210 consecutive patients newly presenting to a psychiatric clinic are assessed. A total of 153 patients fulfilling ICD-9 criteria for anxiety or depression disorder are followed for one year. Prior help-seeking, treatment utilization, explanatory model of illness, and outcome at one year are ascertained by questionnaire, chart review, and telephone interview.

Results: 13% of the 153 patients deny prior treatment; 31% visited a psychiatrist. Explanatory model of illness is not correlated with prior or subsequent treatment utilization. During the one-year follow-up, lack of prior treatment and more formal education are correlated with more visits to the psychiatric clinic, 18.3% report treatment at other psychiatric clinics, and 46.7% report other, nonpsychiatric treatments. Patients who attribute their improvement exclusively to this clinic are less likely to utilize treatments elsewhere. At one year, 45% experienced less than significant improvement, 37% are significantly better, and 18% reported complete remission.

Conclusion: The majority of patients presenting to a psychiatric clinic with anxiety or depressive disorders seek treatment from multiple psychiatric and nonpsychiatric providers. This help-seeking pattern may be related to incomplete resolution of symptoms rather than patients' explanatory model of illness.

NR84 Monday, May 15, 9:00 a.m.–10:30 a.m.

A Comparison of St. John's Wort and SSRI Users

Leonard Lev, M.D., *Department of Psychiatry, NYPH-Cornell Medical, 21 Bloomingdale Road, White Plains, NY 10605*; JoAnne Sirey, Ph.D., Patrick J. Raue, Ph.D., Martha L. Bruce, Ph.D., Barnett S. Meyers, M.D.

Summary:

Objective: St. John's Wort is used as a non-prescription treatment for depression, but little is known about the characteristics of St. John's Wort users. This study compares the demographic, clinical, and attitudinal characteristics of St. John's Wort and SSRI users.

Method: Individuals taking St. John's Wort (SJW, N = 41) or an SSRI (fluoxetine, paroxetine, sertraline, N = 40) were recruited through advertising. Study participants were interviewed to assess depression (DSM-IV MDD criteria, HAM-D), attitudes toward treatment, and patterns of medication and service use.

Results: SJW users were more likely to be employed ($p = .06$), have higher income ($p = .02$), live with family ($p = .03$), and report better self-rated health ($p = .001$). Similar proportions of SJW and SSRI users met criteria for MDD (31.7 vs. 22.5%) and for minor depression (14.6 vs. 17.5%). Most (63%) SJW users had seen a mental health professional in the past. They were less satisfied with mental health contacts than SSRI users ($p = .015$). SJW users used medication less consistently than SSRI users ($p = .032$). SJW users reported greater need for treatment ($p < .001$) and lower self-rated illness severity ($p = .001$).

Conclusions: SJW users have different demographic and attitudinal profile, but present with similar clinical profiles as SSRI users. SJW users should be screened for depression and evaluated for additional service needs.

NR85 Monday, May 15, 9:00 a.m.–10:30 a.m.

Description of an Outpatient Sample of Patients Diagnosed with Depression in a Managed Care Environment

Alisa B. Busch, M.D., *Health Care Policy Department, Harvard Medical School, 180 Longwood Avenue, Boston, MA 02115*; Vanessa Azzone, Ph.D., Shelly F. Greenfield, M.D.

Summary:

Objective: Data from a sample of employed adult enrollees and dependents from five large employers in a large managed behavioral carveout are analyzed to: 1) determine the amount of mental health/substance abuse (MHSA) outpatient treatment provided for major depression; 2) within this population, determine the amount of treatment for psychiatric comorbidity; and 3) determine the proportion diagnosed with major depression remaining in treatment through the continuation phase.

Method: Observational study using 1995–1997 claims and pharmacy data from adult outpatients (n = 12,676) in a managed behavioral health carveout. Frequencies and percentages are obtained on categorical variables.

Results: Preliminary results suggest: 1) 52.4% of the total MHSA outpatient treatment provided was for major depression; 2) within the depressed population, comorbidity treatment included: 0.2% psychotic disorder, 0.3% bipolar disorder, 7% anxiety disorder, 1.5% substance abuse/dependence, 2% adjustment disorder, and 4.3% personality disorder; 3) at least 61% of depressed outpatients did not complete continuation-phase treatment.

Conclusion: Major depression accounts for more than 50% of outpatient treatment in this population. The majority of enrollees diagnosed with major depression did not complete continuation-phase treatment. Further understanding of contributing patient, provider, and/or benefit design factors is a critical next step in ensuring patients receive appropriate care.

NR86 Monday, May 15, 9:00 a.m.–10:30 a.m.

Response to a Partial Hospitalization Treatment Program: A Comparison of Inpatient and Outpatient Referrals

Keri L. Lemmond, M.D., *Department of Psychiatry, Brown University, 345 Blackstone Boulevard, Providence, RI 02904-2702*; Jill I. Mattia, Ph.D., Tina Egan, M.S.W., Rendueles Villalba, M.D.

Summary:

A naturalistic study of the therapeutic effectiveness of a partial hospitalization program (PHP) was conducted. Sixty-eight patients admitted to the Rhode Island Partial Hospitalization Program were administered daily Burns Depression Checklists and Anxiety Inventories. Demographic information, diagnosis, and referral source were prospectively collected. Repeated measures MANCOVAs were performed to compare outpatients and inpatients enrolled in the PHP.

After adjusting for a covariant of baseline severity, effect sizes indicated that while all patients improved during treatment, the largest improvement occurred by day 2 with additional gains evidenced through days 3 and 4. Outpatient versus inpatients began and ended treatment more depressed and anxious, and there was some evidence to suggest that anxious outpatients versus anxious

inpatients improved more quickly from day 1 to day 2. We propose the following explanations: (1) the act of initiating treatment relieves symptoms as hope and a sense of security are instilled, (2) symptom reduction is an early phase of overall improvement with insight and empowerment occurring after stabilization of severe symptoms, or (3) a placebo effect accounts for the pattern of improvement. This study supports the claim that PHP is a rapidly effective approach for stabilizing acute psychiatric illness. Both inpatient and outpatient referrals experienced substantial clinical gains in our partial hospitalization program.

NR87 Monday, May 15, 9:00 a.m.–10:30 a.m.

Treatment of Panic Disorder in an Office-Based Practice

Carlos Blanco, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Imram Khan, M.D., Renee Goodwin, Ph.D.

Summary:

Objective: The authors reviewed the pharmacological treatment of patients with a diagnosis of panic disorder in outpatient private practice and characterized these prescription patterns by patient age, sex, race, payment source, and physician speciality.

Methods: The authors analyzed physician-reported data from the 1992–1996 National Ambulatory Medical Care Survey, comparing visits to psychiatrists and other variables.

Results: Overall, 83,5% of the patients were receiving at least one medication. The most commonly prescribed medications were benzodiazepines (57.3%) and SSRIs (32.7%). There were no differences in the demographic distribution of patients. However, patients seen by a psychiatrist were more likely to have a comorbid psychiatric disorder. There were no changes in prescription patterns from 1992 to 1996.

Conclusions: Many patients with panic disorder do not receive pharmacological treatment. Treatment by psychiatrists is associated with a higher likelihood of receiving medication. No patient characteristics were identified that predicted prescription of psychotropics.

NR88 Monday, May 15, 9:00 a.m.–10:30 a.m.

Initial Experience with a Primary Care Depression Disease Management Program

Catherine J. Datto, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, 7th floor, Philadelphia, PA 19104*; James C. Coyne, Ph.D., Mark A. Miani, M.D., David A. Horowitz, M.D., Ira R. Katz, M.D.

Summary:

We present early experience from a primary care depression disease management program in an academic health system. Of the first 97 patients enrolled, 90 had unipolar depression; and 83 of these had CES-D scores >15. Mean age (SD) was 49 (15), 77% were women, and 76% reported previous episodes of depression. CES-D scores at enrollment were 35.3 (8.9) and those at 12 weeks or the termination were 20.8 (10.4); $F = 119$; $p = <.001$. 42% improved by at least 50%.

Two measures were used to assess AHCPR algorithm adherence: prescription of 'adequate doses' of an antidepressant, and evaluation at four–six weeks with treatment modification as appropriate. Indicator adherence was 73.2% and 40.8%, respectively, and 35.2% to both. Treatment response was significantly related to adherence; F (interaction) = 11.1; $p = .001$. For categorical response, the effect size was 2.1.

Depression disease management is effective in the primary care office and should include quality monitoring with ongoing assessment of adherence. Patient care should include early referral for specialty care when algorithm adherence cannot be achieved in primary care.

NR89 Monday, May 15, 9:00 a.m.–10:30 a.m.

Risperidone Treatment of Chronic Tic Disorder and Tourette's Syndrome

Eun Young Oh, M.D., *Department of Psychiatry, Ajou University, San5 Wonchon-Dong, Paldal-Gu, Suwon, Kyunggi-Do 442-749, South Korea*; Jung-Eun Lee, M.D., Yoon-Mi Shin, M.D.

Summary:

Objective: The purpose of this trial was to investigate the short-term and long-term safety and efficacy of risperidone in the treatment of chronic tic disorders and Tourette's syndrome in children and adolescents.

Method: Twenty-five patients (23 males, two females/14 Tourette's syndrome, 11 chronic motor or vocal tic disorders) participated a 16-week, open-label trial. The patients ranged in age from 6 to 18 years. Clinical responses are measured by the Yale Global Tic Severity Scale (YGTSS). The patients were seen at baseline and for three follow-up visits (four-week, eight-week, 16-week). Risperidone was started at 0.5 mg/day and incresed by 0.5 mg/day or 0.5 mg/b.i.d every five days.

Results: (1) Clinical response revealed a statistically significant reduction on tic scores ranging from 33.17 to 21.78 (mean improvement = 34.33%). (2) Doses of risperidone at the end of the trial ranged from 1 mg to 3 mg (mean = 2.02 mg/day). (3) Most frequent side effect was sedation (9pt, 36%), tiredness (4pt, 16%), weight gain (2pt, 8%), light-headedness (1pt, 4%), nausea (1pt, 4%), no extrapyramidal side effects. (4) Although positive effects were evident in four weeks, statistically significant improvement of tic symptoms appears in eight weeks.

Conclusions: Risperidone appears to be effective in reducing tic frequency and intensity. Low-dose risperidone may be a promising alternative to conventional medications used for treating the symtoms of Tourette's syndrome and chronic tic disorders in Korean children and adolescents.

NR90 Monday, May 15, 9:00 a.m.–10:30 a.m.

Prevalence of Polypharmacy in Different Clinical Settings: It's Relation to Drug-Drug Interactions

Mujeeb U. Shad, M.D., *Psychiatric Research Institute, 1100 North St. Francis, Wichita, KS 67214*; Cheryl Carmichael, B.A., Sheldon H. Preskorn, M.D., Dale Horst, Ph.D.

Summary:

Antidepressant use has grown substantially over the past decade. Virtually every physician-clinician will either use or encounter a patient on an antidepressant. Different classes of antidepressants can interact pharmacodynamically and/or pharmacokinetically with coprescribed medications to alter clinical outcome. This study was done to assess the extent and nature of polypharmacy in patients on antidepressants in five practice settings; a health maintenance organization (HMO), a university outpatient HIV clinic (UHIV), a resident psychiatric outpatient clinic (ROPC), an outpatient community mental health center (CMHC), and a Veteran's Administration medical center (VAMC), with in patients and outpatients treated by either primary care physicians or various specialists. Only patients on at least one antidepressant were included. Pharmaceutical products consisting of more than one drug were counted as separate chemical entities. Analysis of the data showed:

	HMO (n = 1968)	UHIV (n = 67)	RPOC (n = 224)	CMHC (n = 48)	VAMC (n = 1076)
Patients on 1 drug	22%	2%	29%	8%	7%
Patients on 2 drugs	18%	12%	24%	31%	12%
Patients on 3 drugs	16%	9%	17%	9%	13%
Patients on 4+ drugs	44%	77%	30%	52%	68%
$\bar{x}$ # drugs	4	7	3	6	4

Polypharmacy during antidepressant treatment is the rule rather than exception. Hence, a sizable percentage of patients are at potential risk for drug-drug interactions.

NR91 Monday, May 15, 9:00 a.m.–10:30 a.m.

Prevalence of Domestic Violence Against Women in San Juan Teitipac, Oaxaca, Mexico

Alejandra Postlethwaite, M.D., *po box 2709, Calexico, CA 92232*

Summary:

Background: Violence and abuse among Mexican families are not an isolated phenomenon. A clear example is the town of San Juan leitipac, Oaxaca, where this study investigates the prevalence of domestic violence against its women.

Methods: I applied a multiple-choice, 17-question questionnaire to 150 women who where either married or living with their partner, and who lived in San Juan Teitipac. I explained its content and confidentiality.

Results: A total of 52% of the sample women had been physically abused by their spouses. A large percentage of abused women and abusing men where older than age 40. A total of 39.2% of the battered women were illiterate and 65.8% did not complete their elementary education; 39.2% where victimized by their spouses under the influence of alcohol. A total of 65% have more than three children. Only 11.3% of them have filed police reports against their spouses, and 12.6% of the battered women felt comfortable with the abuse.

Interpretation: There exists a large number of abused women in San Juan Teitipac, which implies that the same exists in other parts of Mexico. This problem arises mostly from ignorance and from a culture that doesn't believe in women's rights.

NR92 Monday, May 15, 9:00 a.m.–10:30 a.m.

Depression and Belief in Life After Death Among Geriatric Home-Care Patients

Glen Milstein, Ph.D., *Department of Psychiatry, Weill-Cornell, 21 Bloomingdale Road, White Plains, NY 10605*; Martha L. Bruce, Ph.D.

Summary:

Objective: Studies of geriatric populations report religious belief to be negatively associated with depressive symptoms, in particular among persons with poorer physical health. The goal of this study was to examine the relationship of depression to religious beliefs and practice among elderly homecare patients.

Method: Patients newly admitted to a Visiting Nurse agency were sampled weekly for six months, and assessed by home interviews. Depression was measured with the SCID and GDS. Participants reported religious service participation previous to their physical disability and currently. They rated the personal salience of "strong faith," importance of religion for coping, and belief in life after death.

Results: The 102 participants (65–100 yrs. [M = 78.51], 63% female, 13% nonwhite, 51.6% Catholic, 25.8% Protestant, 8.2% Jewish, 14.4% unaffiliated) reported significantly less religious practice ($p < .001$) subsequent to their physical illness. Current religious practice, salience, and coping were unrelated to depression. A total of 13.6% of participants who believe in life after death had a DSM-IV diagnosis of depression compared with 37% of those who do not believe ($p < .05$). This belief did not differ by religious denomination. Belief in life after death remained negatively associated with depressive diagnosis and symptoms ($p < .05$) when controlling for health status.

Conclusions: Previous research has suggested that religious beliefs counteract hopelessness and feelings of worthlessness by allowing self-esteem to become psychologically unbound to physical abilities. Toward the end of life in medically ill elderly, the belief in life after death appears significant to this psychological process.

NR93 Monday, May 15, 9:00 a.m.–10:30 a.m.

Relationship Between Religiosity and Symptoms of Depression

Sarabjit Singh, M.D., *Department of Psychiatry, UPC-Jefferson, 2751 East Jefferson, Suite 200, Detroit, MI 48207-4100*; Richard Balon, M.D.

Summary:

This study investigated if there is any relationship between patients religiosity and symptoms of depression.

Method: Patients (n = 20) who presented to the psychiatry outpatient clinic and were clinically diagnosed with a depressive disorder (using DSM-IV) were included in the study. They were given three self-rated questionnaires namely; DUREL index (a scale to measure religiosity), CES-D (a scale to delineate cognitive and somatic symptoms of depression) and SINGH index (a scale devised by the investigators to measure religiosity). None of the patients was on any psychotropic medication at the time of participation in the study.

Results: There was a marginally significant correlation between religiosity and the somatic subscal of CES-D. ($r = 0.41$, $p = 0.08$). Patients scoring high on religiosity had significantly higher scores on the somatic subscale of the CES-D. ($P = 0.011$). However, there was no association between religiosity and the cognitive subscale. The SINGH index was strongly correlated with the DUREL index ($r = 0.96$, $p < 0.001$). It also has good internal reliability (Cronbach's alpha = 0.80).

Conclusion: Preliminary data reflect a marginal correlation between religiosity and the somatic symptoms of depression, with there being no correlation with cognitive symptoms. Further studies need to be conducted to validate these findings.

NR94 Monday, May 15, 9:00 a.m.–10:30 a.m.

Career Plans Among Psychiatrists in Training

Babak Mirin-Babazadeghan, M.D., *Department of Psychiatry, Suny-Health Science Center, 450 Clarkson Avenue, Box 1203, Brooklyn, NY 11203*; Jiri J. Danczik, M.D., Zinat Sobhani, M.D.

Summary:

Roughly one third of all psychiatric residents are foreign-born international medical graduates (IMGs) IMG and U.S. medical graduate (USMG) psychiatrists have different practice patterns. Recent surveys showed that the IMGs tended to be older than USMGs, included a higher proportion of women, and were more racially heterogeneous. They worked longer hours, worked more frequently in the public sector, and treated a higher proportion of patients with psychotic disorders. The IMGs also received a higher percentage of their income that USMGs from Medicaid and Medicare, whereas the reverse was true for self-payment.

Objective: Assessment of career plans among psychiatrist in training, and to determine factors influencing these preferences.

Method and setting: We conducted a survey via a questionnaire distributed to the residents and fellows of the department of psychiatry at State University of New York at Brooklyn. The sample of the 32 subjects with mean age of 34 included: 17 (53.1%) male, 15 (46.9%) female 27 (84.4%) IMG, 5 (15.6%) USMG, 17 (53.1%) U.S. citizen or permanent resident, 15 (46.9%) J-visa holder. Twenty-nine (91.6%) of all subjects, including all of the IMGs, spoke one or more language(s) than English.

Results: Analysis of the data indicates that: (1) The majority of respondents preferred to work in outpatient rather than inpatient setting, ^{5}(2) IMGs were more interested than USMGs to work in academic setting, in health professional shortage areas, in urban areas, and with poor mentally ill/minority population, and (3) USMGs were more interested than IMGs to work in rural areas.

Conclusion: Career plans of psychiatrist in training seem to have different pattern among IMGs and USMGs. Further studies are necessary to find implications of this difference.

NR95 Monday, May 15, 9:00 a.m.–10:30 a.m.

Pharmaceutical Industry Impact on Psychiatry Residents' Prescribing Practices

Daniel J. Kuhles II, M.P.H., *Department of Psychiatry, Suny HSC at Syracuse, 750 E. Adams Street, Syracuse, NY 13210*; Thomas L. Schwartz, M.D., Robert J. Gregory, M.D., Alan R. Beeber, M.D.

Summary:

The last decade has seen an increase in interaction between pharmaceutical representatives and psychiatric residents. There is scant literature regarding the impact that sales personnel have on residents' prescribing practices. The authors retrospectively reviewed 100 charts from a psychiatry residency clinic and collected demographic, prescription, and sales-visit data. The timing, length, or number of visits did not lead to any change in prescribing practice. Despite alarm in the medical literature about pharmaceutical sales pressure, it does not appear that these practices lead to an increase in resident prescribing.

NR96 Monday, May 15, 9:00 a.m.–10:30 a.m.

Psychiatric Inpatients Are Not More Likely to Receive Restrictive Measures During Weekends and Holidays

Charles Jin, M.D., *Department of Psychiatry, Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada*; Leo Sher, M.D.

Summary:

Objective: Psychiatrists and mental health professionals often make extra efforts to help their patient to combat so-called "holiday blues" during weekends and holidays. We hypothesized that psychiatric inpatients also have negative changes in their symptoms on weekends and holidays. The negative changes often manifest as episode of anger, aggression, and suicidal behavior in the inpatient population, which often lead to administering additional medications, and restraining and secluding the patint. In this study we used the number of episodes of restraint and seclusion to measure the worsening of the conditions during weekends and holidays.

Method: All restraint and seclusion that occurred during one-year period were identified from a central computer database. The number of episodes of restraint and seclusion occurring during weekday hours was compared with that for weekend or holiday hours using chi-square analysis.

Results: The number of episodes in male patients aged 18–30 and 31–45 and in females aged 31–45 and 46–65 was statistically significantly higher on weekdays than on weekends and holidays ($P < 0.0001$ in all four groups). There was no statistically significant difference in the number of episodes between the rest of age and gender groups. Our results do not support our hypothesis.

Conclusion: Psychiatric patients are not more likely to receive restrain or seclusion during weekends and holidays.

NR97 Monday, May 15, 9:00 a.m.–10:30 a.m.

Unrecognized Comorbid Sexual Dysfunction

Sandra B. Lare, D.O., *Department of Psychiatry, MUSC, 171 Ashley Avenue, Charleston, SC 29425*; Lawrence A. Labbate, M.D.

Summary:

Objective: The purpose of this study was to measure patient report and clinical documentation of sexual function in male psychiatric outpatients.

Methods: Unselected established VA outpatients (N = 99, mean age 50 ± 10) were administered a five-item sexual function questionnaire at the time of their visit to a resident clinic. Questions asked about interest, arousal, orgasm, erections, and overall satisfaction over the past month. Ratings ranged from 1 to 6 (1 = greater than normal, 2 = normal, 3 = minimally diminished, 4 = moderately diminished, 5 = markedly diminished, 6 = totally absent). Diagnoses were as follows: major depression 50%, schizophrenia 24%, PTSD 20%, panic disorder 18%, alcohol dependence 15%, polysubstance dependence 5%. Medical records were evaluated for diagnosis, medications or illnesses that might affect sexual functioning, and the presence of a resident note mentioning sexual functioning within the past four visits.

Results: Mean scores for all items were in the moderately diminished range (means = 3.8–4.3). Patients reported total loss of sexual interest (30%), inability to become excited (20%), anorgasmia (34%), inability to attain erection (24%), or total sexual dissatisfaction (38%). Depressed patients reported lower scores than nondepressed patients ($p < 0.01$) on all measures. Schizophrenic patients reported better sexual function than nonschizophrenic patients ($p < 0.05$) and generally reported only mild impairment. Residents documented sexual function in 34% of patients and were more likely to document with depressed than nondepressed patients (40% vs 19%, $x^2 = 4.3$, $p = .03$). Patients typically took two psychotropics and one other drug known to affect sexual functioning.

Conclusions: These results support data indicating the pervasive prevalence of sexual dysfunction in psychiatric patients; however, sexual function is rarely documented. The authors suggest that resident interviewing more actively target sexual dysfunction.

NR98 Monday, May 15, 9:00 a.m.–10:30 a.m.

Prescribing Conventional Antipsychotics in the Era of Novel Antipsychotics

Xiao-Hong Wang, M.D., *Department of Psychiatry, Suny Health Sciences Center, 750 East Adams St, Syracuse, NY 13210*; Daniel J. Kuhles II, M.P.H., Thomas L. Schwartz, M.D., Sanjay Gupta, M.D., Bhushan S. Agharkar, Jacob Manjooran, M.D., William J. Hardoby, M.D.

Summary:

Atypical antipsychotics are first-line treatment in psychotic disorders, yet conventional antipsychotics are still prescribed in 35% of patients. Clinicians should obtain informed consent from their patients, which includes risk-benefit ratio and alternative drug treatments. We reviewed the charts of 117 outpatients at three New York hospitals: Hutchings Psychiatric Center, Syracuse (HPC); Syracuse Veterans Affairs Medical Center (SVA); and Olean Community Hospital (OGH) on conventional antipsychotics to ascertain why they were maintained on their conventional agent, and whether the treating psychiatrist discussed alternative treat-

ments. Fifty-one percent of the patients were maintained on conventional antipsychotics because of excellent response. Other reasons were patient choice (49%), physician choice (37%), need for depot antipsychotics (13%), lack of response to atypical drugs (7%), family choice (5%), and cost to the patient (3%). Despite the high incidence of TD at all three hospitals (range 12% to 50%), the reasons for continuing the conventional antipsychotic were not discussed between the physician and patient. The treating psychiatrist discussed alternative treatments in only 37.3% of patients at SVA, 57.7% at HPC, and 62.5% at OGH. Similarly, there was a low frequency of discussion about the benefits of atypical antipsychotics (56% to 69%). For patients that are on antipsychotic therapy, discussions about the risk/benefit ratio of treatments are integral for optimal treatment.

NR99 Monday, May 15, 9:00 a.m.–10:30 a.m.

Prescribing Conventional Antipsychotics at Two Veterans Hospitals: Are There Geographic Differences?

Monica Arora, M.D., *Department of Psychiatry, Suny Health Sciences Center, 750 East Adams Street, Syracuse, NY 13210*; Anil Sharma, M.D., Xiao-Hong Wang, M.D., Thomas L. Schwartz, M.D., Subhash C. Bhatia, M.D., Daniel J. Kuhles II, M.P.H., Bhushan S. Agharkar

Summary:

Although atypical antipsychotics are first-line treatment in psychotic disorders, the Expert Consensus Guidelines on Schizophrenia recommends clinicians discuss the risk-benefit ratio of the antipsychotic as well as alternative treatments. In order to examine geographic differences in the informed consent process, the charts of 109 patients at Veterans Administration hospitals in Syracuse, NY, and Omaha, NE, were reviewed to determine how many patients continued use of their conventional antipsychotic, the documented reasons for such continuation, and patient-physician issues that might have influenced the decision to continue the conventional agents. The most common reasons for continuation are excellent response to these agents, patient choice, and physician choice. TD was present in 12% of patients at Syracuse and 3% of those at Omaha. At both VA hospitals, but more so at Omaha, there was a low frequency of discussion (37.3% at Syracuse vs. 2.9% at Omaha, $p < 0.001$) between the physician and patient about alternatives to current conventional antipsychotics, and fewer side effects with atypical antipsychotics (33.3% Syracuse vs. 2.9% at Omaha, $p < 0.001$). The reasons for continuing conventional antipsychotics were discussed with 68% of the patients at the Omaha VA vs. 53% of patients at the Syracuse VA hospital. There may be geographic differences in physicians' prescribing practices of conventional antipsychotics, which need to be addressed with physician education.

NR100 Monday, May 15, 9:00 a.m.–10:30 a.m.

Psychiatric Clinical Research and the Doctor-Patient Relationship

Flavia C. Campos, *Psychiatric Institute, Fed University of Rio Jan, Visconde de Piraja 407/702, Rio de Janeiro, RJ 22410-003, Brazil*; Antonio E. Nard, M.D.

Summary:

Objective: To raise hypotheses about the patient's knowledge of his participation in a six-week clinical trial and to describe the patient's opinions.

Method: We randomly selected 42 patients for a double-blind study in panic disorder (activate drug × placebo). At the end of the treatment a questionnaire with nine qualitative and quantitative items was applied to them.

Results: The answers about the participation in the research were positive in 39 patients. As it was an almost uniform feature (92.8%), the patients' positive thoughts toward the trial did not influence the total results of our trial. A very important point was the answer highlighting the physician's presence in the research clinical assistance.

Conclusion: Although this was a small sample, the patients were enthusiastic about participating in a trial and telling the importance of the physicians' role in it, pointing out the influence of the doctor-patient relationship. The presence of the placebo is absolutely necessary for the critical analysis of the results and it is the "gold standard" for every clinical trial.

NR101 Monday, May 15, 9:00 a.m.–10:30 a.m.

Lack of Psychoeducation in Argentina: Stigma Issues?

Adolfo Canovi, M.D., *Department of Psychiatry, Hospital Italiano, Gascon 450, Buenos Aires, CP 1199, Argentina*; Ricardo L. Perez-Rivera, M.D., Adrian Trajterman, M.D., Gustavo Rozadilla, M.D., Eugenia Dabi, M.D., Eduardo R. Sanchez de Antonio, M.D., Marcela Bonano, M.D.

Summary:

The aim of this study is to test the information on the psychopharmacological treatment that patients received at a psychiatry emergency room.

The present study utilized a sample of 224 outpatients who were treated in the psychiatry emergency room at "Hospital Italiano", between July 1 and November 30, 1999. Fifteen-item, self-administered questionnaire created by residents was completed by each patient to assess the knowledge on their psychopharmacological treatment at that time.

Out of 224 patients, 172 were receiving psychotropics. Within this group, 29% (n = 50) didn't know they were taking these psychiatric drugs, and 88% of them were not under any psychiatric treatment; 67% of the patients that knew they were prescribed psychotropics were under psychiatric treatment. However, the patients explained that they were not given information on side effects (62%), how long the treatment would last (61.5%), and the consequences of interruption of medication (39%).

Conclusion: In this study the majority of the patients who were taking psychotropic drugs were not psychoeducated adequately. This is a concern because most of the patients were under the care of a psychiatrist.

NR102 Monday, May 15, 9:00 a.m.–10:30 a.m.

Stigma in Functional Somatic Syndromes and Comparable Medical Conditions

Karl J. Looper, M.D., *Department of Psychiatry, McGill University, 1033 Pine Avenue West, Room 107, Montreal, QC H3A 1A1, Canada*; Laurence J. Kirmayer, M.D.

Summary:

Objective: To identify sociodemographic and diagnostic correlates of stigma in patients with functional somatic syndromes and comparable medical illnesses.

Methods: 169 patients were surveyed from four diagnostic groups: two organic conditions—rheumatoid arthritis (RA, 43 subjects), and multiple sclerosis (MS, 40); and two functional somatic syndromes (FSS)—fibromyalgia syndrome (FS, 41), and chronic fatigue syndrome (CFS, 45). Instruments included a sociodemographic questionnaire, the depression subscale of the Symptom Checklist 90, the physical functioning subscale of the MOS 36-SF, and a 24-item self-report stigma scale. Groups were compared using univariate statistics, and correlates of stigma were identified in the overall group using multiple linear regression.

Results: The CFS group reported the highest levels of perceived stigma. The MS, FS, and CFS groups reported greater levels of depression than the RA group. Multiple regression analysis identified three significant correlates of stigma (adjusted R^2 = 0.34): depression ($p < 0.001$), functional diagnosis (FSS) ($p < 0.01$), and male sex ($p < 0.05$). Having a FSS accounted for 8% of the variance, and depression accounted for 12% of the variance.

Conclusions: Having a diagnosis of functional syndrome and having depression are important contributors to perceived stigma.

NR103 Monday, May 15, 1:00 a.m.–2:30 a.m.

Schizophrenia: Progressive Prefrontal Gray Changes

Almos I. Nagy, M.D., *Department of Psychiatry, Harvard Medical School, Brockton VA, 940 Belmont Street, Brockton, MA 02301*; Chang U. Lee, M.D., Martha E. Shenton, Ph.D., Dean F. Salisbury, Ph.D., Ashley A. Kricun, B.S., Chandlee C. Dickey, M.D., Robert W. McCarley, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the structural imaging findings in schizophrenia and to discuss the implications of volume measure changes over time.

Summary:

Functional studies in schizophrenia have reported abnormalities in prefrontal cortex, but structural magnetic resonance imaging (MRI) studies have shown less-consistent results. Previously our laboratory showed prefrontal cortical gray matter volume reductions in patients diagnosed as schizophrenic (DSM-IV) at first hospitalization (first episode), compared with first-episode affective psychotic patients and normal controls. This study is a follow-up to determine whether prefrontal cortical volumes change over time in these two patient groups compared with each other and with controls.

Using the same 1.5 T GE MR scanner and SPGR protocol (1.5 mm contiguous slices), we compared high resolution MR measurements of prefrontal gray and white matter volumes at baseline and at follow-up ~1.5 years later (mean interval = 1.39 years) in patients with first-episode schizophrenia (N = 9, mean interscan interval (II) = 1.28 yrs), first-episode affective psychosis (N = 6, N = 5 manic psychosis, N = 1 psychotic depression; mean II = 1.54 yrs) and in normal controls (N = 5, mean II = 1.4 yrs).

Intra-class reliability coefficients (five cases, three raters) for the semiautomatic segmentation were 0.99 for gray and 0.99 for white matter volumes. Prefrontal volume differences between time one scan and time two rescan were determined using a paired t-test and two-tailed significance levels. Schizophrenics showed a significant decrease over time in left gray matter volume ($P = 0.047$) and left white matter volume ($P = 0.021$), while right gray and right white matter volume showed only a nonsignificant tendency to decrease. Seven of the nine schizophrenics showed reductions over time for left gray and left white matter. We also found a significant decrease over time in left white matter volume ($P = 0.026$) in first-episode affective patients (five of six decreased over time). Other volume changes over time were not significant either in affectives or in controls.

These data suggest that in schizophrenia there may be progression of prefrontal left cortical gray matter volume reductions, a finding not present in controls or in affective psychosis, although a larger sample is needed to confirm these preliminary findings.

References:

1. McCarley RW, Wible CG, Frumin M, et al: MRI anatomy of schizophrenia. Biological Psychiatry 1999; 45:1099–1119.
2. Shenton ME, Wible CG, McCarley RW: MRI studies in schizophrenia In: Krishnan KRR, Doraiswamy PM (Eds.) Brain Imaging in Clinical Psychiatry. Marcel Dekker, Inc. 1997 pp. 297–380.

NR104 Monday, May 15, 1:00 a.m.–2:30 a.m.

MRI Analysis of Cortical Gray and White Matter in Patients with Bipolar Disorder

Melissa P. Lopez-Larson, B.S., *Department of Psychiatry, University of Cincinatti, 231 Bethesda Avenue, Cincinatti, OH 45267-0559*; Melissa P. DelBello, M.D., Mark Steed, M.A., Stephen M. Strakowski, M.D.

Educational Objectives:

To recognize abnormalities in cortical gray and white matter in patients with bipolar disorder.

Summary:

Objective: Neuroimaging studies have suggested that there are differences in prefrontal cortical structure and function between patients with bipolar disorder (BP) and healthy volunteers. The aim of our study was to investigate whether differences exist in prefrontal gray and/or white matter volumes in patients with BP compared with healthy volunteers.

Method: Patients with BP hospitalized for a manic episode (n = 17) and healthy volunteers (n = 13) matched for age, sex, and race were recruited. Contiguous 1 mm coronal T1-weighted MRI slices were obtained using a Picker 1.5 Tesla scanner. Regions of interest (ROI) measured were gray and white matter volumes of the total cortex; occipital lobes and right and left prefrontal cortex.

Results: ANCOVA comparing cortical gray and white matter adjusting for sex, education, and substance use duration showed group differences between total gray cortical volume ($F = 6.0$, $df = 24$, $p = 0.02$) and total white cortical volume ($f = 6.04$, $df = 24$, $p = 0.02$). Specifically, patients with BP had larger white matter and smaller gray matter volumes. Furthermore, after adjusting for substance use duration, education, and sex, patients with BP had larger left prefrontal white matter volumes compared with volunteers ($F = 5.6$, $df = 23$, $p = 0.03$). As expected there were no differences in occipital lobe gray or white matter between groups.

Conclusions: Our results suggest that patients with BP have larger cortical prefrontal white matter volumes compared with healthy volunteers, which may represent abnormalities in the frontosubcortical pathways that possibly underlie the pathophysiology of affective illness. Further investigations of specific prefrontal regions are needed.

References:

1. Sax KW, et al: Prefrontal cortical volume and attential performance in bipolar disorder. American Journal of Psychiatry 1999; 156:139–141.
2. Zipursky RB, et al: Deficits in gray matter volume are present in schizophrenia but not bipolar disorder. Schizophrenia Research 1997; 26:85–92.

NR105 Monday, May 15, 1:00 a.m.–2:30 a.m.

Uncinate Fasciculus in Schizophrenia: A Diffusion Tensor Study

Marek Kubicki, Ph.D., *Department of Psychiatry, Harvard Medical School, 940 Belmont Street, Brockton, MA 02301*; Stephan E. Maier, Ph.D., Robert W. McCarley, M.D., Hatsuho Mamata, M.D., Enkeat Teh, M.A., Christopher Allen, B.A., Martha E. Shenton, Ph.D.

Educational Objectives:

To show the advantages afforded by the new MR technique for detecting white matter tract disruptions in the brain; to learn about

the role of the uncinate fasciculus in schizophrenia, a white matter bundle that connects frontal and temporal regions of the brain.

Summary:

There is some evidence to suggest that a disruption in connectivity between frontal and temporal lobes may partly explain the primary symptoms of schizophrenia. Conventional MR studies have not shown compelling evidence for white matter abnormalities, but the component fiber tracts have not been studied, as conventional MR images do not allow their identification. Diffusion tensor imaging, however, represents a new technique that can distinguish between normal and abnormal brain white matter on the basis of water diffusion. The first two studies in schizophrenia to quantify anisotropic diffusion showed lower anisotropy within whole white matter relative to controls.

The aim of this study was to focus on the uncinate bundle, the most prominent connection between the orbital frontal lobe and anterior portions of the temporal lobe. Anisotropic diffusion within this structure (a measure of the density and/or number of white matter fibers), and area were compared between male schizophrenics (n = 6) and male normal controls (n = 4), matched for age, socioeconomic status, and handedness. Images were acquired on a 1.5-Tesla GE Echospeed system. Four-mm thick coronal slices covering the entire brain were acquired perpendicular to the AC-PC line. Using the anisotropy map, the uncinate fasciculus was semiautomatically thresholded and then its area and anisotropy were calculated.

A one-way ANOVA showed a significant reduction of the right uncinate fasciculus area ($p < 0.05$) as well as reduced right uncinate fasciculus anisotropy ($p < 0.05$) in schizophrenics compared with controls. No statistical differences between left sides were found, although descriptive statistics showed that compared with the controls, mean area and anisotropy within uncinate fasciculus on both sides appeared to be lower in schizophrenics.

Despite the fact that our sample was small, this study was able to depict a significant difference between patients diagnosed with schizophrenia and control subjects, suggesting that the symptoms of schizophrenia might, in part, be explained by the difference in the number and/or density of the long interconnecting fibers.

References:

1. Makris N, Worth AJ, Sorensen AG, et al: Morphometry of in vivo human white matter association pathways with diffusion-weighted magnetic resonance imaging. Annals of Neurology 1997; 42:951–62.
2. Peled S, Gudbjartson H, Westin CF, et al: Magnetic resonance imaging shows orientation and asymetry of white matter fiber tracts. Brain Research, 1998; 780:27–33.

NR106 Monday, May 15, 1:00 p.m.–2:30 p.m.

White Matter Abnormalities in Schizophrenia As Measured by Magnetic Resonance Diffusion Imaging

Melissa Frumin, M.D., *Department of Psychiatry, Brockton VA Medical Center, 940 Belmont Street, Brockton, MA 02401*; Carl F. Westin, Ph.D., Robert W. McCarley, M.D., Stephan E. Maier, Ph.D., Hatsuho Mamata, M.D., Marek Kubicki, Ph.D., Martha E. Shenton, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the role of MR diffusion imaging in quantifying both the orientation and density of white matter tracts in the brain. This application has important implications in examining possible disruptions in the connectivity of white matter in patients with schizophrenia.

Summary:

Disruption in the connectivity and organization of white matter fibers has been hypothesized as a possible etiology to explain hallucinations, delusions, and cognitive impairment, the hallmark symptoms of schizophrenia. Magnetic resonance (MR) diffusion imaging is a new technique that can define the orientation and density of white matter tracts. Though there are many studies showing differences in gray matter between patients with schizophrenia and normal controls, there have been few studies using diffusion imaging to define possible differences in white matter.

In this study, six patients who met DSM-IV criteria for schizophrenia and five normal controls were scanned using MR diffusion imaging. An automated program was used to define the corpus callosum (CC), in the mid-saggital plane. As compared with controls, the anisotropy, reflecting less dense and/or less organized white matter in the CC, was lower in patients with schizophrenia. The first eigenvalue of the diffusion tensor, a scalar measurement of diffusion along the principal diffusion direction, measured in the CC, was also lower in patients with schizophrenia as compared to normal controls. These preliminary findings, despite the limitation of small sample size, show a difference in white matter integrity, which warrants further study with a greater number of subjects.

References:

1. Peled S, Gudbjartson H, et al: Magnetic resonance imaging shows orientation and asymmetry of white matter fiber tracts. *Brain Research* 1998; 780:27–33
2. Lim KO, Hedehus M, et al: Compromised white matter tract integrity in schizophrenia inferred from diffusion tensor imaging. *Arch Gen Psychiatry* 1999; 56:367–384

NR107 Monday, May 15, 1:00 p.m.–2:30 p.m.

Cerebellar Function in Children at Risk for Bipolar Disorder

Melissa P. Del Bello, M.D., *Department of Psychiatry, University of Cincinnati, 231 Bethesda Avenue, ML559, Cincinnati, OH 45267*; Patricia McDonough-Ryan, M.A., Sarah M. Graman, B.A., Cesar A. Soutullo, M.D., Molly E. Zimmerman, B.A., H. Lee Rosenberg, B.A., Stephen M. Strakowski, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able recognize cerebellar dysfunction in children at risk for bipolar disorder.

Summary:

Objective: Although traditionally regarded as a regulator of motor function, the cerebellum has also been found to have projections to limbic regions of the brain that modulate mood. Several studies have found abnormal cerebellar anatomy in patients with the diagnosis of bipolar disorder. We hypothesized that compare with healthy volunteers, children with a parent with bipolar disorder would exhibit structural and functional cerebellar abnormalities.

Method: Children (8–12 years) with at least one parent with bipolar disorder (high-risk, N = 17) and children of healthy parents without any DSM-IV Axis I disorder (N = 13), matched for age, sex, socioeconomic status, handedness, and Tanner stage, were assessed using the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS). Contiguous 1mm axial T1-weighted MRI slices were obtained using a 1.5 Tesla scanner. Regions of interest (ROIs) included left and right cerebellar hemispheres and vermal area V1, V2, and V3 volumes. An ataxia battery was administered to all children.

Results: High-risk children performed worse on several ataxia measures (greatest difference, "eyes open stand on left" (EOL), $t = -2.9$, $df = 24$, $p = 0.008$). V3 volume negatively correlated with

control group performance on EOL (Spearman correlation = –0.58, p = 0.04) and "eyes open stand right" (EOR) (Spearman correlation = –0.65, p = 0.02) tasks. However, cerebellar ROI volumes did not correlated with high-risk group performance on any of the ataxia tasks. Additionally, within the high-risk group EOL performance negatively correlated with mood, ADHD, and disruptive behavior symptoms (greatest Spearman correlation = –0.73, p = 0.004).

Discussion: Our results suggest that children at risk for bipolar disorder, particularly those who exhibit mood, ADHD, and distruptive behavior symptoms, may have abnormalities in cerebellar function, suggesting that these abnormalities may be present prior to the onset of bipolar disorder.

References:

1. Soares JC, Mann JJ: The anatomy of mood disorders: review of structural neuroimaging studies. *Biol Psychiatry* 1997; 41:86–106
2. DelBello MP, Strakowski SM, Zimmerman ME, Hawkins JM, Sax KW: MRI analysis of the cerebellum in bipolar disorder: a pilot study. *Neuropsychopharmacology* 1999; 21:63–68

NR108 Monday, May 15, 1:00 p.m.–2:30 p.m.

Age-Related Decline of 5HT-1A Receptor Binding

Johannes Tauscher, M.D., *PET Centre, The Clarke Institute, 250 College Street, Toronto, ON, M5T 1R8, Canada*; Nicolaas P.L.G. Verhoeff, M.D., Doug Hussey, B.S.C., Jeffrey H. Meyer, M.D., Alex Kecojevic, Professor Siegfried Kasper, Shitij Kapur, M.D.

Educational Objectives:

To understand basic principles of 5-HT_{1A} receptor imaging using ROI and pixel-by-pixel analysis of PET data, and recognize the importance of age matching for future neuroimaging studies using [^{11}C] WAY-100635 and PET.

Summary:

Objective: Positron emission tomography (PET) and [^{11}C] WAY-100635 can be used to study the serotonin-1A (5-HT_{1A}) receptor binding potential (BP) in vivo.

Method: After bolus injection of [^{11}C] WAY-100635, PET images were obtained in 17 healthy subjects (7 female/10 male; mean age 37; range: 22–53) with a GEMS 2048-15B camera for 90 minutes. Regions of interest (ROI) were drawn on the coregistered MRI in the frontal, temporal, and cerebellar cortex. 5-HT_{1A} receptor BP were calculated for both cortical regions using a simplified reference tissue method (Gunn et al. 1998). In addition, a voxel-wise analysis was performed using SPM96 with BP images normalized to a ligand-specific template (Meyer et al. 1999).

Results: ROI analysis yielded a mean BP of 3.25 (± .62 SD) in the frontal and 4.55 (± .82 SD) in the temporal cortex. A Pearson correlation coefficient revealed a significant decline of frontal 5-HT_{1A} receptor BP with age (R = –.63; p < .001). SPM96 analysis revealed a significant global effect of age on 5-HT_{1A} BP (set level = .002), but not of gender.

Conclusions: Frontal 5-HT_{1A} BP declined by approximately 10 percent per decade, warranting careful age matching for future studies of 5-HT_{1A} binding potential with [^{11}C] WAY-100635 and PET.

References:

1. Gunn RN, Sargent PA, Bench CJ, et al: Tracer kinetic modeling of the 5-HT_{1A} receptor ligand *[carbonyl-^{11}C]*WAY-100635 for PET. *Neuroimage* 1998; 8:426–440
2. Meyer JH, Gunn RN, Myers R, Grasby P: Assessment of spatial normalization of PET ligand images using ligand-specific templates. *Neuroimage* 1999; 9:545–553

NR109 Monday, May 15, 1:00 p.m.–2:30 p.m.

A Prospective Study of PTSD and Nonadherence in Survivors of a Myocardial Infarction

Eyal Shemesh, M.D., *Department of Psychiatry, Mount Sinai, 1 Gustave Levy Place/Box 1230, New York, NY 10029*; Abraham Rudnick, M.D., Daniela Alon, R.N., Edo Kaluski, M.D., Olga Milovanov, M.D., Zui Verd, M.D., Gad Cotter, M.D.

Educational Objectives:

To diagnose PTSD symptoms in medically ill patients and recognize their importance.

Summary:

Objective: A novel hypothesis suggests that patients who suffer from posttraumatic stress disorder (PTSD) that is related to a medical illness may not take a prescribed medication, since taking it serves as a recurrent reminder of the traumatic experience (the medical disease.) We assessed whether nonadherence is associated with MI-related PTSD and with various psychiatric symptoms in a cohort of MI survivors.

Method: MI survivors were prospectively followed for one year. Adherence was assessed by pill counts of captopril. PTSD symptoms were assessed by the Impact of Event Scale (Horowitz 1979.) The SCL-90-R (Derogatis, 1983) was used to assess psychiatric symptom dimensions. Medical outcome was determined clinically by the occurrence of Severe Adverse Events (SAE).

Results: Of 140 recruited patients, 102 completed one year of follow-up. Nonadherence was associated with SAE (r = 0.93, p = 0.006.) PTSD symptoms, but no other psychiatric or psychosocial variables, were associated with nonadherence (p = 0.05.)

Conclusions: Nonadherence to medications predicts poor outcome after an acute MI. PTSD symptoms are associated with nonadherence and may be a marker for or a direct cause of it. These results extend previous findings and suggest that nonadherence is a response to disease-related stress. Treatment of PTSD may therefore improve adherence and medical outcome.

References:

1. Shemesh E, Lurie S, Stuber, ML et al: A pilot study of postiraumatic stress and nonadherence in pediatric liver transplant recipients. *Pediatrics* 2000; 105:16
2. Stukas AA, Dew MA, Switzer GE, et al: PTSD in heart transplant recipients and their primary family caregivers. *Psychosomatics* 1999; 40:212–221

NR110 Monday, May 15, 1:00 p.m.–2:30 p.m.

Cardiovascular and Metabolic Correlates of PTSD

Sonia P. Yovtcheva, M.D., *Department of Psychiatry, Univ. of VA/Roanoke-Salem Prgm, 1970 Roanoke Boulevard, VAMC, Salem, VA 24153*; Martha M. Kato, M.D., Robert D. Cox, Ph.D., Rezhan Hussein, M.D., Ali Iranmanesh, M.D.

Educational Objectives:

At the conclusion of this presentation the participants should be able to recognize the metabolic changes associated with PTSD.

Summary:

This study was designed to investigate the cardiovascular and metabolic correlates of PTSD. Twenty three men with PTSD (mean age ± SEM: 49 ± 1.3 yrs) and 23 age-matched healthy men (49 ± 1.4 yrs) participated in this study. Height, weight, BP, HR, waist (W), and hip (H) circumferences, W/H ratio, and skin fold triceps, scapula) thickness were measured. Circulating concentrations of glucose, insulin, c-peptide, lipids, leptin, DHEAS, and interleukin-6 were measured in the fasting blood samples collected from each subject. Compared with the normal group, men with PTSD showed significant increases in their waist circum-

ference (37.6 ± 1.1 vs 42.4 ± 1.2; P = 0.006), and waist to hip ratio (0.90 ± 0.01 vs 0.96 ± 0.01, P = 0.005), in the presence of matching BMI (28.7 ± 0.76 vs. 29.9 ±1.15, P = NS), and hip circumference. Altered body composition was accompanied by significant increases in the serum concentrations of triglycerides (157 ± 13.8 vs 275 ± 34.8 mg/dl; P = 0.007) c-peptide (2.2 ± 0.24 vs 3.4 ± 0.35 ng/ml; P = 0.01, insulin (14.8 ± 2.07 vs 39.8 ± 0.72 ulU.ml; P = 0.01), leptin (6.9 ± 0.68 vs 10.4 ± 1.17 ng/ml; P = 0.02) and DHEAS (114 ± 9.45 vs 196 ± 31.4 /ml; P = 0.002). While heart rate was significantly increased in PTSD (69 ± 2.1 vs 74 ± 1.32 beats/min; P = 0.04), measures of systolic (122 ± 2.14 vs 125 ± 1.87 mmHg; P = NS) and diastolic (79 ± 1.25 vs 76 ± 1.41 mmHg) blood pressure were not significantly different. In conclusion, redistribution of fat to the abdominal area characterizes the changed body composition in subjects with PTSD, and is associated with marked increases in triglycerides, insulin, c-peptide, and leptin. The etiology of this phenomenon is unclear, but episodic hypercortisolemia induced by the comorbid conditions, namely alcoholism and depression, could be presumed as a potential mechanism. The metabolic consequences of increased abdominal fat could lead to heightened incidence of diabetes mellitus and coronary artery disease. Alternatively, a protective cardiovascular and immunological role of increased DHEAS in PTSD patients can be postulated, but needs to be further studied.

References:

1. Southwick SM, Yehuda R, Wang SN: Neuroendocrine alterations in posttraumatic stress disorder. *Psychiatric Annals* 1998; 28:8:436–442
2. Han TS, van Leer EM, Seidell JC, et al: Waist circumference action levels in the identification of cardiovascular risk factors: prevalence study in a random sample. *BMJ* 1995; 311:1401–1405

NR111 Monday, May 15, 1:00 p.m.–2:30 p.m.

Testosterone Replacement for Male Depression: Randomized Clinical Trial

Stuart N. Seidman, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Steven P. Roose, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the treatment rationale, clinical indications, efficacy, and risks in using exogenous testosterone in depressed men.

Summary:

Background: Testosterone (T) has psychotropic effects, and evidence suggests that T replacement is mood enhancing in hypogonadal men. The antidepressant efficacy of T replacement is unknown.

Objective: To assess the efficacy of T replacement in depressed men with low T levels.

Method: In a randomized, double-blind trial we enrolled 30 men with low T levels (i.e., ≤350 ng/dl) and major depressive disorder (MDD), and administered T 200mg IM or placebo weekly for six weeks. The primary outcome measure was score on the 24-item Hamilton Rating Scale for Depression (HRSD).

Results: Thirty patients were randomized. The mean age was 52 years, mean T level 262.5ng/dl and mean baseline HRSD score 21; there were no significant demographic or clinical between-group differences. The HRSD scores decreased significantly in both T and placebo groups, and there was no statistically significant between-group difference: reduction in mean HRSD from baseline to endpoint was 10.1 in patients who received T and 10.5 in those who received placebo. Response rate, defined as a 50% or greater reduction in HRSD, was 38.5% (5/13) in patients who received T and 41.2% (7/17) in patients who received placebo. Patients receiving T had some improvement in sexual function.

Conclusion: In this trial, antidepressant effects of T replacement and placebo were not distinguishable.

References:

1. Seidman SN, Walsh BT: Testosterone and depression in aging men. *American Journal of Geriatric Psychiatry* 1999; 7:18–33
2. Seidman SN: The role of testosterone in psychiatry. *Psychiatric Annals* 2000; (in press)

NR112 Monday, May 15, 1:00 p.m.–2:30 p.m.

A Survey of Clinicians' Long-Term Antidepressant Prescribing Practices

Steffany J. Fredman, B.A., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WAC 812, Boston, MA 02114*; Maurizio Fava, M.D., Allison S. Kienke, B.A., Candace N. White, M.Ed., Jerrold F. Rosenbaum, M.D.

Educational Objectives:

At the conclusion of this presentation, participants will be familiar with different approaches to the long-term management of depression

Summary:

Background: Although there is evidence that full-dose, long-term antidepressant treatment is superior to discontinuing medication in recurrently depressed patients, and general guidelines, derived from empirical findings, are available to practicing clinicians, the extent to which clinicians vary in their approach to long-term treatment with antidepressants is unclear.

Methods: We surveyed attendees at the Massachusetts General Hospital annual psychopharmacology review course (N = 801). Prior to lectures on depression and its treatment, we administered a questionnaire regarding long-term prescribing practices for patients suffering from depression.

Results: A total of 432 attendees responded, 93% of whom identified themselves as psychiatrists. Seventy-two percent of respondents reported that they would tend to maintain patients on the same medication dose for six *months to a year* following a *first* major depressive episode, but 83% indicated that they would tend to treat patients for *more than one year* after a *second* episode. While 74% indicated that they would determine to maintain patients on lifetime antidepressant treatment after two to three episodes, only 2% would consider employing lifetime treatment after a single episode.

Conclusion: Despite some evidence that the empirical evidence derived from clinical research has little or no impact on clinical practice, our study results suggest that clinicians select antidepressant treatment maintenance strategies that are consistent with the existing recommended guidelines. Furthermore, the duration of the treatment appears to correlate with the number of prior episodes, and the preferred dosing is the one that has led to remission during the acute phase.

References:

1. Kupfer DJ, Frank E, Perel JM, Cornes C, Mallinger AG, et al: Five-year outcome for maintenance therapies in recurrent depression. Arch Gen Psychiatry 1992; 49(10):769–73
2. Clinical Practice Guideline Number 5: Depression in Primary Care, vol 2. Treatment of Major Depression Rockville, MD: US Dept Health Human Services, Agency for Health Care Policy and Research; April 1993. AHCPR publication 93-0551

NR113 Monday, May 15, 1:00 p.m.–2:30 p.m.

Elevated 5HT-2A Binding Potential in SSRI-Responsive Depression

Jeffrey H. Meyer, M.D., *Mood & Anxiety Program, Clarke Institute, CAMH, 250 College Street, 11th floor, Toronto, ON, M5T 1R8, Canada*; Shitij Kapur, M.D., Beata Eisfeld, B.S.C., Gregory M. Brown, M.D., Sylvain Houle, M.D., Helen S. Mayberg, M.D., Sidney H. Kennedy, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be more informed as to the relationship between 5-HT2A receptor regulation and treatment-responsive depression.

Summary:

Objective: It has been proposed that 5-HT_{2A} receptors may play a role in selective serotonin reuptake inhibitor (SSRI) treatment. The purpose of this study is to evaluate whether 5-HT_{2A} receptor binding potential (BP) may be altered before treatment in SSRI-responsive depressed subjects.

Methods: 21 depressed subjects and 21 age-matched healthy subjects were recruited. Exclusion criteria for patients included antidepressant medication use within six months, a history of suicide attempts within the past five years, other current Axis I disorders including bipolar disorder, and the presence of psychotic symptoms. Using [^{18}F]setoperone and positron emission tomography (PET), 5-HT_{2A} receptor binding potential was assessed using both statistical parametric mapping and region of interest techniques. After scanning, each depressed subject was treated with 20 mg/day of paroxetine for six weeks and 11 subjects had final HDRS <8.

Results: With statistical parametric mapping and analysis of covariance with age as a covariate, treatment-responsive subjects showed globally increased 5-HT_{2A} BP (p(cluster) < 0.001) as compared with age-matched healthy subjects. This was also found on the region of interest data when multivariate analysis of covariance was used ($F_{9,11}$ = 3.4, p = 0.03). No significant findings were present in comparisons between healthy subjects and the remaining depressed subjects.

Conclusions: This finding suggests that upregulation of 5-HT_{2A} receptors could contribute to SSRI responsiveness in depression. (supported by the Medical Research Council of Canada and NARSAD)

References:

1. Meyer JH, Kapur S, Houle S, et al: Prefrontal cortex 5-HT_2 receptors in depression: [^{18}F] setoperone PET imaging. American Journal of Psychiatry 1999; 156(7):1029–1034.
2. Blin J, Sette G, Fiorelli M, et al: A method for the in vivo investigation of the serotonergic 5-HT_2 receptors in the human cerebral cortex using positron emission tomography and ^{18}F labeled setoperone. J Neurochemistry 1990; 54:1744–54.

NR114 Monday, May 15, 1:00 p.m.–2:30 p.m.

An Analysis of Recent Valproate Prescribing Trends

Narayanan Ramesh, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt, 4th floor, Baltimore, MD 21201*; Neil B. Sandson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be to recognize the extent of changes in the use of valproate between 1992 and 1997.

Objective: To determine the extent of changes in the use of valproate in an inpatient psychiatric setting from 1992 to 1997.

Methods: Using a pharmacy data base, Axis I, II, and III diagnoses were compiled on a large sample of inpatients at the Sheppard and Enoch Pratt Hospital who were being treated with valproate in 1992 and 1997. The 1992 sample included all 70 such inpatients for that calendar year. The 1997 sample included the (alphabetically) first 100 such inpatients. Patients were selected without regard to age, sex, race, comorbid illnesses, or any other factors. From each sample, 10% of the charts were reviewed for validation of DSM-IV diagnoses. The compiled diagnoses for each sample were then compared in order to analyze prescribing trends in this setting.

Results: 63% of the 1992 sample was diagnosed with bipolar disorder vs. 43% of the 1997 sample. In contrast, 24% of the 1992 sample was diagnosed with impulse-control-related disorders as compared with 77% in 1997.

Conclusions: The findings of this study suggest an increasing willingness of psychiatrists to prescribe valproate to treat conditions for which it has not yet demonstrated efficacy in controlled studies. While this trend may have merit in clinical practice, caution is clearly warranted.

References:

1. Phenomenology and treatment of agitation, Clinical Psychiatry, 1999.
2. Raskind M, et al: Evaluation and management of aggressive behavior in demented patients. J Clinical Psychiatry, 1999.

NR115 Monday, May 15, 3:00 p.m.–5:00 p.m.

Premenstrual Symptom Changes in Women with Schizophrenia: A Prospective Study

So-Hyun Choi, M.D., *Yongin Mental Hospital, 4 Sanghari, Kunsungmyun, Yongin, Kyunggi-Do 449–910, South Korea*; Sang-Bum Kang, M.D., Sook-Haeng Joe, M.D.

Summary:

Objective: We investigated whether psychiatric symptoms change during the premenstrual phase and the clinical features of the symptom change in female schizophrenic patients.

Methods: We observed 30 female schizophrenic inpatients over one menstrual cycle who met the DSM-IV criteria for schizophrenia and showed regular menstrual cycle. All subjects completed the daily rating form (DRF) every evening and one psychiatrist rated the BPRS once for each of the three menstrual phases (premenstrual, menstrual, postmenstrual phases). Data from 24 subjects who completed the DRF correctly and completely were used for statistical analysis.

Results: Mean total BPRS score for 24 subjects was highest in the premenstrual phase and lowest in the postmenstrual phase and showed statistically significant difference among three menstrual phases in the anxiety-depression group and the withdrawal-retardation group, but not in the psychotic group. When the criterion of 30% change was applied, the items of "depressed mood," "anxious, nervous, restlessness," "hostile, aggressive," and "less, impaired work" showed high frequencies of change in the premenstrual phase on the DRF. Somatic items of "abdominal pain" and "breast pain" showed significant change with 30% change rule on the DRF.

Conclusions: Findings of this study suggest that the premenstrual exacerbation of the symptoms in female schizophrenics may not be a worsening of schizophrenic symptoms themselves, but a concurrence of a specific syndrome that is characterized by a cluster of affective, behavioral, and somatic symptoms.

NR116 Monday, May 15, 3:00 p.m.–5:00 p.m.

Changes in Cortical Excitability in Women with PMS

Mark J. Smith, M.D., *LCS 10/3D41, NIMH, 10 Center Drive, Bethesda, MD 20892*; John C. Keel, B.A., Peter J. Schmidt,

M.D., Linda F. Adams, B.A., David R. Rubinow, M.D., Margaret Nguyen, B.A., Eric M. Wassermann, M.D.

Summary:

Objective: Ovarian steroids appear to modulate cortical excitability, which increases with estradiol (E2), possibly through glutamate potentiation, and decreases with progesterone (P4) metabolites, probably acting through the GABA-A receptor.

Method: Cortical excitability may be measured noninvasively in humans by paired-pulse transcranial magnetic stimulation, which appears to be sensitive to changes in the cortical glutamate/GABA balance.

Results: In the control group of 13 women without premenstrual syndrome (PMS), cortical excitability significantly decreased in the mid-luteal (high E2, high P4) (days 18-27) compared with the mid-follicular phase (high E2, low P4) (days 5-12); F (1,12) = 8.8, p = 0.01, suggesting P4-enhanced GABA activity during the mid-luteal phase. Preliminary data in six women with PMS (meeting premenstrual dysphoric disorder criteria) suggest that cortical excitability was similar in the mid-follicular and mid-luteal phases. The mid-luteal minus mid-follicular difference in cortical excitability tended to be lower in women with PMS than controls (F(1,17) = 4.9; p = 0.055). Two women with PMS tested after treatment with fluoxetine showed lower cortical excitability in the mid-luteal phase.

Conclusions: These results suggest GABA-mediated deficits in the mid-luteal (symptomatic) phase in women with PMS, and that fluoxetine's therapeutic effect in PMS may operate through a GABAergic mechanism.

NR117 Monday, May 15, 3:00 p.m.–5:00 p.m.

Topiramate in Premenstrual Dysphoric Disorder

Seema Hussain, M.D., *605-32 Street West, Prince Albert, SK T2N ITI, Canada*; Zubaida A. Chaudhry, M.B., Mohammad Z. Hussain, M.D.

Summary:

It is estimated that 3% to 5% of women suffer from premenstrual dysphoric disorder. Pharmacological intervention with gonadotropin-releasing hormone agonists, benzodiazepines, selective serotonin reuptake inhibitors, or mood stabilizers is most often used with varying success. However, some females prove resistant or intolerant to these approaches, requiring us to move forward and study alternative drug therapy. Topiramate is an antiepileptic drug with rich pharmacology and broad spectrum of activity with demonstrated therapeutic potential as a mood stabilizer and association with weight loss.

We report on a case series of eight females who were successfully treated with topiramate. Five have received treatment with SSRIs and other medications with little effect and three have tried herbal remedies but no medications. All were obese and concerned about their weight. Topiramate was given at a maximum dose of 100 mg/d and patients were rated on BPRS and subjectively at baseline and at monthly intervals following initiation of topiramate. In addition to relief from premenstrual dysphoria, there was also weight loss with decreased carbohydrate cravings and decreased vulnerability to food overconsumption. From this open study, topiramate promises to be an effective treatment for premenstrual dysphoria especially with those who have overweight concerns.

NR118 Monday, May 15, 3:00 p.m.–5:00 p.m.

Use of Complementary Medicine in Mental Disorders

Benjamin G. Druss, M.D., *Department of Psychiatry, Yale University, 950 Campbell Avenue 116A, West Haven, CT 06516-3861*; Robert A. Rosenheck, M.D.

Summary:

Objective: This study provides the first national estimates for use of practitioner-based complementary treatments by U.S. residents with mental conditions and/or symptoms.

Methods: As part of a national survey, a total of 16,038 adults reported on use of 12 categories of complementary services, mental and medical conditions, and global mental health.

Results: A total of 9.8% of those with a mental condition, 8.3% reporting fair or poor mental health status, 7.9% with a chronic medical condition, and 8.7% of other respondents reported a complementary visit in the past year. In multivariate models, report of a mental condition but not of fair/poor mental health status or a chronic medical condition, predicted a significant increase in odds of a complementary visit. Patients with adjustment disorders were most likely, and those with psychotic and affective disorders least likely, to use complementary therapies to treat their mental condition. Fewer than one-fourth of respondents in any group using complementary therapy told a physician about their visits.

Conclusion: The relatively high prevalence of use of these therapies in mental disorders coupled with lack of physician oversight suggests the potential importance of systematically screening for use of these therapies in mental health settings.

NR119 Monday, May 15, 3:00 p.m.–5:00 p.m.

Neuromotor Signs in Schizophrenia: Their Impact on Social Functioning

Stefanie Berns, Ph.D., *Psychiatric Rehabilitation Department, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004*; Rosemarie Basile-Szulc, Ph.D., Rashmi Rastogi, Ph.D., Judith Jaeger, Ph.D., Pal Czobor, Ph.D., Christina Gomes, B.A.

Summary:

Objective: The etiology and pathophysiology of movement disorders among persistently ill psychiatric patients have been widely researched. Little attention, however, has been focused on the stigmatizing effect of these impairments on social functioning. This study examined the relationship between neuromotor abnormalities and social integration among stabilized schizophrenic andschizoaffective patients reintegrating into the community following an acute exacerbation of their illness.

Method: One hundred-twenty seven patients, aged 18-54, were assessed on a set of neuromotor, disability, and psychopathological measures within six months of their discharge from an inpatient hospitalization. A subset of 100 subjects who consented to be videotaped were rated on a set of social likeability measures.

Results: For schizophrenic subjects but not schizoaffective subjects, the presence and severity of neuromotor abnormalities were associated with a lower level of social functioning, independent of symptomatology. Parkinsonism and gestural and expressive stigmata were associated with reduced social likeability although raters were not told that the subjects had a mental illness.

Conclusion: Movement disorders may represent a significant source of disability and social stigmatization among patients with schizophrenia that is independent of symptomatology.

NR120 Monday, May 15, 3:00 p.m.–5:00 p.m.

Insight, Cognition and Disability in Schizophrenia

Stefanie Berns, Ph.D., *Psychiatric Rehabilitation Department, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004*;

Bonnie Creech, Ph.D., Judith Jaeger, Ph.D., Mark Ast, Ph.D., Pal Czobor, Ph.D.

Summary:

Objective: Research in neurologic patients suggests that frontal lobe functioning is critical for judgments concerning the self (Stuss, 1993), while parietal lobe functioning is related to sensory awareness. Prior schizophrenia research finds relationships between poor insight and executive deficits thought to be mediated by the frontal lobes. We sought to clarify further the neuropsychology of impaired insight and its association with disability.

Method: Subjects with SCID-DSM-IV schizophrenia (N = 70) or schizoaffective disorder (N = 48) received a neuropsychiatric battery within six months of inpatient discharge. An insight rating was derived from the PANSS Judgment item and a distress rating was developed in our laboratory (by BC). Disability was rated using the Social Adjustment Scale (SAS). It was hypothesized that impaired executive functioning would relate to poor insight and lack of distress (LD) and that impaired executive functioning and poor insight/LD would contribute to poor instrumental role functioning.

Results: Significant relationships were found between working memory, dextral laterality, poor insight, and LD. Dextral laterality and LD predicted impairments in SAS social-leisure functioning.

Conclusions: These findings provide support for an association between executive impairment, poor insight/LD, and social dysfunction.

NR121 Monday, May 15, 3:00 p.m.–5:00 p.m.

A Five-Year Follow-Up Study of Deficit and Nondeficit Schizophrenia

Cenk Tek, M.D., *Department of Psychiatry, University of Maryland, MPRC, p o box 21247, Baltimore, MD 21228*; Brian Kirkpatrick, M.D., Robert W. Buchanan, M.D.

Summary:

Objective: Previous studies have suggested that the deficit syndrome, which is characterized by primary and enduring negative symptoms, is a stable subtype of schizophrenia, and patients with the deficit syndrome have neurobiological differences from other people with schizophrenia. We tested the ability of the deficit syndrome to predict clinical features at five years' follow-up in a group of chronically ill outpatients.

Method: Outpatients categorized into deficit (N = 46) and nondeficit (N = 174) groups were assessed at an average of five years after the categorization was made. Raters making the follow-up assessments were blind to the initial categorization.

Results: At follow-up, the deficit patients had poorer quality of life, poorer social and occupational function, and more severe negative symptoms. Despite these differences, deficit patients were less distressed (as measured by depressive mood, anxiety, and guilt). These differences could not be accounted for by more severe hallucinations, delusions, or thought disorder, or by demographic features. The group differences were significant even after accounting for the severity of baseline negative symptoms.

Conclusions: Patients with the deficit syndrome have a set of relatively stable clinical features that are associated with poor outcome.

NR122 Monday, May 15, 3:00 p.m.–5:00 p.m.

Akathisia, Suicidality and Depersonalization

Cem Atbasoglu, M.D., *Department of Psychiatry, University of Ankara, Tahran Caddesi 15/3 Kavaklidere, Ankara 06700, Turkey*; Susan K. Schultz, M.D., Nancy C. Andreasen, M.D.

Summary:

Background: Among motor side effects of antipsychotic medications, akathisia has been uniquely associated with depression and suicidality. Feelings of depersonalization/derealization have also been reported, but it is not clear whether these phenomena are specific to akathisia or nonspecific manifestations of distress.

Methods: The relationship of akathisia with depressive mood and suicidality was examined. Sixty-eight patients (49 men, 19 women) with schizophrenia were evaluated with the Barnes Akathisia Rating Scale (BARS), Hamilton Depression Rating Scale (HDRS), and Brief Psychiatric Rating Scale (BPRS). Twenty-two patients had akathisia (i.e., a global akathisia rating of at least 1).

Results: 1) HDRS and BPRS mean scores did not differ between the groups. 2) Akathisia was associated with higher ratings on three HDRS items: "Suicide," "depersonalization/derealization," and "agitation." 3) Suicidality was also associated with subjective ratings of akathisia. 4) Individual BARS items and the Anxiety-Depression BPRS items were examined in relations to suicidality and depersonalization/derealization. Only "depressive mood" discriminated between suicidal and nonsuicidal patients, whereas the BARS "subjective awareness of distress" predicted depersonalization/derealization.

Conclusions: This study supports the association between akathisia and both suicidality and depersonalization/derealization. However, these symptoms appear to be nonspecific responses to accompanying depressive mood and the subjective awareness of the akathisia syndrome, respectively.

NR123 Monday, May 15, 3:00 p.m.–5:00 p.m.

Neurocognitive Predictors of Functional Decline in Poor-Outcome Schizophrenia

Patrick J. Moriarty, M.A., *Department of Psychology, Hofstra University, 330 East 39th Street, #22-C, New York, NY 10016*; Thomas Coleman, M.A., Joseph I. Friedman, M.D., Philip D. Harvey, Ph.D., Christopher R. Bowie, M.A., Len White, Ph.D., Michael Parella, Ph.D., Kenneth L. Davis, M.D.

Summary:

Cognitive abilities have been shown to be directly related to social, occupational, and adaptive functioning in patients with schizophrenia. However, there is no evidence that impairment on a specific neurocognitive index is associated with functional decline, or whether these measures are all associated with functional impairments due to a global or specific cognitive deficit. In order to test whether any of these neuropsychological measures (verbal learning and memory, praxis, verbal fluency, and confrontational naming) is most associated with functional decline, 68 subjects were chosen from a long-term study of the effects of aging in schizophrenia. Subjects were chosen specifically because they declined functionally from a mildly impaired level of functioning to a moderate or severely impaired level of functioning across two assessments (mean interval = 1.89 years, sd = 1.42 years), based on a global rating of functioning on the Clinical Dementia Rating Scale (CDR). Age and education corrected z-scores were derived for measures of verbal learning, delayed memory, praxic ability, verbal fluency, and confrontational naming, based on performance of healthy controls on these measures as part of the Consortium to Establish a Registry of Alzheimer's Disease (CERAD). Change in performance on these neuropsychological measures was calculated by subtracting the standardized z-score of each measure at the follow-up assessment from the standardized score obtained on each measure at the initial assessment. A repeated measures ANOVA was used to determine if any of these measures were specifically associated with functional decline. Whereas the overall ANOVA was significant ($F(1, 67) = 14.49$, $p < .001$), no specific measure of neurocognitive functioning was able to account for the decline in functional ability (Rao's $R(3, 65) = 1.19$, $p < .321$).

These data suggest that the cognitive decline seen in these patients is generalized, rather than selective. It may be that this functional decline is related to low levels of cortical decline in patients with poor premorbid functioning and a chronic clinical course of illness.

NR124 Monday, May 15, 3:00 p.m.–5:00 p.m.

Impact of Early Intervention with Intramuscular Antipsychotic Medication in an Acute-Care Setting

Hildebrando Salinas, M.D., *Department of Psychiatry, University of Texas, 301 University Blvd route 0197, Galveston, TX 77555-0197*; James M. Russell, M.D., James M. Martinez, M.D., Joan A. Mackell, Ph.D.

Summary:

Introduction: Although there is some evidence that suggests that early and effective intervention in acute psychosis leads to more rapid stabilization of psychotic symptoms (Remington, et al), there is little literature that specifically addresses the impact of this stabilization on patient acuity and resource utilization.

Methods: Five hundred medical records of acutely psychotic patients admitted to the University of Texas Medical Branch at Galveston Hospital between January 1998 and March 1999 were targeted for study eligibility screening. Fifty-two (10.4%) patients received IM antipsychotic medication during their hospitalization and were discharged with a diagnosis of a DSM-IV primary psychotic disorder. The sample was then divided into those patients who received their first IM antipsychotic administration within four hours of presentation (early, n = 31) and those who received it later during their hospitalization (n = 21). Resource utilization, defined as a combination of hospital bed days and number of hours at increased observation levels, was compared between the two groups.

Results: The two groups were similar with respect to gender, age, ethnicity, and discharge diagnosis. Patients with delusions and acute behavioral symptoms were more likely to be treated with early IM antipsychotic medication ($p < 0.05$). Early IM treated patients spent fewer hours on special precautions (median: 46 versus 124 hours, $p < 0.001$). When length of stay (median: 9 versus 11 days) and hours on precautions were combined, patients who received early treatment with IM antipsychotic medication had lower acuity and therefore utilized less hospital resources ($p < 0.01$).

Conclusions: In acute psychotic disorders, early IM antipsychotic medication may lead to more positive outcomes: more rapid stabilization of acute symptoms and reduced hospital resource utilization. Other potential confounds for the decreased resource utilization will also be investigated.

NR125 Monday, May 15, 3:00 p.m.–5:00 p.m.

Increased S100-Beta Protein in Schizophrenia

Clarissa S. Gama, M.D., *Department of Psychiatry, UFRGS-Faculty of Medicine, Rua Pedro Ivo 767, Porto Alegre, RS 90450-210, Brazil*; Diogo R. Lara, M.D., Luis V. Portela, Ph.D., Carlos A. Goncalves, Ph.D., Diogo O. Souza, Ph.D., Paulo B. Abreu, Ph.D.

Summary:

The S100 proteins are a family of calcium-binding proteins found in the central and peripheral nervous system of vertebrates. S100β, the most abundant member of this family in the central nervous system, mediates calcium signal transduction, and shows neurotrophic, gliotrophic, and mitogenic actions that influence the development and maintenance of the nervous system. S100β protein accounts for 96% of the total S100 in the brain. We compared plasma concentration of S100β protein of 20 wash-out medication patients with schizophrenic psychosis and 20 age- and gender-matched healthy controls. Concentrations of S100β protein were measured using a highly specific and sensitive immunoluminometric assay whose detection limit is 0.02 μg/10 (LIA-mat® Sangtec® 100, Sangtec Medical, Bromma, Sweden). Schizophrenic patients showed increased S100β plasma concentrations ($p = 0.014$), and this finding was not related to clinical variables but it correlates negatively with duration of illness ($p = 0.031$). These results are further discussed with respect to the role of S100β release in schizophrenia.

NR126 Monday, May 15, 3:00 p.m.–5:00 p.m.

Schizophrenia With and Without a Comorbid Anxiety Disorder

Sanjay M. Vaswani, M.D., *Department of Psychiatry, Kansas University Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66106*; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Ekkehard Othmer, M.D., Cherilyn M. De Souza, M.D., Marsha R. Read, Ph.D., Edward E. Hunter, Ph.D., William F. Gabrielli, M.D.

Summary:

Objective: To contrast the familial, clinical, and treatment histories of a large group of outpatient schizophrenics who did or did not satisfy criteria for one of three anxiety disorders.

Method: Over a five-year period, all new admissions to the outpatient psychiatry service of a large Midwestern teaching hospital were examined with a structured diagnostic interview and other self-report measures before seeing the clinic physician. Of the 1,458 patients who participated, 192 or 13.2% met Feighner criteria for schizophrenia. Ninety-five of the 192 (49.5%) also met criteria for one or more anxiety disorders. Of the 192 patients with schizophrenia: 15% had OCD only; 8% had only panic attacks; 4% had phobia only; 7% had OCD plus panic; 6% had phobia plus panic attacks; 4% had OCD plus phobia; and 6% had all three anxiety disorders comorbid with schizophrenia. Schizophrenia patients with and without a comorbid anxiety disorder were compared for sociodemographic characteristics and a family history of mental disorder as well as the onset and course of the psychosis, the level of social impairment, utilization of treatments, and psychiatric comorbidity.

Results: Schizophrenics with an anxiety disorder were younger; however no race, gender, religion, marital status, or educational differences were found. Psychosis and anxiety disorder did not distinguish the family histories of the two groups; alcoholism was slightly more prevalent in the anxiety disorder subgroup. Onset of psychosis began earlier in the schizophrenic patients with anxiety disorder. Schizophrenics with anxiety disorder acknowledged significantly more symptoms on the SCL-90 and more psychotic symptoms on the PDI. Psychiatric comorbidity was greater in the anxiety disorder schizophrenic subgroup; this difference was due to an increased prevalence of depression, anorexia nervosa, and somatization disorder. Schizophrenics with comorbid anxiety disorder reported more problems in childhood, poorer health currently, less efficient psychosocial functioning, and lower self satisfaction. Despite the greater severity, diversity of symptoms, and suffering among the schizophrenics with anxiety disorder, no treatment differences were noted, including the number of psychiatric hospitalizations or the kinds of medications prescribed to the two groups.

Conclusions: Our findings suggest that schizophrenics with one or more anxiety disorders may comprise a recognizable subtype with specific treatment needs that must be addressed in order to maximize the therapeutic intervention.

NR127 Monday, May 15, 3:00 p.m.–5:00 p.m.

Evidence of Heterogeneity in Cognitive Performances

Stacey D. Espinet, *York University, 2960 Don Mills Road, North York, ON M2J 3B8, Canada*; R. W. Heinrichs, Ph.D.

Summary:

Objective: To determine whether categorizing schizophrenia patients based on executive function is a promising research direction. The purpose of categorization is to decrease the amount of heterogenity found within the schizophrenic population by classifying the population into subtypes with similar deficits.

Method: Examined the distribution of scores obtained on the Wisconsin Card Sorting Test (WCST) for bimodality in a sample of 104 DSM-III-R schizophrenia patients. Evidence for two performance peaks was apparent on visual and quantitative analysis. The sample was divided into two groups; one intact group (scoring five categories achieved and above), and an impaired group (those scoring four and below categories). T-tests and Chi-square statistics were calculated to determine if these groups varied as a function of age, education, gender, IQ, and other clinical and demographic features.

Results: The groups did not vary in terms of age, education, or gender but did vary in IQ. The subtypes showed a modest stability (Kappa = .51) at a three-year follow-up with 57 of the original patients.

Conclusion: The WCST is one of the most popular standardized measures used to assess cognitive impairment in schizophrenia. However, researchers should be cautious in using the test because reliability is modest and the test may index a transitory cerebral dysfunction rather than a neurobehavioral trait of the illness.

NR128 Monday, May 15, 3:00 p.m.–5:00 p.m.

Metabolic and Cardiovascular Consequences of Prolonged Clozapine Treatment: A Retrospective Study

Martha M. Kato, M.D., *Department of Psychiatry, Univ. of VA/ Roanoke-Salem Prgm, 1970 Roanoke Boulevard, VAMC, Salem, VA 24153*; Sonia P. Yovtcheva, M.D., Carolyn A. Stanley-Tilt, R.N., Rezhan Hussein, M.D., Ali Iranmanesh, M.D.

Summary:

This retrospective study was conducted to determine the metabolic and cardiovascular effects of extended therapy with clozapine. The charts of 19 male patients (mean age ± SEM: 51 ± 1.6 yrs) treated with clozapine were reviewed for height, weight, pulse, systolic and diastolic blood pressure, and serum concentrations of glucose and cholesterol. Clozapine-induced changes were evaluated by comparing the data obtained at baseline (prior to treatment), within one year, and after two years of therapy. A complete lipid profile was checked prospectively in nine of the 19 patients who continued to be active in the clozapine clinic. Results are presented as mean ± SEM, and compared for statistical significance using ANOVA and linear regression analyses. ANOVA did not reveal significant changes in serum glucose concentration, and either systolic or diastolic blood pressure. Although not significant as a group, the responses of weight and body mass index to treatment were variable (no change, increase, decrease) in individual subjects. Alternatively, significant increases were observed in the pulse rate (82 ± 2.9 vs 98 ± 3.2 vs 96 ± 1.9 beats/min; $p < 0.0001$) and serum concentrations of total cholesterol (184 ± 10 vs 198 ± 14 vs 217 ± 12 mg/dL; $p = 0.003$). Linear regression analysis of the prospective lipid data revealed significant positive correlation between serum concentrations of total cholesterol and LDL ($r = 0.9$, $p = 0.009$), but not HDL ($r = 0.52$, $p = 0.09$) or triglycerides ($r = 0.4$, p = NS). It is concluded that in contrast to changes in the body weight, significant increases in pulse rate and serum cholesterol concentration are sustained after prolonged treatment with clozapine. While anticholinergic and peripheral α-blocker properties of clozapine could explain the incidence of chronic tachycardia, the etiology of hypercholesterolemia is not fully clear. Significant positive correlation between circulating concentrations of total cholesterol and LDL after two years of treatment, could imply drug-induced increases in LDL, which requires future investigation. Similarly, the long-term cardiovascular risk of tachycardia and hypercholesterolemia need to be further explored.

NR129 Monday, May 15, 3:00 p.m.–5:00 p.m.

Medication Compliance and Quality of Life in Persons with Schizophrenia

Leticia T. Postrado, Ph.D., *Department of Psychiatry, University of Maryland, 685 West Baltimore, MSTF Room #300, Baltimore, MD 21201*

Summary:

Objective: This paper aims to examine the association of medication compliance with quality of life (QOL) in a schizophrenia sample.

Methods: The Schizophrenia PORT Project team surveyed a stratified random sample of 719 persons with schizophrenia in two states. The survey used the Lehman Quality of Life Instrument to measure subjects' subjective and objective quality of life. A four-point scale was used to determine degree of medical compliance of subjects.

Findings: Compliance with medication was significantly associated with greater overall life satisfaction ($p < .05$), higher satisfaction with social relations ($p < .05$), greater satisfaction with health ($p < .05$), higher self-rating of financial adequacy ($p < .050$), and lower probability of an arrest ($p < .01$), controlling for patients' demographic and clinical characteristics.

Conclusion: Quality of life maybe useful for enhancing the quality of care to promote better compliance among persons with schizophrenia. More studies with longitudinal design should be conducted to ascertain the causal influence of medication compliance on quality of life.

NR130 Monday, May 15, 3:00 p.m.–5:00 p.m.

Depression Is Not Associated with Short-Term Outcome in Acute Schizophrenia

Thomas Szafranski, M.D., *Department of Psychiatry, IPIN, Sobieskiego 1/9, Warszawa 02-957, Poland*; Zuzanna Konieczynska, Ph.D.

Summary:

Objective: Presence of depressive symptoms during the exacerbation of schizophrenia is usually associated with positive prognosis. The aim of our study was to evaluate the prognostic value of depression for short-term outcome in acute schizophrenics.

Methods: Two independent samples of patients with DSM-IV diagnosis of schizophrenia were assessed with PANSS and Calgary Depression Scale at admission and discharge. First sample consisted of 80 consecutive admissions to inpatient ward and the second sample consisted of 60 patients admitted to the daily treatment center. Patients were treated with various antipsychotics. Data were analyzed using Spearmen Rank Correlations and Mann-Withney U Test.

Results: In both samples depression scores (CDSS) at admission were not correlated with total PANSS reduction (end point vs. baseline [%]). Patients were divided into two groups with high or low depression scores. Both groups did not differ in regard to total PANSS, PANSS positive and negative symptoms at admis-

sion and discharge, difference between groups in total PANSS reduction.

Conclusions: Presence of depressive symptoms at admission was not associated with more favorable short-term outcome.

NR131 Monday, May 15, 3:00 p.m.–5:00 p.m.

Methylphenidate Treatment of Psychiatric Symptoms from Central Pontine Myelinolysis

Denise C. Bridgeford, M.D., *Psychiatry, Denver VAMC, 1055 Clermont Street 116, Denver, CO 80220*; David B. Arciniegas, M.D., Marcelo Fernando Batkis, M.D., Brandon K. Martin, B.A., Thomas P. Beresford, M.D.

Summary:

Objective: Central Pontine Myelinolysis (CPM) is a demyelinating disease of the brain stem that can affect extrapontine brain areas. It is believed to be a polyetiologic syndrome linked to hyponatremia, hypokalemia, and chronic alcoholism. To date few treatment cases have been reported, owing to fatal complications of CPM. Once diagnosed only postmortem, the illness can now be diagnosed antemortem with MRI.

Method: We describe a case of MRI verified CPM with myelinolysis extending to the basal ganglia in a 55-year-old chronic alcoholic patient. Reasoning that psychostimulants have improved similar symptoms after traumatic brain injury, with patient and family consent we undertook an off-on-off-on trial of methylphenidate over a one-month period. Target psychiatric symptoms were apathy, amotivation, lack of social propriety, inattention to activities of daily living, cognitive slowing, and depressed mood. These were measured with the UCLA Neuropsychiatric Inventory.

Results: Significant mood and frontal lobe symptom relief resulted only with drug treatment and quickly returned in the absence of methylphenidate.

Conclusion: medication aimed at alleviating symptoms of depression, psychosis, and frontal lobe impairment may be useful in treating CPM. This case suggests that an increase in dopaminergic transmission may help compensate for the neural impairment of CPM.

NR132 Monday, May 15, 3:00 p.m.–5:00 p.m.

Semantic Retrieval in Older Schizophrenia Patients

Angela O. Udebiuwa, M.D., *Department of Psychiatry, University of Maryland, 22 South Greene Street, box 351, Baltimore, MD 21201*; Richard B. Rosse, M.D., Stephen I. Deutsch, M.D., Jill A. RachBeisel, M.D.

Summary:

Investigators are increasingly interested in understanding neurocognitive deficits in schizophrenia. It is postulated that these deficits are the core symptoms of schizophrenia that lead to functional disability. This study examined semantic memory function in schizophrenia. Semantic memory refers to general knowledge that includes knowledge about words, concepts, and their relations. A variety of language problems have been identified in schizophrenia patients, most notably on verbal fluency tests. Such deficits reflect disturbances in strategic search and organization of semantic structures. We further examined retrieval from semantic memory in older nondemented schizophrenia patients (age 50–71 yrs, M = 56.8) and control subjects using a standard test of lexical fluency and a novel word-retrieval task, in which subjects produced words to definitions. Patients retrieved fewer words and were slower to produce words compared with control subjects. Patients' word-retrieval ability was correlated to performance on the lexical fluency test. In addition, we observed a marginally significant relation between word retrieval and scores on the Thought Language and Communication Scale (TLC, Andreasan, 1986). Results suggest impairments in semantic search strategies in older schizophrenia patients that might relate to symptoms of formal thought disorder, as measured by the TLC.

NR133 Monday, May 15, 3:00 p.m.–5:00 p.m.

Neuropsychological Correlates of Schizophrenic Syndrome

Steffen Moritz, Ph.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20246, Germany*; Burghard Andresen, Ph.D., Dieter Naber, M.D., Martin Lambert, M.D., Michael Krausz, Ph.D., Anne Karow, M.D.

Summary:

There is a great deal of evidence that schizophrenic symptomatology is best represented by three syndromes (positive, negative, disorganized). Both the disorganized and negative syndrome have been found to correlate with several neurocognitive dysfunctions. However, previous studies investigated samples predominantly treated with typical neuroleptics, which frequently induce parkinsonoid symptoms that are hard to disentangle from primary negative symptoms and may have inflated correlations with neurocognition. A newly developed psychopathological instrument called Positive And Negative And Disorganized Symptoms Scale (PANADSS) was evaluated in 60 schizophrenic patients. A total of 47 participants treated with atypical neuroleptics performed several neurocognitive tasks.

A threefactor solution of schizophrenic symptomatology emerged. Negative symptomatology was associated with diminished creative verbal fluency and digit span backward, whereas disorganization was significantly correlated with impaired Stroop, WCST, and Trail-Making-Test B performance.

Data suggest that disorganization is associated with tasks that demand executive functioning. Previous findings reporting correlations between negative symptomatology and neurocognition may have been confounded by the adverse consequences of typical neuroleptics.

NR134 Monday, May 15, 3:00 p.m.–5:00 p.m.

Gender, Gamma Activity and Schizophrenia

Shameran Slewa-Younan, B.A., *Department of Psychological Medicine, University of Sydney, Westmead Hospital, Wentworhville 2145, Australia*; Evian Gordon, Ph.D., Leanne Williams, Ph.D., Elkwonon Goldberg, Ph.D.

Summary:

This study explores the possibility that the more favourable clinical prognosis in females with schizophrenia may be associated with their greater network interconnectedness, which is possibly reflected in enhanced gamma (40Hz) electrical brain activity. An auditory "oddball" task was administered to 35 patients with schizophrenia and 35 age- and sex-matched controls (25 males and 10 females). Peak gamma amplitude (from a time series of gamma activity averaged for 40 target stimuli and the immediately preceding 40 background tones) was examined across 19 sites. Peak gamma activity occurred 250 to 450ms in targets and 350 to 550ms in backgrounds. Multiple within and between group MANOVAs were conducted analyzing both peak gamma amplitude (microvolts) and latency (milliseconds). Within-group, the control males showed a pattern of earlier gamma latency in the right compared with the left hemisphere ($F(1, 33) = 3.70$, $p < 0.06$), while control females exhibited delayed latency frontally compared with the posterior region ($F(1,33) = 6.25$, $p < 0.04$). This male lateralization finding and the anterior/posterior gradient in females is consistent with Goldberg's predictions. The patient group however, failed to show this male lateralized and female frontal-poste-

rior pattern of gamma activity, suggesting sub-optimal network integration in the patient group, in both males and females.

NR135 Monday, May 15, 3:00 p.m.–5:00 p.m.

Trends in the Treatment of Schizoaffective Disorder

Julianne Flynn, M.D., *Department of Psychiatry, Walter Reed, 6900 Georgia Avenue, Washington, DC 20307-5001*; Thomas A. Grieger, M.D., David M. Benedek, M.D.

Summary:

Background: Treatment of patients with schizoaffective disorder continues to evolve, particularly given the availability of newer pharmacotherapies. The demographics of these patients, nature of symptoms present at hospitalization, and factors that precipitate rehospitalization are not well studied. Understanding the epidemiology and response to treatment in this population may improve the delivery of care.

Method: Outcome data were extracted from the charts of 70 patients with a diagnosis of schizoaffective disorder during the period from September 1993 to October 1999. Demographic data, comorbid substance use, age at onset of illness, living situation, employment, primary mood symptoms, presence of psychosis, and psychotropic medications at admission and discharge, were extracted from the records. Rate of functional improvement was also assessed.

Results: Demographic data are described. A total of 94% of patients presented with psychosis; 21% presented without mood symptoms. The use of lithium and "typical" antipsychotics decreased and the use of divalproex sodium and newer antipsychotics increased during the period studied. Hospital days to stabilization remained constant during the period studied.

Conclusion: Most patients with schizoaffective disorder are hospitalized with active psychosis. Newer pharmacologic treatments have not improved time to stabilization during hospitalization.

NR136 Monday, May 15, 3:00 p.m.–5:00 p.m.

Factors Predicting Compliance with Appointments in Women Discharged from a Psychiatric Hospital in Turkey

Aykut Ozden, M.D., *Department of Psychiatry, Beth Israel Medical Center, 321 East 13th Street, # 11-B, New York, NY 10003*; Huseyin H. Ozsan, M.D., Bedriye Oncu, M.D., Handan Tugcu, Ph.D.

Summary:

Objective: We know that psychiatric patients' compliance with their appointments is generally low. The aim of this study is to find the characteristics of psychiatric patients who were discharged and did not comply with the appointments, which may be helpful in predicting such behavior.

Method: Seventy-six female patients discharged from the ward for female psychotics in the psychiatry clinic of the University of Ankara, Turkey, are followed prospectively. One month after discharge, patients are divided into two groups as compliant and noncompliant with the appointments and they are compared regarding their sociodemographic and psychiatric characteristics. BPRS is used for assessment of their psychiatric condition before discharge.

Results: Of the 76 patients, 73.8% of them (n = 56) complied with the appointments given. The noncompliant patients are relatively older, widowed or divorced, living out of the city, did not improve much with the admission, and who evaluated their stay in the hospital negatively.

Conclusion: These results showed that the noncompliant female psychotic patients with the appointments could be predicted from the aforementioned variables. We must be particularly cautious when we evaluate these patients for discharge.

NR137 Monday, May 15, 3:00 p.m.–5:00 p.m.

Suspiciousness As a Specific Risk Factor for Major Depressive Episodes in Schizophrenia

Erick L. Messias, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, Baltimore, MD 21201*; Brian Kirkpatrick, M.D., Ranganathan Ram, M.D., Allen Y. Tien, M.D.

Summary:

Objective: Serious depression is a common and important complication of schizophrenia. In a prospective, population-based study, we tested the hypothesis that suspiciousness increases the risk for the later development of depression in schizophrenia.

Method: Data came from the Epidemiological Catchment Area (ECA) study. Baseline clinical and demographic features were used to predict the onset of new episodes of depression at one-year follow up. As ECA diagnoses were based on lay interviews, which may have low sensitivity compared with clinical diagnoses, two overlapping groups of putative schizophrenia patients were defined.

Results: Suspiciousness was associated with an increased risk of new episodes of depression in both patient groups, after accounting for demographic variables. There was no association between an increased risk of depression and either disorganization or hallucinations and delusions.

Conclusions: Suspiciousness appears to be a specific risk factor for depression in psychotic groups. Interventions that decrease suspiciousness or mitigate its isolating effects might decrease the risk of serious depression and suicide.

NR138 Monday, May 15, 3:00 p.m.–5:00 p.m.

Old Schizophrenics: Gender, Symptoms, Course and Outcome

Uma Naidoo, M.D., *Department of Psychiatry, Mass. Mental Health Center, 74 Fenwood Road, Boston, MA 02115*; Carl Salzman, M.D., Omar Rahman, M.D., Emily Schwab, B.S., Kelly Czworka, A.B.

Summary:

Objective: To present the symptom profile, demographic characteristics, course of illness, and level of functioning of early-onset elderly schizophrenic patients.

Method: A chart review was conducted at a major public sector mental health center to investigate the demographic, gender, and psychosocial data on current outpatients over the age of 65 years, who carry the diagnosis of schizophrenia or schizoaffective disorder. (N = 33)

Results: Of 33 patients, 24 patients were women. In addition, 21 patients (72%) were paranoid at the time of the chart review. At the onset of their illness, 13 (62%) of these patients were paranoid, suggesting that the symptom profile of this illness changed in approximately 40% with age. Since the literature suggests that late onset schizophrenia is entirely a paranoid illness, this raises the question of whether the development of paranoid symptoms is related to age in some patients. In terms of outcome, the age of onset of illness did not predict the level of functioning scores (GAF: global assessment of functioning) in old age.

Conclusion: Old people with moderately severe early-onset schizophrenia who attend a public mental health Continuing Care Clinic were found to be predominantly female, and suffer primarily from paranoid symptoms. These observations confirm and extend other retrospective surveys of similar age populations who are less severely and more severely ill. Although some early onset elderly schizophrenia patients had paranoid symptoms at the on-

set of their illness, others became paranoid as they aged. In this group the initial severity of symptoms did not predict the level of functioning in old age. These data suggest that elderly outpatients with early-onset schizophrenia represent a heterogeneous group of female individuals who require further study.

NR139 Monday, May 15, 3:00 p.m.–5:00 p.m.

Morbidity from Catatonia in a Chronic Population

Chitra Malur, M.D., *Department of Psychiatry, Suny Stony Brook, Health Science Center T-10, Stony Brook, NY 11794-8101*; Andrew J. Francis, Jr., M.D.

Summary:

Objective: To screen for undetected and untreated catatonia in a chronic hospital to assess the morbidity from catatonia in a long-term institutional population.

Method: A random sample of 103 patients was obtained; 52 were not examined for practical reasons, such as lack of capacity or consent. Ages ranged from 23 to 58 and hospitalization from one month to 40 years. Chart diagnoses were schizoaffective disorder (15), schizophrenia paranoid (11), undifferentiated (14), disorganized (1), residual (2) types, depression NOS (2), polysubstance dependence (1), bipolar disorder (4), psychosis NOS (1). Patients were rated on the Bush Francis Catatonia Scale and the Simpson Angus Parkinsonism Scale.

Result: Eight patients met criteria for retarded catatonia (16%) of whom seven had no known history of catatonia. Their primary diagnoses were schizophrenia types but not catatonic. Catatonia coexisted with Parkinsonism in four patients. Two were prescribed lorazepam for periodic agitation and one for negative symptoms.

Conclusion: Undetected and untreated catatonia occurs in a chronic psychiatric hospital (point prevalence 16%). Unrecognized catatonia is often mislabeled, and untreated catatonia may lead to significant morbidity and prolong hospitalization. Catatonia can be distinguished from but may coexist with other motor disorders.

NR140 Monday, May 15, 3:00 p.m.–5:00 p.m.

SPECT Brain Imaging in Catatonia

Chitra Malur, M.D., *Department of Psychiatry, Suny Stony Brook, Health Science Center T-10, Stony Brook, NY 11794-8101*; Corazon Cabahug, M.D., Andrew J. Francis, Jr., M.D.

Summary:

Objective: To test the hypothesis that catatonia is a motor syndrome with cortical dysfunction, we studied the regional cerebral blood flow in 10 catatonic patients with single photon emission tomography (SPECT).

Methods: Ten catatonic inpatients (five male, five female, with various psychiatric diagnoses) were identified with at least four catatonic signs. Nine had retarded and one excited catatonia. All were investigated with Tc 99m HMPAO SPECT while catatonic. In four cases, a second SPECT scan was obtained following resolution of catatonia defined by absence of catatonic signs. The SPECT scans were summarized qualitatively.

Results: Asymmetrical fronto-parietal hypoperfusion was found in all 10 cases of catatonia, five predominantly left sided and five right sided. Of four cases in remission, three showed normalization, and one showed significant improvement in the original hypoperfusion.

Conclusions: Decreased activity in SPECT scans of the 10 patients suggests the involvement of frontal and parietal areas in catatonia. The laterality is unexplained but has been reported in other studies. Normalization of activity with resolution of catatonia parallels psychopathological studies that catatonia is a syndromic state phenomenon.

NR141 Monday, May 15, 3:00 p.m.–5:00 p.m.

Catatonia in Post-ECT Delirium

Chitra Malur, M.D., *Department of Psychiatry, Suny Stony Brook, Health Science Center T-10, Stony Brook, NY 11794-8101*; Andrew J. Francis, Jr., M.D.

Summary:

Objective: Catatonia secondary to several medical conditions is recognized, but catatonic signs in post-ECT delirium have not been described. The DSM-IV criteria for catatonia secondary to a general medical illness exclude delirium, but often the same factors that promote delirium also induce catatonia.

Method: We noted three cases of catatonia emerging during post-ECT delirium and reviewed their course and clinical management.

Results: Three patients without catatonia (two with schizoaffective disorder and one bipolar disorder with mental retardation) received ECT and developed delirium after ECT session #4, #10, and #7, respectively. During this time, they became catatonic by Bush-Francis criteria (two retarded, one excited). Catatonia resolved and delirium improved with oral lorazepam in two and clonazepam in one.

Conclusions: Catatonic signs may occur in post-ECT delirium and may respond to benzodiazepines, which also improve or resolve the delirium. These cases argue that the DSM criteria for secondary catatonia should not exclude delirium, and that usual treatments for catatonia (e.g., benzodiazepines) that are not first-line choices for managing other forms of delirium may be useful for delirium with catatonic features.

NR142 Monday, May 15, 3:00 p.m.–5:00 p.m.

A Follow-Up Study Comparing Clinical and Endocrine Effects of Clozapine and Risperidone

Norberto M. Zelaschi, M.D., *Department of Psychiatry, PRA-Korn Hospital, 520 Y 175, LaPlata, BA 1900, Argentina*; Juana L. Rodriguez, M.D., Sergio Gaitan, M.D., Sergio Panizzo, B.A., Azucena Sobrera, B.A., Angelica Lopez, B.A., Ferando Archuby, B.A.

Summary:

This study describes clinical data, rate of relapse, and prolactin (PRL) serum levels after a long-term antipsychotic drug trial comparing clozapine (CLOZ) and risperidone (RIS).

Method: We have studied 23 patients suffering from schizophrenic disorder—DSM-IV diagnosis criteria; the complete period of follow up is for two years. A clinical criterion for relapse was used, which were previously validated in former trials. After 56 weeks of continuous and uninterrupted treatment, PRL serum levels performed by ELISA were compared between patients receiving CLOZ (n = 9 $\bar{x}$ age; 41 +/– 6.29), RIS (n = 14, $\bar{x}$ age 56 =/ – 11.98), and a sample of normal subjects (n = 19 $\bar{x}$ age; 25 =/ – 4.50).

Results: Eleven patients relapsed with RIS and one dropped out for developing neutropenia with CLOZ; eight patients responded to CLOZ and four to RIS. The difference for the rate of relapse is statistically significant (x^2 = 11.27, p = .0008). PRL serum levels increased with RIS ($\bar{x}$33.03 =/– 15.92, ng/ml) and decreased with CLOZ ($\bar{x}$ = 10.22 =/– 2.32 ng/ml), when compared with normal subjects ($\bar{x}$ = 17.33 =/– 4.33 ng/ml). ANOVA test followed by the Tukey's test for multiple comparisons F = 26.65, p = .000000.

Comments: There are relatively few studies showing simultaneously the rate of relapse and the values of serum PRL during prolonged trials with CLOZ and RIS. Our data suggest that the patients with sustained intervention of DA-5HTA2 blocking agents, showed clinical differences, which reflect pharmacological properties of atypical antipsychotic drugs. Moreover, the low risk of relapse associated with a decrease of PRL observed with CLOZ

could indicate a clinical balanced relationship between a weak DA and a strong 5HTA2 antagonism. On the other hand, prolactogenic activity found with RIS could indicate this potent DA blocking activity.

NR143 Monday, May 15, 3:00 p.m.–5:00 p.m.

Vlaproic Acid Increases Gene Expression of Superoxide Dismutase (SOD1)

Xin-Min Li, M.D., *Department of Psychiatry, University of Saskatchewan, 103 Hospital Drive, Saskatoon, SK S7N OW8, Canada*; Ou Bai, Augusto Juorio, Vern Bennett, M.D., Rudy Bowen, M.D.

Summary:

Objectives: Mood stabilizing agents have been used effectively in the treatment of bipolar disorder. Neuroanatomical studies have shown that bipolar disorders are associated with neuronal atrophy or loss. This study is to test whether valproic acid regulates the mRNA of superoxide dismutase (SOD1), which reduces the oxidative stress of the neuron.

Methods: Valproic acid was administered to PC12 cells in culture. Its effect on SOD1 mRNA levels were analyzed by northern blot after 24 or 48 hours of treatment.

Results: Valproic acid upregulates SOD1 mRNA in a time- and dose-dependent manner, whereby the greatest upregulation was seen at longer time points and higher doses.

Conclusion: These findings suggest that valproic acid has the ability to positively regulate a neuroprotective gene, and ongoing treatment for bipolar affective disorder, even during remission may be very critical.

NR144 Monday, May 15, 3:00 p.m.–5:00 p.m.

Venlafaxine Extended Release in Bipolar Depression

Jose M. Artadi, M.D., *Department of Psychiatry, University of Miami Medical Sch, D79 1400 NW 10 AVE, # 304A, Miami, FL 33136*; Manuela Georgescu, M.D., Paul J. Goodnick, M.D., Blanche Freund, Ph.D., C. Lindsay De Vane, Ph.D., Charles L. Bowden, M.D., Peyton White, A. Kumar, Ph.D.

Summary:

The treatment of depression in the bipolar disorders has not been established. Although data, particularly from open studies, support the use of bupropion...as well as others, little has been definitive. Venlafaxine, with effects on serotonin, norepinephrine, and dopamine, particularly at higher doses may combine benefits of both bupropion and the SSRIs. Thus, it was hypothesized that venlafaxine at a dose of 225 mg/day might be effective in patients with major depression in the context of bipolar history, as well as that their response might be related to baseline measures of platelet 5HT content, as previously seen with SSRIs (Goodnick et al, 1995), and of plasma MHPG, as seen with bupropion (Goodnick et al, 1998).

In this initial open label study, those with DSM-IV MDE, single episode or recurrent, with history of mania or hypomania, aged 18–65 years, with baseline HDRS of ≥18 (17-item), received 112.5 mg venlafaxine XR for days 1–7, then 225 mg for days 8–57. Patients were evaluated on the HDRS, BDI, YMRS at screening, baseline, and end of weeks 1, 2, 4, and 8. Blood samples were collected for evaluation of platelet 5HT content, plasma MHPG at baseline, and of platelet 5HT content, plasma MHPG, and venlafaxine blood levels at conclusion.

To date, data are available on eight patients of whom six have completed: four men and four women, mean age = 48.1 years. HDRS has improved from 21.2 to 17.4 at week 1 ($p < .01$) and final 5.4 ($p < .001$); BDI, from 30.6 to final 11.2 (= .001). No changes found in YMRS, HR, BP, RR, weight; Plasma results pending. Thus, venlafaxine merits further double-blind studies to establish efficacy in bipolar major depression.

NR145 Monday, May 15, 3:00 p.m.–5:00 p.m.

Onset of Response to Fluoxetine As Assessed by the Symptom Questionnaire

David Mischoulon, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WAC 812, Boston, MA 02114*; Shamsah B. Sonawalla, M.D., Andrea C. Hutchins, B.A., Margarita L. Delgado, B.A., Mary J. Johnson, M.A., John J. Worthington III, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Summary:

Objective: Previous studies have evaluated onset of response to antidepressant medication and have found that symptoms of depression may respond at separate time periods. The purpose of this study was to examine the onset of response to fluoxetine across the different subscales of the Symptom Questionnaire.

Methods: We evaluated 169 depressed outpatients (99 women; mean age: 40.3 ± 10.6 years) meeting DSM-III-R criteria for major depressive disorder. All patients completed the Symptom Questionnaire (SQ) at baseline and at weeks 2, 4, 6, and 8. We defined onset of response as a ≥ 50% reduction in scores on each scale of the SQ (Anger/Hostility, Depression, and Anxiety).

Results: The proportion of patients who obtained a ≥ 50% reduction in SQ scores at week 2 was 35% for anger/hostility, 19% for depression, and 18% for anxiety; at week 4, the proportion was 54% for anger/hostility, 36% for depression, and 32% for anxiety; and at week 8 (endpoint) the proportion was 67% for anger/hostility, 50% for depression, and 50% for anxiety.

Conclusion: Our preliminary results suggest that psychological symptoms of depression such as anger and hostility, as measured by the SQ, may respond earlier and perhaps more robustly than other symptoms.

NR146 Monday, May 15, 3:00 p.m.–5:00 p.m.

Effects of Mirtazapine on Sleep Polygraphic Variables

Michel Schittecatte, M.D., *Department of Psychiatry, Hopital Van Gogh, Rue de L'Hopital 55, Charceroi 6030, Belgium*; Francoise Dumont, M.D., Robert Machowski, Ph.D., Catherine Cornil, Francis Lavergne, M.D., Jean Wilmotte, M.D.

Summary:

Objective: To study, in depressed patients, the effects of mirtazapine on sleep polygraphic variables.

Method: Mirtazapine was administrated on a flexible schedule (30 – 60 mg at night time) in a sample of 17 drug-free patients meeting DSM-IV criteria for a major depressive episode. Severity of depression was evaluated using the HAMD, the MADRS, and the CGI. Sleep polygraphic recordings were performed before and during acute and chronic treatment. Subjective assessment of changes of sleep were quantified using the Leeds Sleep Evaluation Questionnaire.

Results: In acute administration (first two days), mirtazapine (15 mg) significantly increases total sleep time, sleep efficiency, stage II, stage REM, and slow wave sleep percent, and decreases sleep latency and stage awake percent (all p's < 0.05). These effects persist after two weeks of treatment and remains significant for total sleep time, sleep efficiency, and stage awake percent. Subjectively, mirtazapine induces a improvement of sleep with a significant easier and quicker than usual go to sleep and a more restful quality of sleep.

Conclusions: This open, noncontrolled study suggest that mirtazapine ameliorates the sleep disturbances encountered in de-

pressed patients both objectively and subjectively. Controlled studies are needed to confirm these preliminary results.

NR147 Monday, May 15, 3:00 p.m.–5:00 p.m.

Alpha2-Adrenoreceptor Sensitivity As a Marker of Depression

Michel Schittecatte, M.D., *Department of Psychiatry, Hopital Van Gogh, Rue de L'Hopital 55, Charceroi 6030, Belgium*; Francoise Dumont, M.D., Robert Machowski, Ph.D., Eric Fontaine, Catherine Cornil, Julien Mendlewicz, M.D., Jean Wilmotte, M.D.

Summary:

Objective: To determine if α2-adrenoceptor subsensitivity is a state or a trait marker of depression by the use of the REM sleep response to the α2-agonist, clonidine.

Method: Thirty-two drug-free depressed patients were consecutively challenged with a Clonidine REM Suppression Test (CREST) and treated with fluvokamine, a SSRI with no or little effects on NA receptors (Group 1), or mirtazapine, a NaSSA acting via α2 adrenoceptors blockade (Group 2). The first 10 patients of of each group who recovered were given a second challenge. The CREST of these two groups of 10 patients in both states were compared between them and with the CREST of a group of 10 normal subjects.

Results: Before treatment, the REM sleep response to clonidine was highly significantly different of the response in the healthy subjects in the two groups. After treatment, we still observed a blunted REM sleep response to clonidine in the fluvoxamine treated patients, despite clinical recovery, but a normalized response in the mirtazapine treated patients.

Conclusions: These results suggest that α2-adrenoceptor subsensitivity is a trait marker of depression, in accordance with previous studies using the growth hormone (GH) response to clonidine as a probe.

NR148 Monday, May 15, 3:00 p.m.–5:00 p.m.

Characteristics of Individuals Seeking Treatment for Gambling Problems and Reporting Excessive Tobacco Use

Marc N. Potenza, M.D., *Department of Psychiatry, Yale University, 34 Park Street, New Haven, CT 06519*; Marvin A. Steinberg, Ph.D., Susan McLaughlin, Dawn Hemstock, Ran Wu, M.S., Bruce J. Rounsaville, M.D., Stephanie S. O'Malley, Ph.D.

Summary:

Objective: To investigate the characteristics of individuals seeking treatment for gambling disorders with regard to presence or absence of excessive tobacco use. We hypothesized that individuals with disordered gambling reporting excessive tobacco use would represent a group more susceptible to addictive disorders and therefore experience more severe gambling problems.

Methods: Information from the 1260 calls obtained during a year-long period from 1998 to 1999 to a gambling helpline serving the Southern New England region of the United States were analyzed with respect to reported presence or absence of excessive tobacco use by the identified gambler.

Results: Statistically significant differences were observed with regard to education level, income, gambling patterns, legal problems, lifetime money lost to gambling, financial problems, interpersonal problems, drug and alcohol problems, suicidality, and patterns of mental health care treatment.

Conclusions: These results have implications for both the provision of care to individuals with gambling disorders and the theoretical framework within which disordered gambling is conceptualized. Further investigation is needed to more precisely define the relationships between nicotine use and gambling behaviors.

NR149 Monday, May 15, 3:00 p.m.–5:00 p.m.

Switching Versus Augmentation: A Prospective, Naturalistic Comparison in Depressed, Treatment-Resistant Patients

Michael A. Posternak, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Introduction: Switching antidepressant and augmentation are the two main pharmacologic alternatives a clinician has when faced with treatment-resistant depression. While double-blind studies have independently validated their effectiveness, the two strategies have never been directly compared against each other.

Method: In a naturalistic, open-label design, prospective assessments were made on all depressed outpatients who were treatment-resistant. Short- and long-term outcomes of switching versus augmentation were compared using the Clinical Global Impression scale.

Results: In the acute phase, 11 of 25 (44.0%) patients whose antidepressant was switched, compared to 9 of 21 (42.8%) whose antidepressant was augmented, responded—a nearly identical rate. Almost all of the latter group (87.5%) maintained their response for at least 6 months, while a slightly lower percentage of patients whose antidepressant was switched (66.7%) maintained a positive response. No decrement in response rates was found on subsequent trials.

Conclusions: Switching and augmentation appear to be equally effective interventions in treatment-resistant depression. For patients who do not respond to an augmentation or switch, our results suggest that subsequent trials are just as effective.

NR150 Monday, May 15, 3:00 p.m.–5:00 p.m.

Therapeutic Drug Monitoring of Olanzapine

Matthias Dobmeier, M.D., *Department of Psychiatry, University of Regensburg; Universitatsstr 53, Regensburg D-93053, Germany*; Ekkehard Haen, M.D., Juergen Mueller, M.D., Helmfried E. Klein, M.D.

Summary:

Olanzapine is mainly eliminated by Cytochrom P (CYP) 1A2 but also by CYP 2C19, 2D6 and FMO3. If both CYP 1A2 and 2D6 are involved, metabolism can easily be influenced by environmental factors, such as smoking; ingestion of coffee, tea, grapefruit juice; and concomittened medication, inducing or inhibiting these enzymes. But also gender, age, and weight seem to influence the plasma level. Therapeutic drug monitoring (TDM) with this new neuroleptic drug was started to detect differences in the plasma levels and to get better information about the decreasing or increasing factors. Steady state plasma levels of olanzapine were determined by high-liquid chromatography (HPLC) with electrochemical detection. Over 150 patients on olanzapine were examined. A total of 291 blood samples from these patients were analyzed. The range was between 0 and 200 ng/ml olanzapine. Some patients obviously did not take their medication. No linear correlation between daily dose and plasma level could be found. Patients with levels below 10 ng/ml had a poor clinical response, measured by GCS. On the average women had higher olanzapine plasma levels than men. Some drugs like valproate decrease, whereas others such as carbamazepine increase the plasma level markedly. Older patients tend to have higher plasma levels. Some of the patients with adverse drug events (ADE) had plasma levels above 100 ng/ml. Therefore, we believe that TDM of olanzapine

is a valuable instrument to improve the safety of pharmacological treatment.

NR151 Monday, May 15, 3:00 p.m.–5:00 p.m.

Gabapentin in Bipolar Depression

Po W. Wang, M.D., *Stanford University, 401 Quarry Road, 2124, Stanford, CA 94305*; Claudia M. Santosa, M.A., Connie M. Strong, M.S., Debbie L. Tate, Terence A. Ketter, M.D.

Summary:

Objective: In bipolar disorder patients, gabapentin (GBP) monotherapy does not appear effective in mania or treatment-resistant rapid cycling, but adjunctive GBP may attenuate depressive symptoms. Hence, we studied adjunctive GBP in bipolar depression.

Method: We added open GBP (900–2700 mg/day) to stable doses of mood stabilizers for 12 weeks in fourteen (7 women, 7 men, mean age 37.6) depressed bipolar disorder (5 bipolar I, 9 bipolar II) outpatients, and performed weekly 28-item Hamilton Depression (HAM-D) Ratings.

Results: Six of fourteen (43%) patients responded with moderate to marked improvement (≥50% HAM-D decrease). Mild to moderate baseline depression (18 < HAM-D < 30) was related to better outcome, as 5/5 responded compared with only 1/9 patients with severe (HAM-D ≥ 30) baseline depression (Fisher's Exact $p = 0.003$). Overall mean Ham-D ratings decreased 42% from 32.9 ± 8.7 at baseline to 19.1 ± 13.7 at week 12 (LOCF, $t = 5.1$, $df = 13$, $p = 0.0002$). GBP was well tolerated with minimal somatic adverse effects, and no patient developed mania.

Conclusion: Adjunctive GBP may offer benefit in mild to moderate bipolar depression. Controlled studies are indicated to explore the utility of this approach.

NR152 Monday, May 15, 3:00 p.m.–5:00 p.m.

Effect of SSRI on 5HT

Charl Els, *Department of Physiology, U. Free State, c/o AHP, p o box 1000, Ponoka, AB T4J 1R8, Canada*; W.E. Nel, M.D., J.M.C. Oosthuizen, M.D., E.H. de Wet, M.D., P.H. du Preez, B.S., P.T. Austin, B.S.

Summary:

Introduction and aim: Fenfluramine and dexfenfluramine are mediated by central serotonergic pathways in the brain. Dexfenfluramine, fenfluramine, and serotonin reuptake inhibitors (SSRIs) increase central serotonin concentrations. Dexfenfluramine and fenfluramine increase peripheral serotonin concentrations, possibly responsible for cardiac valvular pathology (reported in recent literature). The aim of this study was to investigate the effect of SSRIs on peripheral serotonin concentrations.

Method: Ethics committee approval was obtained, and informed patient consent. Thirteen patients completed the parallel, double-blind, randomized study. Patients were treated with paroxetine or fluoxetime, prescribed by a psychiatrist (CE). Venous blood was collected from each patient on two occasions, i.e., before commencement of treatment (before) and one month later (after). The serum was analysed according to recognized standard laboratory procedures.

Results: Paroxetine group: n = 7; age: 36.6 ± years; males = 4, females = 3; before [5-HT]; 158.7 ± 93.5 ng/ml; after [5-HT]: 102.1 ± 59.9 ng/ml; median difference (after vs. before): 46 ng/ml = 64.3% decrease. Fluoxetine group: n = 6; age: 30.2 ± 10.4 years; females = 6; before [5-HT]; 152.8 ± 68.1 ng/ml; after [5-HT]; 105.7 ± 14.8 ng/ml; median difference (after vs. before): 18.5 ng/ml = 84.8% decrease.

Conclusion: The results suggest that paroxetine and fluoxetine decrease peripheral serotonin concentrations, which is not in accordance with expectation and warrants further investigation.

NR153 Monday, May 15, 3:00 p.m.–5:00 p.m.

Adjunctive Gabapentin in Treatment-Resistant Depression

Sarah Yasmin, M.D., *Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906*; Linda L. Carpenter, M.D., Zelko Leon, M.D., Jason M. Siniscalchi, M.S., Lawrence H. Price, M.D.

Summary:

Background: Previous studies in predominantly bipolar patients have suggested that gabapentin may be useful in treating mood disorders. This report describes its efficacy and tolerability as an adjunctive agent in treatment-resistant depression.

Methods: A chart review was conducted on 27 outpatients with predominantly nonbipolar depressive disorders in whom gabapentin was added to ongoing treatment with a conventional antidepressant to which patients had not responded after at least six weeks. Clinical state and adverse effects were assessed retrospectively at each visit.

Results: Mean gabapentin trial duration was 15.2 ± 7.8 weeks, with a mean final dose of 904 ± 445 mg/day (range, 300–1800 mg/day). Clinician-rated measures of clinical state improved significantly from baseline to endpoint. Overall, 37.0% (n = 10) of patients were responders at endpoint; another 18.5% (n = 5) manifested a transient response not sustained to endpoint. Gabapentin was well tolerated; the most common adverse effects were fatigue, sedation, dizziness, and gastrointestinal symptoms.

Conclusion: These findings in primarily nonbipolar patients suggest that gabapentin may be of adjunctive benefit in the management of treatment-resistant depression. Limitations of the study included uncontrolled treatment and retrospective efficacy assessments.

NR154 Monday, May 15, 3:00 p.m.–5:00 p.m.

Medication Outcomes in a Veterans Administration Domiciliary Program

Christopher P. Camilleri, M.D., *Ward 23C, Veterans Administration Medical Center, 940 Belmont Street, Brockton, MA 02301*; David N. Osser, M.D., Paul Block, Ph.D., Eviline T. Meleka, M.D., Jagdish Ragade, M.D.

Summary:

Objective: To evaluate the effectiveness of pharmacotherapy in a three-to-four-month residential rehabilitation program for complex, treatment-resistant homeless veterans.

Method: 300 veterans were evaluated by the program's psychiatrist. Three psychiatrist raters retrospectively reviewed treatment records and assessed the outcomes of all medication trials on a three-point scale: markedly improved, slightly improved, or not improved.

Results: Preliminary analyses are reported on 69 patients (128 trials). The most common target diagnoses for medication were: anxiety disorders other than PTSD (12), PTSD (11), major depression (11), other depressive disorders (9), and bipolar disorders (7); 90% had a history of alcohol or substance abuse/dependence prior to admission. There were no differences in the outcomes of completed trials by diagnosis (ANOVA: $F = 0.983$, $p = 0.465$).

Examining the last outcome before discharge, 53% markedly improved, 30% improved slightly, and 17% did not change. Also, 42% had other comorbid Axis I disorders: these patients received an average of 2.1 trials, and 59% improved markedly. The 58% without comorbidity had 1.7 trials, and 49% improved markedly.

These differences were nonsignificant by chi-square, but the trends may reach significance in the full sample. By diagnosis, the number of medication trials ranged from 1.5 per patient for major depression to over 2.0 for PTSD and other anxiety disorders, bipolar disorder, and psychotic disorders. These differences also suggested trends.

Conclusions: Pharmacotherapy was eventually helpful for most (83%) of these dual-diagnosis patients treated in the context of a structured program. However, there were trends that the psychopharmacologist had to pursue more medication trials to achieve positive outcomes in patients with non-substance-related Axis I comorbidity, anxiety disorders, and bipolar mood disorders.

Data on the full sample will be presented at the meeting.

NR155 Monday, May 15, 3:00 p.m.–5:00 p.m.

Efficacy of Mirtazapine in Panic Disorder

Joseph Berger, M.D., *Emory University, 1841 Clifton Road, Atlanta, GA 30329*; Philip T. Ninan, M.D., Bettina Knight, B.S.N., Amy Selvig, B.S., Charles B. Nemeroff, M.D.

Summary:

Several pharmacological agents are effective in the treatment of panic disorder, including antidepressants (SSRIs and tricyclic antidepressants) and benzodiazepines. However, many individuals are intolerant of these antidepressants and concern with discontinuation effects limit the use of benzodiazepines. Buspirone, a serotonin IA partial agonist, is not effective in panic disorder, suggesting that specific pharmacological effects are needed for therapeutic benefit.

Objective: We tested the tolerability, safety, and efficacy of mirtazapine in panic disorder. The pharmacological effects of mirtazapine includes antagonism of the alpha-2 adrenoreceptor as well as serotonin 2 and 3 receptors.

Method: Subjects gave informed consent and met DSM-IV criteria for panic disorder with or without agoraphobia based on the SCID interview. Subjects who had two full panic attacks during a single-blind placebo lead in for four to 14 days were subsequently treated with open-label mirtazapine (15–45 mg daily) for eight weeks (Phase I). Subjects kept a daily diary recording panic symptoms and anticipatory anxiety. Assessment of phobic avoidance, depressive symptoms, as well as functional measures were also obtained at each visit. Response was operationally defined as a CGI improvement score of 1 or 2 and a 50% reduction in the number of panic attacks. Responders entered a double-blind phase with randomization to placebo or continuation of mirtazapine for an additional 24 weeks (Phase II).

Results: Sixteen subjects entered the study, with 10 successfully completing phase 1 currently. Only one terminated early because of side effects, and no serious adverse events occurred. Nine (90% completers, 56% intent to treat) met criteria for response and entered phase II. Detailed results will be presented.

Conclusion: Preliminary data support the safety, tolerability, and efficacy of mirtazapine in the treatment for panic disorder.

NR156 Monday, May 15, 3:00 p.m.–5:00 p.m.

Antipsychotic Tolerance, Rebound and Supersensitivity Psychosis with Quetiapine

Howard C. Margolese, M.D., *Department of Psychiatry, Allan Memorial Institute, 1025 Pine Avenue West, Montreal, QC H3A 1A1, Canada*; Guy Chouinard, M.D., Linda Beauclair, M.D., Marie-Claire Belanger, R.N.

Summary:

Objective: To determine long-term efficacy of quetiapine monotherapy in schizophrenia.

Methods: A total of 23 stable male outpatients with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder were selected from 350 outpatients to enter a three-year open-label study (5077IL/0051) at our center. Patients were previously stable on 460.12 ± 422.84 mg/day chlorpromazine units (n = 17), and/or 6.05 ± 3.99 mg/day of risperidone (n = 10). Patients were hospitalized for 13-day treatment initiation (5077IL/0072).

Results: Only five patients (21.7%) completed 77 to 96 weeks of the study, which was terminated by the sponsor for administrative reasons (approval of the drug by health authorities). Initial dose was 200 mg/day in divided doses, mean ending dose 487 ± 209.6 mg/day. For those completing 12 weeks or less (n = 11) mean ending dose was 362 ± 184.8 mg/day, for those completing 25 weeks or more 592 ± 178.2 mg/day (n = 12). The dose of those initially stabilized had to be continually increased for all but three patients. Furthermore, 6/23 patients met Chouinard diagnostic criteria for SSP. To date only 2/23 (8.7%) remains on quetiapine.

Conclusions: Rebound psychosis or SSP appears more easily with quetiapine. Quetiapine binds loosely to the D2 receptor and is easily displaced, even by dopamine. Thus, multiple daily doses would initially enhance D2 receptor downregulation but then cause increased receptor density to compensate for quetiapine's loose and short D2 occupancy. Therefore, quetiapine monotherapy given once daily may reduce development of tolerance, rebound, and SSP.

NR157 Monday, May 15, 3:00 p.m.–5:00 p.m.

Olanzapine Treatment of Adult Stuttering: An Open-Label Prospective Analysis

Nathan E. Lavid, M.D., *Department of Psychiatry, Univ. of CA - Irvine, 101 The City Drive, South, Orange, CA 92868*; David L. Franklin, M.S., Gerald A. Maguire, M.D.

Summary:

As previously reported by Lavid et al., olanzapine has been successfully used in the management of stuttering in two children and one adolescent. This observation has been extended to a similar result in four adult patients. A 50-year-old white male, a 42-year-old male, a 32-year-old male, and a 31-year-old female, all with developmental stuttering, have been followed prospectively for three months to two years after receiving olanzapine to control their symptoms. The patients' fluency before treatment ranged from severe to moderate, which was scored as a 6 to 4 via the Clinical Global Impression (CGI) scale. All of the patients are receiving a maintenance dose of 2.5 mg at bedtime. Three of the patients now have CGI scores of 1 (minimal stuttering) and the fourth is rated as a 2 (mild stuttering). All of the patients have noted that their fluency has improved on the trial. Mild weight gain has been noted in all four subjects. This side effect has been managed with some success with diet and exercise. These results indicate that olanzapine may be useful in the treatment of stuttering in adults.

NR158 Monday, May 15, 3:00 p.m.–5:00 p.m.

Citalopram Treatment of Social Phobia

Charles A. Cloutier, *Department of Psychiatry, Duke University, 2213 Elba Street, Durham, NC 27710*; Indu Varia, M.D., P. Murali Doraiswamy, M.D.

Summary:

Objective: SSRIs are used as treatments for generalized and specific social phobias (social anxiety disorders). The efficacy of citalopram, an SSRI, for the treatment of social phobia has not been fully investigated. The purpose of this retrospective case observation was to evaluate the use of the SSRI citalopram in the treatment of generalized social phobia.

Method: We report the use of citalopram for the treatment of generalized social phobia in five patients with disabling social phobia at an academic outpatient clinic. Three of these patients had failed a prior SSRI trial. Main outcome measures were the HAM-D, HAM-A, Liebowitz Social Anxiety Scale, and CGI.

Results: At 12 weeks, all five patients experienced full or partial improvement in symptoms with meaningful improvement in social and occupational functioning. The mean dose of citalopram at endpoint was 50mg.

Conclusions: These data suggest that citalopram may be an effective treatment for social anxiety disorder and that a second SSRI may be helpful in patients who have failed prior SSRI trials. A larger placebo-controlled study of citalopram is warranted.

NR159 Monday, May 15, 3:00 p.m.–5:00 p.m.

Mirtazapine Versus Fluoxetine in Panic Disorder

Flavio Kapezinski, Ph.D., *Department of Psychiatry, UFRGS, Otavio Dutra 174/1003, Porto Alegre, RS 90810-230, Brazil*; Luciana Ribeiro, M.D., Joao V. Busnello, Marcia K. Sant'Anna, Marcelo Madruga, Joao Quevedo, M.D., Ellis D. Busnello, M.D.

Summary:

Background: Mirtazapine is an antidepressant with a different side-effect profile in comparison with the first-line agents used in the treatment of panic disorder. Up to now mirtazapine had not been tested in a double-blind manner for the treatment of panic disorder. This study compared the effectiveness and safety of mirtazapine and fluoxetine in the treatment of PD.

Method: The study was a double-blind, randomized trial comparing mirtazapine and fluoxetine in PD. After a one-week placebo run-in, 27 patients entered into an eight-week, double-blind phase of treatment with either mirtazapine or fluoxetine.

Results: There were no statistical differences between the two groups at endpoint for the primary outcome measures: ratio of endpoint to baseline panic attacks, panic free status and high end state functioning. There were also no significant differences between groups as measured by Panic Diary, the CGI-S, CGI-I, HAM-A, Sheehan Phobic Scale, and Patient Global Evaluation of Phobic Anxiety. Adverse events that were different among groups were: weight gain, that occurred more frequently in the mirtazapine group, and nausea and paresthesias that occurred more often in the fluoxetine group.

Conclusion: Results suggest that mirtazapine may be an alternative for the current treatments of PD. Organon-Brazil provided mirtazapine for this trial.

NR160 Monday, May 15, 3:00 p.m.–5:00 p.m.

5HT Syndrome: A Review of Cases

Jimmy O. Ibikunle, M.D., *Department of Psychiatry, Penn State University-Hershey Medical Ctr, 500 University Drive, Hershey, PA*

Summary:

Serotonin syndrome is a toxic, potentially fatal hyperserotonergic state. It has been reported at initiation, in overdose, and combination of serotonergic agents. It also occurs in recreational substance abuse. Sternbach's diagnostic criteria include autonomic, neuromuscular, and cognitive symptoms and signs.

Method: A retrospective chart review of toxicology consults at a university medical center for reported or suspected overdose and drug interactions involving at least one known serotonergic agent was done. Individuals with substance intoxication and animal bites were excluded.

Results: Of the 173 cases, over a five-year period, five met criteria for serotonin syndrome, constituting 2.89%. Mean age was 34.4. Four patients were female. One required ICU stay; others were discharged within 24 hours; all survived. Three cases occurred in the course of medication adjustments: switching from fluoxetine to trazodone, augmenting fluoxetine with lithium and simultaneously increasing doses of fluoxetine and trazodone. Two cases involved intentional overdose: one with venlafaxine and the other with sertraline; the latter followed a recent switch to fluvoxamine. Cognitive symptoms were the most common initial presentation.

Conclusion: Occurrence during medication changes supports an iatrogenic etiology. No cases involved a MAOI, notorious for its precipitant effect, and fluoxetine's pharmacokinetics suggests its predisposition.

NR161 Monday, May 15, 3:00 p.m.–5:00 p.m.

Overdose: A Review of 100 Cases

Jimmy O. Ibikunle, M.D., *Department of Psychiatry, Penn State University-HersheyMedical Ctr, 500 University Drive, Hershey, PA 17033*; Suzi R. Levens, M.D.

Summary:

Patients who overdose represent a significant challenge for consultation-liaison psychiatrists.

Methods: A retrospective chart review of 100 patients over 18 consecutively admitted from July through December, 1998 by the toxicology service following overdose warranting hospitalization was performed. Diagnoses were based on DSM-IV criteria.

Results: Seventy-eight percent of the 100 toxicology cases reported suicidal intent. The age range was 18 to 79; the mean was 34.8. Fifty-five percent were female. The primary psychiatric diagnoses are as follows: 64% mood disorder, 16% substance-related disorder, 8% adjustment disorder, 7% psychotic disorder, 2% anxiety disorder, 3% other. Sixty-eight percent had a prior Axis I diagnosis other than substance abuse. Forty-one percent were currently receiving psychiatric treatment. Sixty-four percent had coexisting substance abuse. Twenty-nine percent ingested at least one substance of abuse as part of the overdose. Forty-six percent had previously attempted suicide. Seventy-five percent identified a stressful life event.

Conclusion: Adult overdose patients share risk factors for suicidal behavior including the presence of an Axis I diagnosis, particularly a mood disorder, lack of current psychiatric treatment; history of prior suicide attempt; and significant life stressors. Substance abuse represents a significant independent and comorbid risk factor for overdose.

NR162 Monday, May 15, 3:00 p.m.–5:00 p.m.

Fluoxetine in the Treatment of Huntington's Disease

Nicola de Marchi, M.D., *Department of Psychiatry, University of Naples, Largo Madonna Delle Grazie, Naples 80138, Italy*; Alfredo Dama, M.D., M. Antonietta Ragone, M.D., Fabiana Daniele, M.D., Maria G. Ariano, M.D.

Summary:

We describe here two patients with Huntington's disease (HD), who showed an excellent response to the selective serotonin reuptake inhibitor (SSRI) fluoxetine. These patients had not responded to previous pharmacological treatments and were in an advanced HD stage. In both subjects, we detected a remarkable improvement of agitation and irritability after a few weeks of treatment. An improvement in the motor domain of these patients was also observed after three months of fluoxetine administration, with a mean decrease of 40% in the score at the HD Scale (HDS). This amelioration has persisted for a number of years. In patient 1, we observed a surprising cognitive improvement, which started after six months of treatment, when this patient became testable with the Mini Mental State Examination (MMSE). It is noteworthy

that these clinical results are still visible after six years of treatment, whereas HD displays an inesorably progressive course of illness.

Fluoxetine was chosen because these two patients belong to a large HD pedigree, showing a high prevalence of obsessive-compulsive disorder (OCD). The positive response to this drug support the hypothesis that we might have identified a particular subtype of HD, of which OCD may represent a significant clinical marker.

NR163 Monday, May 15, 3:00 p.m.–5:00 p.m.

Risperidone and Clozapine: A Five Add-On APD in Acute Psychosis

Amresh K. Shrivastava, M.D., *Silver Mind Hospital, Gokhale Road Thane West, Mumbai 400602, India*; Meghana Thakar, M.A., Supriya Ghalsasi, D.P.M.

Summary:

Objective: Acute exacerbation of psychosis in emergency is mostly treated by a combination of linloperidole(HAL) and benzodiazepine (BZ). Outcome & safety-efficacy profile in usage of such a combination is often related to clinical difficulties, intolerable side effects, longer duration of admission, and inadequate control of psychosis. Feasibility of introducing novel antipsychotic needs to be explored during management of acute state. We attempted to study safety and efficacy of novel APD in combination with HAL in acute state management.

Method: An open-level naturalistic design study of acute psychotic episode in chronic schizophrenia in a hospitalized sample (N = 50) was examined using HAL as sole APD (group t, N = 20) and in combination with clozapine (CLZ) (group II, N = 15), and risperidone (RISP) (group III, N = 15). Selection criteria were based purely on clinical situation.

Results: It was observed that patients receiving atypical APD along with HAL showed good tolerability. No patient showed any unusual side effect (SE). Two patients in Group I exhibited signs of incipient NMS .60% in group 1, 80% in CLZ group & 80% patients in RISP group did not show any SE EPS was seen in 25% receiving HAL alone & 20% receiving RISP with HAL .20% in CLZ group showed common SE. Mean dose of HAL alone was 26.7 mg, while it dropped to 14 mg when combined with CLZ & 15 mg with RISP. Number of patients requiring BZ was reduced by 55% in CLZ group & by 15% in RISP group. Mean duration of hospitalization diminished from 5.6 weeks for HAL to 3 weeks in CLZ & 3.6 weeks in RISP group. Mean dose of CLZ was found to be 230 & RISP 5.0 mg per day 70% in I .80% in II & 80% in III group showed better than 'good' recovery on CGI.

Conclusion: Combining novel APD with haloperidole in required cases in acute suite management appears feasible & beneficial.

NR164 Monday, May 15, 3:00 p.m.–5:00 p.m.

Use of Topiramate as a Mood Stabilizer

Lou Ann Eads, M.D., *Psychiatry, UAMS, 4301 West Markham, Little Rock, AR 72205*; R. Greg Wooten, M.D., Thomas A. M. Kramer, M.D.

Summary:

Topiramate is one of the newer antiepileptic drugs. Recently, we performed a retrospective chart review. Review of 17 consecutive treatment refractory patients started on topiramate, at an assertive community program, was undertaken. Topiramate in these patients was used as either the primary mood stabilizer or as an adjunctive mood stabilizer. There were eight males and nine females, ranging in age from 29 to 56 years of age. Eight of these patients showed an eight- to 20-point increase in their GAF. One patient showed no increase in their GAF, but was felt to be benefiting from the addition of topiramate, according to their treating physician; incidently, this person's care was complicated by AIDS. Lastly, eight of the patients discontinued topiramate because of various CNS side effects, such as dizzyness, confusion, fatigue, somnolence, and impaired concentration. The total daily dosage ranged from 50 to 1600 mg/d. In summary, topiramate appears to show promise as either an adjunctive or primary maintenance treatment for mood disorders, especially mood disorders with psychotic features. These positive results strongly support further investigation into the use of topiramate.

NR165 Monday, May 15, 3:00 p.m.–5:00 p.m.

Head Trauma: Litigants Versus Nonlitigants

Reed Goldstein, Ph.D., *Department of Psychiatry, Pennsylvania Hospital, 210 West Washington, 8q Mezzanine, Philadelphia, PA 19106*; Howard S. Sudak, M.D., Gary S. Bruss, Ph.D.

Summary:

Forty consecutively referred patients (20 plaintiffs; 20 non-litigants) who were diagnosed with motor vehicle accident-related mild traumatic closed head injury (MTCHI)/postconcussional disorder and administered measures of neuropsychological functioning (Halstead-Reitan Test Battery; Wechsler Intelligence and Memory Scales) and personality functioning (MMPI-2). The two groups were matched for SES, age, education, severity of injury (Glasgow Coma Scale, duration of loss of consciousness, results of brain image studies), and post-injury time to cognitive and personality assessment). Sixty-five percent of subjects in each group were females.

No significant differences were found between litigants and non-litigants for IQ scores; Halstead-Reitan Impairment Index; measures of overall memory function. Litigants were more impaired on individual measures of attention ($t = 3.1$, $p < .05$), short-term auditory memory ($t = 2.1$, $p < .05$), and speed of processing ($t = 3.2$, $p < .05$). On the MMPI-2, non-litigants attempted to present themselves in a mildly favorable light and answered items in a nonexaggerated manner; coping skills were intact. Litigants obtained a validity profile consistent with overdramatization and exaggeration of emotional symptoms. It is important to include an assessment of personality functioning as well as legal status in the evaluation of MTCHI.

NR166 Monday, May 15, 3:00 p.m.–5:00 p.m.

A Novel Functional MRI Memory Test for the Assessment of Early Alzheimer's Disease

Lauretta Baucher, *Department of Psychiatry, Duke University, box 3018 c/o Dr. Doraiswamy, Durham, NC 27710*; Gene Chen, B.S., Jeffery Petrella, M.D., Amishi Jha, Ph.D., Gregory McCarthy, Ph.D., Halla Husn, P. Murali Doraiswamy, M.D.

Summary:

There is an urgent need to develop sensitive imaging markers to assess neuronal function at the earliest stages of Alzheimer's disease (AD). Such markers may be useful to evaluate subjects at risk, differentiate age-related memory changes from prodromal AD, and monitor the effects of novel therapies. We report here the development of an event-related functional MRI (fMRI) working memory test and its initial application in patients with progressive mild memory impairment (MMI). The test is designed to assess local hemodynamic response to component processes of working memory: encoding, maintenance, and retrieval. MMI subjects (delayed recall deficits, CDR = 0.5, normal MMSE and function, clinical diagnosis of questionable AD) and matched elderly controls (CDR = 0, normal MMSE, memory and function) underwent fMRI using a delayed response working memory task with an S1–S2 interval of 18-sec between visual stimuli. Faces comprised the working memory set. Both groups of subjects completed the fMRI,

successfully supporting the feasibility of this test in elderly patients. Memory load-related fMRI activation differences were present during encoding and retrieval in frontal and temporal lobe regions in both the MMI and controls groups, reaching significance ($p < 0.05$) in the controls. Our work in progress (N = 12) also suggests that prefrontal and temporal cortical activation tends to be decreased in MMI. These data will be discussed in relation to the clinical promise of using fMRI to evaluate component processes of working memory in elderly patients with early signs of Alzheimer's disease.

NR167 Monday, May 15, 3:00 p.m.–5:00 p.m.

Delirium Predisposal Factors

Adolfo Canovi, M.D., *Department of Psychiatry, Hospital Italiano, Gascon 450, Buenos Aires, CP 1199, Argentina*; Ricardo L. Perez-Rivera, M.D., Cecilia J. De Simone, M.D., Gustavo Rozadilla, M.D.

Summary:

Introduction: It is well accepted that delirium or acute confusional state is a multifactorial syndrome in which the patient's vulnerability or predisposed factors interact with the precipitant factors or organic causes.

Objective: Our objective was to detect and determine the frequency of psychiatric disorders antecedents as vulnerability factors, in those patients who have suffered delirium.

Methods: We evaluated 56 inpatients. The data were collected by the patient's clinical evaluation, family interview, and clinical charts review.

Results: Sixteen of the 56 inpatients evaluated suffered delirium that represented 29% of the population evaluated. Compared with the group who had not suffered delirium, this group's mean age was older and with predominance of females. Also, 100% (n = 16) of the delirium group showed abnormal laboratory test (blood analysis) and received medications; 75% (n = 12) suffered cronical illness; 63% (n = 10) have psychiatric antecedents; and 50% (n = 8) were in post-surgical states. The most prevalent psychiatric antecedent was major depressive disorder (n = 5), followed by dementia (n = 4), alcohol abuse (n = 3), and delirium (n = 1).

Conclusion: The frequency of psychiatric antecedents in delirium was important and therefore could be considered as vulnerability or predisposed factor to develop delirium.

NR168 Monday, May 15, 3:00 p.m.–5:00 p.m.

Irritable Bowel Syndrome Treated with Amitriptyline: An Open Trial with 19 Patients

Hildeberto J. Tavares, M.D., *Department of Psychiatry, IPQ-HC = USP, R Ovidio Pires de Campos S/N, Sao Paulo, SP 05403-010, Brazil*; Hyong-Jin Cho, M.D., Carlos R. Silva, M.D., Aytan M. Sipahy, M.D., Aderson D. Moreira, M.D., Wagner F. Gattaz, Ph.D.

Summary:

Irritable bowel syndrome (IBS) is a chronic functional gastroenterological disorder, often associated with psychiatric disorders, mainly depression and anxiety. This syndrome has recently been treated with antidepressants, even when there is no comorbid psychiatric conditions. The present study evaluates the response obtained with amitriptiline 50 mg-a-day, psychiatric comorbidity and the influence of psychiatric disorders in this IBS sample. Nineteen adult subjects fulfilling Rome criteria for IBS were included in the study after medical and psychiatric evaluation and after a one-week placebo wash-out period. The patients were evaluated in weeks 0, 1, 2, 4, and 8 with the following instruments: Visual Analogical Scale (VAS) for 10 abdominal symptoms, Clinical Global Impressions (CGI) scale, Hamilton's depression scale (HAMD), and Hamilton's anxiety scale (HAMA). Psychiatric disorders were found in 68.4% of the patients and 42.1% of the patients had depression and/or dysthymia. Abdominal pain, flatulence, eructation, abdominal distension, CGI, HAMA, and HAMD improved significantly in Wilcoxon statistic test. The improvement in CGI, HAMD, and HAMA was significantly (Mann-Whitney test) greater in the group with psychiatric comorbidity. The authors concluded that amitriptiline 50 mg-a-day improved abdominal and extra-abdominal symptoms of IBS, both in patients with or without psychiatric comorbidity.

NR169 Monday, May 15, 3:00 p.m.–5:00 p.m.

Malingering in the Military

Nancy A. Harpold, D.O., *Department of Psychiatry, US Army and Med. College of GA, 1515 Pope Street, Augusta, GA 30912-3800*; Judith K. Denton, M.D., Paul C. Burney, M.D., Christopher Lange, M.D., William J. Evans, M.D.

Summary:

Objective: This study sought to investigate specific characteristics of malingering in a military population.

Method: A comprehensive retrospective chart review was performed on 161 patients admitted to the inpatient psychiatric unit of an Army medical center from 1993 to 1996. Exclusion criteria included substance dependence, mood disorders, and psychotic disorders.

Results: Of the 161 charts reviewed, 24% (38) met the criteria for malingering according to DSM-IV. In the malingering population, 29% met criteria for antisocial personality disorder, compared with 17% in the total population. There was no statistically significant difference in the percentage of females in the malingering population (29% female) compared with the total charts reviewed (28% female.) In the malingering population, 24% were endorsing legal difficulties, compared with 30% in the total population.

Conclusion: Our study suggests that in the military population, malingering is not strongly associated with a medicolegal presentation. These findings are in contrast to the DSM-IV recommendation to strongly suggest malingering in the mediolegal presentation. There appears to be a higher percentage of antisocial personality disorder in the military malingering population. This is consistent with DSM-IV. In the military population, there does not appear to be a higher incidence of malingering in one particular sex.

NR170 Monday, May 15, 3:00 p.m.–5:00 p.m.

Dopamine and Electroretinogram in Cocaine-Dependent Patients

Jeffrey A. Berman, M.D., *Department of Psychiatry, New Jersey Medical School, 30 Bergen Street ADMC 1507, Newark, NJ 07107*; Abir Marcus, M.D., Benito Gonzalez, PA-C, Alec Roy, M.D., Monique Roy, M.D.

Summary:

Objective: Cocaine has its reinforcing effects by influencing dopaminergic transmission in brain reward centers. Dopamine (DA) is found in high concentrations in the retina. Cocaine-dependent patients, recently withdrawn, have been shown to have significantly reduced blue cone ERG b-wave amplitudes. We examined the relationship of the ERG responses and homovanillic acid (HVA) levels in cerebrospinal fluid (CSF) in cocaine-dependent patients.

Methods: Subjects met DSM-IV criteria for cocaine dependence at East Orange VA Hospital. They were drug free two weeks prior to ERG and lumbar puncture. HVA was measured by high-pressure liquid chromatography. Independent sample t-test was used.

Results: We used an ERG blue cone b-wave amplitude >0.5 mV to divide patients into normal ERG responders and blunted responders. Blunted ERG responders (n = 9) had significantly higher concentrations of CSF HVA (mean 45.5 pmol, SE = 15.4) than responders (n = 4) (mean 24.2, SE = 15.04 pmol/ml. ($t = 2.32$, $p < 0.05$).

Discussion: This preliminary investigation is the first to substantiate a possible use of ERG amplitudes as an index of DA metabolism. Further studies are needed to determine whether this ERG marker may be useful in identifying a subgroup of cocaine-dependent patients for specific psychopharmacological treatment studies.

NR171 Monday, May 15, 3:00 p.m.–5:00 p.m.

Testosterone and Pathological Gambling

Carlos Blanco, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Angela Ibanez, M.D., Enrique Baca-Garcia, M.D., Carmen Blanco-Jerez, B.S., Jeronimo Saiz-Ruiz, M.D., Luis Orensanz, Ph.D.

Summary:

Objective: Testosterone has been previously related to impulsive-aggressive behaviors. We investigated the possible association between testosterone levels and pathological gambling, an impulsive, non-aggressive behavior.

Method: Levels of testosterone of 30 DSM-IV male pathological gamblers and 30 age- and gender- matched healthy volunteers were determined at 9 a.m.

Results: Testosterone levels were 472.4 (SD = 36.0) pg/ml in pathological gamblers and 553.7 (SD = 34.3) in controls ($t = 12.15$; $df = 58$; $p < 0.001$).

Conclusion: High testosterone levels are not associated with pathological gambling. High testosterone levels may be more closely associated to aggressive than impulsive behaviors.

NR172 Monday, May 15, 3:00 p.m.–5:00 p.m.

Deep Brain Stimulation in OCD: A Reversible Last-Resort Therapeutic Option?

Loes Gabriels, M.D., *Department of Psychiatry, UZ Antwerpen, Wilrijkstraat 10, Edegem B-2650, Belgium*; Paul Cosyns, M.D., Bart Nuttin, M.D.

Summary:

Objective: To explore if electrical stimulation in specific brain sites improves symptomatology in treatment-resistant obsessive-compulsive disorder (OCD).

Method: Randomized double blind, stimulation ON-OFF, cross-over study. Psychiatrist-rated Yale-Brown Obsessive-Compulsive Scale (Y-BOCS-psy) prior to surgery, at the end of each crossover branch, and after six months continuous stimulation (CS), as well as weekly Y-BOCS self-rating scales (Y-BOCS-SRS) were completed.

Results: Patient 1: Y-BOCS-psy scores were 38 (max 40) before surgery, 30 in ON, 35 in OFF, and 31 after six months CS, but Y-BOCS-SRS remained 40/40 during the whole protocol. Patient 2 and 3: Y-BOCS-psy dropped from 33 and *30* before surgery to 20 and *18* in ON. Patient 2 ended OFF with Y-BOCS-psy 29. Patient 3 refused to support OFF, after having experienced ON. After six months CS, scores were 27 and *16*. Mean Y-BOCS-SRS were 35 and *28.8* before surgery; 24,5 and *20.4* in ON; 28 for patient 2 in OFF; 21 and *15.8* after six months CS.

Conclusions: These preliminary results are promising and DBS may alleviate OCD symptomatology, therefore being an answer to the ethical considerations about the irreversibility of psychosurgery versus the obligation to present all appropriate options to OCD patients who failed available pharmacotherapy and psychotherapy.

NR173 Monday, May 15, 3:00 p.m.–5:00 p.m.

Cyclooxygenase and Brain Development: Implications in Rett's Syndrome

Carolina Stamu, M.D., *Department of Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Pl p o box 1228, New York, NY 10029*; Giulio M. Pasinetti, Ph.D., Lap Ho, Ph.D., Fitzroy Willis, Ph.D.

Summary:

Cyclooxygenase (COX)-2, the inducible form of COX known for its role in prostanoid biosynthesis, belongs to a subset of genes localized to dendritic spines that are regulated by synaptic activity. Altered COX-2 expression in dendrites of brains of cases affected by Rett's syndrome, a form of profound psychomotor retardation, has been reported. Thus, alteration of neuronal COX-2 may play an important role in abnormal development and possibly in a mechanism leading to mental retardation. To further explore the role of COX-2 in brain, we generated a transgenic mouse model with neuronal overexpression of human (h)COX-2 and used DNA microarray techniques to identify clusters of genes differentially expressed in the brains of COX-2 transgenics. Because the genes screened in the DNA microarray were clustered by an algorithm designed to group genes into functional families, we were able to identify a pattern of changes within distinct biochemical hierarchies that were affected by COX-2 overexpression. Data from this analysis indicated that genes involved in cell cycle/division (cycle dependent kinases, CDK-1) and cell growth (glial derived growth factor, GDNF) are affected in brain of COX-2 transgenics. The result of the analysis suggests that COX-2 may play an important role in brain development. We hypothesize that COX-2 expression may indirectly influence the mechanism involved in abnormal dendritic development in Rett's syndrome.

NR174 Monday, May 15, 3:00 p.m.–5:00 p.m.

Olanzapine Augmentation for SSRI-Apathy Symptoms

Christopher R. Johnson, M.D., *Department of Psychiatry, Baylor College of Medicine, One Baylor Plaza, # 110D, Houston, TX 77030*; Michael Barber, Ph.D., Barbara Kertz, M.A., Kimberly K. Cress, M.D., Paul J. Carlson, M.D., Leanne Vogelson, B.A., Lauren B. Marangell, M.D.

Summary:

Objective: This open-label, flexible-dose study was undertaken to assess the efficacy of olanzapine (2.5–20 mg) in treating residual apathy in patients taking SSRIs for the treatment of depression.

Method: Participants to date are 13 men and women who met DSM-IV criteria for major depression, in remission (MADRS ≤ 12), with significant symptoms of apathy as assessed by the Apathy Evaluation Scale (AES ≥ 30), MADRS-item 8 (inability to feel ≥ 2), and the Clinical Global Impression (CGI ≥ 3). Subjects with a personal or family history of psychosis were excluded. Olanzapine was titrated in 2.5 mg increments at weekly intervals, based on side effects and clinical response.

Results: Improvement was clinically evident and demonstrable on all symptoms assessments; LOCF: AES (–21.4 [SD 11.8]; $p = 0.002$), CGI (–2.5 [SD 1.3]; $p = 0.002$), MADRS (–6.46 [SD 5.61]; $p = 0.007$), and MADRS-item 8(–2.5 [SD 1.5]; $p = 0.002$). The mean dose of olanzapine was 4.6 (SD = 5.8) mg.

Conclusions: These preliminary data suggest that olanzapine may be effective in treating residual apathy symptoms in patients taking SSRIs.

NR175 Monday, May 15, 3:00 p.m.–5:00 p.m.

fMRI to Assess Chinese Schizophrenia

Dein-Wen Lee, *Department of Psychiatry, Veteran General Hospital, 201, SEC 2, Shi-Pai Road, Taipei, Taiwan*; Chen-Hong Yang, M.D., Tung-Ping T. Su, M.D., Jen-Chuen Hsieh, M.D.

Summary:

Object: We applied a verbal fluency task in Chinese schizophrenic patients during three Tesla MRI scanning to approach the pathogenesis of schizophrenia in Chinese population.

Method: Some declared that schizophrenia might be the pay for human being language development. So we adopted verbal fluency task in block design to access Chinese schizophrenics in fMRI. Chinese is quite different from English due to its ideographical script in contrast to alphabetic script. Single Chinese characters often don't manifest a concept. It is often that a compound word represents a concept in Chinese. Our experimental design comprised one phonemic generation task and two categorical generation tasks. During phonemic generation, the subject was instructed to generate as many compound words as possible in responding to a given single word. Because the schizophrenics often showed a tendency toward concrete thinking, animal generation and tool generation were included in our study design of categorical generation task. We also hoped to see different object representations at inferior temporal lobe as described by Damasio. Repetition was taken as baseline. Our data were analyzed with statistical parametric mapping (SPM 99 from the Wellcome Department of Cognitive Neurology, London, UK) implemented in MATLAB on a SUN workstation. The motion artifacts were corrected via realignment procedure. All images were then normalized to Talairach and Tournoux standard brain.

Results: The common activation region including: M1 (mid to lower level corresponded to mouth representation), Brodmann area 44, 47, 18, 24. Schizophrenia patients showed less frontal activation in both phonemic generation and tool generation; they also showed less deactivation of posterior temporal region and posterior cingulate gyrus, Brodmann area 39, 40, 22, 23.

Conclusions: Our data support the notion about the pathogenesis of schizophrenia, that is, a fronto-temporal disconnection.

NR176 Monday, May 15, 3:00 p.m.–5:00 p.m.

M-CPP/PET in Impulsive/Aggressive Personality Disorders

Diedre A. Reynolds, M.D., *Department of Psychiatry, Mt. Sinai Medical Center, 130 West Kingsbridge Rd, #116A, Bronx, NY 10468*; Antonia S. New, M.D., Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Vivian Mitropoulou, M.A., Marianne Goodman, M.D., Larry J. Siever, M.D.

Summary:

Background: We have previously reported reduced cerebral glucose metabolism following oral administration of the serotonergic agent d,l-fenfluramine in orbital and ventral medial prefrontal cortex in impulsive personality disordered subjects compared with normals (Siever et al, 1999). In this study, the effect on regional brain glucose metabolism in response to the intravenous administration of 0.08 mg/kg mCPP and placebo was evaluated to test the hypothesis that mCPP-induced changes in brain metabolism of the orbital frontal cortex and adjacent ventral medial frontal cortex as well as temporal and cingulate cortex are blunted in patients with impulsive/aggressive personality disorders. These studies build on a body of evidence that reduced serotonergic activity as reflected in reduced neuroendocrine responses to serotonergic challenges or diminished concentrations of serotonin metabolites is associated with impulsive aggression in personality disorder patients. They provide an opportunity to directly visualize serotonergic modulation of metabolism of key brain regions implicated in the regulation of aggression.

Methods: 13 impulsive personality disordered patients (as defined by DSM-IV criteria) and five normal volunteer control subjects were studied. 0.08 mg/kg mCPP were administered intravenously and placebo in a randomized, double-blind, placebo-controlled design on two separate days before FDG positron emission tomographic (PET) scanning. Blood samples were obtained for prolactin and mCPP levels prior to and following mCPP and for prolactin following placebo administration. Images were reconstructed using reverse Tailarach method. Repeated measures ANOVA was conducted using drug vs placebo, hypothesized regions (orbital cortex, cingulate) vs control region (occipital cortex), by diagnosis (impulsive vs normal).

Results: Preliminary data suggest decreased regional metabolic response to mCPP in impulsives compared with normals in orbital cortex but not in the occipital cortex. Results will be updated at presentation.

Conclusions: These findings, in conjunction with previously reported findings, suggest that the orbital cortex may be a key region in the modulation of aggression through a serotonergic mechanism.

NR177 Monday, May 15, 3:00 p.m.–5:00 p.m.

NPSLE, Age and the Neurodevelopmental Model

Avram H. Mack, M.D., *Department of Psychiatry, Harvard-Longwood, 330 Brookline Avenue, Rabb 2, Boston, MA 02215*; Gregory L. Fricchione, M.D., Malcolm Rogers, M.D.

Summary:

Objective: To describe the neurologic and psychiatric syndromes that occur secondary to systemic lupus erythematosus (NPSLE) in terms of age and to compare such findings with those predicted by Weinberger's "windows of vulnerability" hypothesis of the neurodevelopmental pathogenesis of mental disorders.

Method: Literature search and manual review provided cases of NPSLE. The particular NPSLE diagnoses and the ages at which they occurred were compiled. We then determined ranges and means of age of onset of the various syndromes. We compared those with the ranges and means of age of onset of psychiatric disorders postulated by the "windows" model.

Results: A total of 826 NPSLE events were identified in 559 patients. Variations were found including a nine-year difference between the mean onset of psychosis (30.59) and depressed mood (39.65). The mean ages of onset and the ranges were similar to those proposed by Weinberger both absolutely and in temporal relation to each other.

Conclusion: NPSLE syndromes differ in terms of age in a manner consistent with, and in support of, the "windows of vulnerability" neurodevelopmental model of mental disorders. Independently, or in combination, study of both the "windows" model and NPSLE may produce important findings about psychopathology and should be pursued.

NR178 Monday, May 15, 3:00 p.m.–5:00 p.m.

Neuroendocrine Response to Intravenous Clomipramine in Treatment-Resistant OCD

Sanjay J. Mathew, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, box 84, New York, NY 10032*; Brian A. Fallon, M.D., Kathryn Perko, Jeremy D. Coplan, M.D.

Summary:

Objective: The investigators examined the neuroendocrine response to intravenous clomipramine (IV CMI) in treatment-resistant OCD patients on day 1 and day 14 of treatment to identify predictors and mechanisms of response.

Methods: Thirty-five OCD patients with an inadequate response to oral CMI were begun at 25 mg IV CMI, increasing to 250 mg over 14 days. On day 1, plasma levels of prolactin (PRL), growth hormone (GH), and cortisol (CORT) were obtained immediately before the infusion, and at five 30-minute time points after the infusion. On day 14, hormonal samples were obtained in a similar fashion. Response was assessed by the Y-BOCS.

Results: Low PRL_{MAX} to IV CMI and low CORT levels overall on day 1 were both significantly associated with clinical response. An overall increase in GH secretion during the day 14 challenge was associated with positive response. A pronounced PRL response to IV CMI on day 14 was exhibited by the nonresponders, whereas a smaller and later but significant increase in PRL was noted in the responders.

Conclusion: Neuroendocrine measures reflective of low serotonergic tone positively predicted response to IV CMI. Enhancement of 5-HT neurotransmission was necessary but not sufficient for clinical response.

NR179 Monday, May 15, 3:00 p.m.–5:00 p.m.

Valproate Increases the mRNA Levels of Bcl-2

Shumin Zhao, M.D., *Department of Psychiatry, Wayne State University, 2751 East Jefferson, #200, Detroit, MI 48205*; Husseini K. Manji, M.D., Guang Chen, M.D.

Summary:

A previous study demonstrated that both lithium and VPA treatments increased mRNA levels and the DNA binding activity of the transcription factor PEBP2β in frontal cortex. Both treatments also increased the protein level of Bcl-2, a neuroprotective protein known to be transcriptionally regulated by PEBP2β. We thought that VPA and Li may first turned on PEBP2β gene expression and then PEBP2 transcription factors turn on Bcl-2 gene expression, resulting in increase in protein levels of Bcl-2. Based on this model, the increase in levels of Bcl-2 mRNA is a critical intermediate step, but has not been approved. The mRNA levels of Bcl-2 in frontal cortex is low and difficult to detect using conventional method. Therefore we developed a sensitive RT-PCR method for Bcl-2 mRNA, and β-actin levels were also detected alone with Bcl-2 detection to control experimental varies causing by both PCR and sample preparation. Rats were treated with sodium valproate, and the blood valproic levels were about 39 μg/ml. In these rats we found chronic VPA treatment resulted in a significant increase in Bcl-2 mRNA in frontal cortex, and the finding supported the notion that VPA increased bcl-2 protein through enhanced its gene expression.

NR180 Monday, May 15, 3:00 p.m.–5:00 p.m.

Visuospatial Memory Dysfunction in OCD: A Neuropsychological and PET Study

Kyung-Heup Ahn, M.D., *Department of Psychiatry, Seoul National Univ. Hospital, 28 Yeon-Gun dong, Jong-Ro gu, Seoul 110-744, Korea*; Jae-Seung Lee, M.D., Myung-Chul Lee, M.D., Dong-Woo Lee, M.D., In-Kyoon Lyoo, M.D., Dong-Soo Lee, M.D., Jun-Soo Kwon, M.D.

Summary:

Objective: Neuropsychological and functional neuroimaging methods were combined to investigate biological substrate of obsessive-compulsive disorder (OCD).

Method: Twelve OCD patients met DSM-IV criteria (by SCID-IV, mean age, 29.8 ± 10.1) and eight healthy normal controls (mean age, 26.5 ± 7.3) were compared by using a neuropsychological battery (Wisconsin Card Sorting Test, Letter Fluency Test, Category Fluency Test, Rey-Osterrieth Complex Figure Test (RCFT), Trail Making Test, Digit Span), and [18F]FDG-PET scan. Thirty-four regions of interest (ROI) were compared.

Results: Scores of Trail Making Test-A, immediate recall, and delayed recall of RCFT in OCD subjects were significantly lower than those of healthy comparison subjects (ANCOVAs, $F = 9.06$, $df = 18$, $p = 0.009$; $F = 4.96$, $df = 18$, $p = 0.043$; $F = 4.62$, $df = 18$, $p = 0.05$, respectively). OCD subjects showed lower glucose metabolism in left (ANCOVA, $F = 6.19$, $df = 19$, $p = 0.025$) and right (ANCOVA, $F = 3.93$, $df = 19$, $p = 0.066$) superior parietal area and significantly higher glucose metabolism in left basal ganglia (ANCOVA, $F = 5.00$, $df = 19$, $p = 0.041$) than normal control subjects. Glucose metabolism asymmetry ((Left − Right)/(Left + Right)) of central frontal area is significantly higher in OCD patients (ANCOVA, $F = 7.67$, $df = 19$, $p = 0.014$). There was a significant correlation between scores of immediate recall in RCFT and glucose metabolism of left superior parietal area ($r = 0.51$, $p = 0.025$). In addition, scores of Trail Making Test-A were highly correlated with glucose metabolism asymmetry in central frontal area ($r = -0.65$, $p = 0.003$).

Conclusions: These results emphasized the role of visuospatial memory deficits mediated by parietal lobe hypofunction in OCD subjects.

NR181 Monday, May 15, 3:00 p.m.–5:00 p.m.

Treatment-Resistant Schizophrenia: Predictive Factors

Jorge Henna, M.D., *Department of Psychiatry, Projesq-HC = IPQ, R. Ovidio Pires de Campos S/N, Sao Paulo, SP 05403-010, Brazil*; Helio Elkis, M.D.

Summary:

Treatment resistant schizophrenia (TRS) has been described in the last 40 years. A significant proportion of patients were described as symptomatic despite the high doses of antipsychotics and other therapeutics strategies. It is now estimated that in Brazil 100,000 to 250,000 patients are TRS. Some predictive factors of response to antipsychotic therapy have been extensively studied. In the present study we sought to identify predictors of treatment resistance comparing patients with TRS versus non TRS.

59 DSM-III-R patients with schizophrenia or schizoaffective disorders (40 TRS, 19 controls) were evaluated at five time points within six weeks of interval. The SADS-L was used for interviewing and the BPRS-A and the PANSS for psychopathological assessment. Neuroleptic resistance was defined according to KANE's criteria.

TRS was associated with an earlier age of onset, greater number of hospitalizations, high levels of the totals scores of the BPRS and the PANSS at baseline, and a reduction of 20% of BPRS and 10% of PANSS after treatment with clozapine.

The present study suggests that male patients with an earlier age of onset and who have high number of previous hospitalizations and high levels of psychopathology at baseline are probable TRS.

NR182 Monday, May 15, 3:00 p.m.–5:00 p.m.

Topographic Analysis of the Regional Brain Atrophy in Alzheimer Patients Using an Area-Based Radial Transformation Study

Ju-Han Kim, *Harvard Medical School, 21 Autumn Street, 4th Floor, Boston, MA 02215*; Jung-Hie Lee, M.D., Jong-Inn Woo, M.D.

Summary:

Objective: To determine the quantitative topographic distribution of brain atrophy in Alzheimer patients.

Method: We investigated 26 Alzheimer patients (age, 72.2 ± 7.0) according to NINCDS-ADRDA criteria and 22 normal control subjects (age, 71.5 ± 5.4). Using a polar coordinate system with its origin at the center of the lateral symmetry line, we performed an area-based radial transformation of each axial brain MR image into a unit circle so as for each pixel in the circle to represent the same tissue volume of the original image. This allowed topographic analysis of brain atrophy patterns.

Result: Topographic analysis with direct comparison and digital subtraction techniques revealed an uneven topographic distribution with temporo-parietal accentuation in Alzheimer patients, which is consistent with the topographic patterns reported by previous PET and postmortem histopathological studies. Contrary to the symmetrical lateral ventricular shapes in control subjects, the body and occipital horn of left lateral ventricle dilated more rostrally and the occipital horn of right lateral ventricle more caudally in Alzheimer patients. Lateral symmetry test both by paired t-test ($p < .05$) and by left-to-right digital subtraction analysis demonstrated lateral asymmetry in ventricular dilatation of Alzheimer patients. Discriminant analysis with the topographic profiles correctly separated Alzheimer patients from the control subjects with improved sensitivity (76.9%) and specificity (86.4%).

Conclusion: The uneven topographic distribution and the asymmetrical lateral ventricular dilatation provided the possible diagnostic importance. Providing detailed topographic profile in addition to the volumetric indices, area-based radial transformation analysis may be useful as a complementary morphometric method to the traditional volumetry and region of interest studies.

NR183 Monday, May 15, 3:00 p.m.–5:00 p.m.

99 Tc-ECD Brain SPECT in Alzheimer's Disease: Mexican Experience

Jose A. Santos, *Department of Psychiatry, Instituto Mexican, Averida Mexico Xochimilco, Mexico D.F. 14370, Mexico*; Juan C. Garcia, M.D., Oscar Ugalde, M.D., Gabriela Galindo, David E. Saucedo, M.D.

Summary:

Introduction: Single photon emission computed tomography (SPECT) measures regional cerebral blood flow (rCBF). We aim demonstrate correlation between Alzheimer disease (AD) symptoms and low rCBF.

Study design: Descriptive-longitudinal at the "Instituto Mexicano de Psiquiatria".

Patients:—55 patients with probable AD diagnosis were included, AD diagnostic criteria from NINCS-ADRDA and DSM-IV. Memory loss, depression, praxis, gnosias, and language disorders featured. Magnetic resonance image (MRI) and SPECT aimed tracing regions of interest: bilateral temporal, frontal, and parietal lobes with low rCBF.

Method: Non-parametric analysis was done between clinical symptoms and low rCBF.

Results: We found memory loss 89%, gnosia and praxis disorders 56%, language disorders 33%. Low rCBF was found on the following lobes: left temporal 96%, right temporal 94%, left frontal 69%, right frontal 52%, left parietal 47%, right parietal 29%, left and right (49% and 32%) frontoparietal association areas. Significative correlation exists between praxis disorders-left parietal lobe low rCBF ($p = 0.011$); behavioral disorders-left temporal lobe rCBF ($p = 0.033$); language disorders-left temporal lobe low rCBF.

Conclusions: Relation between low rCBF and AD symptoms are shown through SPECT. Thus, it may be useful to establish diagnosis and prognosis.

NR184 Monday, May 15, 3:00 p.m.–5:00 p.m.

Decreased Repetitive Behaviors in Response to Oxytocin Challenge in Adult Autistic Disorders

Sherie L. Novotny, M.D., *Department of Psychiatry, Mt Sinai School Medical School, 1 Gustave Levy Place Box 1230, New York, NY 10029*; Eric Hollander, M.D., Andrea Allen, Ph.D., Bonnie A. Aronowitz, Ph.D., Concetta DeCaria, Ph.D., Charles Cartwright, M.D., Rona Yaffe

Summary:

Considerable evidence suggests that abnormalities exist in the peptide systems, particularly the oxytocin system, in patients with autism and Asperger's disorder. To assess the effect of oxytocin on autistic and obsessive-compulsive behavior, synthetic oxytocin (pitocin) infusion was studied in adult autistic patients and matched normal controls.

Methods: Fifteen adult patients with autism or Asperger's disorder (14 male, one female, mean age = 32.9 yrs, range = 19.4–55.6) were compared with seven healthy controls (six male, one female, mean age = 32.3 yrs, range = 18.5–43.3). All subjects were randomized in a double-blind manner to single-dose oxytocin (10ug/ml in 1.0L normal saline infused over two hours with q15 minute rate increases from 10 ml/hour until maximum dose of 700ml/hour) and placebo (normal saline infusion) comparison challenges, separated by one week. Behavioral measures (Autism Behavior Checklist (ABC) and Clinical Challenge Obsessive Compulsive Rating Scale (CCOCRS)) were measured at baseline and throughout the challenges. Student's paired t-test was used to analyze both the ABC data (following a square root transformation because the data was not normally distributed) and the CCOCRS (with no transformation). The 240 min time point was used due to the time for maximum effect of oxytocin in addition to the initial slow rate of infusion.

Results: Patients with autism or Asperger's disorder showed fewer repetitive behaviors as measured by the ABC following pitocin infusion (mean 1.21 ± 1.58) vs. placebo infusion, (mean 2.00 ± 1.81) ($t = -2.280$, $df = 13$, $p = 0.04$). As expected, the controls showed no significant differences in behavioral response to oxytocin vs. placebo challenges ($t = 1.24$, $df = 6$, $p = 0.261$). At time point 240 following oxytocin infusion, patients showed a nonsignificant trend toward less obsessive-compulsive behaviors (mean = 0.200 ± 0.414), as measured by the CCOCRS, compared with the same time point following placebo (mean = 0.643 ± 1:151) ($t = 1.883$, $df = 13$, $p = 0.082$).

Conclusions: Repetitive behavior in autism may be related to abnormalities in the oxytocin system, and may be partially ameliorated by synthetic oxytocin infusion.

NR185 Monday, May 15, 3:00 p.m.–5:00 p.m.

Is St. John's Wort a Mood Stabilizer in Bipolar Children and Adolescents?

Frederic J. Kochman, M.D., *Child Psychiatry, EPS Lille Saint-Andre', 304 Avenue Motte, Roubaix, NO 59100, France*; Ginette Hamm, M.D., Daniel Bavart, M.D.

Summary:

Quite surprisingly, despite its safety and tolerability, we present herein the first study focusing on the efficacy of hypericum extracts in children and adolescents. It has been demonstrated that the attenuation of protein kinase C (PKC) activity may play a major role in the therapeutic effects of mood stabilizers. It has also been found that hypericum specifically inhibits PKC.

Objectives: To evaluate the potential mood stabilizing properties and safety of hypericum in bipolar children and adolescents.

Methods: Eleven children and adolescents (aged 9–17) meeting all the DSM-IV criteria for bipolar disorder according to Kiddie-SADS semi-structured interview were included. In a 12-month

prospective open-label study, we compared for each patients a six-month period without any treatment and a following six-month period with hypericum (555 mg daily with 5% hyperforin), using the Kiddie Life Chart Method (NIMH-K-LCM), CGI, CGAS, Child Depression Inventory (CDI), and Young Mania Rating Scale (YMRS).

Results: The number and severity of mood disorders were strikingly lower in all patients but one, after the treatment, with an excellent tolerability profile. Statistically significant improvements were found, especially in the CGI ($p < 0.001$) and CGAS ($p < 0.001$).

Conclusion: We bring herein the first evidence for the potential mood stabilizing properties of St John's Wort in bipolar patients, which should be considered more as a mood stabilizer than an antidepressant.

NR186 Monday, May 15, 3:00 p.m.–5:00 p.m.

Trauma, PTSD and Personality in Adolescents

Siham Muntasser, M.D., *Department of Psychiatry, Tulane University, 3123 Camp Street, New Orleans, LA 70115*; James W. Lowe, M.D., Jamet Rice, Ph.D., Lee Matthews, Ph.D.

Summary:

Objectives: To assess the relationship between trauma and abuse with PTSD and personality features in a group of adolescents hospitalized in an acute psychiatric unit.

Method: Participants were 252 adolescents, 132 males and 120 females, with an age range between 12–18, admitted to an acute psychiatric unit. Upon admission, each patient was subjected to a full clinical evaluation, and a series of psychopathology measures, such as RCMAS for anxiety, BDI for depression, BAI for anxiety, TSCC for PTSD, MACI for personality features.

Results: Analysis of variance (ANOVA) indicated a significant association between anxiety and depression with PTSD. PTSD was also strongly associated with an elevation in the borderline scale of the MACI. Our data revealed the presence of a subset of patients with a significant elevation in the PTSD scales, with high levels of anxiety and depression, but without any obvious history of trauma. This subset showed the same elevation in the borderline scale of the MACI.

Discussion: Considerable debate exists in the literature regarding the relationship between child abuse with PTSD and personality features. Our data indicate the presence of a subset of adolescents who present with a clinical picture that is very similar to PTSD but without any obvious history of trauma. Our data suggest an association between trauma and borderline personality features.

NR187 Monday, May 15, 3:00 p.m.–5:00 p.m.

A Systematic Open-Label Trial of Mirtazapine in Autism and Related Pervasive Developmental Disorders

David J. Posey, M.D., *Department of Psychiatry, Indiana University, 702 Barnhill Drive, Room 3701, Indianapolis, IN 46202-5200*; Krista D. Guenin, B.A., Arlene Kohburn, B.A., Naomi B. Swiezy, Ph.D., Christopher J. McDougle, M.D.

Summary:

Objective: Few medications have been shown to be efficacious and safe in the treatment of associated symptoms of autism. Following consistent demonstrations of abnormalities in serotonin, several medications affecting this system have been studied. The objective of this study was to conduct a systematic, open-label examination of the efficacy and tolerability of mirtazapine, an antidepressant with both serotonergic and noradrenergic properties, in the treatment of associated symptoms of autism and other pervasive developmental disorders (PDDs).

Method: Twenty-six subjects (five females, 21 males), (ages 4 to 23 years) with PDDs (20 with autistic disorder, one with Asperger's disorder, one with Rett's disorder, and 4 with PDD not otherwise specified) were treated with open-label mirtazapine (dose range, 7.5 mg to 45 mg daily). Nineteen had mental retardation; 15 were taking concomitant medications. At endpoint, subjects' primary caregivers were interviewed using the Clinical Global Impressions (CGI) scale, the Aberrant Behavior Checklist, and a side-effect checklist.

Results: Twenty-three of 26 subjects completed at least four weeks of treatment. Seven of 26 patients (26.9%) were judged responders ("much improved" or "very much improved" on the CGI) based on target symptoms of aggression, self-injury, anxiety, depression, agitation, and sleep. Adverse effects were minimal and included sedation, weight gain, and irritability.

Conclusions: Mirtazapine was well tolerated, but showed only limited efficacy for treating the associated symptoms of autistic disorder and other PDDs.

NR188 Monday, May 15, 3:00 p.m.–5:00 p.m.

A Psychoeducational Group for Bipolar Adolescents

Kiki D. Chang, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305*; Joyce Dorado, Ph.D., Jacqueline Martin, Ph.D.

Summary:

Background: Psychoeducational therapy has been proposed to be helpful for bipolar adults in maintaining lithium compliance, preventing manic relapse, and improving psychosocial outcome (Perry et al., 1999). Psychoeducational group therapy has also been used successfully with families of affectively ill children (Brent et al., 1993), but has not been studied when applied to bipolar children themselves. We used various rating scales to study the efficacy of a psychoeducational/support group for bipolar adolescents.

Methods: Eight adolescents 15–17 years old with Bipolar I or II disorder participated in a 10-week group, meeting once/week for one hour. Mean age was 15.8 years, and there were three boys and five girls. The group consisted of psychoeducational sessions alternating with supportive sessions. Topics covered included an overview of BD (epidemiology, phenomenology, etiology), medications (types, purposes, side effects), therapies, substance abuse, and peer relations. Pre- and post-group rating were done with the Clinical and Functional Assessment Scale (CAFAS), Childhood Depression Inventory (CDI), Child and Adolescent Mood State Scale (CAMSS), and a Bipolar Informational Quiz (BIQ). Parents completed pre-group the Child Behavior Checklist (CBCL), and Parental Stress Inventory (PSI).

Results: Group participants showed a high level of pre-group dysfunction, with a mean CBCL score of 76.3 +/– 8.9 (>67 is clinically significant), and a PSI of 97.2 +/– 2.5 (maximum is 100). There were no significant differences between pre- and post-group scores for the CDI, CAMSS, or BIQ. However, participants showed significant improvement by the CAFAS, with a mean pre-group score of 110.0 +/– 12.9, and a post-group score of 48.6 +/– 24.1 (lower numbers indicate better functioning, $p = .02$). Participants showed particular improvement in subscales of School/Work ($p = .01$), Home ($p = .02$), Moods ($p = .02$), Substance Use ($p < .05$), and Thinking ($p < .05$).

Conclusions: Adolescents with bipolar disorder may benefit from psychoeducational/support groups. Group participants did not demonstrate an overall increase in BD-related knowledge and reported finding the supportive element of the group most important to them. Improvements in mood symptoms may not be detected by self-report scales. However, improvements in overall

psychosocial functioning and mood may be detected by clinician rated parental and participant report. Further studies are necessary using larger numbers of participants and waiting list control groups.

NR189 Monday, May 15, 3:00 p.m.–5:00 p.m.

Autosomal Dominant Macrocephaly and Autism

Syed S. A. Naqvi, M.D., *Department of Psychiatry, Cedars-Sinai Hospital, 5209 Thalians, 8730 Alden Drive, Los Angeles, CA 90048*; John M. Graham, Jr., M.D.

Summary:

Cole and Hughes (1991) reported a syndrome consisting of progressive postnatal macrocephaly, marked obesity, distinctive facial features, and mental retardation with family history for macrocephaly. Subsequently, Stevenson et al (1997) emphasized a link between progressive postnatal macrocephaly, and autism, suggesting this might comprise a recognizable autism syndrome. We report a child with autosomal dominant macrocephaly and autism, which may represent a unique variant of this syndrome. The patient was delivered by cesarean section with normal Apgar scores and normal head size. Lack of speech at 22 months, with perseverative behavior, stereotypic movements, and lack of social communication established the diagnosis of autism and mental retardation. At that age, his head circumference was +2 standard deviation (S.D.) above the mean for age (upper limit of normal). A brain MRI revealed mild prominence of ventricles. By 4 1/2 years, head circumference was +3 S.D. and repeat MRI at eight years revealed a large brain with enlarged posterior corpus callosum and hypoplastic superior cerebellar vermis. At 14 years, his head circumference is +4.2 S.D. Mother's head circumference was normal, but father's is +2.75 S.D. (abnormal). We believe this represents a new recognizable, progressive paternal autosomal dominant macrocephaly, genetic syndrome within the autistic spectrum.

NR190 Monday, May 15, 3:00 p.m.–5:00 p.m.

Gender Differences in the Relevance and Effect of Depression Post-Unstable Ischemic Syndrome

Syed S. A. Naqvi, M.D., *Department of Psychiatry, Cedars-Sinai Hospital, 5209 Thalians, 8730 Alden Drive, Los Angeles, CA 90048*; Peter J. Panzarino, Jr., M.D., Yulius Mustafa, M.D., Haidar Sadeghi-Razlighi, M.D., Russell M. Poland, M.D., Tasneem Z. Naqvi, M.D.

Summary:

Background: We examined the influence of gender on the rate of recurrent acute ischemic cardiac events following unstable angina (UA) or acute myocardial infarction (MI).

Methods: Patients were mailed a Zung Self-Assessment Questionnaire two weeks post discharge for UA or MI and followed for three to 14 months. Depressed patients were offered treatment in a four-month randomized study involving psychotherapy with or without Paxil.

Results: A total of 363 pts were surveyed (257 males, 68 ± 13 years, 106 females (29%), age 68 ± 12 years. Of the 222 responders, there were 55 women (25%), and 167 males (75%). Twenty-eight women were not depressed (SDS 40 ± 6) and 27 (49%) depressed (SDS 56 ± 7). A total of 94 males (56%) were non-depressed (SDS) and 73 depressed (SDS 58 ± 9, p = 0.4). Three women (64 ± 12) and 12 men (69.8 ± 11 years) participated in treatment. Women who were depressed and did not participate were significantly older than non-depressed women (76 ± 10 vs 69 ± 15 yr, p = 0.05), participant women (p = 0.059), non-participant depressed men (76 ± 10 vs 68 ± 13, p = 0.007) and participant depressed men (p = 0.04). Over an 8 ± 4 month follow up, there were four admissions in non-depressed women due to a cardiac event. Eight out of 24 depressed non-participant women were admitted with a cardiac event. Cardiac causes were the leading cause of re-admissions in non-depressed and non participant depressed men (18 and 18, respectively).

Conclusion: (1) Depression afflicts older women compared with men post UIS and spares younger women. Depression in both genders increases the risk of acute cardiac events. Depressed older women are reluctant to seek treatment. Psychosocial issues regarding reluctance to treatment need to be explored in both genders, particularly in older depressed women.

NR191 Monday, May 15, 3:00 p.m.–5:00 p.m.

Recognition of Mental Disorders by Residents in a Gastroenterology Unit

Phillippe M.J. Persoons, M.D., *Department of Psychiatry, UZ Gasthuisberg, Herestraat 49, Leuven 3000, Belgium*; Benjamin Fischler, M.D., Koen Luyckx, M.A., Lukas Van Oudenhove

Summary:

Objectives: to assess if medical residents recognize Axis I disorders at the end of a gastroenterology or hepatology admission.

Methods: Axis I disorders were assessed by the PRIME-MD Patient Health Questionaire (PHQ). A standard questionnaire about psychiatric diagnostical status was completed by medical residents blinded for the PHQ. Patients were divided into three major groups: functional intestinal disorder (FID), inflammatory bowel disorder (IBD), and other organic gastroenterological or hepatological disorder (OOD). HAD was used to assess the intensity of anxiety and depression.

Results: For 150 inpatients both questionnaires were completed. Any Axis I was recognized in 27.2%, major depression in 9.1%, other depressive disorders in 13.8%, any anxiety disorder in 9.1%, possible alcohol abuse in 33.3%. Any psychiatric disorder and any mood disorder were better recognized in FID (respectively, 50.0% and 53.2%) and in women (p = 0.08). Neither degree of disability, anxiety, depression, or age seemed to influence recognition significantly.

Conclusion: The degree of recognition of Axis I disorders in hospitalized patients by medical residents is extremely low, especially in men and in organic disorders, despite the impact of mental disorders on health-related quality of life. The systematic use of the PRIME-MD PHQ could raise the recognition of psychiatric disorders on medical wards.

NR192 Monday, May 15, 3:00 p.m.–5:00 p.m.

Panic Disorder in Mitral Valve Prolapse

Chau-Shoun Lee, M.D., *Department of Psychiatry, Poh-Ai Hospital, No. 83 Nan-Chang Street, Lo-Tung Ilan 265, Taiwan*; Jung-Chen Chang, Ph.C.

Summary:

Objective: This study examined the prevalence of panic disorder (PD) and its demographic risk factors in patients with mitral valve prolapse (MVP).

Methods: Consecutive MVP patients confirmed by standard echocardiographic methods were considered for this study. A total of 36 MVP patients were interviewed to make clinical diagnoses according to DSM-IV criteria. Their mean age was 31.7 ± 12.3, 14 (28.9%) male, 18 (50.0%) married, 16 (44.4%) single, and education years 11.9 ± 3.7.

Results: Of the 36 MVP patients, 16 (44.4%) had PD, 11 (30.6%) had psychiatric disorders other than PD, and nine (25.0%) had no psychiatric disorders. Patients without any psychiatric disorders were younger than those with PD or other disorders (ANOVA; F = 3.9, df = 2, p = 0.03). Female patients were more likely to have

PD or other psychiatric disorders ($\chi^2 = 8.1$, df = 2, p = 0.02). Being married was significantly associated with PD or other psychiatric disorders ($\chi^2 = 12.3$, df = 2, p = 0.002).

Conclusions: The high prevalence of PD in our hospital-based sample highlights the importance of psychiatric consultation for those MVP patients. Efforts may focus on high risk patients, such as those who are elderly female, or married.

NR193 Monday, May 15, 3:00 p.m.–5:00 p.m.

Quetiapine Fumarate Treatment of Delirium

Thomas L. Schwartz, M.D., *Department of Psychiatry, SUNY Health Sciences Center, 750 E Adams Street, Syracuse, NY 13210*; Prakash S. Masand, M.D.

Summary:

Introduction: Delirium, an organic psychiatric syndrome, occurs in 10% of hospitalized patients and is characterized by fluctuating consciousness and impaired cognition, perception, and behavior.

Methods: Charts were retrospectively reviewed of 11 consecutive patients with delirium who were given quetiapine fumarate, a novel antipsychotic, as first-line treatment for their symptoms. A control group of 11 patients treated with haloperidol, the standard treatment for delirium, during the same time period was also evaluated. The Delirium Rating Scale was used to evaluate the efficacy of each treatment.

Results: Ten of 11 patients in both groups had ≥50% improvement in DRS scores. There was no difference in onset of symptom resolution, duration of treatment, and overall clinical improvement. Quetiapine fumarate was better tolerated in these medically ill patients.

Conclusion: Ours is the first report of quetiapine fumarate in treating delirium. Quetiapine fumarate appears to be an efficacious and well tolerated treatment for delirium. Further prospective studies are warranted.

NR194 Monday, May 15, 3:00 p.m.–5:00 p.m.

Psychological Structure of Patients with Diabetic Polyneuropathy

Vladimir M. Diligenski, M.D., *Department of Psychiatry, Dragisa Misovic, Milana Tepica 1, Beograd 11000, Yugoslavia*; Natasa M. Sikanic, M.D., Svetlana F. Jelic, Zorica M. Caparevic, M.D., Gradimir V. Bojkovic, Nada P. Kostic, M.D.

Summary:

We investigated 44 patients who were admitted in the Department of internal Medicine by an internist, neurologist, or psychiatrist. The diagnosis of the polyneuropathy was given based on the neurologist's findings. These patients were divided into the following two groups, both with 22 patients: experimental group with polyneuropathy and control group without polyneuropathy.

The psychological structure of these patients was followed continually by the semistructured interview with 32 items in connection with the origin, course, treatment, and psychological acceptance of diabetes. The assessment was also made with Zung Depression Scale, MMPI, and Analog Scale for Measuring Pain.

It was found that degree of the neurotic expression on MMPI, Zung scale, and interview were in direct proportion with the degree of the pain experience in the experimental and control group. Pain experience was found in 32% of the control group without polyneuropathy. Specifically, high scores were found on the depression, paranoid, and social introversion scales.

The objective assessment of polyneuropathy, which was checked by the EMG methods, is not in the same ratio with the degree of the neurotic scores and pain experience that was in total contrast to our expectations.

NR195 Monday, May 15, 3:00 p.m.–5:00 p.m.

A Pilot Study of Psychiatric Disorders in Adults with Irritable Bowel Syndrome

Catharine J. Munn, M.D., *Department of Psychiatry, McMaster Medical Center, 1200 Main Street, West, Hamilton, ON L8N 3Z5, Canada*; Michael A. Van Ameringen, M.D., Catherine L. Mancini, M.D., Peter Farvolden, Ph.D., Gervais Tougas, M.D.

Summary:

Psychiatric disorders have been described as being extremely common amongst patients with irritable bowel syndrome (IBS) in studies in the United States, particularly those patients presenting to hospital-based gastroenterology clinics. The present pilot study aims to measure the incidence of and describe the psychiatric disorders present in patients with IBS in a Canadian, hospital-based gastroenterology clinic. Patients completed self-report measures evaluating physical symptoms (Rome and Manning criteria, McGill Pain Questionnaire), psychiatric symptoms (Mini International Neuropsychiatric Inventory, Symptom Checklist 60 — Revised, Eating Attitudes Test, Anxiety Sensitivity Index - Revised), quality of life (The IBS Quality of Life), presence of abuse history (Ontario Child Health Study), as well as the patient's understanding of their bowel and psychiatric symptoms and their coping methods. Preliminary results from 30 patients indicate that psychiatric disorders, though common, are not as common in our sample as has been described previously. The results of our study will be reported and compared with the results of previous studies in which similar measures have been used. Implications for the assessment and management of IBS and further research will be discussed.

NR196 Monday, May 15, 3:00 p.m.–5:00 p.m.

The Quality of Life in Cancer Patients in Korea

Kwangil Kim, M.D., *Department of Psychiatry, Yonsei University, Shinchondong 134 CPO box 8044, Seoul 120-752, Korea*; Sung-Kil Min, M.D., Youngchul Jung, M.D.

Summary:

The quality of life in cancer patients has influence on the course and prognosis of the disease. Evaluating how cancer patients perceive their quality of life and comparing its characteristics, will make better interventions possible for the disease.

In our study 58 cancer patients, 202 patients with different diseases, and 228 controls, assessed by WHOQOL, Korea version, undewent the evaluation of the quality of life.

The results of this study were that the score of the cancer patient group was lowest, followed by the patients with different diseases, and the controls. These differences between groups were influenced by the physical domain, the psychological domain, the independent domain, the environmental domain, the spiritual domain, while the social domain showed no difference. Among these domains, the physical domain and the independent domain showed the lowest scores in cancer patients and the patients with other diseases. The statistical results through path analysis showed that the general quality of life and the psychological domain were more influenced by other domains, suggesting that the psychological quality of life is the most important in Korea.

NR197 Monday, May 15, 3:00 p.m.–5:00 p.m.

Healer Choice in a Multi-Ethnic Adolescent Population

Cathy K. Bell, M.D., *Department of Psychiatry, University of Hawaii, 1356 Lusitana St., 4th floor, Honolulu, HI 96813*; Deborah A. Goebert, M.S., Naleen N. Andrade, M.D., Ronald

C. Johnson, Ph.D., John F. McDermott, Jr., M.D., Earl S. Hishinuma, Ph.D., Barry S. Carlton, M.D.

Summary:

Objective: To identify demographic and development factors in a large community-based multiethnic adolescent population that predict healer choice (nonmedical instead of medical).

Method: The sample consisted of 4,136 grade 9-12 high school students (Native Hawaiian, Caucasian, Filipino, Japanese, and mixed). Variables included demographic physical/mental health, academic, family relationships, healer preference/use, and ethnic and cultural identity. Correlation and multiple logistic analyses were performed for the Hawaiian, non-Hawaiian, and combined groups.

Results: While most preferred physicians for their health care, 24.7% preferred alternative healers, and 9.9% were using them. As expected, more Hawaiians preferred Native-Hawaiian healers ($P < 0.0001$). For the non-Hawaiian group, mental health needs ($P < 0.01$) predicted alternative healer preference. For both groups, valuing the Native-Hawaiian culture (cultural identity) was the strongest predictor of alternative healer preference ($P < 0.0001$), independent of SES.

Conclusion: In this first large-scale, NIMH-funded, community-based study of a multiethnic adolescent population, *cultural identity,* i.e., culturally determined values, overrides *ethnic* identity in determining choice of alternative healers. Implications are developmental, i.e., crossing traditional boundaries during adolescence, and social, i.e., mental health over physical health influencing alternative healer choice.

NR198 Monday, May 15, 3:00 p.m.–5:00 p.m.

The Relationship Between Irritable Bowel Syndrome and Panic Disorder in Mumbai, India

Titiksha V. Kubal, M.D., *Department of Psychiatry, Suny Upstate Medical Center, 750 East Adams Street, Syracuse, NY 13210*; Charles Pinto, M.D., Sumeet Sharma, M.D., Subhdeep Virk, M.D., Sarah Vandervoort, Sanjay Gupta, M.D., Prakash S. Masand, M.D.

Summary:

Irritable bowel syndrome (IBS) has been reported in 10%–20% of adults. Amongst patients seeking medical attention for IBS 70%–90% may have psychiatric comorbidity, most commonly major depression. In contrast, few studies have looked at the prevalence of IBS in psychiatric patients. Using a semistructured clinical interview to study the prevalence of IBS among panic disorder patients in Mumbai, India, we compared 52 patients seeking treatment for panic disorder in a psychiatric outpatient setting to a control group of 40 patients who were seeking treatment for medical illnesses in a medicine inpatient unit of Nair Hospital (university hospital affiliated to T.N. Medical College) Mumbai, India. The control group did not have any Axis I disorder. IBS was diagnosed according to the criteria of Drossman et al. Fifteen patients (28.85%) with panic disorder met the criteria for IBS, in contrast to eight patients (20.0%) in the control group ($P = 0.4663$). Patients with panic disorder and IBS were more likely to report symptoms of backpain, weakness, and heartburn as well as a history of bowel disease as compared to patients with panic disorder but without IBS. IBS is fairly common in patients seeking treatment for panic disorder in Mumbai, India. In a similar study, the prevalence of IBS in U.S. patients with panic disorder was 46.3% versus 2.5% patients in the control group ($p < 0.000005$). The differences in the control groups will be addressed. Prospective studies should address the question whether treatment of panic disorder leads to an improvement or resolution of the symptoms of IBS.

NR199 Monday, May 15, 3:00 p.m.–5:00 p.m.

Outcome of Recognizing Major Depression Among Chinese Patients in Primary Care

Albert Yeung, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Saniford Street, Suite 401, Boston, MA 02114*; Shauna Howarth, B.A., Andrew A. Nierenberg, M.D., Raymond Chan, B.S., Jonathan E. Alpert, M.D., David Mishoulon, M.D., Maurizio Fava, M.D.

Summary:

Objective: To investigate the outcome of recognizing depressed Asian Americans in primary care.

Method: Chinese patients in a primary care clinic were screened for depression using the Beck Depression Inventory (BDI) (Chinese Version) (cut-off point ≥16). Diagnosis was confirmed using SCID performed by a psychiatrist. Primary care physicians (PCPs) of patients diagnosed with depression received a letter notifying them of their patients' diagnosis. Recognized depressed patients were interviewed and their medical records reviewed three months later for outcome.

Results: A total of 680 patients were approached, 410 (60%) filled out the BDI; among them 69 (17%) scored ≥ 16. Fifty patients received the SCID interview, and 40 depressed Asian Americans were identified (58% female, 42% male, mean age 48). None of the depressed patients were receiving treatment for depression. After receiving the letter, PCPs discussed treatment of depression with 19 (48%) patients; among them 13 (33%) declined referral to mental health service, four (10%) accepted referred but only three showed up at a mental health service, and two (5%) were started on an antidepressant by PCPs. PCPs did not intervene on the remaining 21 (53%) patients.

Conclusion: Recognizing depressed Asian Americans in primary care is *not* enough to facilitate patient referral to a mental health service or to improve treatment of depression. Possible solutions will be discussed.

NR200 Monday, May 15, 3:00 p.m.–5:00 p.m.

The Association Between Schizophrenia and Cancer: A Population-Based Study

Mary E. Cohen, M.D., *Department of Psychiatry, University of Virginia, Box 986, Charlottesville, VA 22908*; Bruce Dembling, John B. Schorling, M.D.

Summary:

Background: There has been speculation that persons with schizophrenia may have a reduced incidence of cancer. Few well-designed studies have been done to evaluate this possibility. We used a national database to determine the lifetime prevalence of cancer in persons with schizophrenia compared with the general population.

Methods: Data from the 1986 National Mortality Follow-back Study (NMFS) were analyzed. The NMFS sampled 1% of all deaths in the U.S. that year. In addition to death certificates, information was gathered from hospital records and interviews with other informants. We compared the rates of having a diagnosis of cancer for persons with schizophrenia ($N = 130$) with those for other decedents ($N = 18,603$) using logistic regression and standardizing cases for age at death.

Results: The prevalence of cancer in persons with schizophrenia was 19% vs. 28% for other decedents (odds ration 0.62; 95% CI 0.40–0.96). After controlling for age, race, gender, marital status, education, net worth, smoking, and hospitalization in the year prior to death, the odds ratio for the diagnosis of cancer in persons with schizophrenia was 0.58 (95% CI 0.37–0.90).

Conclusions: In this population-based study, we demonstrated a statistically significantly reduced prevalence of cancer among individuals with a diagnosis of schizophrenia.

NR201 Monday, May 15, 3:00 p.m.–5:00 p.m.

Characteristics of Depressive Symptoms in Koreans

Jin-Yeong Kim, M.D., *Department of Psychiatry, Seoul National University Hosp, 28 Yeon-Gun dong, Jong Ro gu, Seoul, Korea*; Sung-Mi Choi, M.A., Guk-Hee Seo, M.D., Seong-Jin Cho, M.D., Maeng-Je Cho, M.D.

Summary:

Objective: In order to explore culturally different expressions of depressive symptoms, factor structure of depressive symptoms in Koreans was examined using data taken through the Korean version of the Center for Epidemiologic Studies Depression Scales (CES-D).

Method: Door-to-door visiting survey was conducted by trained interviewers for the nationwide probability sample of 5,805 subjects, between ages 15 and 69, among whom 4,589 completed the CES-D scale. Using data from this sample, we analyzed factor structure of depressive symptoms according to the gender, and the four age groups with different socio-cultural backgrounds.

Results: Different factor structures were found as compared with other reports from Western countries. Somatic symptoms and affective symptoms were combined as one factor, and emotional hardship and interpersonal factor as another separate factor. There were no differences in factor structures between men and women. In adolescents below 20 years, somatic symptoms are separated from affective symptoms and in the elderly 60 years and over, interpersonal factor is separated from emotional hardship.

Conclusions: We found unique factor structures in Korean people. In addition, adolescents, adults, and elderly showed culturally different modes of expression of depressive symptoms according to generation, respectively. This suggested that different approaches for the diagnosis and treatments of depressive symptoms were needed in Koreans according to age groups.

NR202 Monday, May 15, 3:00 p.m.–5:00 p.m.

Effects of Perceived Health on Psychiatric Outcome

Richard Thompson, Ph.D., *Department of Psychiatry, University of Pennsylvania, 11 Gates/HUP 3400 Spruce, Philadelphia, PA 19104*; Tina L. Harralson, Ph.D., Alan C. Regenberg, B.A., Tiffany Purnell, B.A., Ira R. Katz, M.D., James C. Coyne, Ph.D., Trevor Hadley, Ph.D.

Summary:

Objective: The purpose of this study is to examine the relationship between health perception and psychiatric outcome in a sample of persons enrolled in treatment in a behavior managed care setting.

Method: Participants included 125 persons (67% women, 12% minority) who completed a telephone battery prior to their first appointment with a mental health clinician. Follow-up telephone interviews were conducted at 4, 8, and 12 weeks. The battery included Center for Epidemiologic Studies Depression scale (CES-D) and the Outcome Questionnaire (OQ), a general self-report measure of psychiatric well-being, as well as a measure of perceived health (PH). Mean age for this sample was 52.8 years (range 22–88).

Results: Preliminary analyses revealed a significant relationship between PH and concurrent CES-D ($r = .27$, $p < .01$), and between PH and both concurrent OQ ($r = .33$, $p < .01$) and OQ at 4 weeks ($r = .45$, $p < .01$), 8 weeks ($r = .45$, $p < .01$), and 12 weeks ($r = .52$, $p = .03$) follow-up. These results remained significant when controlling for the initial OQ score and were not mediated by psychological distress or negative affect.

Conclusion: Perceived health may be an important independent predictor of success in psychiatric treatment. Implications for clinical intervention will be discussed and a more complete data set will be reported.

NR203 Monday, May 15, 3:00 p.m.–5:00 p.m.

Odontological Problems in Patients Exposed to Lithium Therapy

Mariana F. Tatsch, M.D., *Department of Psychiatry, IPQ-HC= USP, R Ovidio Pires S/N, Sao Paulo, SP 05403-010, Brazil*; Renata Kkrelling, M.D., Valentim Gentil, M.D.

Summary:

Case notes from 209 private patients with mood disorders (bipolar, scizoaffective, or depressive) consecutively seem in a private practice between March 1977 and May 1999 and exposed to lithium, were screened for information on dental and peridontal problems. These were mentioned in 130 (62.2%) cases, and were grouped according to onset (pre or post lithium), severity, and demography. No record or absence of odontological problems accounted for 111 (53.1%) of the sample. In 63 (30.1%) patients, dental or periodontal problems preceeded exposure to lithium (in 18 [8.6%] the outcome was very severe, often leading to an edentulous state). In 43 (20.6%) cases the problems had onset after lithium exposure for variable amounts of time (in 11 [5.3%], very severe).

The breakdown by sex and age of first exposure to lithium will be presented. These results support previous observations of significant odontological problems in patients exposed to lithium treatment for mood disorders, but the specific role of lithium as opposed to other drugs or metabolic factors remains unclear.

NR204 Monday, May 15, 3:00 p.m.–5:00 p.m.

The Role of Preinjury IQ in the Assessment of Intelligence Impairment Due to Traumatic Head Injury

Beilin Gao, M.D., *Shenzhen Kangnin Hospital, Guizhu Road #1080, Guang Zhou Shenzhe 518020, China*; Siqing Li, M.D.

Summary:

Objective: To explore the value of preinjury intelligence quotient (pre-IQ) in the assessment of intelligence impairment due to head injury.

Methods: With the statistical software of the Wechsler Adult Intelligence Scale Revised in China (WAIS-RC), the data of the current intelligence quotient (CIQ) and the pre-IQ from 17 subjects with the head trauma were analyzed. Comparing the analyzing results with the technological examination, the clinical diagnoses in these 17 subjects were retrospectively reevaluated with and without using the index of pre-IQ.

Results: Three of 17 subjects were not clinically evaluated as "the intelligence deficit" because their CIQs were more than a score of 70 and didn't meet the criteria of intelligence deficit of WAIS. Using the index of pre-injury intelligence, the CIQs of these three subjects were significantly lower than the pre-IQ, which was supported by the abnormal signs on the technological examination (CT or MRI). It is suggested that "the intelligence deficit due to the brain injury" might be made in these three subjects.

Conclusion: The pre-IQ is a relatively objective index assessing the intelligence damage of the individuals with head injury. It is reliable method to combine CIQ with pre-IQ in the assessment of intelligence impairment.

NR205 Monday, May 15, 3:00 p.m.–5:00 p.m.

Gender Role in Fitness-to-Stand-Trial Exams

Gary R. Collins, M.D., *Forensic Psychology Department, New York University, 305 West 13th Street, #2G, New York, NY 10014*; Stephen B. Billick, M.D.

Summary:

Method: 50 cases, randomly selected from the Manhattan Criminal Court Clinic files, were examined for examiner's gender, defendant's gender, and outcome of the examination of fitness to proceed with the trial. Each defendant was examined by two forensic examiners, yielding a total of 100 examinations.

Results: There were six female defendants and 44 male defendants. There were 75 examinations done by male examiners and 25 exams done by female examiners. Of 100 examinations done, male examiners found male defendants fit/not fit at about the same rate as female examiners. However, male examiners found female defendants fit at a much greater rate than female examiners. Male/male gender examining teams found male and female defendants fit at a higher rate than male/female gender examining teams did.

Conclusion: Female forensic examiners tended to be more likely to find defendants, both male and female, not fit to stand trial than were their male forensic examiner counterparts.

NR206 Monday, May 15, 3:00 p.m.–5:00 p.m.

An Association Between Bipolar Disorder and Synaptobrevin-Like 1 Gene (SYBL1)

Takuya Saito, M.D., *Department of Psychiatry, Albert Einstein College of Medicine, 1300 Morris Park Avenue, room F103, Bronx, NY 10461*; Sam Parsia, M.D., Demitri F. Papolos, M.D., Herbert M. Lachman, M.D.

Summary:

There is some evidence for a bipolar disorder (BPD) susceptibility gene on Xq28 in a subset of patients with apparent X-linked inheritance. We have analyzed one gene in this region, *SYBL1*, which encodes a synaptobrevin-like gene. Synaptobrevins are members of the family of proteins involved in synaptic vesicle exocytosis. *SYBL1* maps to the X-Y pseudoautosomal region but behaves genetically like a typical X-linked gene, since it is not expressed on either the Y or inactive X-chromosomes. Mutation analysis of *SYBL1* resulted in the detection of a G->C transversion in the polypyrimidine tract (PPT) at the 3′ splice acceptor site preceding exon 6. Although the PPT is important for splicing, the biological effect of the G->C polymorphism is not known. We analyzed this polymorphism in 110 patients with BPD not selected for sex-linked transmission and 119 controls. No significant differences in allele frequencies were found females patients and controls. However, a trend towards significance for an increase in the "C" allele ($p = 0.06$, chi square = 3.46) was detected in males with BPD. Considering these preliminary findings in unselected bipolar male patients, the *SYBL1* PPT polymorphism should be more thoroughly investigated as a candidate gene for "X-linked" BPD.

NR207 Monday, May 15, 3:00 p.m.–5:00 p.m.

The Role of Gender in Determining Neuropsychiatric Outcome Following Mild or Moderate Head Injury

Ariel K. Dalfen, M.D., *Department of Psychiatry, Univ of Toronto-Sunny Brook, 2075 Bayview, Toronto, ON M4N 3M5, Canada*; Alison Jardine, O.T., Donna Ouchterlony, M.D., Scott R. McCullagh, M.D., Andrea Protzner, M.A., Anthony Feinstein, M.D.

Summary:

Background: The role of gender in predicting neurobehavioral outcome following traumatic brain injury (TBI) has received little attention. With respect to severe TBI, limited data suggest a better outcome in females, while the converse may apply to mild injuries.

Objective: To determine the role of gender on neuropsychiatric outcome in patient with mild to moderate TBI.

Methods: A sample of 60 patients seen at a TBI clinic with mild to moderate closed head injury, defined as Glasgow Coma Scale (GCS) ≥13 and posttraumatic amnesia (PTA) ≥one week, were assessed for symptoms of postconcussion disorder (Rivermead Scale (RS), psychological distress (28-item General Health Questionnaire (GHQ), global outcome (Glasgow Outcome Scale (GOS), and psychosocial outcome (Rivermead Follow-up Questionnaire (RFUQ). The data were compared with respect to gender differences.

Results: Thirty-five men and 25 women were seen 150 (sd = 80.7) days post injury. The mean sample age was 34 (sd = 12) years. There were no statistically significant gender differences on any demographic nor injury-related measures. Similarly, the gender neuropsychiatric profiles were similar (viz. RS: $p = .7$; GHQ: $p = .9$; GOS: $p = .9$; RFUQ: $p = .3$).

Conclusions: Our data show that there are no significant differences between men and women on an array of neuropsychiatric outcomes following mild to moderate brain injury. The significance of these findings is discussed in light of earlier limited data devoted to the subject.

NR208 Monday, May 15, 3:00 p.m.–5:00 p.m.

Attention and Eye Movement Control in OCD

Chiang-Shan R. Li, M.D., *Department of Psychiatry, Chang Gung Memorial Hospital, 5 Fu-Hsiang Street, Taoyuan 333, Taiwan*; Yong-yi Yang, M.D., Hsuen-ling Chang, M.D., Sho-fen Lin, M.S.

Summary:

Objective: Previous work revealed in patients with obsessive-compulsive disorder (OCD) abnormalities in the cortico-striatal circuitry and in executive control. The present study aimed to pursue along and examine the coordination of attention and oculomotor processes in OCD by studying the effect of spatial cueing on saccade latency.

Methods: Four medication-free patients with OCD and four matched controls participated in reaction-time experiments involving visual and cued saccades. The fixation light (FL) was straight ahead and peripheral target (T) 6 deg to the left or right of the FL in all experiments. One-third of the trials were visual and two-thirds cued saccades in which a cue preceded T by a variable onset asynchrony (0.1, 0.2, 0.4, 0.7 or 1.2 sec). In experiment 1, the peripheral cue did not predict the location of T. The cue did in 75% of the trials in experiment 2. In experiment 3, the cue was a change of the FL color; red (green) signaling T to appear at left (right) in 75% of the trials and blue not predictive. Latencies of the cued and visual saccades were compared.

Results: We reproduced the cost and benefit effects in saccade latency, depending on the cue validity and the paradigm. Interestingly, we obtained robust results that patients with OCD exhibited a different time course of inhibition of return in oculomotor programming.

Conclusion: The findings suggested that the cortico-striatal circuitry might play a role in orchestrating eye movement and attentional shifting.

NR209 Monday, May 15, 3:00 p.m.–5:00 p.m.

Facial Expression Analysis of Psychiatric Patients

Georg Fuckel, M.D., *Department of Psychiatry, LMU, Nussbaumstr 7, Munich 80336, Germany*; Annuschua Praessl, Birgit Graf, Paraskevi Mavrogiorguv, M.D., Hans F. Moeller, M.D., Ulrich Hegerl, M.D.

Summary:

Objective: Facial expression are often said to be the window of the soul. Changed facial expressions are one of the core symp-

toms of psychiatric diseases such as schizophrenia or major depression. Analyses of facial expressions by different methods found in general reduced activity in schizophrenic and depressive patients. It was, however, assumed that facial expressions of psychiatric patients are more specifically disturbed in the details of single facial movements.

Method: So-called active measurements of motor activity allow to analyze facial movements in detail. Markers, which are fixed in distinct points of the face and send ultrasonic signals in high frequency, give a direct measure of facial movements with high spatial-temporal resolution. Using such a method, schizophrenic and depressive patients watching a movie (Mr. Bean) were investigated.

Results: Compared with healthy controls, this movie caused similar emotions in both the schizophrenic and depressive patients. However, the facial movements resulting in laughing were specifically changed: the corners of the mouth reached significantly quicker their maximal position in the schizophrenic patients than in the healthy controls, while in the depressive patients this speed of the corners of the mouth was slower than in the controls.

Conclusions: It is assumed that such analyses of facial expressions could contribute to solving difficult diagnostic problems like the differentiation of beginning schizophrenia from depression.

NR210 Monday, May 15, 3:00 p.m.–5:00 p.m.

The Merger of Two Psychiatry Residency Training Programs

Anjali M. Gupta, M.D., *MHCC, VA Medical Center, 10 North Greene Street, Baltimore, MD 21201*; Lisa B. Dixon, M.D., Laura R. Gaffney, M.D., Patricia N. Nnadi, M.D.

Summary:

Objectives: This study examined the attitudes of faculty and residents at Shepard Pratt (SP) and the University of Maryland (UMD) on the effects of the merger of their residency programs.

Method: Two years post-merger, residents and full-time faculty at UMD and SP were surveyed with a questionnaire addressing education, morale, program implementation, governance, and impact on faculty. Responses (43% rate) from 36 faculty and 25 residents were received. PGY1-2's were combined program residents (CP). PGY3-4's were affiliated with their respective institutions (UMD and SP). Faculty defined their affiliation with either of the three groups.

Results: The CP group felt the merger enhanced the balance between service and education ($P < .03$), increased level of input to administration ($P < .04$), and increased enthusiasm ($P < .02$) compared with UMD. The CP group felt the merger provided a unique philosophy ($P < .04$) and an improvement in residency education ($P < .04$) compared with SP. The SP group but not the UMD group rated increased tension between CP residents and single-program residents.

Conclusion: This study suggests that residency program mergers create transition challenges that have some specificity to each institution's perceived role in the merger. These data suggest how future residency mergers, now increasingly common, should target efforts to assist with smooth transitions.

NR211 Monday, May 15, 3:00 p.m.–5:00 p.m.

Stress, Psychopathology and Cytokines in In Vitro Fertilization Patients

Florina Haimovici, M.D., *Department of Psychiatry, Harvards Shore, 63 Adeline Road, Newton, MA 02459*; Raina Fichorova, M.D., Janis Anderson, Ph.D., Wright Bates, M.D., Vincent Carey, Ph.D., Randy S. Glassman, M.D., Deborah J. Anderson, Ph.D.

Summary:

Major depressive disorder has been hypothesized to modulate several aspects of the immune response including cytokine production. Research shows that psychological stress and major depression play a role in infertility. We previously found evidence of cytokine effects on implantation. We hypothesize that expression and function of cytokines and growth factors in the human genital tract can be modulated by stress and also are altered in major depression. This pilot study was designed to assess cytokine profiles in female and male genital tract secretions, which correlate with infertility along with perceived stress and psychiatric symptoms. Infertile couples (mean age 35) who qualified for in vitro fertilization (IVF) were assessed at the time of egg retrieval for psychological variables and cytokine levels in cervicovaginal lavages (CVLs), follicular fluid (FF), semen, and peripheral blood serum. IVF outcome (fertilization and pregnancy) and concentrations of $TGF\beta_1$, IL-2, IL-1β, IL-6, IL-10, and IL-15 in biological fluids were correlated with visual analog rating scales (VAS) for stress, anxiety, and depression and numeric stress ratings for current (DSI) and long-term stress (LISRES). Interleukins were detectable in genital tract fluids and at much lower levels in serum. TGFβ was detectable at high levels in all serum samples and variable levels in all genital tract fluids. IL-2 was undetectable in any biological fluid tested, and IL-1β and IL-15 were undetectable in FF and CVLs, respectively. In only one of the 15 couples who completed this preliminary study, both partners scored high in all three VAS (scores >50 for stress, depression, and anxiety). Moreover, this was the only couple in which fertilization failed. This couple demonstrated lowest levels of IL-15 in semen, and lower levels of TGFβ in CVL and FF as compared with couples with successful fertilization/pregnancy. A large-scale study is in progress to investigate further the correlation between stress, psychopathology, and mucosal immune function in infertile patients.

NR212 Monday, May 15, 3:00 p.m.–5:00 p.m.

Quality of Life Among Schizophrenics: Is Age a Contributing Factor?

Joanne Fenton, M.D., *Department of Psychiatry, University of Maryland Medical School, 22 South Greene Street, box 351, Baltimore, MD 21201*; Lisa B. Dixon, M.D., Janine C. Delahanty, M.A.

Summary:

Objective: The purpose of this study is to assess the impact of advanced age on quality of life and symptoms among persons with schizophrenia.

Methods: The Schizophrenia Patient Outcomes Research Team (PORT) conducted a 90-minute interview of 719 persons with schizophrenia sampled from a variety of community and treatment settings. Persons who were >65 years ($N = 42$) were compared with persons who were 44–65 ($N = 261$) and 18–44 ($N = 415$) on the Lehman's Quality of Life Interview.

Results: In multiple regression models controlling for age and race, the oldest age group had significantly greater subjective satisfaction with family relations ($p < .05$), social relations ($p < .05$), daily activities ($p < .01$), and safety ($p < .001$) than the youngest group, and significantly higher quality of life with regard to daily activities ($p < .001$). The oldest age group also had significantly greater subjective satisfaction with living situation and finances (p's $< .001$) as well as objective quality of life in terms of social relations ($p < .001$) compared with both younger age groups. The older group had significantly less psychotic and depressive symptoms ($p < .001$).

Conclusions: This study suggests that among those persons with schizophrenia who survive to the age of 65, quality of life may improve and symptoms may diminish over time.

NR213 Monday, May 15, 3:00 p.m.–5:00 p.m.

On-Site Geropsychiatric Services in Senior Housing: Preliminary Findings

Nancy C. Maruyama, M.D., *Department of Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 02809-1001*; Blaine S. Greenwald, M.D., Phyllis Tobin, Grace S. Nierenberg, Donna Del Cielo, M.S.W., Barbara Vogel, M.S.W., Arlene Feuerman

Summary:

Senior housing is emerging as an alternative health/mental health delivery setting coincident with a market-driven deemphasis of hospital-based treatment. Despite the boom in senior housing, very limited data are available addressing psychiatric/psychosocial phenomena in senior housing, or the programmatic elements of on-site geropsychiatric services.

Objective: To report on the first 25 referents to a new geropsychiatry program in subsidized senior housing and naturally-occurring retirement communities (NORCs); and to describe the initial program model.

Method: Residents were referred for geropsychiatric assessment by social workers serving senior housing/NORCs in Queens, N.Y. All consecutive referents (N = 25) were assessed in their apartments from the program's inception in 10/99, and were evaluated by a geropsychiatrist. A chart-review survey of computerized medical records was conducted and demographic, psychosocial, diagnostic, treatment, and short-term outcome information were systematically extracted.

Results: Mean age = 80 +/– 7.8 years; 76% were women. 64% were widowed, 28% married, 8% divorced/never married. All had medical problems (mean number = 2.9 +/– 1.1). 44% had family involvement; 32% had assistance with household chores; 44% needed personal care; and 28% help with ambulation. Forty percent met DSM-IV criteria for dementia, 16% for major depression, and 32% for adjustment disorders with anxious/depressed moods. Initial evaluations required one and a half hours face-to-face plus additional corroborative data collection. F/u visits required 30–60 minutes. Over the first three months, 8% required psychiatric hospitalization; 8% died; and 84% continually maintained in the community. All hospitalized patients returned home.

Conclusions: Typical initial referent profile for geropsychiatric assessment is an "old-old" woman living alone with limited family contact, significant ADL/cognitive compromise, anxious/depressive symptomatology, who requires significant time to complete an assessment. Evaluation and subsequent on-site treatment were greatly facilitated by laptop computer and cellular-phone. Early analysis indicates successful on-site geropsychiatric assessment/treatment is achievable, but may be too time-consuming to sustain fee-for-service MD Medicare reimbursement. Experiences suggest alternative, more cost-efficient models.

NR214 Monday, May 15, 3:00 p.m.–5:00 p.m.

Subtypes of OCD and Symptom Severity

Craig Springer, *Department of Psychiatry, North Shore Hospital, 400 Community Drive, Manhasset, NY 11030*; Francine J. Spinowitz, M.A., Juliana R. Lachenmeyer, Ph.D., Yoav Cohen, Regina Uccello, B.A.

Summary:

Previous literature has suggested that it may be important to distinguish between categories of obsessive-compulsive disordered patients (Steketee, Grayson, and Foa, 1985). Research using the Compulsive Activity Checklist (CAC) has identified two major subtypes of obsessive-compulsive disordered patients: (1) washers, who exhibit compulsions involving washing and cleaning rituals, and (2) checkers, who exhibit compulsions involving checking things such as stoves and locks (Fruend, Steketee, and Foa, 1987). More recently, research has explored these subtypes in relation to personality traits and has found that washers are more likely than checkers to have personality disorders (Horesh, Dolberg, Kirschenbaum-Aviner, and Kotler, 1997). The purpose of the present study was to examine whether different types of compulsions were related to severity of OCD symptoms. Eighty participants, 37 males and 43 females with a mean age of 35 years, were classified into groups based on the kinds of compulsions reported in the CAC: washers, checkers, or both. Severity of symptoms was also reported on the CAC. Data were analyzed using multiple t-tests with the Bonferroni posthoc adjustment. Results indicated that washers (Mean 20.2) had significantly more severe symptoms than did checkers (Mean 11.5). Implications of the results for differential treatment will be discussed.

NR215 Monday, May 15, 3:00 p.m.–5:00 p.m.

Violence in Inner-City, State Psychiatric Patients

Denise De Guzman, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, 4th flr, Baltimore, MD 21201*; Anthony F. Lehman, M.D., Lisa B. Dixon, M.D., Corey B. Smith, M.A., Patricia W. Kendall, Ph.D.

Summary:

Objective: To assess the prevalence and correlates of violence and victimization among a cohort of acute inpatients three months pre-hospitalization at an inner city, state psychiatric facility.

Method: 223 voluntary patients at an urban, state psychiatric facility were surveyed upon readmission to an inpatient psychiatric unit. Bivariate data analyses were performed to assess relationships between patient characteristics and violence, victimization, interim services and support and other outcomes.

Results: 39% of patients experienced violent tendencies, defined as either the impulse or threat to hit, injure, or harm someone; or threats to hurt or kill yourself. 24% of patients manifested violent behavior (hit or injured someone) and 24% of patients experienced victimization. Married patients were less likely to be victimized upon discharge from the initial inpatient program ($p = 0.05$). Educated patients were less likely to exhibit violent behavior in the interim period between hospitalizations ($p < 0.05$). In contrast, patients with higher frequency of prescribed medication were more likely to exhibit violent behavior ($p < 0.05$). Age and family involvement were unrelated to violence or victimization. Overall, patients had very significant post-discharge problems (homelessness, incarceration, lack of goal-directed activity, suicidal ideation, ongoing substance abuse) and few were receiving ongoing mental healthcare. While 81 patients (38%) reported any outpatient mental health care and 91 patients (44%) had no post-discharge prescribed medication, 132 patients (62%) had an emergency room or crisis center visit.

Discussion: The 24% of patients in this study manifesting violent behavior prior to their rehospitalization is significantly higher than previous estimates of approximately 10% in similar patient populations. The relationship between education and marital status with violence are consistent with previous studies examining risk factors for violence. The striking findings of post-discharge problems reported by patients, coupled with the lack of routine outpatient care, underscores the need for improved aftercare and expanded efforts to engage families in the aftercare process for these patients.

NR216 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Diffusion Tensor MRI in the Schizophrenia Spectrum

Lina S. Shihabuddin, M.D., *Department of Psychiatry, Mt. Sinai School of Medicine, 1 Gustave Levy Place, box 1505, New York, NY 10029;* Monte S. Buschsbaum, M.D., Cheuk Tang,

Ph.D., Adam M. Brickman, B.A., Michael B. Fleischman, B.A., Antonia S. New, M.D., Larry J. Siever, M.D.

Educational Objectives:

Better understand new imaging techniques to visualize white matter areas and better understand the relationship between deficits in these areas and schizophrenia.

Summary:

Psychopharmacology and animal circuitry studies have suggested cortico-striatal abnormalities in schizophrenia. These abnormalities have been studied with functional and anatomical neuroimaging techniques. Diffusion tensor imaging is a new magnetic resonance imaging (MRI) sequence designed to assess white matter tract integrity. Through the quantification of directionality of restricted diffusion (anistotropy), this technique allows the direct assessment of large axons stretching from the prefrontal cortex to the striatum.

Structural MRI and diffusion tensor imaging were obtained on 65 patients with schizophrenia, 11 patients with schizotypal personality disorder (SPD), and 35 age- and sex-matched normal controls. Preliminary analysis showed decreased anistotropy in frontal-striatal white matter, which implies reduced frontal-striatal connectivity in schizophrenia compared with normal controls.

These findings suggest that cortico-striatal circuitry interruptions are part of the disease process in schizophrenia. Further analysis, including the SPD sample, is being performed. Implications of these findings in the neuropathology of the schizophrenia spectrum disorders will be discussed.

References:

1. Buchsbaum MS, Tang CY, Peled S, Gudbjartsson H, et al: MRI white matter diffusion anisotropy and PET metabolic rate in schizophrenia. Neuroreport 1998; 9: 425–430
2. Lim KO, Hedehus M, Moseley M, de Crespigny A, et al: Compromised white matter tract integrity in schizophrenia inferred from diffusion sensor imaging. Arch Gen Psychiatry 1999; 56: 367–374

NR217 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Motor Dysfunction in Schizophrenia

Douglas R. Dolnak, D.O., *Department of Psychiatry, University of CA/San Diego, 8950 Vill La Jolla Dr, Suite 2243, La Jolla, CA 92103;* Mark H. Rapaport, M.D., Caligiuri Michael, M.D., Golshan Shahrokh, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be familiar with motor dysfunction in schizophrenia by (1) assessing motor dysfunction subjectively via rating scales, (2) assessing motor dysfunction objectively via novel electromechanical measures, (3) recognizing future implications of improving precision in clinical research with these measures.

Summary:

This study compares and contrasts the effects of olanzapine and risperidone on extrapyramidal symptoms. We employed objective measures to ascertain whether there are clinically significant differences between olanzapine and risperidone on two important, but difficult to reliably measure, motor features: hyperkinesia and bradykinesia. We hypothesized that olanzapine will have fewer extrapyramidal problems than risperidone because: (1) differences in in vitro binding profiles, (2) differences in behavioral pharmacology, and (3) differences in c-fos expression. Electromechanical measures were used to assess objectively dyskinesia, bradykinesia, and tremor. Motor function was subjectively assessed with the Abnormal Involuntary Movement Scale, Simpson Angus Scale, and the Barnes Akathisia Scale. Subjects were 18–65 years of age, medically stable, and met DSM-IV diagnosis of schizophrenia. Forty subjects were randomized to either olanzapine or risperidone treatment for eight weeks. Preliminary analysis (n = 18) demonstrated that hand-force instability at baseline was 6.03 (3.3) for the risperidone treatment group and 6.56 (5.4) for the olanzapine treatment group. After eight weeks of treatment, hand-force instability had decreased 29% for the risperidone group and 57% for the olanzapine group (F = 4.1; p = .05). Preliminary analysis did not differentiate olanzapine and risperidone on subjective measures of motor impairment. Final analysis of a larger group of patients will be presented.

References:

1. Caligiuri MP, Lohr JB: A disturbance in the control of muscle force in neuroleptic-naive schizophrenic patients. Biol Psychiatry 1994; 35: 104–111
2. Caligiuri MP, Lohr JB: Fine force instability: a quantitative measure of neuroleptic-induced dyskinesia in the hand. J Neuropsychiatry Clin Neurosci 1990; 2: 395–398

NR218 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Obesity As a Risk Factor for Antipsychotic Noncompliance

Peter J. Weiden, M.D., *Department of Psychiatry, SUNY HSC at Brooklyn, 450 Clarkson Avenue, Brooklyn, NY 11203;* David B. Allison, Ph.D., Joan A. Mackell, Ph.D., Diana McDonnell, A.B.D.

Summary:

Objectives: Although the newer atypical antipsychotics have been a major improvement in terms of side effects, weight gain remains a vexing problem. Therefore, it is increasingly important to understand whether there is a relationship between obesity and medication compliance.

Methods: Cross-sectional eight-page questionnaires, focusing on treatment and health issues, were mailed to people with schizophrenia identified through NAMI and NMHA. Self-reported frequency of missing medication was the primary dependent variable. The primary independent variable was BMI, categorized as normal (<25, n = 73), overweight (25–30, n = 104), or obese (>30, n = 100). Other independent variables included demographics, reported reasons for stopping medication, medication attitude, and treatment satisfaction.

Results: There was a significant association between obesity and noncompliance, with obese people almost three times more likely to report missing their medication (OR = 2.9, CI 1.1-7.3). This relationship was stronger for women. Obese respondents were also more likely to stop medication because of weight gain (OR = 13.8, CI 2.0-95.4). Respondents' attitudes toward medication attenuated, but did not eliminate, the relationship between obesity and noncompliance.

Discussion: There seems to be a significant association between obesity and noncompliance even when accounting for other possible confounding factors.

References:

1. Allison D, Fontaine KR, Heo M, et al: The distribution of Body Mass Index among individuals with and without schizophrenia. Journal of Clinical Psychiatry 1999; 60 (4): 215–220

NR219 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Cognitive Therapy of Schizophrenia: Toronto Trial

Neil A. Rector, Ph.D., *Mood and Anxiety Department, Clarke Institute, 250 College Street, Toronto, ON M5T IR8, Canada;* Mary V. Seeman, M.D., Zindel V. Segal, Ph.D.

Educational Objectives:

Participants will learn about the principles and intervention strategies of cognitive therapy for schizophrenia. They will also recognize potentially suitable candidates for this therapy. Finally, they will be able to demonstrate a knowledge concerning the efficacy of this intervention following the aggregated (meta-analytic) summary of all studies conducted to date.

Summary:

A significant proportion of patients with schizophrenia continue to experience distressing and disabling psychotic symptoms that are, in part, resistant to the benefits of pharmaocotherapy.

Objective: The primary aim of this study was to assess whether patients with a DSM-IV diagnosis of schizophrenia and medication-resistant symptoms show superior clinical outcomes following adjunctive treatment with cognitive therapy.

Method: A randomized controlled study was completed with 61 patients assigned to either cognitive therapy and routine care or routine care only. Routine care consisted of pharmacotherapy and case management. Cognitive therapy was conducted on an individual basis and lasted for six months. Clinical outcomes were completed by blind assessors.

Results: Patients who received cognitive therapy and routine care demonstrated significantly better symptom outcomes than patients who received routine care only. Significant differences were noted on the scale total score of the Positive and Negative Symptom Scale (PANSS) and this difference was largely accounted for by differences on the positive and negative symptom subscale scores of the PANSS.

Discussion: The efficacy of cognitive therapy for schizophrenia appears well supported. A quantitative summary of all randomized controlled trial studies conducted to date will be provided.

References:

1. Kuipers E, et al. London-East Anglia randomized controlled trial of cognitive-behavioural therapy for psychosis: effects of the treatment phase, 1997; 171: 319–327
2. Drury V, Birchwood M, Cochrane R, MacMillan F: Cognitive therapy and recovery from acute psychosis: a controlled trial, impact on psychotic symptoms. British Journal of Psychiatry 1996; 169: 593–601

NR220 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

The Effectiveness of the Family-to-Family Education Program

Lisa B. Dixon, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, Room 476, Baltimore, MD 21201;* Betty Stewart, B.A., Joyce Burland, Ph.D., Alicia Lucksted, Ph.D., Janine C. Delahanty, M.A., Marcia Hoffman, M.A., Leticia T. Postrado, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the outcomes for which the Family to Family Education Program has been shown to be effective.

Summary:

Purpose: This study assesses the effectiveness of the 12-week NAMI Family to Family Education Program (FFEP), a peer-based structured program for families members of persons with severe mental illness (SMI) that is widespread throughout the nation. The program provides support, education, problem-solving skills training, and crisis intervention help for families in accordance with best-practices standards.

Methods: A total of 38 consenting family member FFEP participants were assessed prospectively at baseline, post-intervention, and six months post-FFEP. Trained family member interviewers conducted assessments. Repeated measures analyses of variance were used to assess within-subject change over time.

Results: Participants had *significantly* increased gains in self-perceived knowledge about mental illness, empowerment, ability to cope with the mental health system, and ability to cope with their ill family member. Subjective burden of mental illness including worry and displeasure with the ill family member also *significantly* declined. Most importantly, post-program gains were sustained after six months.

Conclusions: This study provides substantial evidence that the FFEP, a consumer-run, volunteer-driven program that has received considerable financial support from the states, is effective at improving the experience of families of persons with SMI. A more rigorous controlled study to test the effectiveness of FFEP is merited.

References:

1. Dixon L, Goldman HH, Hirad: State policy and funding of services to families of adults with serious and persistent mental illness. Psychiatric Services 1999; 50: 551–552
2. Dixon L. Providing services to families of persons with schizophrenia: present and future. Journal of Mental Health Policy and Economics 1999; 2: 3–8

NR221 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Preventing Jail and Hospital Recidivism Among Adults with Severe Mental Illness

J. Steven Lamberti, M.D., *Department of Psychiatry, University of Rochester, 1650 Elmwood Avenue, Rochester, NY 14620;* Robert L. Weisman, D.O., Rudo Mundondo-Ashton, M.S., Nancy Price, R.N.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to (1) demonstrate clinical strategies to promote treatment adherence among patients with histories of jail and hospital recidivism, and (2) describe the design, operation and effectiveness of Project Link, an integrated approach to prevention of jail and hospital recidivism.

Summary:

Objective: Persons with severe mental illness are overrepresented in jails and prisons. This study is designed to determine whether Project Link, recipient of the APA's 1999 Gold Award, is effective at reducing jail and hospital utilization among outpatients with criminal justice histories:

Method: Fifty-four outpatients referred to Project Link were studied using a pre-post design to compare outcomes one year before and after enrollment. Subjects met DSM-IV criteria for schizophrenia or other chronic psychotic disorders, and had histories of noncompliance, arrest, and incarceration. Three subjects were lost to follow-up. Service utilization data were obtained through chart reviews and monitored prospectively. The Multnomah Community Ability Scale (MCAS) and the Global Assessment of Functioning (GAF) scale were administered at enrollment and one year later to assess community functioning.

Results: Mean (SD) yearly jail days per patient dropped from 108.7 (132.4) to 39.8 (114.9) ($Z = -3.9$, $P < .001$; Wilcoxon test, two-tailed), and mean (SD) yearly hospital days dropped from 104.8 (125.7) to 13.7 (38.5) ($Z = -4.8$, $P < .001$; Wilcoxon test, two-tailed). Significant improvement was noted in MCAS and GAS scores.

Conclusions: This study suggests that integrated outpatient programs like Project Link can reduce jail and hospital recidivism among high-risk patients. Controlled studies are needed.

Supported by a grant from the Robert Wood Johnson Foundation's Local Initiative Funding Partners Program

References:

1. Lamb RH, Weinberger, LE: Persons with severe mental illness in jails and prisons: A review. Psychiatric Services 1998; 49(4): 483–492

2. Prevention of jail and hospital recidivism among persons with severe mental illness. Project Link, Department of Psychiatry, University of Rochester, Rochester, New York. Psychiatric Services 1999; 50(11): 1477–1480

NR222 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Fluoxetine in Adolescents with Major Depression

Jack R. Cornelius, M.D., *Department of Psychiatry, University of Pittsburgh, WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593;* Oscar G. Bukstein, M.D., Kevin G. Lynch, Ph.D., Boris Birmaher, M.D., Samuel Gershon, M.D., Ihsan M. Salloum, M.D., Duncan B. Clark, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should know the therapeutic response of adolescents with comorbid major depression and an alcohol use disorder to fluoxetine, as demonstrated in an open-label trial.

Summary:

Background: Recently, a first placebo-controlled study of a SSRI medication was conducted among adolescents (Emslie et al., 1997). That study demonstrated efficacy for fluoxetine versus placebo for treating major depression.

Objective: The authors investigated whether fluoxetine decreases the depressive symptoms and the drinking of adolescents with comorbid major depression and an alcohol use disorder.

Method: The authors conducted a 12-week, open-label study of fluoxetine (20 mg) in 13 adolescents with comorbid major depression and an alcohol use disorder.

Results: The mean HAM-D-24 score dropped by 19 points, from a baseline mean score of 26.5 +/– 6.4 to an end of study mean of 6.4 +/– 4.8 ($p < .001$). The number of drinks per drinking day also demonstrated a significant drop ($p < .005$). On the Clinical Global Impressions scale, all patients demonstrated "much" or "very much" improvement in depressive symptoms at the end of the trial, while seven of the 13 patients (53.9%) showed "much" or "very much" improvement in symptoms of alcohol dependence.

Conclusions: These data suggest promise for fluoxetine for decreasing both the depressive symptoms and the drinking of adolescents with comorbid major depression and an alcohol use disorder.

References:

1. Cornelius JR, Salloum IM, Ehler JG, et al: Fluoxetine in depressed alcoholics: A double-blind, placebo-controlled trial. Archives of General Psychiatry 1997; 54: 1031–1037

2. Cornelius JR, Salloum IM, Haskett, RF, et al: Fluoxetine versus placebo in depressed alcoholics: A 1-year follow-up study. Addictive Behaviors in press.

NR223 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Decreased Benzodiazepine Binding in PTSD

J. Douglas Bremner, M.D., *Dept. of Psychiatric Research, Yale University, 184 Liberty Street, New Haven, CT 06519;* Robert B. Innis, M.D., Steven M. Southwick, M.D., Lawerence Staib, Ph.D., Sami Zoghbi, Ph.D., Dennis S. Charney, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should have an appreciation for the role of the benzodiazepine receptor in stress and changes in benzodiazepine receptor binding in PTSD.

Summary:

Objective: Animals exposed to stress developed a decrease in benzodiazepine receptor binding in frontal cortex. No studies have examined central benzodiazepine receptor binding in patients with posttraumatic stress disorder (PTSD). The purpose of this study was to examine measures of benzodiazepine receptor binding in PTSD.

Methods: A quantitative measure related to benzodiazepine receptor binding (Distribution Volume (DV)) was obtained with single photon emission computed tomography (SPECT) imaging of [^{123}I]iomazenil and measurement of radioligand concentration in plasma in patients with Vietnam combat-related PTSD and case-matched healthy comparison subjects. DV image data were analyzed using statistical parametric mapping (spm96).

Results: Lower values for measures of benzodiazepine receptor binding (DV) was found in frontal cortex (Brodmann's area 9) in PTSD patients relative to comparison subjects.

Conclusions: These findings of lower values for measures of benzodiazepine receptor binding are consistent with smaller number of benzodiazepine receptors and/or reduced affinity of receptor binding in medial prefrontal cortex in PTSD. Alterations in benzodiazepine and/or GABA function in this area may underlie many of the symptoms of PTSD.

References:

1. Bremner JD, Southwick SM, Charney DS: The neurobiology of posttraumatic stress disorder: An integration of animal and human research, in Posttraumatic Stress Disorder: A Comprehensive Text. Edited by Saigh PA, Brenner JD. Allyn & Bacon, New York, 1999, pp. 103–143

2. Bremner JD: Does stress damage the brain? Biol Psychiatry 1999; 45: 797–805

NR224 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

A Three-Week, Double-Blind, Randomized Trial of Ziprasidone in the Acute Treatment of Mania

Paul E. Keck, Jr., M.D., *Biological Psychiatry Dept., UCMC College of Medicine, 231 Bethesda Ave/PO Box 670559, Cincinnati, OH 45267-0559;* Kathleen Ice, Ph.D.

Summary:

Objective: A randomized, double-blind study to compare flexible-dose oral ziprasidone 80–160 mg/day ($n = 131$) with placebo ($n = 64$) over three weeks in inpatients with acute mania.

Method: Bipolar patients with acute mania who provided written informed consent and had a baseline SADS-C Mania Rating Scale Score (MRS) ≥14 were assessed using the SADS-C, PANSS, CGI-S, Simpson-Angus, Barnes Akathisia, and AIMS scales. The SADS-C was administered at days 2, 4, 7, 14, and 21. Primary efficacy analysis was change from baseline to endpoint (LOCF) on the SADS-C MRS (ANCOVA, controlling for baseline and center).

Results: Groups were comparable at baseline. Robust improvements in the MRS score were observed with ziprasidone compared to placebo at all time points beginning at day 2 ($p \leq 0.05$). Ziprasidone was also effective in reducing overall psychopathology. The effective dose range was similar to that for acute exacerbation of schizophrenia and schizoaffective disorder. Ziprasidone was well tolerated.

Conclusions: Ziprasidone was well tolerated and appears to offer a rapidly effective treatment for patients with bipolar mania.

References:

1. Keck Jr P, Buffenstein A, Ferguson J, Feighner J, Ziprasidone Study Group et al: Ziprasidone 40 and 120 mg/day in the acute exacerbation of schizophrenia and schizoaffective disorder: a 4-week placebo-controlled trial. Psychopharmacol 1998; 140(2): 173–184
2. Frye MA, Ketter TA, Altshuler LL, Denicoff K, et al: Clozapine in bipolar disorder: treatment implications for other atypical antipsychotics. J Affect Disord 1998; 48(2–3): 91–10

NR225 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Affect in Salivary Cortisol in Bosnian Refugees Suffering from PTSD

Aida Spahic-Mihajlovic, M.D., *Department of Psychiatry, Loyola Medical Center, 2160 South First Avenue, Maywood, IL 60153;* Edward J. Neafsey, Ph.D., John W. Crayton, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to understand the basic symptomatology of PTSD in a refugee population from Bosnia, especially the disturbance in affect known as "numbing" and the relation of this to heightened HPA axis sensitivity.

Summary:

Emotion and salivary cortisol levels were studied in 21 male Bosnian refugees diagnosed with PTSD and 17 male Bosnian control subjects. Emotion was assessed using Lang's "Looking at Pictures" test. The pictures all had assigned "normal" valence and arousal scores. Valence ratings of PTSD subjects were normal. However, while the control subjects, like normal subjects, found both pleasant and unpleasant images arousing, the PTSD subjects found only unpleasant images arousing, with pleasant images very commonly (11/21 subjects) rated as almost completely non-arousing. Both control and PTSD subjects also provided salivary cortisol samples at 8:00 a.m. and 4:00 p.m. on two consecutive days, with a dexamethasone tablet (0.5 mg) taken at 10:00 p.m. after the first day's samples. A three-way ANOVA (group by day by time) of the salivary cortisol measurements data was significant overall ($F = 3.286$, $p = .004$) with significant main effects of group (PTSD < control, $F = 8.343$, $p = .005$) and day (day 2 < day 1, $F = 5.787$, $p = 0.18$) were found, confirming previous reports that HPA axis sensitivity is intact or even enhanced in PTSD. The finding of a selective disturbance of "pleasant arousal" in PTSD suggests that different mental illnesses may selectivity alter either positive or negative affective arousal.

References:

1. Lang PJ, Greenwald MK, Bradley MM, Hamm AO: Looking at pictures: Affective, facial, visceral, and behavioral reactions. Psychophysiology 1993; 30: 261–273
2. Yehuda R: Sensitization of the hypothalamic-pituitary-adrenal axis in posttraumatic stress disorder. Ann N Y Acad Sci 1997; 821: 57–75

NR226 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

Heavy Drinking: Alcohol Disorders in Social Phobia

Rosa M. Crum, M.D., *Department of Epidemiology, Johns Hopkins University, 2024 E. Monument St. #2-500, Baltimore, MD 21205-2223;* Laura Pratt, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should further his/her understanding of the epidemiology of heavy drinking and alcohol abuse and dependence among individuals with social phobia.

Summary:

Objectives: Using prospective data, we assessed the risk of heavy drinking and alcohol disorders among individuals with DIS/DSM-III social phobia, and a subclinical social phobic syndrome (an irrational fear of social situations, without significant impairment or avoidance).

Methods: Probability samples were selected by census tracks and households as part of the Epidemiologic Catchment Area program. The baseline interview for the Baltimore site was completed in 1981, and between 1993 and 1996, 73% of survivors were re-interviewed. From the baseline interview, we identified a cohort of 1152 individuals who were at risk for episodes of heavy drinking or alcohol use disorders. Logistic regression was used to assess the association between DIS/DSM-III social phobia and subclinical social phobia with risk for incident alcohol abuse and dependence, as well as incident heavy drinking.

Results: Among those with DIS/DSM-III social phobia only one developed heavy drinking at follow-up, and none developed incident alcohol abuse or dependence. Among those with *subclinical* social phobia, the cumulative incidence of heavy drinking and alcohol abuse or dependence was 119 per 1000, and 95 per 1000, respectively. After adjustment for covariates, the estimated relative risk (RR) for heavy drinking among those with subclinical social phobia was 2.39 (95% CI (confidence interval), 1.10-5.18, $p = 0.028$); and the RR for alcohol abuse or dependence was 2.27 (95% CI 0.99-5.24, $p = 0.053$) relative to those without social phobia or subclinical social fears.

Conclusions: The data may improve our understanding of the comorbid relationship of social phobia with risk for alcohol conditions.

References:

1. Kushner MG, Sher KJ, Erickson DJ: Prospective analysis of the relation between DSM-III anxiety disorders and alcohol use disorders. American Journal of Psychiatry 1999; 156(5): 723–732
2. Magee WJ, Eaton WW, Wittchen H-U, McGonagle KA, Kessler RC: Agoraphobia, simple phobia, and social phobia in the National Cormorbidity Survey. Archives of General Psychiatry 1996; 53: 159–168

NR227 Tuesday, May 16, 9:00 a.m.-10:30 a.m.

The Quality of Care for Depressive and Anxiety Disorders in the United States

Alexander S. Young, M.D., *Department of Psychiatry, UCLA, 10920 Wilshire Blvd, Suite 300, Los Angeles, CA 90024;* Ruth Klap, Ph.D., Cathy D. Sherbourne, Ph.D., Kenneth B. Wells, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand that quality of care for depressive and anxiety disorders can be measured, know the approximate level of treatment quality for these disorders in the U.S., know factors that increase the risk of not receiving appropriate care in the U.S., and appreciate the need for quality improvement.

Summary:

Objective: Little is known about the quality of care for psychiatric disorders nationally. We estimate the rate of appropriate psychotropic medication or counseling among the U.S. population with depressive and anxiety disorders, and examine factors affecting use of appropriate care.

Method: A total of 1641 adults with a probable 12-month depressive or anxiety disorder were drawn from a national sample. Data are from a telephone survey during 1997–1998.

Results: During the past year, 82% of adults with probable depressive or anxiety disorders saw a health care provider, and 31% used some appropriate treatment. Most visited medical providers only, and these people had significantly lower rates of appropriate treatment than people visiting specialists. Rates of appropriate treatment were lower for men, African Americans, the less educated, and adults under 30 or over 59 years old. Insurance status and income did not have unique effects on use of appropriate care.

Conclusions: The majority of adults with a probable depressive or anxiety disorder receive no appropriate care. While this holds across diverse groups, rates of appropriate care are lower in certain demographic subgroups. Public education and practice-level quality improvement efforts are broadly needed, and should also target these subgroups.

References:

1. Sturm R, Gresenz C, Sherbourne C, Minnium K, et al: The design of healthcare for communities: a study of health care delivery for alcohol, drug abuse, and mental health conditions. Inquiry 1999; 36: 221–33
2. Brook RH, McGlynn EA, Cleary PD: Quality of health care. Part 2: measuring quality of care. N Engl J Med 1996; 335: 966–970

NR228 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Panic Disorder Patients at the Time of Air Strikes

Vladan Starcevic, M.D., *c/o Hunter Mental Health Service, James Fletcher Hospital, PO Box 833, Watt Street, New Castle 2300 NSW, Australia;* Goran Bogojevic, M.D., Katarina Kelin, M.D.

Summary:

Objective: To assess the impact of a real danger situation of air strikes on several aspects of the panic disorder (PD) patients' psychopathology and on their functioning.

Methods: At the time of the 11-week NATO air strikes on Belgrade in 1999, 84 PD patients (61 women, 23 men, mean age 35.3 years) with a previously diagnosed and treated DSM-IV PD, who were in partial or complete remission and were followed up regularly, were administered Panic and Agoraphobia Scale (PAS), which measures the severity of PD and is a part of the regular follow-up assessment battery. The majority of patients (49; 58.3%) were still taking antipanic medications at the time of the PAS assessments.

Results: Compared to the PAS assessments made prior to the onset of air strikes, those made during the period of air strikes, showed the following results: 1) a non-significant trend towards a decrease in the frequency, severity and duration of panic attacks (mean of 1.04 [SD = 2.08] vs. 1.09 [SD = 1.97]); 2) almost identical scores on the measures of agoraphobic avoidance (mean of 0.79 [SD = 1.66] vs. 0.80 [SD = 1.65]); 3) a significant increase ($p < 0.001$) in the frequency and intensity of anticipatory anxiety (mean of 1.89 [SD = 1.64] vs. 1.38 [SD = 1.50]); 4) a significant decrease ($p < 0.001$) in overall disability (mean of 1.41 [SD = 1.68] vs. 2.07 [SD = 1.84]).

Conclusions: These results suggest a lack of relationship between real danger and panic attacks, but suggest that real danger may be associated with increased anticipatory anxiety in PD patients. The results also lend support to the notion that panic attacks and fear induced by real danger are different phenomena. Contrary to the expectations of many PD patients, the presence of real danger does not affect their functioning adversely.

NR229 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Combined Treatments in Panic Disorder with Agoraphobia Revisited

Vladan Starcevic, M.D., *c/o Hunter Mental Health Service, James Fletcher Hospital, PO Box 833, Watt Street, New Castle 2300 NSW, Australia;* Goran Bogojevic, M.D., Dusan Kolar, M.D., Eberhard H. Uhlenhuth, M.D.

Summary:

Objective: To compare efficacy of cognitive-behavior therapy alone (CBT) with efficacy of a controversial but apparently common practice of combining CBT with a high-potency benzodiazepine (HPB; alprazolam, clonazepam) (CBT1) and of combining CBT with a HPB and a selective serotonin reuptake inhibitor (SSRI; fluoxetine) (CBT2) in the treatment of panic disorder with agoraphobia (PDA).

Methods: Of 88 outpatients with the DSM-IV diagnosis of PDA, 24 were treated with CBT, 43 with CBT1, and 21 with CBT2. The main treatment efficacy variable was a score on the Panic and Agoraphobia Scale (PAS), a clinician-administered instrument for comprehensive assessment of the severity of PDA. The methodological innovation was that the three groups of patients were compared in terms of their PAS scores at the end of treatment, while controlling for the differences in their baseline PAS scores and that the analysis of covariance was used after determining that the regression lines in all groups were parallel.

Results: At the end of treatment, there was a significant difference ($p = 0.03$) when adjusted, total mean PAS scores were compared: 11.03 (SD = 5.23) for CBT vs. 9.71 (SD = 4.92) for CBT1 vs. 6.90 (SD = 4.96) for CBT2. There was no significant difference ($p = 0.33$) when the PAS scores were compared between CBT and CBT1, while significant differences emerged when such comparisons were made for CBT vs. CBT2 ($p = 0.01$) and for CBT1 vs. CBT2 ($p = 0.03$).

Conclusions: These results suggest that effects of combination treatments in PDA may depend on what is being combined; while a combination of CBT and a HPB does not confer additional benefit in comparison with CBT alone, use of an SSRI together with CBT and a HPB leads to significantly larger treatment gains in comparison with both CBT alone and CBT combined with a HPB.

NR230 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Modulation of 5HT-2C and 5HT-1A Receptor Responsiveness by Clomipramine Treatment or Aerobic Exercise in Patients with Panic Disorder

Andreas Broocks, M.D., *Department of Psychiatry, University of Lubeck, Ratzeburger Allee 160, Luebeck 23538, Germany;* Eckart Ruether, M.D., Ullrich Munzel, Ph.D., Goeran Majak, M.D., Borwin Bandelow, M.D.

Summary:

Objective: The study addresses the question whether antidepressant medication (clomipramine) or a non-pharmacological treatment (aerobic exercise) will modulate central serotonergic responsiveness in patients with panic disorder.

Method: A total of 45 patients with panic disorder and/or agoraphobia were randomly allocated to a ten-week period of endurance training, clomipramine or placebo treatment. Before and after treatment, the psychobehavioral and neuroendocrine effects of orally-administered m-Chlorophenylpiperazine (m-CPP; 0.4 mg/kg), ipsapirone (0.3 mg/kg) and placebo were examined.

Results: In comparison with the baseline challenges, the psychological responses to m-CPP and ipsapirone, as measured by the NIMH rating scales were significantly reduced both after exercise and clomipramine treatment. Neuroendocrine responses to m-CPP were also reduced in these two treatment groups; in contrast, administration of ipsapirone was associated with a trend

toward increased cortisol secretion both after clomipramine and exercise treatment.

Conclusion: A ten-week protocol of aerobic exercise leads to similar changes in 5-HT2C and 5-HT1A receptor responsiveness as does pharmacological treatment with clomipramine in patients with panic disorder. These results are in agreement with a study in marathon runners, indicating that regular endurance exercise is associated with downregulation of central 5-HT2C receptors.

NR231 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Prevalence and Correlates of Panic in Postmenopause

Jordan W. Smoller, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114;* Albert Oberman, M.D., Robert P. MacMahon, Ph.D., Judith Hsia, M.D., Mark H. Pollack, M.D., Sylvia Wassertheil-Smoller, Ph.D., David S. Sheps, M.D., Bruce A. Barton, Ph.D., Susan Hendrix, Sandra Daugherty, Rebecca Jackson, M.D., Donna Kearns, Tammy Dicken,

Summary:

Objective: To determine prevalence and correlates of panic attacks in postmenopausal women.

Methods: A total of 1176 women ages 50–79 enrolled in the MIMS, a 10-center ancillary study of the Women's Health Initiative (WHI), underwent 24-hour ambulatory electrocardiogram monitoring (AECG) and completed questionnaires on symptoms of ischemia and panic.

Results: 10.5% reported panic attacks in the past 6 months defined as a positive response to feeling suddenly frightened or anxious, accompanied by 4 or more symptoms on the panic symptom checklist. Prevalence was higher among blacks (20.3%) than non-blacks (10.0%), p = .016, among women ages 50–59 (15.4%) than those over 60 years (7.5%), p < .0001, and among diabetics (25%) than non-diabetics (10.2%), p = .016. Prevalence was not related to living alone, marital status, education, or hormone replacement therapy. Women with panic attacks in the past six months were more likely to be current smokers (OR = 2.47, 95% CI:1.27-4.81), to be depressed (based on a measure derived from the CES-D) (OR = 6.02, 95% CI:3.86-9.39), and to report chest pain during AECG monitoring (OR = 4.2, 95% CI:2.28-7.64).

Conclusion: These data indicate that panic attacks may be relatively common among postmenopausal women and are associated with cardiovascular risk factors (diabetes, smoking, and depression) as well as chest pain during AECG.

NR232 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

TDT Analysis of Behavior Inhibition Using Candida

Jordan W. Smoller, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114;* Jerrold F. Rosenbaum, M.D., Joseph Biederman, M.D., Jerome Kagan, Ph.D., Nancy Snidman, Ph.D., Stephen V. Faraone, Ph.D., John Kennedy, B.S., Alyssandra Schwarz, B.A., Susan Slaugenhaupt, Ph.D.

Summary:

Objective: To test polymorphisms in candidate genes for association with behavioral inhibition to the unfamiliar (BI), a heritable temperamental predisposition that appears to be a risk factor for the development of panic and phobic anxiety disorders, in a sample of children at risk for anxiety disorders.

Mouse models of behavioral inhibition and fear behavior can provide candidate genes for the genetic analysis of BI. Two such genes are preproenkephalin (PenK)—because the PenK knockout mouse exhibits decreased fear behavior in unfamiliar environments-and the adenosine A1a receptor gene (A1aR) because it maps to a region homologous to mouse chromosomal regions containing QTLs influencing fear behavior.

Method: Children aged 21 months, 4 years, or 6 years underwent behavioral assessments for BI. Candidate gene testing was performed using the transmission/disequilibrium test (TDT) on trios consisting of an inhibited child and two parents. Genotypes are available for 55 trios (58 informative transmissions) for PenK and 58 trios (48 informative transmissions) for A1aR.

Results: No association between BI and PenK or A1aR was observed in this sample.

Conclusion: This study illustrates an approach to the genetic dissection of panic and phobic anxiety disorders based on candidate genes derived from mouse models of behavioral inhibition.

NR233 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Follow-Up Results of Treatment of Social Phobia

Tone T. Haug, M.D., *Department of Psychiatry, University of Bergen, Haukeland University Hospital, Bergen 5022, Norway;* Svein Blomhoff, M.D., Kerstin Hellstrom, Ph.D., Ingar Holme, Ph.D., Hans P. Madsbu, Jan E. Wold, M.D.

Summary:

Both pharmacological and cognitive-behavior treatments are effective in social phobia, but it has been difficult to identify treatments that are clearly superior to others. The patients preference and availability of treatments are important for the decision of which treatment to be chosen. Long-term effectiveness of treatment will also be important. In an earlier study patients with social phobia were treated with sertraline and placebo, both groups combined with exposure therapy or general medical care for 24 weeks. Combined sertraline and exposure therapy (p = 0.001), sertraline alone (p = 0.001), and exposure therapy (p = 0.04) were all superior to placebo on measures of social phobia at the assessment at 24 weeks.

Method: In this study we made a follow-up assessment after one year of that study applying the same instruments as at baseline and at end of treatment (24 weeks).

Results: All treatment groups had a significant improvement from baseline to week 52 on all psychometric assessment (p = 0.00). Patients who had received exposure therapy seemed to have a further improvement on scores on social phobia from week 24 to week 52, while the patients who had medication had no improvement after end of treatment but the improvement at week 24 seemed to be maintained at week 52.

NR234 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Affective and Anxiety Comorbidity in PTSD Treatment Trials of Sertraline

Kathleen T. Brady, M.D., *Department of Psychiatry, Medical University of SC, 67 President Street, box250861, Charleston, SC 29425-0742;* Matthew J. Friedman, M.D., Gail M. Farfel, Ph.D.

Summary:

Objective: Comorbidity of mood and anxiety disorders is common for patients suffering from Posttraumatic Stress Disorder (PTSD). We examined the results from two trials of sertraline and placebo in the treatment of PTSD to assess whether comorbidity affected response to treatment.

Method: Two multicenter, 12-week, double-blind, flexible dose studies of adult outpatients from the general population with a DSM-III-R diagnosis of PTSD were conducted at U.S. centers (n = 12 and 14) to evaluate the safety and efficacy of sertraline (50–200 mg/day) compared to placebo in the treatment of PTSD. The total severity score of the Clinician-Administered PTSD Scale

(CAPS-2) and the Davidson Trauma Scale (DTS) total score were used to examine the effect of comorbidity on treatment outcome.

Results: There were 208 and 187 subjects enrolled in the two trials. The mean duration of PTSD was approximately 13 years in both studies. Rates of comorbid depressive disorders were 50% and 37% in Studies 1 and 2, respectively, while rates of comorbid anxiety disorders were 20% and 16%. In the two studies pooled, patients treated with sertraline improved significantly ($p \leq .05$) compared to placebo-treated patients on both the CAPS-2 and DTS whether or not they had a comorbid depressive disorder. Similarly, patients treated with sertraline were significantly improved ($p < .01$) compared to placebo subjects whether or not they had a comorbid anxiety disorder. Sertraline was generally safe and well-tolerated in these studies.

Conclusion: Sertraline (50–200 mg/day) is effective and well-tolerated in the treatment of PTSD for patients with or without comorbid affective or anxiety disorders.

NR235 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Improvement of CCK-4-Induced Panic by Vigabatrin

Peter Zwanzger, M.D., *Department of Psychiatry, LMU Munich, Nuss Baumstrasse 7, Munich 80336, Germany;* Thomas C. Baghai, M.D., Cornelius Schuele, M.D., R.J. Boerner, M.D., Hans J. Moeller, Rainer Rupprech, M.D.

Summary:

Objectives: Vigabatrin increases GABA-levels by irreversible inhibition of the GABA-catabolizing enzyme GABA-transaminase (GABA-T). Preclinical studies showed anxiolytic effects in vigabatrin treated rats. Anxiolytic effects in patients with panic disorder (PD) could therefore be expected. Administration of cholecystokinin-tetrapeptide (CCK-4) provokes panic-like symptoms both in healthy volunteers and patients with PD which are prevented by benzodiazepines. To evaluate putative anxiolytic properties of vigabatrin in humans, CCK-4 induced panic symptoms were studied in healthy volunteers before and after vigabatrin treatment.

Methods: After placebo-controlled administration of 25 μg CCK-4 ten healthy volunteers received vigabatrin for seven days with a daily dosage of 2 g. The treatment period was followed by a second CCK-4 challenge. Panic and anxiety were assessed using the API-score, a DSM-IV derived panic-symptom scale and visual analogue self-rating scales. In addition cortisol and prolactin plasma levels were determined during the CCK-4 challenge.

Results: All subjects reported a marked reduction of CCK-4 induced panic symptoms and anxiety after seven days of vigabatrin treatment. API-score, PSS and subjects self-rating scores showed a significant reduction after treatment. Moreover there was a significant reduction of CCK-induced elevation of cortisol levels following vigabatrin treatment.

Conclusion: Our data show a marked improvement of CCK-4-induced panic symptoms following vigabatrin treatment in healthy volunteers and suggest that GABA-transaminase inhibitors might be useful in ameliorating panic symptoms also in patients with PD.

NR236 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Sexual Dysfunctions: A Neglected Complication of Social Phobia and Panic Disorder

Ivan L.V. Figueira, M.D., *Department of Psychiatry, UFRJ, Rua Dona Mariana 182, BL1A 1503, Rio de Janeiro, RJ 22280-020, Brazil;* Elizabete G.M. Possidente, M.D.

Summary:

Little is known about sexual dysfunction comorbid with anxiety disorder. The aim of the present study was to evaluate retrospectively the sexual function of social phobic patients in comparison with a panic disorder sample. We examined 30 patients with social phobia and 28 with panic disorder using the DSM-IV criteria to obtain the sexual dysfunction diagnoses. Their sexual life was investigated with a semi-structured interview developed by the authors. We used an another semi-structured interview (SCID-I) to obtain the diagnoses of social phobia and panic disorder according to the DSM-IV. We excluded the DSM-IV's "C" criterion, which states that "The sexual dysfunction is not better accounted for by another Axis I disorder...." Panic disorder patients reported a significantly greater proportion of sexual disorders compared with social phobics: 75.0% (21/28) vs 33.3% (10/30) ($p = 0.0034$;). Aversive sexual disorder was the most common sexual dysfunction in both male and female panic disorder patients: 35.7%; 5/14 and 50.0%; 7/14 respectively. Premature ejaculation was the most common sexual dysfunction in male social phobic patients: 47.4% (9/19). These results suggest that sexual dysfunctions are a neglected complication of social phobia and panic disorder.

NR237 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Results of a 24-Week Extension Study of Sertraline in PTSD

Peter D. Londborg, M.D., *Seattle Clinical Research, 901 Boren Avenue, Suite 1800, Seattle, WA 98104-3508;* William Patterson, M.D., Mark Hegel, Ph.D., Carolyn R. Sikes, Ph.D., Gail M. Farfel, Ph.D.

Summary:

Objective: As no data are published addressing whether long-term pharmacological treatment of Posttraumatic Stress Disorder (PTSD) is safe or effective, the objective was to assess whether six months of open-label sertraline following a three month, double-blind trial sustained clinical response.

Method: Outpatients with PTSD who completed one of two 12-week, double-blind studies of sertraline and placebo were eligible to enter a 24-week open-label trial of sertraline (50–200 mg/day) in the treatment of PTSD. Primary efficacy measures were the Clinician-Rated PTSD Scale (CAPS-2), CGI ratings of Severity and Improvement, and the Impact of Event scale.

Results: Patients ($n = 249$) in the 24-week study showed statistically significant ($p < .05$) improvement assessed from baseline to endpoint on all primary efficacy parameters. Significant improvement was seen both in patients who had received placebo and those who had received sertraline in the 12-week feeder studies. The extent of improvement in this study was greater in those who had previously been randomized to placebo: a 40% decrease on the CAPS-2, versus 31% for those who had previously received sertraline. Sertraline was generally well-tolerated. The most frequently reported adverse events (≥10%) were headache, upper respiratory infection, insomnia, diarrhea, nausea, malaise, and fatigue. Treatment discontinuations due to adverse events or lab abnormalities occurred in 10% of patients.

Conclusion: Sertraline (50–200 mg/day) sustained clinical response during 24 weeks of open-label treatment for PTSD patients who had previously received either sertraline or placebo. Sertraline was shown to be a well-tolerated treatment for patients with PTSD.

NR238 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Effects of Sertraline and Placebo in Men with PTSD

Matthew J. Friedman, M.D., *National Center for PTSD, VA Medical Center (116-D), White River Juncti, VT 05009-0001;* Charles R. Marmar, M.D., Gail M. Farfel, Ph.D.

Summary:

Objective: Although pharmacologic treatment trials in PTSD were originally conducted in male combat veterans, epidemiologic studies have now shown that PTSD is more common in women.

Previously, we have shown sertraline to be an effective treatment for women with PTSD in two large, placebo-controlled trials. The objective of this analysis is to use data from three large, randomized trials of sertraline and placebo in a civilian population with PTSD to examine the effect in men.

Method: Three U.S. multicenter, 12-week, double-blind, flexible dose studies of adult men and women with a DSM-III-R diagnosis of PTSD were conducted to evaluate the safety and efficacy of sertraline (50–200 mg/day) and placebo in PTSD. The total severity score of the Clinician-Administered PTSD Scale (CAPS-2), the Impact of Event Scale, the Clinical Global Impressions (CGI) ratings of severity and improvement, and the Davidson Trauma Scale were the primary efficacy parameters used in these studies.

Results: Approximately 25% of subjects enrolled in each of the trials were men, the majority Caucasian, with a mean age of approximately 41 yrs, mean duration of illness of approximately 11 yrs, and approximately 19% and 46% of male subjects had comorbid anxiety and depressive disorders, respectively. Two of the three studies demonstrated sertraline to be efficacious in treating PTSD in the overall study population, and a post-hoc gender analysis showed strong evidence of efficacy in women. However, efficacy in men was not demonstrated on any of the primary efficacy parameters. There were two predictors of a positive response to sertraline in men: having a history of childhood abuse, or a history of drug abuse. Furthermore, the proportion of subjects classified as responders (a 30% CAPS-2 decrease plus a CGI-I ≤ 2) were similar in the cohorts of men and women. Sertraline was generally well-tolerated in these studies.

Conclusion: The effect of sertraline and placebo in the treatment of PTSD in men will be discussed, and questions will be posed for future research into this effect.

NR239 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Survival Analysis of Discontinuation from Clinical Trials As a Measure of Effectiveness in GAD: Comparison of Venlafaxine Extended Release with Placebo

Stuart A. Montgomery, M.D., *Imperial College of London, p o box 8751, London W13 8WH, United Kingdom;* Vincent Hahe, M.D., Vincent Haudiquet, David Hackett, M.S.C.

Summary:

Background: Dropout during clinical trials is an outcome not given due weight in efficacy analyses.

Method: Two double-blind randomized, placebo-controlled, six-month studies of venlafaxine XR in the treatment of GAD (DSM-IV) were examined. The first compared a flexible dose of 75–225 mg venlafaxine XR with placebo in 251 patients. The second compared three fixed doses with placebo in 541 patients. Survival curves for time to discontinue due to lack of efficacy were estimated using the Kaplan-Meier method.

Results: In the first study, 10 (8%) venlafaxine XR-treated patients discontinued because of lack of efficacy compared with 28 (22%) of placebo-treated patients. In the second study, six (4%), 13 (10%), and 24 (17%) patients treated with venlafaxine XR at 150 mg, 75, and 37.5 mg respectively, discontinued because of lack of efficacy compared with 27 (21%) of placebo-treated patients. Survival analysis showed a highly statistically significant difference (log-rank) between venlafaxine XR and placebo in each study, with a dose-response in the second study. Through the six-month period the curves continued to separate.

Conclusion: Survival analysis of discontinuations from clinical trials is a clinically relevant measure of assessing effectiveness of treatment, which includes all randomized patients in the data-set.

NR240 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

The SSRI Citalopram Is Effective in the Treatment of OCD: Results from a Double-Blind, Fixed-Dose, Placebo-Controlled Trial

Stuart A. Montgomery, M.D., *Imperial College of London, p o box 8751, London W13 8WH, United Kingdom;* Professor Siegfried Kasper, K. Bang

Summary:

Introduction: Citalopram, the most selective SSRI, is effective in the treatment of depression and panic disorder. It has been shown that SSRIs are effective in the treatment of obsessive compulsive disorder (OCD). Studies in adults and children suggest that citalopram is also effective in the treatment of OCD. This study was conducted to evaluate citalopram in the treatment of OCD over the antidepressant dose range of 20–60 mg/day.

Methods: This was a multicenter, double-blind, parallel group, fixed-dose study. Patients meeting DSM-IV criteria for OCD were randomized to placebo or citalopram at doses of 20 mg/day, 40 mg/day, or 60 mg/day for 12 weeks. Efficacy measures included the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Clinical Global Impressions of Improvement (CGI-I) scale.

Results: A total of 401 patients were randomized. All doses of citalopram produced significant reductions in Y-BOCS scores relative to placebo; significant improvement was observed after one week of double-blind treatment. CGI-1 scores were significantly improved versus placebo in each of the citalopram treatment groups. After 12 weeks, 63%, 54%, and 62% of patients randomized to citalopram 20 mg/day, 40 mg/day, and 60 mg/day, respectively, were rated as "1" (very much improved) or "2" (much improved) on the CGI-I. Citalopram was well tolerated at all dose levels.

Conclusions: Citalopram at doses of 20 mg/day, 40 mg/day and 60 mg/day, is well tolerated and significantly more effective than placebo in the treatment of patients with OCD.

NR241 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Mirtazapine and Onset of Action of Antidepressant Activity

Stuart A. Montgomery, M.D., *Imperial College of London, p o box 8751, London W13 8WH, United Kingdom;* Albert J. Schotte, Paul D. Reimitz, Ph.D.

Summary:

Three double-blind controlled studies of mirtazapine (MIR) vs fluoxetine (FLU), paroxetine (PAR) or citalopram (CIT) in depressed patients were re-analyzed. Data from the FLU and PAR studies (using HAMD-17) were combined (387 patients), whilst that of the CIT study (using MADRS) was analyzed separately (269 patients). Decrease in HAMD-17 was significantly greater on MIR than FLU/PAR at 7, 14, 21, 28 and 42 days and there was a significantly greater proportion of responders ($\geq$50% reduction in HAMD-17) on MIR than FLU/PAR on days 7, 14, 21, and 28. MADRS decreased significantly more on MIR than on CIT at day 14; differences at days 21 and 28 approached significance ($p = 0.07$). The responder rate ($\geq$50% reduction in MADRS) rate was higher on MIR than CIT at 14, 21, and 28 days (ns). The proportion of remissions (HAMD ≤ 7 or MADRS ≥ 12) was greater on MIR than SSRI at all times, with the differences achieving significance at days 21 and 28 for FLU/PAR and day 21 for CIT. At no time point for any parameter was there an advantage for SSRI over MIR. These results provide strong evidence that MIR has a faster onset of action than the SSRIs. Supported by Organon.

NR242 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Depression, Anxiety, Anger and Somatic Symptoms in BDD

Katharine A. Phillips, M.D., *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906;* Susan L. McElroy, M.D., Jason M. Siniscalchi, M.S.

Summary:

Background: Body dysmorphic disorder (BDD), a distressing and impairing disorder, is being increasingly researched. However, little is known about non-BDD symptoms and well-being in this disorder.

Methods: A total of 74 consecutive patients with DSM-IV BDD completed the self-report Symptom Questionnaire, a reliable, valid, and widely used scale that assesses distress, symptoms, and well-being in the areas of depression, anxiety, anger-hostility, and somatic symptoms. BDD severity and delusionality were assessed using reliable and valid published scales.

Results: The following scores were obtained on the Symptom Questionnaire: depression: 16.6 ± 6.4; anxiety: 16.5 ± 5.2; anger-hostility: 13.3 ± 6.6; and somatic symptoms: 11.0 ± 6.2. Scores on all four scales were notably higher than normative scores for normal controls. Scores on the depression, anxiety, and anger-hostility scales were higher than norms for psychiatric patients, whereas the somatic symptom score was similar to that of psychiatric patients. Scores on all four scales were significantly correlated with BDD severity (depression: $r = .64$, $p = .00$; anxiety: $r = .30$, $p = .02$; anger-hostility: $r = .44$, $p = .00$; somatic symptoms: $r = .27$, $p = .03$). Scores on the depression ($r = .65$, $p = .00$) and anger-hostility ($r = .43$, $p = .02$) scales were significantly correlated with delusionality. Scores on all four scales significantly decreased in subjects treated in an open-label fluvoxamine trial ($n = 18$).

Conclusion: Patients with BDD have high levels of distress, are highly symptomatic, and have poor well-being in the areas of depression, anxiety, and anger hostility. Despite being classified as a somatoform disorder, somatic symptom severity is similar to that of other psychiatric patients. Fluvoxamine treatment significantly decreased symptoms and improved well-being.

NR243 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Sensory Phenomena and Treatment Response in OCD

Roseli G. Shavitt, M.D., *Department of Psychiatry, University of Sao Paulo, Rua Ovidio Pires de Campos S/N, Sao Paulo 05403-010, Brazil;* Maria C.R. Rosario-Campos, M.D., Raquel C. Valle, Euripedes C. Miguel, M.D.

Summary:

Background: There is considerable evidence supporting the notion that OCD patients comprise an heterogeneous population. Sensory phenomena (SF) are general uncomfortable feelings, urges or mental/bodily sensations that can precede repetitive behaviors in OCD patients. Miguel et al. (1997) observed that patients with tic-related OCD presented more sensory phenomena, preceding their repetitive behaviors when compared to patients with non tic-related OCD. These phenomenologic differences could predict different treatment responses:

Method: Twenty-nine consecutive, drug-free outpatients (21 women, age-range = 17–50 years) have been studied. The Structured 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 and 12 weeks of exclusive clomipramine treatment (75-300mg daily).

Results: The degree of response (mean delta initial-final YBOCS scores) was significantly lower for patients with SF than for those without SF, with a special significance for the just-right ($p = 0.005$) and the tension/pressure ($p = 0.007$) mental phenomena.

Conclusions: The presence of sensory phenomena in OCD patients seems to predict a poorer response to clomipramine in the short term. If this finding is confirmed by a further analysis with a larger sample, we should consider offering this subgroup of patients a more comprehensive therapeutic approach, in order to achieve better treatment results.

NR244 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Pregabalin Treatment of GAD

Atul C. Pande, M.D., *CNS Clinical, Parke-Davis Pharmaceuticals, 2800 Plymouth Rd, Ann Arbor, MI 48105-2430;* Jerri G. Crockatt, M.A., Carol Janney, M.S., Douglas E. Feltner, M.D.

Summary:

Objective: To assess the safety and efficacy of pregabalin, a novel anxiolytic, for the treatment of generalized anxiety disorder (GAD).

Methods: Three, multicenter, controlled trials of similar design were conducted in patients with GAD. A one week lead-in period was followed by double-blind randomized treatment with either placebo, pregabalin 50 mg TID, pregabalin 200 mg TID, or lorazepam 2 mg TID. Following four weeks of treatment, dose was tapered over one week. Severity of anxiety was assessed at baseline and at weekly clinic visits using the Hamilton Anxiety Scale (HAM-A). Withdrawal symptoms were assessed using the Rickels Physician Withdrawal Checklist.

Results: Two studies showed pregabalin 600 mg/d and lorazepam 6 mg/d to be superior to placebo in reducing symptoms of GAD as measured by HAM-A total score. One study also showed a significant treatment effect of pregabalin 150 mg/d. One study did not differentiate among treatment groups. The most frequently occurring adverse effects associated with pregabalin were somnolence and dizziness. The frequency of these effects was dose dependent. Preliminary data did not suggest an abstinence syndrome attributable to pregabalin.

Conclusions: In two of three controlled trials, pregabalin was an effective and well-tolerated treatment for GAD. Sponsored by Parke-Davis Pharmaceutical Research.

NR245 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Ages of Onset for Anxiety Disorders

Jill I. Mattia, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 593 Eddy Street POB-430, Providence, RI 02903;* Mark Zimmerman, M.D.

Summary:

Objective: The purpose of this study was to examine the ages of onset of DSM-IV anxiety disorders.

Methods: A consecutive series of 500 individuals presenting to a general adult outpatient practice were interviewed with an expanded version of the Structured Clinical Interview for DSM-IV disorders (SCID).

Results: Three hundred and eight subjects (61.6%) in the sample were diagnosed with at least one lifetime anxiety disorder diagnosis. Approximately half (51.3%) of these subjects had two or more anxiety disorders. The mean age of onset for social phobia was 11.0 ($SD = 6.8$), specific phobia 14.3 ($SD = 11.2$), obsessive-compulsive disorder 18.5 ($SD = 11.3$), generalized anxiety disorder 19.2 ($SD = 13.9$), posttraumatic stress disorder 21.2 ($SD = 14.5$), panic disorder with agoraphobia 24.5 ($SD = 12.5$), panic disorder 28.5 ($SD = 14.6$), agoraphophobia without history of panic 29.1 ($SD = 19.0$), and acute stress disorder 33.4 ($SD = 11.4$). Of

those subjects with more than one anxiety disorder, social phobia was most likely to have emerged first (33.5% of the time), and approximately 25% of comorbid subjects placed the onset of at least two of their anxiety disorders at the same age.

Conclusions: There appears to be a range of ages at which anxiety disorders first manifest themselves and social phobia on average seems to emerge the earliest.

NR246 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Combined Effects of Pharmacotherapy and Cognitive-Behavior Therapy in Treating OCD

David M. Direnfeld, M.A., *Community Mental Health Center, Buffalo General Hospital, 80 Goodrich Street, Buffalo, NY 14203;* Michele T. Pato, M.D.

Summary:

Objective: To examine the additive effect of exposure and ritual prevention (EX/RP) to an adequately medicated sample of individuals with obsessive-compulsive disorder (OCD). In addition, to determine if the combined treatment confers an advantage beyond that of medication alone.

Method: A total of 38 individuals with OCD were provided with EX/RP adjuvant treatment, delivered in a group format, following an adequate trial (≥8 weeks) of a SRI. OC severity, assessed using the Yale-Brown Obsessive-Compulsive Scale (YBOCS), was measured before and after EX/RP treatment. A sub-sample (n = 23) had OC severity assessed before starting medication, in addition to EX/RP treatment.

Results: EX/RP lead to a significant improvement in YBOCS scores (17% reduction) in individuals who had an adequate trial of a SRI, with 34% (13) achieving a treatment response (≥25% improvement in YBOCS scores). In the sub sample (n = 23), a significant improvement in YBOCS scores (15% reduction) was obtained following an adequate trial of a SRI, with 17% (4) achieving a treatment response (≥25% improvement). When EX/RP was added, patients experienced an additional significant improvement in YBOCS scores (20% reduction), with 61% (14) achieving a treatment response (≥25% improvement). The combined treatments resulted in an overall improvement of 32% in YBOCS scores, with 74% (17) achieving a treatment response (≥25% improvement).

Discussion: These results demonstrate that adding EX/RP as an adjuvant to pharmacotherapy not only adds significantly more improvement, but also increases the likelihood that an individual will be considered a treatment responder. It appears that the additive treatment (74% treatment responders) of EX/RP was more efficacious for more people than the mono-therapy of SRIs. Furthermore, it is noteworthy that the behavior therapy was provided in an efficient and cost-effective group setting rather than the more traditional individual treatment.

NR247 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Subthreshold PTSD: Impairment and Comorbidity

Randall D. Marshall, M.D., *Anxiety Disorders, NY State Psychiatric Institute, 1051 Riverside Drive, Unit 69, New York, NY 10032;* Mark Olfson, M.D., Fred Hellman, B.S., Carlos Blanco, M.D., Mary T. Guardino, B.A., Elmer Struening, Ph.D.

Summary:

Objective: PTSD, like major depression, is a common disorder associated with high disability and comorbidity. Unlike the depressive disorders, however, very little is known about subthreshold symptoms in PTSD. This study investigates subthreshold PTSD in a large community sample.

Method: On National Anxiety Disorders Screening Day 1997, 9184 individuals were screened for affective and anxiety disorders (including PTSD) at 1521 U.S. sites. A total of 2607 individuals reported at least one PTSD symptom persisting > one month. Impairment, rates of comorbid disorders, and suicidality were examined and compared (MANOVA) for each subthreshold score.

Results: Impairment, number of comorbid disorders, comorbid major depression, and suicidal ideation all increased significantly with number of subthreshold PTSD symptoms. For each additional symptom (1–4, respectively), number of comorbid anxiety disorders were 1.7, 2.0, 3.2, and 3.7; percentage of subjects with comorbid major depressive disorder increased from 56%, 70%, 80%, to 88%; percent with current suicidal ideation increased from 13%, 15%, 23%, to 33% (ANOVA $p < .0001$).

Conclusions: Subthreshold PTSD, almost entirely neglected to date, is associated with significant impairment and comorbidity. Such findings significantly broaden the scope of public health concern regarding posttraumatic symptoms. Screening for both full and subthreshold PTSD is important to identify individuals in need of services.

NR248 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Controlled Trial of Paroxetine in Chronic PTSD

Randall D. Marshall, M.D., *Anxiety Disorders, NY State Psychiatric Institute, 1051 Riverside Drive, Unit 69, New York, NY 10032;* Franklin R. Schneier, M.D., Blair Simpson, M.D., Carlos Blanco, M.D., Katherine L. Beebe, Ph.D., Michael R. Liebowitz, M.D.

Summary:

Practice guidelines for the treatment of PTSD recently recommended SSRIs as a first-line medication treatment. This presentation discusses interim results of an ongoing double-blind, placebo-controlled trial of paroxetine for chronic PTSD. To date, 44 adults have been randomized, with independent evaluator ratings conducted at weeks 0,5, and 10, and analyses conducted on N = 30 patients (at least five weeks' treatment). Responders were defined by a Global Improvement rating of 1 (very much improved) or 2 (much improved). Chi-square analysis demonstrated significantly different response rates between the paroxetine (11/16, 68%) versus placebo (4/14, 28%) groups (chi square = 4.82, p = .028). On the Clinician Administered PTSD Scale (CAPS), total score was reduced 25.1 for paroxetine vs 8.5 for placebo (from 79.8 and 76.9, respectively). Similarly, random regression analyses were significant for reduction from baseline for paroxetine (slope −2.56, SE .772, p = .003) but not placebo (slope −1.08, SE 0.876, p = .227). Repeated measures ANOVA showed a significant treatment by time interaction for the week 0 to week 5 (F = 4.11, p = .05), but not week 5 to week 10 (F = .303, p = NS). Between-group effects were not significant but power is insufficient at this sample size.

Conclusion: Findings from this interim analysis of data from a small sample size are consistent with promising open trial findings, and suggest that paroxetine is effective in ameliorating the symptoms of PTSD.

NR249 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Fluoxetine in Panic Disorder: A Randomized, Placebo-Controlled Study

David Michelson, M.D., *Dept. of Neuroscience, Eli Lilly and Company, Lilly Corporate Center DC 0721, Indianapolis, IN 46285;* Neena Sarka, Ph.D., Craig Pemberton, B.S.

Summary:

Objective: Only one previous study has been reported assessing the efficacy of fluoxetine in panic disorder under double-blind, placebo-controlled conditions. The current study was de-

signed to provide further information concerning the efficacy of fluoxetine in this disorder.

Methods: Patients meeting DSM-IV criteria for panic disorder with at least two full panic attacks during a two-week evaluation were randomized to fluoxetine (initiated at 10 mg/day for the first week) 20–60 mg daily (N = 90) or placebo (N = 90) and evaluated biweekly for 12 weeks in a multicenter study conducted in Europe. The protocol-defined primary outcome measure was the percentage of panic-free patients in the final visit interval at endpoint.

Results: At endpoint, more patients receiving fluoxetine were panic-free compared with patients receiving placebo (fix 42%, pla 28%, p = 0.02). Mean reductions in CGI severity, HAM-A, State Anxiety Inventory, and Sheehan work and social impairment scores were also statistically significantly greater among fluoxetine-treated patients. The median final dose was 20 mg. Overall numbers of adverse events were similar between both treatment groups.

Conclusion: Fluoxetine is efficacious and well-tolerated in the treatment of panic disorder.

NR250 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Valproic Acid in Panic Disorder: A Study in Fluvoxamine-Refractory Patients

Antonio E. Nardi, M.D., *Department of Psychiatry, Federal Univ. Rio de Janeiro, R. Visconde de Piraja, 407/702, Rio de Janeiro 22410-003, Brazil*

Summary:

Valproic acid, an anticonvulsant that increases GABAergic transmission, was openly evaluated in panic disorder outpatients who were non-responders to fluvoxamine. Thirty-seven patients with panic disorder (DSM-IV) were openly treated for three months with fluvoxamine (300mg/day). Twelve patients (32.4%) were considered non-responders. After two-week placebo wash-out they were treated openly with valproic acid. The main efficacy measure—number of panic attacks—was obtained throughout the trial. The patients had a diary from which weekly data were taken after investigator review. After eight weeks of treatment panic attacks were reduced 65% from baseline. Seven patients (58.3%) were completely free of panic attacks. No relationship was observed between efficacy and valproic acid concentration. The mean dose was 1,724 ± 67 mg daily. The most frequent side effects were headache (41.7%), nausea (41.7%), and decreased libido (16.7%). Valproic acid was found to be statistically and clinically effective antipanic agent in fluvoxamine-refractory panic disorder patients.

NR251 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

OCD and Comorbid Disorders in Rheumatic Fever Patients

Pedro G. Alvarenga, *Department of Psychiatry, Psychiatric Institute, Rua Ovidio Pires de Campos SN, Sao Paulo, SP 05403-010, Brazil;* Lisia G. Prado, Marcos T. Mercadante, M.D., Max Grimberg, Ana G. Hounie, M.D., Juliana B. Diniz, Euripedes C. Miguel, M.D.

Summary:

Background: Previous studies have demonstrated a higher prevalence of OCD and related disorders (OCD, OC symptoms, tic disorders and attention deficit hyperactive disorder) in children with acute onset of RF.

Methods: Thirty adult patients with past history of RF and 27 controls were assessed. The major depressive disorder and generalized anxiety disorder components from the Structured Clinical Interview for DSM-IV were used. ADHD was assessed using the Schedule for Affective Disorders and Schizophrenia Epidemiological Edition. The Yale Global Tic Severity Scale, Yale Brown Obsessive Compulsive Scale, and Beck Depression and Anxiety Inventories were also used.

Results: We found a higher prevalence of obsessive-compulsive symptoms (46%) and motor tics (16%) in the RF group when compared with controls (p = 0.02; p = 0.03, respectively). Four of the five patients with motor tics (RF group) had concomitant OCS.

Conclusion: Adults with past history of RF present with higher prevalence of OCS and tics, isolated or in combination. This finding suggests that if this symptoms are associated to RF, they are not necessarily related to an acute rheumatic episode, being also found in remission states.

NR252 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Evaluation of Hydroxyzine in the Treatment of GAD

Christian Spadone, M.D., *Department of Psychiatry, Saint Anne Hospital, 1 Rue Cabanis, Paris 75014, France;* Pierre M. Llorca, M.D., Olivier Sol, M.D., Emmanuelle Corruble, M.D., Dominique Servant, M.D., Thierry Bougerol, M.D., Jean-Paul Macher, M.D.

Summary:

Objective: Evaluation of the efficacy and safety of hydroxyzine (50 mg/day) in outpatients suffering from generalized anxiety disorder according to DSM-IV classification.

Methods: French, multicenter, parallel, randomized, double-blind, placebo-controlled, and versus bromazepam (6 mg/day) trial including two weeks of single-blind, run-in placebo, 12 weeks of double-blind randomized treatment, and four weeks of single-blind, run-out placebo. A total of 334 out of 369 selected outpatients were randomized before entering the double-blind period. The primary outcome criterion was the evolution of the Hamilton-Anxiety Scale score from baseline to 12 weeks of double-blind treatment with hydroxyzine compared with placebo.

Results: In the intent-to-treat analysis, the evolution of the mean scores from baseline to endpoint was −12.16 ± 7.74 for hydroxyzine and −9.64 ± 7.74 for placebo (p = 0.019). Results of responder and remission rates, CGI-1, HAD, and efficacy maintenance also confirmed the efficacy of hydroxyzine over placebo (p < 0.03). The study did not show any statistically significant difference between hydroxyzine and bromazepam.

Except for drowsiness, more frequent with bromazepam, safety results were comparable in the three groups.

Conclusion: Hydroxyzine showed both efficacy and safety in the treatment of generalized anxiety disorder and appears as an effective alternative treatment to benzodiazepine prescription.

NR253 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Paroxetine Treatment of GAD: A Double-Blind, Placebo-Controlled Trial

Kevin M. Bellew, B.S., CNS, *Smith, Kline and Beecham, 1250 South Collegeville Road, Collegeville, PA 19426;* James P. McCafferty, B.S., Malini Iyengar, M.D., Rocco M. Zaninelli, M.D.

Summary:

Method: This was a multicenter study in adults who met DSM-IV criteria for generalized anxiety disorder (GAD). Excluded were patients with a current diagnosis of major depression or an Axis I anxiety disorder other than GAD. For inclusion, candidates were required to have a HAM-A score ≥20 and a MADRS score <18. Qualified patients were randomized to receive either paroxetine 20 mg/day, paroxetine 40 mg/day, or placebo for eight weeks. Efficacy and safety assessments were carried out weekly. The protocol identified a single primary outcome measure, the change in Total HAM-A score. The secondary measures included clinical

global impression in severity of illness and improvement scores, as well as the anxiety and tension items from the HAM-A.

Results: The study enrolled 566 patients, average age was 42, 56% were females. Over 75% completed eight weeks of treatment. Compared with placebo, paroxetine produced a statistically significant reduction in the total HAM-A score that was corroborated by results seen in the secondary measures. Based on the proportion of responders (CGI improvement score of 1 or 2), the effect is dose dependent.

Mean Change (SE)	Placebo	20 mg	40 mg
N	140	143	143
HAM-A Total	-10.7 (0.7)	-13.8 (0.6)[44]	-13.9 (0.6)[44]
HAM-A Anxiety Item	-1.1 (0.1)	-1.6 (0.1)[44]	-1.6 (0.1)[44]
HAM-A Tension Item	-1.0 (0.1)	-1.5 (0.1)[44]	-1.7 (0.1)[44]
CGI Severity Score	-1.1 (0.1)	-1.8 (0.1)[44]	-1.8 (0.1)[44]
Responders	52%	68%[4]	81%[44]

[4]$p < 0.01$ [44]$p < 0.001$

Conclusion: Paroxetine is an effective treatment in patients with GAD who do not have comorbid major depression.

NR254 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

OCD with History of Rheumatic Fever: A Different Subtype?

Juliana B. Diniz, Department of Psychiatry, Psychiatric Institute, R Dr Ovidio Pires de Campos SN, Sao Paulo, SP 05403-010, Brazil; Priscila Chacon, Maria C.R. Rosario-Campos, M.D., Helena Prado, Ana G. Hounie, M.D., Roseli G. Shavitt, M.D., Euripedes C. Miguel, M.D.

Summary:

Background: OCD is an heterogeneous disorder with different possible subtypes. A hypothetical subtype may be related to Rheumatic Fever (RF). In this study, 13 OCD plus RF patients (found by clinical history) were compared with 63 OCD patients without RF seen consecutively in our Clinic.

Methods: Patients were assessed using a Structured Interview for DSM-IV (SCID; KID-SADS), Yale Global Tic Severity Scale, Yale Brown Obsessive-Compulsive Scale, Beck Depression and Anxiety Inventories, and USP-HARVARD Repetitive Behavior Interview assessing sensory phenomena (SP) preceding their compulsive behaviors.

Results: We found a higher frequency of co-morbidities in the OCD plus RF group ($p = 0.04$), including Body Dismorphic Disorder (BDD) ($p = 0.02$). Although without statistical differences, 10 (77%) patients with OCD plus RF had an early onset (age < 10) of their OCS (mean = 11) compared with 29 (46%) in the group of OCD without RF (mean = 7.5); 12 (92%) had SP, and five (38.5%) had Tic Disorders.

Conclusion: Patients with OCD and RF tend to have a higher number of comorbidities, including BDD,Tic disorders, early onset and SP, similar to what was described previously in OCD patients with an early onset. More studies are necessary to determine if these patients have a different prognosis and response to treatment.

NR255 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

The Efficacy of Sertraline in Panic Disorder: A Combined Fixed-Dose Analysis

Javaid I. Sheikh, M.D., *Department Of Psychiatry, Stanford University, Stanford School of Medicine, Stanford, CA 94305-5546;* Peter D. Londborg, M.D., Cathryn M. Clary, M.D.

Summary:

Objective: Sertraline has demonstrated efficacy in the treatment of panic disorder in daily doses ranging from 50–200 mg. To have sufficient power to assess whether there is a dose-response relationship for the efficacy and tolerability of sertraline in panic disorder, with or without subsyndromic depression, a condition commonly seen comorbidly with panic disorder in clinical practice, data from two fixed-dose studies were pooled and analyzed.

Methods: The current investigation combined results from two identical 12-week, double-blind, fixed dose studies of sertraline conducted in males and non-fertile females who met DSM-III-R criteria for moderate-to-severe panic disorder and comparing placebo with three fixed daily doses of sertraline (50 mg, 100 mg, or 200 mg). Outcome was assessed by a conservative endpoint (LOCF) analysis of frequency of major or limited symptom panic attacks, change in panic burden (attack frequency X severity), CGI-improvement, as well as the effect on outcome of mild-to-moderate levels of subsyndromic depression.

Results: A total of 82 patients were randomized to placebo (67% male; mean age, 38 yrs; 49% with agoraphobia; mean weekly panic attack frequency, 11.8); vs. 240 patients randomized to the three doses of sertraline (60% male, mean age, 40 yrs; 51% with agoraphobia; mean weekly panic attack frequency, 9.7). There were no significant differences in baseline values among the three sertraline dose levels. All 3 sertraline dose levels demonstrated significant efficacy compared to placebo, with no consistent evidence of a dose-response effect. For the subset of patients with subsyndromic depression at baseline, sertraline yielded a significantly higher panic-free rate compared to placebo ($p = 0.021$) at LOCF endpoint. Finally, sertraline was well-tolerated at all dose levels, with no significant between-dose differences in patients discontinuing due to adverse events.

Conclusions: 50 mg of sertraline demonstrated equivalent anti-panic efficacy to 100 mg and 200 mg doses, and all doses were well-tolerated.

NR256 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Pregabalin Treatment of Social Phobia

Douglas E. Feltner, M.D., *CNS Clinical, Parke-Davis, 2800 Plymouth Road, Ann Arbor, MI 48105;* Mark H. Pollack, M.D., Jonathan R.T. Davidson, M.D., Murray B. Stein, M.D., Rise A. Futterer, M.D., James W. Jefferson, M.D., R. Bruce Lydiard, M.D.

Summary:

Objective: To assess the safety and efficacy of pregabalin, a novel anxiolytic, for the treatment of social phobia, generalized type.

Methods: A total of 135 patients were randomized to 11 weeks of double-blind treatment with either low-dose pregabalin (150mg/day, n = 42), high-dose pregabalin (600mg/day, n = 47), or placebo (n = 46) given TID. The primary efficacy parameter was change from baseline to endpoint in the Liebowitz Social Anxiety Scale (LSAS) total score. Safety was assessed through clinical and laboratory monitoring and recording spontaneously reported adverse events.

Results: LSAS total score was significantly decreased by high dose pregabalin treatment compared with placebo ($p = 0.024$, ANCOVA). Significant differences ($p \leq 0.05$) between high-dose pregabalin and placebo were seen on several secondary measures. Low-dose pregabalin showed numeric superiority over placebo on several measures, but was not significantly better than placebo on any. Improvement for high dose pregabalin was comparable to other recently published U.S. multicenter trials of effective compounds, was evident by the end of one week of treatment, and continued to the end of the study. Somnolence and dizziness were the most frequently occurring adverse events among high dose pregabalin patients.

Conclusions: In this study, pregabalin (600 mg/day) was an effective and safe treatment for social phobia.

NR257 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Effect Size As a Measure of Specific Activity of Venlafaxine Extended Release in the Treatment of GAD

Paolo Meoni, Ph.D., *CNS, Wyeth Ayerst, 80 Avenue du General de Gaulle, Paris la Defense 92031, France;* David Hackett, M.S.C., Yves Brault, Eliseo Salinas, M.D.

Summary:

Objective: To determine the symptom-specific activity of venlafaxine XR in the treatment of generalized anxiety disorder (GAD).

Method: Itemized effect sizes of the Hamilton Anxiety Rating (HAM-A) scale were obtained from outpatients with GAD (DSM-IV) evaluated in five double-blind, placebo-controlled studies of similar design, comparing venlafaxine XR (n = 1289, at doses ranging from 37.5 to 225 mg/day) with placebo (n = 540). An effect size cut-off of 1 (ES^1) was used to characterize the items with the largest changes from baseline (LOCF), while a cut-off of the difference in effect sizes of 0.3 ($ES_{diff0.3}$) between drug and placebo was used to characterize drug specific changes.

Results: At week 8, placebo treatment produced no ES^1. Venlafaxine XR treatment produced an ES^1 for the HAM-A items 1 (Anxious mood), 2 (Tension), and 14 (Behavior at interview). Venlafaxine XR showed an $ES_{diff0.3}$ at week 8 for items 1, 2, and 6 (Depressed mood) and at month six for items 1, 2, 4, (Insomnia), 5 (Cognitive), 6, and 14. These correspond closely to the diagnostic symptoms for GAD.

Conclusion: The efficacy of venlafaxine XR in the treatment of GAD is characterized over the range of anxiety specific symptoms.

NR258 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Quality-of-Life Improvement in PTSD with Sertraline Treatment: Results of a Multicenter, Placebo-Controlled Trial

Mark H. Rapaport, M.D., *Department of Psychiatry, UCSD School of Medicine, 8950 Villa La Jolla Dr, #2243, La Jolla, CA 92037;* Phebe M. Tucker, M.D., Gail M. Farfel, Ph.D., Cathryn M. Clary, M.D.

Summary:

Objective: Previous research has shown that PTSD impairs quality of life (QOL) more than does MDD or OCD, but that SSRIs such as sertraline or fluoxetine improve QOL/functional status with short-term treatment.

Method: Data from a previously reported multicenter, randomized, placebo-controlled, 12-week trial of sertraline 50-200 mg (starting dose 25 mg; N = 187) with DSM-III-R chronic PTSD were utilized to assess QOL at baseline and end of study. Assessments include the Quality of Life Enjoyment and Satisfaction Questionaire (Q-LES-Q), questions from the Medical Outcomes Study (MOS) SF 36 and other QOL items, as well as investigator and subject-rated PTSD symptom scales, including the CAPS-2, IES, Davidson Trauma Scale, and CGI-S and CGI-I.

Results: QOL and functional status as assessed by the Q-LES-Q was significantly impaired at baseline in both groups (54.5 ± 11.2; 57.4 ± 13.4 in sertraline/pbo, respectively), with the sertraline subjects showing statistically superior improvement to placebo subjects at ITT endpoint (11.7 ± 2.1; 3.3 ± 1.9 in sert/pbo, respectively). Other QOL assessments and results on the Q-LES-Q subscales confirmed this finding and will be presented, as well as correlations between the Q-LES-Q, MOS and PTSD symptom scales at baseline/endpoint. Responders to sertraline in PTSD specific symptom scales showed significantly more improvement in QOL than placebo responders ($p < 0.05$ on 3 responder criteria).

Conclusion: Acute sertraline treatment of chronic PTSD is associated with significant improvements in quality of life.

NR259 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

A 24-Week Prevention of Relapse of Generalized Social Phobia Study in Responders to 20 Weeks of Sertraline Treatment

John R. Walker, Ph.D., *Department of Psychology, St. Boniface Hospital, 409 Tache Avenue, Winnipeg, MB R2H 1W2, Canada;* Michael A. Van Ameringen, M.D., Richard P. Swinson, M.D., Roger M. Lane, M.D.

Summary:

Objective: Demonstrate the efficacy and tolerability of sertraline in the prevention of relapse of generalized social phobia (GSP).

Method: Fifty adult GSP patients with CGI-I much or very much improved after 20 weeks sertraline treatment (50–200 mg/day) were randomized double-blind in 1:1 ratio to continue sertraline or switch to placebo for 24 weeks. Primary efficacy assessments; number relapsing (CGI-S) increase of >2 points over continuation baseline and/or discontinuation for lack of efficacy (LOE); CGI-I 1 or 2; mean score changes from continuation baseline on CGI-S, social phobia sub-scale of Marks Fear Questionnaire (MFQ), and Duke Brief Social Phobia Scale (BSPS) at study endpoint.

Results: In ITT, LOCF analyses 1/25 (4%) in sertraline group and 9/25 (36%) in placebo-switch group had relapsed at study endpoint ($p = 0.01$). Mean CGI-S, MFQ social phobia subscale, and BSPS total scores were reduced by 0.07, 0.34, and 1.86 in the sertraline group and increased 0.88, 4.09, and 5.99 in the placebo-switch group ($p < 0.03$), respectively. There was no significant difference in CGI-I responders. Eighty-eight percent of sertraline and 40% of placebo-switch patients completed the study. Discontinuations for LOE were 4% in sertraline and 28% in placebo-switch ($p < 0.05$).

Conclusions: Sertraline is effective in preventing relapse in GSP.

NR260 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Is the DSM-IV Criteria of 13 Panic Symptoms Valid for Japanese Patients?

Hisanobu Kaiya, M.D., *Imon Nagoya Building, Panic Disorder Research Center, 1-16 Tsubakicho Nakamuraku, Nagoya 453-0015, Japan;* Natsuko Kaiya, Shin Yasuda, M.D., Seiji Harata, M.D., Noriya Ishida, M.D., Isao Kitayama, M.D.

Summary:

Three-hundred eighty-three Japanese patients who fulfill the DSM-IV criteria for panic disorder or have had limited symptom attacks were included in the present study. They were asked if, in the first panic attack, they had experienced 13 panic symptoms in the DSM-IV criteria and an additional nine other symptoms. When patients experienced symptoms other than those stated, they were asked to describe the concrete symptoms. To mention the most frequent symptoms in order: palpitation (89%); feeling of choking (74%); fear of dying (55%); fear of losing control or going crazy (52%); sweating (49%); feeling dizzy, unsteady, lightheaded, or faint (49%); trembling or shaking (48%); sensation of shortness of breath or smothering (47%); nausea or abdominal distress (33%); derealization or depersonalization (32%); thirst (31%); chest pain or discomfort (29%); paresthesias (28%); chills or hot flushes (25%); feeling paralyzed (19%); blurred vision (16%); headache (14%); tinnitus (13%); urination (12%); urge to have bowel movement (10%); grasping and pulling feeling of stomach (6%); and nasal congestion (0.8%). These results show that chills or hot flushes are replaced by thirst in Japanese patients. In the meeting, we will report more detailed analysis of the data.

NR261 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

A Comparison of the Activity of Central and Peripheral Chemoreceptors in Panic Disorder Patients and Healthy Volunteers

Martin A. Katzman, M.D., *Anxiety Clinic, Clarke Institute-CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada;* Lukasz M. Struzik, B.S.C., Nishka Vijay, Aimee M. Coonerty-Femiano, B.A., Safraaz Mahamed, B.S.C., James Duffin, Ph.D.

Summary:

Introduction: Klein (1993) has suggested that panic disorder patients possess a false suffocation alarm that may be associated with a lowered threshold for carbon dioxide detection. We compared the thresholds and sensitivities of the central and peripheral chemoreflexes between panic disorder patients and age- and sex-matched healthy volunteers to test this hypothesis.

Method: We used a modified version of Read's rebreathing technique to examine the peripheral and central chemoreflex characteristics in these two populations. Subjects were examined during three rebreathing tests: training, hyperoxic (central chemoreflex alone) and hypoxic (combined central and peripheral chemoreflex).

Results: Preliminary comparisons between five panic disorder patients with agoraphobia and five healthy volunteers showed no significant differences in sensitivities or thresholds. However, the thresholds for panic disorder patients were lower than those of the volunteers for both the hypoxic and hyperoxic rebreathing tests.

Conclusion: Although Klein's hypothesis is not supported by these data, the sample size is too small to allow a definitive conclusion. Further experimentation should reveal whether the current trends in chemoreflex thresholds reaches statistical significance and if sensitivities are also different.

NR262 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

A Dose-Finding and Discontinuation Study of Clomipramine in Panic Disorder

Francisco Lotufo-Neto, M.D., *University of Sao Paulo, Rua Oliveira Dias 345, Sao Paulo, SP 01433-030, Brazil;* Marcio A. Bernik, M.D., Renato Ramos, M.D., Laura Andrade, M.D., Clarice Gorenstein, Ph.D., Taki Cordas, M.D., Valentim Gentil, M.D.

Summary:

Eighty-one panic disorder patients with or without agoraphobia were treated with flexible doses of clomipramine under single-blind conditions. Fifty-seven (70.3%) reached operational criteria for full remission in 16.2 ± 6.5 weeks, with a mean dose of 89.1 ± 8.2 mg/day. Fifty-four (81%) of them received a continuous post-remission maintenance treatment at full doses of clomipramine for four to six months. No patient relapsed during the clomipramine maintenance phase. Their medication was then tappered and discontinued with placebo substitution under double-blind conditions. Fifty-one (63%) patients were followed up until relapse or recurrence for up to three years, with periodic assessments. Three different outcome groups were identified: the first (n = 19, 19; 37.2%) experienced an early/immediate relapse (5.2 ± 4.9 weeks after drug discontinuation); the second group (n = 22, 22; 43.1%) experienced recurrence after 42.9 ± 35 weeks following discontinuation; and the third group (n = 10, 10; 19.6%) remained assymptomatic and functionally well throughout the follow-up. Predictors of early relapse were discussed.

NR263 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Dimensional Personality Models and the Anxiety and Depression Interface

Francisco Paez, M.D., *Clinical Research Department, F. Bernardino Alvarez Psychiatric Hospital, AV San Fernando y Nino Jesos S/N, Mexico City, DF 14000, Mexico;* Rebeca Robles, M.Psy.

Summary:

To determine the differences and shared variances between three dimensional personality models and pure forms of depression and anxiety disorders, comorbid forms and mixed anxiety and depression (MAD) disorders as well as dimensional measures of symptoms, 292 patients consecutively evaluated at the Fray Bernardino Alvarez Psychiatric Hospital in Mexico City were studied. A control group of 132 subjects were also studied Diagnoses were assigned using the SCID for DSM-IV diagnosis. Patients answered Cloninger's temperament and character inventory, Eynseck's personality questionnaire, Watson and Clarck's positive and negative affect scale, and Becks anxiety and depression inventories. Reliability of translated versions were properly evaluated.

Results: 185 (63.3%) had a pure mood disorder (PMD), 37 (12.6%) a pure anxiety disorder, 23 (7.8%) comorbid Anxiety-depression disorders (CAD), and 47 (16.1%) MAD. Positive and negative affect scores were significantly lower for DM and MAD groups compared with controls. Eysenck's neuroticismo scale was significantly lower in all categories. Cloninger's harm avoidance scale differed in all diagnosis against controls mut MAD also differed against CAD forms. The combinations of these scales explained 60% of the variance of depressive symptoms and 30% of anxiety symptoms.

Conclusion: some evidence supports MAD as a distinctive disorder.

NR264 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Pharmacotherapy of BDD: A Chart-Review Study

Ralph S. Albertini, M.D., *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906;* Katharine A. Phillips, M.D., Ajaz Khan, M.D., Marshall Robinson, M.A.

Summary:

Background: Body dysmorphic disorder (BDD) is a distressing, impairing, and relatively common disorder. However, research on its pharmacotherapy is very limited. No placebo-controlled studies, and no maintenance, continuation, or discontinuation studies have been done. Only one open-label augmentation study has been published.

Methods: This chart review study included 92 outpatients with DSM-IV BDD treated for up to more than eight years by the first or second author in their clinical practice. Response to a variety of medications, and the relapse rate with medication discontinuation, were determined using standard rating scales.

Results: All subjects received psychotropic medication, with a total of 178 adequate medication trials (2.0 ± 1.7, range = 0–7 adequate trials per subject). All subjects received an SRI, with 1.4 ± .8 (range = 0–5) adequate SRI trials per subject. A total of 63.8% (n = 58) of adequate SRI trials resulted in improvement in BDD symptoms, with similar response rates for each type of SRI. Of those subjects who failed an initial adequate SRI trial, 38.5% responded to at least one subsequent adequate SRI trial. Discontinuation of an effective SRI resulted in relapse in 83.4% (n = 31) of cases. Response rates to SSRI augmentation were as follows: clomipramine, 44% (n = 4) of trials; buspirone, 33% (n = 12) of trials; and neuroleptics, 15% (n = 2) of trials.

Conclusions: These findings from a clinical setting suggest that a majority of BDD patients improve with an SRI and that all SRIs

appear effective. Certain SRI augmentation strategies may be beneficial. The high relapse rate with SRI discontinuation suggests that long-term treatment is often necessary. These preliminary findings require confirmation in placebo-controlled efficacy studies and in effectiveness studies.

NR265 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Personality and Mood Characteristics of Female Athletes

Karyn E. Hood, M.Ed., *Anxiety Clinic, CAMH-Clarke Division, 250 College Street, Room 1109, Toronto, ON M5T 1R8, Canada;* Martin A. Katzman, M.D.

Summary:

Introduction: Performance variables such as competition anxiety and motivation have been extensively researched in the sports psychology literature. Measures assessing personality dimensions like anxiety sensitivity, worry, perfectionism and mood disturbances however, have been largely overlooked.

Objective: In the current study, we examined personality traits of female athletes on an elite women's athletic team, and their relationship to mood and eating disorders.

Method: Twenty-five members (aged 19 to 28) completed several self-report measures including the Anxiety Sensitivity Inventory (ASI), Penn State Worry Questionnaire (PSWQ), Dysfunctional Attitudes Scale (DAS), Frost Multidimensional Personality Scale (MPS-F), Beck Depression Inventory (BDI-II), and the NEO Personality Inventory-Revised (NEO-PI-R).

Results: Preliminary analyses revealed mean ASI scores for the team in the moderate range, but above what would be expected from a non-clinical population. Significant score elevations were observed on the concern over mistakes, doubts about actions, and personal standards subscales of the MPS-F. Elevations were also noted on the DAS need for approval subscale, but not on the DAS perfectionism subscale. Additional personality data from the NEO-PI-R data will be presented.

Conclusion: Elevations in anxiety sensitivity and perfectionism may represent core features of elite athletes. However, these attributes may also put them at an elevated risk for psychopathology including depression, anxiety and eating disorders.

NR266 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Gabapentin in PTSD: Effects on Sleep Disturbances

Mark B. Hammer, M.D., *Department of Psychiatry, Ralph H. Johnson, 109 Bee Street, #116A, Charleston, SC 29401-5703;* Lawrence A. Labbate, M.D., Jeffrey P. Lorberbaum, M.D., Helen G. Ulmer, M.S.N., Clare Tyson, B.S., Charlotte C. Teneback, B.S.

Summary:

Objective: Insomnia, nightmares, and other sleep disturbances are common symptoms in PTSD. Although many PTSD symptoms improve significantly with antidepressant medications, sleep difficulties are often refractory. Gabapentin, indicated for adjunctive treatment of partial complex seizure disorders, has been of interest in psychiatry as a potential mood stabilizer and anxiolytic agent (possibly via increased brain levels of GABA). The agent also has a relatively benign drug interaction and side effect profile.

Method: We reviewed records of 23 patients meeting DSM-IV criteria for PTSD associated with combat, diagnosed in a multidisciplinary PTSD clinic. Gabapentin was added to the existing medication regimens of patients who had continued sleep disturbances. The dose of gabapentin ranged from 300–900mg, generally given at bedtime.

Results: All patients were noted to have moderate or greater improvement in duration of sleep and most noted a decrease in the frequency of nightmares. Sedation and mild dizziness were the only reported side effects.

Conclusions: This preliminary retrospective series suggests that gabapentin may be efficacious for sleep difficulties associated with chronic PTSD. Controlled studies are needed to further explore this clinical observation and to investigate effects of gabapentin on core PTSD symptoms.

NR267 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

The Cognitive Burden of Lewy Bodies

Michael J. Serby, M.D., *Department of Psychiatry, The Mount Sinai Medical Center, 1 Gustave L Levy Pl Box 1230, New York, NY 10029;* Adam M. Brickman, B.A., Vahram Haroutunian, Ph.D., Dushvant P. Purohir, M.D., Kenneth L. Davis, M.D.

Summary:

Introduction: We recently demonstrated a significant correlation between degree of dementia and the number of Lewy bodies present in brain. We now present data that underscore this relationship further.

Methods: We compared three groups of patients from a well-characterized nursing home population (the Jewish Home and Hospital [JHHA]): definite AD (by autopsy; n = 49), Lewy body variant (LBV) of AD (n = 16), and pure Lewy body dementia (LBD; n = 10).

Results: The three groups did not differ in age at admission to the nursing home (AD group = 85.8 ± 8.0 years; LBV = 82.7 ± 7.2; LBD = 84.6 ± 7.8), age at death (AD = 89.4 ± 8.9; LBV = 86.3 ± 7.8; LBD = 85.2 ± 6.7), total time in the nursing home (AD = 3.6 ± 3.2; LBV = 3.6 ± 2.5; LBD = 3.2 ± 2.9) or gender ratios.

Despite these similar clinical pictures, the groups differed on Clinical Dementia Rating (CDR) scores. The LBV group had a mean CDR (4.25 ± 1.13) which was worse than either AD (3.2 ± 1.44) or LBD (3.0 ± 1.6) (between groups ANOVA significant at .025 level). There was a significantly greater number of Lewy bodies in LBV than in LBD brains ($p < .001$).

Discussion: It appears that the co-occurrence of AD and Lewy body pathology is associated with higher numbers of Lewy bodies and greater dementia than when classical AD or Lewy body lesions occur alone. It is unclear why brains with AD pathology would have more Lewy bodies. In this regard, it is interesting to note the high prevalence of parkinsonism as AD progresses, and the overlapping risk factors for AD and LBD. These two pathological states may interact at molecular levels in ways that are undefined currently.

NR268 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Serum Melanotranferrin, P97 in Alzheimer's Disease

Min-Kyung Seo, M.S.W., *Samsung Medical Center, #50 Kanngnami-Gu Ilwon-Dong, Seoul, Korea;* Doh-Kwan Kim, Sang-Sun Kang, Shin-Won Lim, Seonwoo Kim, Jong-Won Kim, Bernard J. Carroll, M.D.

Summary:

Objective: A biomarker of Alzheimer's disease (AD) has not been developed for clinical use. We investigated whether serum concentrations of the melanotransferrin (p97) could be useful in diagnosis.

Method: We measured serum p97 concentrations and apolipoprotein E (ApoE) allele genotype in 211 subjects: 71 patients with AD, 56 patients with non-AD-type dementia, and 84 normal control subjects.

Results: Age-adjusted serum p97 concentrations were elevated in patients with AD(13.69 ± 4.16 pg/μl) compared with patients

with non-AD dementia (4.54 ± 3.99 pg/μl) or normal subjects (3.58 ± 1.99 pg/μl). These group differences were highly significant (p = 0.0001). Serum p97 concentrations were significantly elevated even in early AD, but were not significantly related to the degree of dementia. The optimal serum p97 concentration to distinguish AD was 10.0 pg/μl. By age-adjusted analysis in the total sample, this threshold yielded sensitivity 0.915, specificity 0.914, overall accuracy 0.915. By analysis without age adjustment in demented patients only, this threshold yielded sensitivity 0.901, specificity 0.857, overall accuracy 0.882. Serum p97 concentrations did not differ among the ApoE genotypes or in the presence of the ϵ4 allele.

Conclusion: An elevated serum p97 concentration may represent a biochemical marker of AD, even in the early stage of the illness.

NR269 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Reduction of Psychotic Symptoms by Olanzapine in Patients with Possible Lewy Body Dementia

Todd M. Sanger, Ph.D., *Lilly Research Lab, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;* W. Scott Clark, Ph.D., Jamie S. Street, M.D., Alan F. Breier, M.D.

Summary:

Objective: A *post hoc* analysis was performed on the results of a double-blind, six-week study of nursing home patients (n = 206) with dementia to determine the efficacy and safety of olanzapine in reducing psychosis and behavioral disturbances.

Methods: The effects of 5, 10, and 15 mg/day olanzapine were assessed relative to placebo in patients who had possible Lewy body dementia (n = 29), determined by a nonzero score on the Simpson-Angus Scale and a nonzero score on the *hallucinations* item of the NPI/NH. All data are reported as mean changes.

Results: Patients receiving 5 mg/day of olanzapine improved by 82.9% on the NPI/NH Delusions and hallucinations combined score, compared with 17.4% for placebo (p = .015). On the *delusions* item, olanzapine-treated patients improved by 77.8%, compared to 29.0% for placebo (p = .012). Olanzapine-treated patients showed 85.7% improvement in Occupational Disruptiveness related to the NPI/NH delusions and hallucinations items. Placebo-treated patients showed only 14.0% improvement (p = .002). Significant improvement (p = .042) was also found on the Mini-Mental State Exam for olanzapine-treated patients (2.4-point improvement), compared with placebo (0.1-point worsening). Changes in EPS were not statistically or clinically significantly different for patients treated with olanzapine.

Conclusions: Compared with placebo, 5 mg/day of olanzapine significantly improved psychotic symptoms and behavioral disturbances in patients with possible DLB. Additional well-controlled studies are needed to confirm these results.

NR270 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

An Economic Evaluation of Donepezil in Mild to Moderate Alzheimer's Disease Patients: Results of a One-Year, Double-Blind, Randomized Trial

Anders Wimo, M.D., *P O Box 16, HC Bergsjo S-82070, Sweden;* Bengt Winblad, M.D., Vera Mastey, Anders Haglund, Peter Hertzman, Robert Miceli, Lena Jacobson, Ponni Subbiah, M.D.

Summary:

Objective: To evaluate the annual costs and consequences of donepezil or placebo in patients with mild to moderate AD.

Methods: Patients with possible or probable AD from five Nordic countries received donepezil (n = 142; 5–10 mg/day) or placebo (n = 144). Based on prospectively collected patient and caregiver heath care resource utilization and caregiver time and work status, a cost consequence analysis was conducted from a societal perspective. The unit costs for resource utilization were assessed in 1997 Swedish krona (SEK).

Results: Patients gained significant functional benefits from donepezil treatment. These benefits were obtained at no significant increase in direct costs. The total annual direct costs of care were comparable (22,962,723 SEK for donepezil, 21,483,250 SEK for placebo). The net difference in per-patient costs (12,520 SEK) was about 8% of the total direct costs. Inclusion of caregiver time and work status reduced this cost to 6,943 SEK.

Conclusions: Donepezil-treated patients attained a significant clinical benefit at an annual cost similar to placebo patients.

NR271 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Effects of a Novel M-1 Selective Agonist on Behavioral Symptoms in Patients with Mild to Moderate Alzheimer's Disease

Katherine L. Beebe, Ph.D., *CNS, Smith, Kline and Beecham, 1250 South Collegeville Road, Collegeville, PA 19426;* James P. McCafferty, B.S., Rajinder Kumar, M.B., Julia Loudon, Ph.D., Matthew Truman, M.S.C., Eve Cedar, M.S.C., Kevin M. Bellew, B.S.

Summary:

Behavioral dysfunction in AD may be related to progressive cholinergic deficiency. Sabcomeline, a novel, highly potent, muscarinic partial agonist was tested among patients with mild to moderate dementia of the probable Alzheimer's type. In two six month, placebo-controlled clinical trials, the Neuropsychiatric Inventory (NPI) was used as a secondary outcome measure to assess behavioral disturbance.

A post-hoc meta-analysis combining data from the individual studies was conducted on patients stratified by baseline NPI scores (NPI < 10, Mild symptoms; NPI 10–20, Moderate symptoms; NPI > 20, Severe symptoms). The Clinician's Interview Based Impression of Change, (CIBIC-Plus) assessed global improvement.

Overall, the sabcomeline group showed a trend towards stabilization of behavioral symptoms compared to placebo. Statistically significant effects were observed in sabcomeline patients with the most severe neuropsychiatric disturbance baseline (NPI > 20) compared with placebo patients (placebo: n = 48, mean Δ ± se = 1.7 ± 2.7; sabcomeline 25 ug bid: n = 46, −4.0 ± 2.8, p = 0.0432; 50 ug od: n = 57, −6.1 ± 1.8, p = 0.019). This change was associated with marked clinical improvement on the CIBIC-Plus (0.77-points over placebo, p < .01). Benefit over placebo was further identified among NPI items including, hallucinations, anxiety, elation, and apathy. Sabcomeline was safe and well tolerated in the study population.

These findings suggest that sabcomeline may ameliorate certain aspects of severe neuropsychiatric disturbance among AD patients. Further investigation is needed to replicate these data prospectively.

NR272 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Validation of the Delirium Rating Scale Revised-98 (DRS-R-98)

Paula T. Trzepacz, M.D., *Neuroscience Research Dept., Eli Lilly and Company, Lilly Corporate Centre, Indianapolis, IN 46285;* Dinesh Mittal, M.D., Rafael A. Torres, M.D., Kim Kanary, B.S., John Norton, M.D., Nita Jimerson, M.S.N.

Summary:

Background: The DRS-R-98 is a revision of the Delirium Rating Scale (DRS) (1988), a widely used, well-validated 10-item scale

that has been translated into nine languages. The DRS-R-98 has 13 severity and three diagnostic items with descriptive anchors for each level.

Methods: We prospectively validated the DRS-R-98 among five DSM-IV Dx groups: delirium, dementia, depression, schizophrenia and "other" hospitalized Ss at the Univ. Mississippi affiliated hospitals. Psychiatrist raters for the DRS and DRS-R-98 were blind to Dx. The Cognitive Test for Delirium (CTD) and the Clinical Global Impression (CGI) scale were done independently by others.

Results: There were 68 Ss, 24 with delirium. Mean age, race, and sex did not differ between groups. Mean DRS-R-98 scores were significantly higher (ANOVA, $p < .001$) in delirious Ss than in each other Dx group. In delirious Ss: DRS-R-98 total and severity scores correlated significantly ($p < .001$) with DRS scores ($r = .84$ and $r = .80$, respectively); DRS-R-98 severity scores correlated significantly ($p = .001$) with CGI severity ($r = .61$) and with the CTD ($r = -.63$); and age did not correlate with any scale. DRS-R-98 interrater reliability was >.98 (ICC) among 3 raters. Cronbach's alpha for scale reliability was high (.90); when each item was removed from the scale, the correlations remained >.88, suggesting high internal consistency. DRS-R-98 mean scores significantly decreased after treatment ($p < .001$), as did CTD, CGI and DRS scores, indicating that the DRS-R-98 is sensitive to change in delirium severity. ROC analysis for delirium vs. all other Dx groups resulted in 92% sensitivity and 95% specificity for a DRS-R-98 with cutoff score of 17.75 points, even though some mild delirium and severe dementia cases were included.

Summary: The DRS-R-98 is a valid, sensitive, and reliable instrument for rating delirium symptom (Sx) severity. It has advantages over the original DRS for repeated measures and phenomenological studies due to its enhanced breadth of Sx and separation into severity and diagnostic subscales.

NR273 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Long-Term Efficacy of Olanzapine in the Control of Psychotic and Behavioral Symptoms in Patients with Alzheimer's Dementia

Jamie S. Street, M.D., *Lilly Research Labs, Eli Lilly & Company, Lilly Corporate Center, DC0538, Indianapolis, IN 46285;* W. Scott Clark, Ph.D., Beth E. Juliar, M.S.C., Peter D. Feldman, Ph.D., Deborah L. Kadam, M.A., Alan F. Breier, M.D.

Summary:

Objective: A multicenter study was conducted to determine long-term efficacy and safety of olanzapine in treating psychotic symptoms and behavioral disturbances associated with Alzheimer's disease.

Methods: Elderly nursing home patients (mean age: 83.1 years) with dementia ($n = 137$) who successfully completed a six-week double-blind study entered an open-label phase of up to 18 weeks during which they received olanzapine (dose range: 5, 10, or 15 mg/day). Mean change in the sum of the agitation, delusions, and hallucinations items of the NPI/NH was used as the primary efficacy measure (Core Total).

Results: Following treatment with olanzapine, patients' scores improved significantly on the Core Total (mean, −7.55; SD = 8.53; $p < .001$), Total (mean, −17.85; SD = 23.72; $p < .001$), and 10 of the 13 individual item scores of the NPI/NH, including Occupational Disruptiveness (mean, −2.84; SD = 3.24; $p < .001$). Barnes Akathisia scores improved significantly from baseline (mean, −0.22; SD = 0.80; $p = .002$). Simpson-Angus and AIMS scores were not significantly changed. No significant changes occurred in patient ECGs, including QT_c interval, nor in any other vital sign or in weight. Treatment-emergent symptoms included somnolence (26%), accidental injury (25%), and rash (22%).

Conclusion: These data suggest that olanzapine is an effective, generally safe, and well-tolerated long-term treatment for psychotic symptoms and behavioral disturbances in elderly patients with Alzheimer's dementia.

NR274 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Attentuation in the Progression of Cognitive Deterioration in Alzheimer's Disease with Rivastigmine: A Dose-Dependent Effect

Martin K. Farlow, M.D., *Department of Neurology, Indiana University, 541 North Clinical Drive, Suite 583, Indianapolis, IN 46202-5111;* John Messina, Pharm.D., Ravi Anand, M.D., Richard Hartman, Ph.D., Jeffrey Veach, M.S.

Summary:

Possible disease modifying effects of rivastigmine have been suggested by analyses using a variation of the randomized start design; however the results were somewhat confounded by differing attrition rates. We report on an alternative method investigating whether increasing doses reduce the rates of cognitive decline in patients who continue treatment.

The effect of dose on the rate of decline seen on Alzheimer's Disease Assessment Scale-Cognitive Subscale was explored for patients in a long-term (130 weeks) extension of a 26-week, placebo-controlled trial using two methods: a weighted least squares regression analysis using each individual's slope and a weighted analysis of variance comparing the slopes of patients categorized by dose (≤6 mg/day or >6 mg/day).

The results from 408 patients included in the weighted least squares analysis estimated the rate of decline to attenuate by −1 point/yr for every 3 mg/day increase ($p < 0.0001$). The average annual rate of decline for patients whose mean dose was >6 mg/day was 4.5 (95% CI 5.1, 3.9) while for patients with a mean dose of ≤6 mg/day a decline of 8.2 (95% CI 9.1, 7.3) points was seen.

These data further support earlier results suggesting that rivastigmine reduces the rate of progression of cognitive deterioration in AD.

NR275 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Donepezil Preserves Functional Status in Alzheimer's Disease

Richard C. Mohs, Ph.D., *VA Medical Center, Mt. Sinai School of Medicine, 130 W. Kingsbridge Road, Bronx, NY 10468;* Rachelle S. Doody, M.D., John C. Morris, M.D., John R. Leni, Ph.D., Sharon L. Rogers, Ph.D., Carlos A. Perdomo, M.S., Raymond D. Pratt, M.D.

Summary:

Objective: To examine the effects of donepezil compared with placebo on the preservation of function over time in patients with Alzheimer's disease (AD) in a prospective, one-year double-blind study.

Methods: Patients were required to have a diagnosis of probable AD (NINCDS criteria), MMSE of 12–20, CDR of 1 or 2, and modified Hachinski Ischemia score ≤4. Patients had to be able to perform five of six basic Activities of Daily Living (ADLs) and eight of ten instrumental ADLs. Patients in the donepezil group received 5 mg/day for 28 days and 10 mg/day thereafter. Outcome measures were the Alzheimer's Disease Functional Assessment and Change Scale, MMSE, and CDR. At each visit, investigators determined whether pre-defined criteria for clinically evident decline in functional status had been met. If criteria were met, patients were discontinued from the study.

Results: A total of 431 patients were randomized. The median time to clinically evident functional decline was 208 days [95% CL = (165, 252)] for the placebo group and 357 days [95% CL = 280] for the donepezil group. At 48 weeks, the probability of sur-

vival was 51% for the donepezil group and only 35% for the placebo group (Kaplan-Meier analysis).

Conclusion: In this study of one-year duration, donepezil treatment extended the median time to clinically evident decline in function by 5 months versus placebo.

NR276 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Motoric Subtypes of Delirium: Relationship to Symptom Profile, Etiology and Management

David J. Meagher, M.D., *Department of Psychiatry, Crichton Royal Hospital, Dumfries DG1 4TG, Scotland;* Paula T. Trzepacz, M.D., Donal T. O'Hanlon, M.D., Edmond O'Mahony, Patricia R. Casey, M.D.

Summary:

Background: Delirium is considered a unitary syndrome that is a final common pathway for multiple etiologies. However, clinically defined subtypes may differ regarding key aspects of clinical profile. This study addresses the relationship between motoric subtypes, non-motoric symptoms, etiology, and management.

Methods: Consecutive C-L referrals with ICD-10 delirium were separated into motorically defined subtypes. These were compared with regard to symptom profile (rated with the Delirium Rating Scale), etiology, and treatment with pharmacological and environmental strategies.

Results: Mean age was 60 years. Fourteen subjects were hyperactive, 11 hypoactive, and 21 of mixed motoric profile. Motoric groups had similar levels of cognitive disturbance but differed across a range of individual symptoms and overall symptom severity. Cases of drug-related etiology had higher scores for multiple symptoms and total DRS. Psychotropic medications were used more frequently in patients of hyperactive motoric profile. Greater use of environmental strategies was associated with overall delirium severity, agitation, mood lability and sleep-wake cycle disturbance but not with degree of cognitive impairment.

Conclusions: Motorically defined subtypes of delirium differ in symptom profile, relationship to etiology and management practices. These differences may reflect underlying pathophysiologies and possibly confer differing treatment responsivities.

NR277 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Intravenous Dopamine Increases the Risk for Delirium

Barbara R. Sommer, M.D., *Department of Psychiatry, Stanford University, Stanford Medical School, Stanford, CA 94305-5723;* Lowell Wise, D.Sc., Helena C. Kraemer, Ph.D.

Summary:

We hypothesized that the administration of intravenous dopamine (DA) increases the risk for delirium as manifested by need for haloperidol. We evaluated records of all inpatient admissions to Stanford University Hospital over a one year period (N = 21, 844). To examine the unique contribution of DA in the prediction of need for haloperidol, a multivariate logistic regression model was used. DA administration nearly tripled the odds of also needing the antipsychotic drug ($\chi^2 = 101$, d.f. = 1, p = .0001, odds ratio 2.9), second as a predictor only to ICU admission.

With stratification by illness acuity, DA continued to produce an odds ratio of about three. Further, we found that in the ICU setting (N = 3309), not even age was as highly correlated with need for haloperidol as was DA administration.

While ours is a retrospective analysis, it is the first attempt to fully evaluate DA administration as an independent risk factor for delirium. Despite the retrospective nature of this study and the inexact method to assess acuity (DRG weights) and presence of delirium, it seems likely that the use of DA in either the ICU or non-ICU setting significantly increases the risk for delirium. This study suggests the need for prospective studies to evaluate pretreatment for delirium to decrease morbidity.

NR278 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Trial of a Geriatric Delirium Service

Martin G. Cole, M.D., *Psychiatry, St. Mary's Hospital Ctr., 3830 Lacombe Avenue, Montreal, PQ H3T1M5, Canada;* Jane McCusker, M.D., Francois Bellavance, Ph.D., Francois J. Primeau, M.D., Robert F. Bailey, M.D., Michael V. Bonnycastle, M.D.

Summary:

Objective: To determine if systematic detection and treatment of delirium in elderly medical inpatients could increase the rate of cognitive recovery, and reduce time to recovery.

Methods: Patients aged 65 or over and newly admitted to the medical services of a primary acute care hospital were screened using the Confusion Assessment Method. A total of 227 patients with delirium (DSM-III-R criteria) were randomly allocated to the treatment group (n = 113) or control (n = 114) groups. Subjects in the treatment group were managed according to a protocol similar to the APA practice guidelines for the treatment of delirium by a geriatric specialist consultant and an intervention nurse. The primary outcome measure was the Mini-Mental State Examination. Subjects were assessed three times during the first week and weekly thereafter for eight weeks in hospital by a research assistant blind to study group.

Results: Overall, there were no significant benefits of the intervention. However, in a subgroup of patients without dementia (n = 69), rate of recovery (intervention vs control) was 61% vs 47% (NS) and time to recovery was 4.5 vs 6.7 days (NS).

Conclusion: Systematic detection and treatment of delirium may be useful for elderly medical inpatients without dementia.

NR279 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Sertraline for Depression in Remitted Schizophrenia

Donald E. Addington, M.D., *Department of Psychiatry, University of Calgary, 1403-29 Street, NW, Calgary, AB T2N 2T9, Canada;* Jean M. Addington, Ph.D., Scott B. Patten, M.D., Gary J. Remington, M.D., Javad Moamai, M.D., Alain Labelle, M.D., Linda Beauclair, M.D.

Summary:

Background: The effectiveness of selective serotonin reuptake inhibitors as treatment for depression in remitted schizophrenia has not been clearly demonstrated. They are, however, widely used in clinical practice.

Method: A randomized, double blind, prospective, placebo-controlled study of 48 subjects meeting DSM-IV criteria for both schizophrenia in remission and for a major depressive episode after one week open treatment with benztropine. Depression was assessed with the Calgary Depression Scale for Schizophrenia (CDSS).

Results: A total of 27 patients were randomized to placebo, 21 to sertraline. Mean CDSS at randomisation was 14.0. Ninety-five percent of patients completed the six-week study. Both groups showed significant improvements with one-half showing a 50% reduction in level of depression. There were no statistically significant differences in outcome between either treatment group.

Conclusions: The small sample size limits the strength of the conclusions that can be drawn from this study. The results highlight the need for further research on the role of antidepressant treatment of depression in remitted schizophrenia.

NR280 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

5HT Transporter Polymorphism and SSRI Response

Bruce G. Pollock, M.D., *Geriatric Psychopharmacology, Western Psych. Inst. & Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213-2593;* Robert E. Ferrell, M.D., Benoit H. Mulsant, M.D., Mark D. Miller, M.D., Robert A. Sweet, M.D., Stephanie Davis, M.Ed., Margaret A. Kirshner, B.A.

Summary:

The serotonin transporter gene promoter region polymorphism is known to affect transporter expression and function. We hypothesized that those patients possessing the *ll* genotype for rapid serotonin reuptake would-be more responsive to treatment with a serotonin reuptake inhibitor than those with the dominant *s* allele. DNA samples were obtained from 95 patients, aged 74 years, undergoing a protocolized treatment for depression with paroxetine (20 mg for four weeks, followed by scheduled dosage increases for partially responsive patients) or nortriptyline (therapeutic range: 50 to 150 ng/ml). *S* (484 bp) and *l* (528 bp) alleles were determined using DNA amplification and established flanking primers. Patients were treated for up to 12 weeks and assessed weekly. Twenty-one of the paroxetine-treated subjects were found to have the *ll* genotype, 24 were *sl,* and 6 *ss.* There were no differences between these groups in pretreatment Hamilton Rating Scale for Depression (HRDS) scores, age, gender, or cognitive status. The mean decrease from baseline, in HRDS scores at two weeks was significantly greater for patients with the *ll* genotype (10.5 ± 4.2 vs 5.9 ± 4.0; p = 0.0002) than for those possessing an *s* allele. At the conclusion of the study, there was no difference between groups in the number of responders (HRDS ≤10). Onset of response to nortriptyline was not affected. Allelic variation of 5-HTTLPR may contribute to the variable initial response of older patients treated with an SSRI.

NR281 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Treatment of Behaviors in Dementia with Citalopram

Bruce G. Pollock, M.D., *Geriatric Psychopharmacology, Western Psych. Inst. & Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213-2593;* Jules Rosen, M.D., Benoit H. Mulsant, M.D., Robert A. Sweet, M.D., Robert S. Marin, M.D., N.J. Jacob, M.D., Kimberly A. Huber, B.A.

Summary:

Conventional antipsychotics were, until recently, the most prevalent pharmacotherapy for psychosis and behavioral disturbances accompanying dementia and are still frequently utilized. The purpose of this federally funded study was to examine the acute efficacy of the selective serotonin reuptake inhibitor (SSRI) citalopram in comparison with the neuroleptic perphenazine in a double-blind, placebo-controlled study of behavioral disturbances associated with dementia. Eighty-three inpatients (53 women; mean age 80.6 ± 8.4 years; mean MMSE score of 8.57 ± 6.84) with moderate to severe scores on one of the target symptoms (disinhibition, motor agitation, hostility, suspiciousness, hallucinations, and/or delusions) participated in this 17-day study. Citalopram dosing started at 10 mg and was titrated to 20 mg; perphenazine dosing started at 0.1 mg/kg and was titrated to 0.2 mg/kg. Patients treated with citalopram or perphenazine both improved significantly compared with placebo. Mean reductions of total E-Behave-AD scores for citalopram, perphenazine, and placebo were 5.7 ($p < .005$), 3.2 ($p < .05$), and 0.2 (ns), respectively. E-Behave-AD scores for both citalopram ($p < 0.005$) and perphenazine ($p < 0.05$) were found to be significantly different from placebo. In conclusion, the SSRI citalopram and the neuroleptic perphenazine were equally beneficial in the acute treatment of both psychotic and nonpsychotic symptoms associated with behavioral disturbances of dementia.

NR282 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

A Chronic-Disease Model for Disease Management of Depression in the Primary Care Elderly

James C. Coyne, Ph.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Room 758, Philadelphia, PA 19104;* Gregory Brown, Ph.D., Ira R. Katz, M.D., Herbert C. Schulberg, Ph.D., Ellen Brown, Ed.D.

Summary:

As part of the NIMH-supported PROSPECT study's evaluation of collaborative mental health care for older primary-care patients, we screened 353 subjects (61.2% female; mean age 73.5) at six primary care practices of the Philadelphia PROSPECT site to estimate the size of the population with indicators of depression as a chronic condition. 5.7% screened positive for current depression with CES-D > 20 (PPV 68%); 13.8% were taking psychotropic medications including 7.3% taking antidepressants; 23.8% reported a history of depressive symptoms; and 16.1%, a history of depressive disorder. CES-D scores were higher for those taking antidepressants ($t = 3.72$; $p = .001$) but not those taking other psychotropics. They were higher in those with a history of depressive disorder ($t = 3.88$; $p < .001$) but not for a history of depressive symptoms. Of those with CES-D >10 and <21, 2.3% were taking antidepressants and were likely to have depression in partial remission; and 4.0% had a history of depressive disorder and were likely to have a partial recurrence. From a lifetime perspective, 15.9% of those who screened negative had a history of depression or were currently taking antidepressants. Thus, the number of individuals who would benefit from depression disease management significantly exceeds the number of patients with current symptoms.

NR283 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Effects of Cognitive and Affective Status on the Recovery Trajectory of Geriatric Patients After Discharge from Medical Rehabilitation

Joel E. Streim, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Room 766, Philadelphia, PA 19104;* Thomas R. Ten Have, Ph.D., Lan Zhou, Ph.D., Ira R. Katz, M.D.

Summary:

Objective: This NIMH-supported longitudinal study examined the effects of affective and cognitive status on the continued recovery trajectory of elderly medical rehabilitation patients after discharge home.

Method: A convenience sample of 48 patients, age ≥65 years, was recruited from an acute hospital-level and subacute nursing home-level medical rehabilitation unit. Subjects' affective, cognitive, and functional status were assessed at discharge, and functional status was reassessed weekly for three months after discharge. Affective status was assessed with the 15-item Geriatric Depression Scale (GDS); cognitive status with the Minimental State Examination (MMSE); and functional status with the Functional Independence Measure (FIM) and the Instrumental Activities of Daily Living (IADL) scale. Recovery trajectory and the effects of covariates were evaluated using random regression analyses.

Results: For the entire group, FIM and IADL scores showed a significant positive slope over the three-month period. Cognitively intact subjects (MMSE ≥24) had a favorable recovery trajectory for IADL (–2.50, SE = 1.02, P = .02) but not FIM (5.91, SE = 4.00, P = .15); impaired subjects (MMSE <24) had favorable recovery on the FIM (18.79, SE = 8.82, P = .04) but not IADL (0.78, SE = 2.14, P = .7). Non-depressed subjects (GDS ≤5) had a favorable trajectory for IADL (–2.33, SE = 1.08, P = .04) and marginally on the FIM (7.86, SE = 4.37, P = .08); and mildly to moderately

depressed subjects (GDS >5, mean = 7.39 ± 1.75) did not show favorable recovery on IADL (–0.72, SE = 1.86, P = .7) or FIM (10.00, SE = 7.63, P = .2)

Conclusions: Older adults can experience continued recovery after a rehabilitation stay. However, expectations within domains of functional recovery may differ according to cognitive and affective status.

NR284 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Reliability of a Telephone Screen for Depression Among Elderly Primary Care Patients

Tina L. Harralson, Ph.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, room 762, Philadelphia, PA 19104;* Thomas R. Ten Have, Ph.D., Alan C. Regenberg, B.A., Margaret M. Rider, B.A., Michael J. Kallan, M.S., Joel E. Streim, M.D., Mary Ann Foreciea, M.D.

Summary:

Objective: The purpose of this study was to test the reliability of a telephone-administered health assessment in terms of agreement with an analogous in-person administered mental health assessment. Both the telephone and in-person assessments included the Hamilton Depression Rating Scale (HDRS) and the short forms of the Geriatric Depression Scale (GDS) and the Center for Epidemiologic Studies Depression scale (CESD).

Method: This sample included 76 paid volunteers recruited from an integrated geriatric medical/psychiatry primary care setting (mean age = 75.9 years; 68% women; 48% minority). Persons were randomly assigned to receive either an in-person or telephone interview first. Ninety-four percent of the repeat interviews were conducted within one week. Reliability between the in-person and the telephone assessments were calculated using the intraclass correlation (ICC) and the corresponding 95% confidence interval (CI).

Results: Seventy-one percent of the subjects attending the practice for general medical (MED) reasons and 29% were visiting a geriatric psychiatrist (PSYCH). Mean depression scores were higher among PSYCH patients. ICC and CI for the total sample are as follows: HDRS: ICC = .77 (CI: 0.65, 0.85); CES-D: ICC = .70 (CI: 0.55, 0.81); GDS: ICC = .77 (CI: 0.64, 0.86). Reliability for PSYCH patients alone was as follows: HDRS: ICC = .61 (CI: 0.39, .077), CES-D: ICC = .78 (CI: 0.53, 0.91), and GDS: ICC = .86 (CI = 0.63, 0.95). Reliability among MED patients was: HDRS: ICC = .84 (CI: 0.64, 0.94), CES-D: ICC = .57 (CI: 0.34, 0.73), and GDS: ICC = .52 (CI: 0.26, 0.71).

Conclusions: The telephone assessment of depression using HDRS, CES-D, and GDS is reliable in that it agrees statistically with the in-person assessments according to ICC coefficient guidelines proposed by Fleiss (1986): Furthermore, telephone screening for depressive symptoms may prove to be a cost- and time-efficient way to improve patient care in a primary care setting.

NR285 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Depression and General Medical Comorbidity in a Behavioral Health Management Care Setting

Tina L. Harralson, Ph.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, room 762, Philadelphia, PA 19104;* Pamela E. Brody, Ph.D., James C. Coyne, Ph.D., Alan C. Regenberg, B.A., Ira R. Katz, M.D., Richard Thompson, Ph.D., Trevor Hadley, Ph.D.

Summary:

Objective: This report estimates the prevalence of general medical comorbidity, its association with symptoms of depression, and its relationship to health-related quality of life in an age-stratified random sample of persons newly seeking services in a behavior health managed care organization over a three-month period. These preliminary findings are part of an ongoing study designed to evaluate the impact of medical comorbidity on care outcomes.

Method: Participants included 129 persons (67% women, 12% minority) who completed a telephone battery prior to their first mental health appointment. Assessments included the Center for Epidemiologic Studies Depression scale (CES-D), Hamilton Depression Rating Scale (HDRS), SF-12 mental health (MCS) and health-related quality of life (PCS) subscales, and a general medical comorbidity (GMC) checklist. Mean age was 52.8 yrs. (range 22–88 yrs.)

Results: Mean baseline depression scores were CES-D 25.3 (s.d. = 12.8) and HDRS 15.0 (s.d. = 8.8). Seventy-five percent of all persons interviewed reported ≥ 1 GMC at the baseline (22% of persons < 36 yrs; 60% of 36–49 yrs; 87% of 50–65 yrs.; 94% of person >65 yrs reported ≥1 GMC). Based on sample weightings, we estimate that 52% of the clients seeking referrals have ≥1 GMC. In this sample, there was a low, but significant correlation between MCS and PCS (r = .21 p = .02). Number of GMC was related to PCS (r = –.54, p < .001). Correlations between GMC and PCS by age were r = –.28, p = .28 (<36 yrs); r = –.41, p = .01 (36-49 yrs); r = –.51, p < .01 (50–65 yrs); and r = –.49, p < .01 (>65 yrs). GMC was not associated with MCS except for persons aged 50–65 yrs (r = –.40, p = .02). Baseline CES-D and HDRS were correlated with GMC as follows by age group: CES-D: r = –.10, p = .70; HDRS: r = –.02, p = .95 (<36 yrs); CES-D: r = –.07, p = .67; HDRS: r = –.11, p = .52 (36–49 yrs); CES-D: r = .40, p = .02; HDRS: r = .45, p < .01 (50–65 yrs); and CES-D: r = .01, p = .94; HDRS: r = .12, p = .50 (>65 yrs). These findings suggest that although GMC is greatest in the elderly, it may have the greatest impact on the nature and/or severity of the problems that led patients to seek care in middle-aged persons. Further research will probe the impact of comorbidity on the outcomes of care.

NR286 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Recognition of Depression in Elderly Homecare Patients: An Educational Intervention for Homecare Nurses

Ellen Brown, Ed.D., *Department of Psychiatry, Cornell University, 21 Bloomingdale Road, box 187, White Plains, NY 10605;* Martha L. Bruce, Ph.D., Barnett S. Meyers, M.D., Patrick J. Raue, Ph.D.

Summary:

Objective: Depression is prevalent, underrecognized, and untreated in older homecare patients. This pilot study tested an educational intervention aimed at improving the homecare nurses' ability to recognize depression in homecare patients and instruction in making appropriate referrals to psychiatric evaluation.

Methods: Homecare nurses at a certified home health agency were randomized to a multiple session educational intervention group (n = 10) or control group (n = 10) and followed for 13 weeks.

Results: During the follow-up 14 patients were referred by intervention group nurses versus two patient referrals by nurses in the control group. 50% of nurses in the intervention group made a psychiatric referral versus 20% in the control group. Of all referred patients, 56% (n = 9) were started or adjusted on a psychotropic treatment regimen and 69% (n = 11) were referred or received further mental health services.

Conclusions: These pilot data suggest an educational intervention can improve management of depression in the homebound elderly by homecare nurses.

NR287 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Anterior Cingulate Dysfunction and Treatment Response in Geriatric Depression

Balu Kalayam, M.D., *Department Of Psychiatry, New York Presbaterian Hospital, 21 Bloomingdale Road, White Plains, NY 10605-1504;* George S. Alexopoulos, M.D., Joe Deasis, M.D., Alfredo Toro, B.A., Robert C. Young, M.D.

Summary:

Objective: Preliminary findings are reported from an investigation of depressed geriatric patients and controls examined for differences in error negative wave component (ERN) of evoked response, and the relationship of ERN to antidepressant treatment response in patients. Support for the investigation is provided by findings in the literature of an association for ERN with anterior cingulate activity, and the relationship in elderly depressed patients for clinically defined prefrontal dysfunction with poor or delayed antidepressant response.

Method: Twenty depressed elderly subjects were studied before and after six weeks of adequate antidepressant treatment and compared with ten psychiatrically normal controls. Subjects were tested for ERN using the Stroop Color Interference test, which is sensitive to anterior cingulate activity. ERN was recorded for wrong responses to incongruent stimuli using scalp electrodes placed according to the International 10–20 system. Recovery in 11 patients was associated with treatment for six weeks with nortriptyline (75mg daily), citalopram (>30mg daily), or sertraline (>75mg daily).

Results: Depressed patients had longer ERN latency for incongruent stimuli compared with control subjects ($t = 3.1$, $p < 0.01$). Non-responders ($n = 9$) compared with responders ($n = 11$) had longer latency and larger ERN amplitude at left frontal than at right frontal recording sites ($p < 0.03$; Repeated Measure analysis). The association of a left frontal ERN deficit with poor response to treatment was not explained by differences in clinical characteristics, neuropsychological Stroop performance, or treatment intensity between responders and non-responders.

Conclusion: Our findings complement findings in young depressed adults of poor response to antidepressants being associated with hypometabolism of the rostral anterior cingulate pathway, and provide support for a controlled treatment study in a larger sample of geriatric depressed patients.

NR288 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Five-Year Dementia Outcome of Elderly Depressives With and Without MRI Signal Hyperintensities

Blaine S. Greenwald, M.D., *Department of Psychiatry, Hillside Hospital, 75-59 263rd Street, Lowenstein Bldg, Glen Oaks, NY 11004;* Elisse Kramer-Ginsberg, Ph.D., K. Ranga R. Krishnan, M.D., Manzar Ashtari, Ph.D., Jian Hu, M.D., Neil J. Kremen, M.D., Mahendra C. Patel, M.D.

Summary:

Signal hyperintensities on T-2 weighted magnetic resonance imaging (MRI) brain scans likely reflect underlying cerebrovascular and/or degenerative age-related abnormalities. However, limited information is available on whether such changes are associated with dementia outcome at long-term follow-up.

Objective: To compare five-year dementia outcome in elderly depressed patients and controls with and without brain MRI signal hyperintensities in periventricular (PVH), deep white matter (DWMH), and subcortical gray matter (SGMH) locations.

Methods: A follow-up telephone survey was conducted in elderly depressives and controls who had undergone MRI scans five years earlier that had been visually rated blind to diagnosis for frequency/severity of signal hyperintensities employing a standardized rating system (modified Fazekas scale). Age-similar depressed and normal comparison subjects were characterized as demented/non-demented according to DSM-IV criteria.

Results: 83% (71/86) of subjects were successfully contacted. Amongst depressives ($n = 38$), 26% had PVH, 13% DWMH, and 16% SGMH. 29% of depressives were demented at five-year follow-up. Amongst controls ($n = 33$), 21% had PVH, 6% DWMH, and 6% SGMH. 0% of controls were demented at follow-up, 67% (4/6) of depressives with SGMH were demented at f/u compared with 22% (7/32) of depressives without SGMH ($p = .03$). In contrast, depressives with and without PVH and DWMH did not significantly differ in the percent distribution with dementia at follow-up. In addition, logistic regression considering all hyperintensity variables and age found only SGMH significantly predicted dementia outcome (76% correct classification; $p = 0.03$).

Conclusions: Hyperintensity lesion location (SGMH but not PVH or DWMH) appears to influence cognitive outcome. Since more severe SGMH likely reflect complete and incomplete lacunar infarctions, these preliminary data suggest that occlusive vasculopathy in subcortical gray matter of elderly depressives may presage dementia.

NR289 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Managing Behavioral Symptoms in Alzheimer's Disease

Thomas D. McRae, M.D., *Pfizer Incorporated, 235 East 42nd Street, New York, NY 10471;* Teresa Griesing, Ph.D., Ed Whalen, Ph.D.

Summary:

Objective: In a controlled trial, this study explored combining a ChEI (donepezil) and an SSRI (sertraline) to treat behavioral symptoms in non-depressed AD patients.

Methods: A total of 276 patients meeting Neuropsychiatric Inventory (NPI) criteria began open-label (OL) donepezil (don) treatment for eight weeks at 26 outpatient sites. A total of 245 patients who continued to meet criteria were then randomized to sertraline (ser- 25 to 200 mg/day depending on response and tolerability) or placebo (pla) for 12 weeks, while continuing OL don. Outcomes included the NPI, CGI-I, and the Cohen-Mansfield Agitation Inventory (CMAI-C).

Results: Both active drugs were well tolerated; completion rates were 82.3% ser + don and 81% pla + don. While CGI-I improved for both, ser had statistically significantly better ratings than pla at Wks 13 ($p = 0.048$), 17 ($p = 0.006$) and 18 ($p = 0.032$) and the overall double-blind period ($p = 0.007$). NPI total at baseline for the whole group was 26.3 and improved –7.5 by wk 20($p = 0.0001$). When NPI symptoms likely related to the serotonergic system (anxiety, irritability, and agitation/aggression) were combined, ser treated patients showed improvement at Wk 20—–1.3 vs –0.8 for pla ($p = 0.063$). At Wk 20, the ser group was significantly improved on the CMAI-C verbally aggressive subscale –1.4 vs –0.5 ($p = 0.045$).

Conclusion: Mean NPI improved with OL don. Patients with serotonergic symptoms showed greater improvement by adding ser versus pla. Combining don and ser was well-tolerated and appears safe.

NR290 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Sertraline in the Treatment of Elderly Depression: Results of a Large, Multicenter, Placebo-Controlled Trial

Lon S. Schneider, M.D., *Department of Psychiatry, University of Southern CA, 1975 Zonal Avenue, KAM-400, Los Angeles, CA 90033;* Cathryn M. Clary, M.D., Sanford I. Finkel, M.D., K. Ranga R. Krishnan, M.D., P. Murali Doraiswamy, M.D.

Summary:

Objective: Although SSRIs are the first-line agents used in the treatment of elderly depression, and comparator trials of SSRIs and TCAs have shown comparable efficacy, little placebo-controlled data exist to support such use.

Method: This was a multicenter, double-blind, randomized, placebo-controlled, eight-week flexible dose trial of sertraline 50–100 mg in the treatment of outpatients aged ≥60 years old (76% ≥65 years old) with DSM-IV major depressive disorder and 17-item Ham-D scores at baseline of ≥18. An attempt was made to include patients with the typical medical comorbidity seen in the depressed elderly, although unstable medical conditions and other primary Axis I diagnoses were excluded.

Results: A total of 752 subjects were randomized in the study (mean age 70 yrs, range 60–92; 56% female), and 595 (79%) completed. Overall, statistically significant differences in favor of sertraline were found on all three of the primary outcome measures, Ham-D change score, CGI-Improvement score, and change in CGI-Severity ($p < 0.05$ on all), with the difference starting at week 2. Sertraline was well tolerated, with 14% of sertraline and 5% of placebo patients discontinuing for adverse events, and <1%/3% for lack of efficacy, in sertraline and placebo, respectively.

Conclusion: In this first placebo-controlled study of sertraline in elderly depression, the drug was effective, safe, and well-tolerated.

NR291 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Depression and Self-Reported Functional Status in Older Primary Care Patients

Jeffrey M. Lyness, M.D., *Department of Psychiatry, University of Rochester, 300 Crittenden Boulevard, Rochester, NY 14642-8409;* Paula A. Sinclair, B.A., Deborah A. King, Ph.D., Christopher Cox, Ph.D., Eric D. Caine, M.D.

Summary:

Objective: To examine the association between depression and self-reported functional status, controlling for examiner-rated functional status, in order to better understand the influence of depression on such self-report measures.

Method: The subjects were 304 patients age 60 years and older recruited from primary care settings. Measures included examiner ratings of depressive symptoms and disorders, self-reported and examiner-rated functional assessments, and examiner-rated medical illness burden. Multiple regression techniques were used to determine the independent association of depression with self-reported function.

Results: Depressive symptoms were independently associated with self-reported functional disability even after controlling for examiner-rated disability and medical illness burden. The statistical significance of depression diagnosis association with self-reported disability was more variable depending on the other covariates. Both depressive symptoms and diagnoses were significantly independently associated with self-attributed physical and emotional disability, after controlling for examiner-rated medical burden and physical and psychiatric disability, respectively.

Conclusions: Clinicians and researchers should recognize that depression can "confound" the self-reporting of functional disability. Future study is needed to better understand the complex relationships among depression, medical burden, and functional status.

NR292 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Clinical Significance of Depression in Primary Care

George S. Alexopoulos, M.D., *Department of Psychiatry, Cornell University Med College, 21 Bloomingdale Road, White Plains, NY 10605;* Martha L. Bruce, Ph.D., Thomas R. Ten Have, Ph.D., Ellen Brown, Ed.D., Herbert C. Schulberg, Ph.D.

Summary:

Objective: Geriatric depression may contribute to medical morbidity, disability, and compromised quality of life. However, the level of depressive symptoms required in order to influence the clinical picture remains unclear. This study compared the clinical characteristics of syndromic and sub-syndromic depression in a representative sample of patients from primary care practices that participate in the ongoing NIMH-supported PROSPECT Study.

Methods: A total of 699 randomly selected primary care patients had a telephone interview using the CES-D. All patients with CES-D scores above 20 and 5% of patients with a CES-D score below 20 had an in-person interview using the SCID and other instruments.

Results: Of the 699 patients, 71 (10%) had a CES-D score above 20, and of these, 26 (37%) met DSM-IV criteria for major or minor depression. Only two of the 71 patients with high CES-D were receiving antidepressant treatment. Compared with subjects with high CES-D scores and no depression diagnoses ($N = 45$), patients who received a depression diagnosis ($N = 26$) had higher severity of depression (HDRS $t = 11.0$, $p < 0.0001$), lower scores in the Positive Affect Scale ($t = 2.4$, $p < 0.02$), more current suicidal ideation (SSI $t = 3.25$, $p < 0.001$), and greater scores of neuroticism (NEO $t = 2.64$, $p < 0.01$). However, these groups had similar scores in anxiety, history of suicidal ideation, negative affect, disability, social interactions, optimism, and subjective and instrumental social support. Moreover, patients with high CES-D and no depression diagnoses had more symptoms of depression (HDRS $t = 2.2$, $p < 0.03$) and anxiety (CAS $t = 2.26$, $p < 0.03$), less positive affect ($t = 3.51$, $p < 0.0007$), lower optimism (NEO $t = 2.06$, $p < 0.04$), greater perceived ($t = 2.43$, $p < 0.02$) and actual disability ($t = 2.16$, $p < 0.03$) than patients with CES-D below 21.

Conclusions: These findings suggest that elderly, primary care patients with major depression, minor depression, and even subsyndromal depressive complaints have more anxiety, personality dysfunction, and disability than patients free of depressive symptoms. Primary care services need to be equipped to identify and treat patients with syndromal and subsyndromal depression effectively.

NR293 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Socioeconomic Status Differences in Screening for Depression

Martha L. Bruce, Ph.D., *Department of Psychiatry, Cornell Medical School, 21 Bloomingdale Road, White Plains, NY 10605;* George S. Alexopoulos, M.D., Thomas R. Ten Have, Ph.D., Gail J. McAvay, M.S., Herbert C. Schulberg, Ph.D.

Summary:

Objective: This analysis examines sociodemographic differences in the CESD's utility as a screen for depression in primary care elderly.

Methods: The Cornell site of the PROSPECT study screened a representative sample of 699 patients age ≥60 from six primary care practices. All patients who screened positive (CESD ≥20) and a 5% random sample of patients who screened negative were interviewed with the SCID (total $n = 131$).

Results: The sensitivity and specificity of the CESD for major or minor depression was 100% and 58%, respectively. Specificity did not differ by gender, age, or education, but was greater in high vs. low income (70% vs. 47%, $p < .04$) and white vs. black patients (65% vs. 45%; $p < .10$). In multivariate models, both race and income contributed to specificity.

The predictive value of the CESD's four subscales varied by socioeconomic status. Only depressed mood uniformly predicted depression. The positive affect and somatic subscales predicted diagnosis in high income patients only. The interpersonal subscale were negatively related to depression in white patients only.

Conclusions: The findings suggest that effective screening for depression must accommodate socioeconomic variation in symptom experience and expression. Whether or not these findings also reflect actual differences in the nature of depression needs further investigation.

NR294 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Signal Hyperintensities in Geriatric Mania

Jose M. De Asis, M.D., *Department of Psychiatry, Cornell University, 21 Bloomingdale Road, White Plains, NY 10605;* Robert C. Young, M.D., George S. Alexopoulos, M.D., Blaine S. Greenwald, M.D., Tatsu Kakuma, Ph.D., Manzar Ashtari, Ph.D.

Summary:

Objective: Brain vascular changes may contribute to the pathophysiology of mood disorders in the elderly, including manic states. We therefore compared signal hyperintensities on magnetic resonance imaging (MRI) in geriatric manic patients and controls. We hypothesized that hyperintensity scores would be greater in patients.

Method: Geriatric patients aged ≥60 years meeting RDC for manic disorder and same-aged normal controls were studied using MRI. Signal hyperintensities were rated blind using the modified Fazekas (F) and Boyko (B) classifications. Frontal deep white matter and periventricular hyperintensities, and subcortical gray matter hyperintensities were assessed.

Results: Forty patients (mean age = 69.8 yrs; S.D = 6.73 yrs) and 15 controls (mean age = 70.5 yrs; S.D. = 6.5 yrs) were studied. Cumulative logistic regression taking age and sex into account revealed that frontal deep white matter scores were greater in the patients than the controls (F: right $p < 0.01$, left $p < 0.001$; B: right $p < 0.01$, left $p < 0.001$). The group scores overlapped in the other regions assessed.

Conclusion: These preliminary findings support hypothesized group differences. Examination of clinical correlates of signal hyperintensities in geriatric mania is of further interest.

NR295 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Compliance with Medical Treatment in Patients with Alzheimer's Disease

Elizabeth Crocco, M.D., *Department of Psychiatry, University of Miami, 4300 Alton Road, MSMC Psychiatry, Miami, FL 33140;* Ruben Bravo, M.D., Ranjan Duara, M.D., Raymond L. Ownby, M.D.

Summary:

Objective: Multiple studies have shown that patients do not take medications as prescribed. Patients with memory problems, such as those with Alzheimer's disease (AD) may be at increased risk for medication noncompliance. The purpose of this study was to assess issues related to medication compliance among patients with memory impairments.

Method: Fifty-three patients consecutively evaluated at a multidisciplinary memory disorders clinic were administered a medication compliance questionnaire based on the model of adherence developed by Park (Park & Jones, 1997).

Results: Patients' and caregivers' estimate of compliance were significantly different, with caregivers reporting lower compliance rates than patients. Compliance varied by condition and its perceived seriousness, with compliance lowest for psychiatric disorders such as depression and anxiety. These conditions were rated as less serious than other medical conditions.

Conclusion: These results confirm low rates of compliance among patients with memory complaints, especially for psychiatric conditions such as depression. This study confirms the need for further development of strategies to improve medication adherence in these patients.

NR296 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Neuropsychological Impairment in the Elderly with Mild to Moderate Depression

Armin von Gunten, M.D., *Department of Psychogeriatrics, Lausanne University, 10 Av. De Morges, Lausanne, VD 1004, Switzerland;* Rene Duc

Summary:

Objectives: To characterize the cognitive syndrome of elderly mildly to moderately depressed patients as compared with normal controls.

Method: Study design: open cross-sectional study; neuropsychologist unaware of diagnosis *Setting:* university old-age outpatient clinic. *Subjects:* 44 French-speaking subjects (11 men; 33 women; mean age 72.3 y) with an ICD-10 diagnosis of depressive disorder of a mild to moderate intensity and not fulfilling NINCDS-ADRDA criteria for dementia; 44 normal control subjects closely matched in pairs as to age, gender, and education.

Main outcome measures: MMSE-M, PECPA-2r Lausanne, RBMT (pictures and drawings), co-morbidity (hypertension, cardiovascular disease, diabetes etc).

Statistics: non parametric Mann-Whitney test

Results: Statistically significant differences as to immediate and delayed recall both verbal and visual as well as cued and non-cued recall and as to temporal orientation, clock drawing test, and verbal fluency.

No statistically significant differences as to global MMSE-M and PECPA-2r scores or in any practo-gnosic test

Comorbidity is identical in both groups.

Conclusion: Mild to moderate depressive elderly are impaired in memory and executive functions, but not in phasic or practognosic capacities. Memory impairment suggests an underlying impairment of both instrumental and executive memory dysfunction.

NR297 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Estrogen Therapy and Cognitive Function in Postmenopausal Women with Dementia

Helen H. Kyomen, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478-9106;* John Hennen, Ph.D., Jeanne Y. Wei, M.D.

Summary:

Objective: To evaluate estrogen therapy as an intervention for cognitive decline in postmenopausal women with dementia using metaanalytic techniques.

Method: Data Sources: Computerized biomedical literature databases from January 1966 through September 1999, supplemented by manual review of potentially relevant reports and direct contact with researchers. *Study Selection:* Published reports on randomized, placebo-controlled trials with data evaluating the effects of estrogen vs. placebo on cognitive decline among postmenopausal women with dementia. *Data Extraction:* Identified studies were evaluated for several design characteristics, including presence of a placebo control group, randomized assignment, severity range of dementia within the study group, longitudinal nature of the data, and comparison with baseline status. Data abstracted included means, ranges, and standard deviations on

two standardized measures of cognitive ability in each of the studies.

Results: Standardized mean effect sizes based on the Mini-Mental State examination (MMSE) and one other cognitive scale in each of the three studies were obtained. In this meta-analysis, the standardized mean (95% CI) estrogen vs. placebo difference was −0.54 (−4.98 to +3.90); this mean effect was not significantly different from zero ($z = -0.24$, $p = 0.81$).

Conclusions: Available double-blind, placebo-controlled trial data suggest that, in short-term, controlled intervention studies, estrogen therapy has no effect on cognitive decline in elderly, postmenopausal women with dementia.

NR298 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Olanzapine in the Prevention of Psychosis Among Nursing Home Patients with Behavioral Disturbances Associated with Alzheimer's Disease

W. Scott Clark, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;* Jamie S. Street, M.D., Todd M. Sanger, Ph.D., Peter D. Feldman, Ph.D., Alan F. Breier, M.D.

Summary:

Objectives: A multicenter study was conducted to determine the efficacy and safety of olanzapine in treating psychotic symptoms and behavioral disturbances associated with Alzheimer's disease. This analysis was performed *post hoc* among nursing home patients who did not yet have delusions or hallucinations to assess the appearance of such psychotic symptoms.

Methods: Onset of psychotic symptoms was determined with the NPI/NH during treatment with either placebo or a fixed dose of 5, 10, or 15 mg/day of olanzapine for up to six weeks of therapy.

Results: Among patients entering the study with neither hallucinations nor delusions ($n = 76$), there was a significantly greater increase in development of these psychotic symptoms among placebo patients compared with olanzapine patients ($p = .006$). For the larger subset of patients without hallucinations at baseline ($n = 155$), significantly fewer olanzapine-treated patients (7.4%) developed hallucinations compared with placebo (21.9%, $p = .045$). Olanzapine had a favorable safety profile in each symptom-subgroup of patients. Changes in extrapyramidal symptoms, labs, and vital signs were not statistically or clinically significantly different for patients treated with olanzapine compared to placebo.

Conclusion: These results suggest that olanzapine may be a safe and well-tolerated antipsychotic that may benefit patients with Alzheimer's dementia by reducing the appearance of psychotic symptoms.

NR299 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Drug Treatment in Depressed Elderly in the Dutch Community

Caroline M. Sonnenberg, M.D., *Department of Psychiatry, Vrye Universiteit, De boelelaan 1081C, room 0-534, HV Amsterdam 1081, Netherlands;* Aartjaw T.F. Beekman, Ph.D., Dorly H. Deeg, Ph.D., Willem V. Tilburg, Ph.D.

Summary:

Objective: In older people, a diagnosis of depression is frequently missed, and proper medical treatment is similarly hampered. We investigated which characteristics and risk factors are associated with (non-)treatment in depressed elderly.

Method: In a random, age- and sex-stratified community sample of 3107 older Dutch people (55 to 85 years), demographic variables, mental and physical health, and medication use were assessed. Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D) and the Diagnostic Interview Schedule (DIS).

Results: 2% had a major depression. 80% of this group did not use antidepressants, but 40% used anxiolytics (benzodiazepines). Depressed men used twice as often antidepressants as depressed women. In the nontreated group, benzodiazepine use was 45% in depressed women versus none in depressed men. These sex differences in medication use could not be explained by anxiety symptoms, which were equally prevalent in both groups. The use of antidepressants in both depressed men and women was not associated with the presence of physical illness or seeing a doctor recently.

Conclusions: Depressed older people are severely undertreated, women even more so than men. Recognition of the depressive disorder by the physician and administering adequate medical treatment seem to be problematic.

NR300 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Poorer Social Networks Increase Rehospitalization Risk in Older Veterans

Joan Rosansky, M.S.W., *VAGLAHS, 11301 Wilshire Boulevard, Suite 116S, Los Angeles, CA 90073;* Ritesh Mistry, M.P.H., James McGuire, Ph.D., Charles McDermott, M.S.W., Lissy F. Jarvik, M.D.

Summary:

Objectives: To determine whether social isolation risk is associated with higher re-hospitalization rates among elderly male veterans.

Methods: A total of 144 patients from the UPBEAT (Unified Psychogeriatric Biopsychosocial Evaluation and Treatment) mental health care coordination demonstration at the West Los Angeles VA Healthcare Center were evaluated using Lubben Social Network Scale (LSNS) and Rand 36-Item Health Survey Short Form. Inpatient utilization was tracked the year following enrollment.

Patients were categorized as isolated, or at high, moderate, or low risk for isolation. A logistic regression model of isolation risk and other demographic covarites was developed to explain rehospitalization. Bivariate analysis (Chi-squared; t-test) was conducted between re-hospitalization and LSNS items.

Results: Regression model was significant (Chi-square = 26.9; $p = .0007$). Significant variables: SF-36 physical (OR = .92; $p = .000$) and mental health status (OR = .93; $p = .04$), education (OR = 1.2; $p = .04$) and social isolation (OR = 3.2; $p = .01$). The group including patients isolated or at moderate to high risk for isolation was three times more likely to be rehospitalized than were low-risk patients. Bivariate analyses indicated patients without rehospitalizations had more close relatives ($t = 2.54$; $p = .01$) and people to talk to about important decisions ($t = 2.07$; $p = .04$).

Conclusions: Social isolation is an important risk factor; health care interventions promoting social networks may reduce rehospitalizations.

NR301 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Late-Onset Schizophrenia

Luis Aguera-Ortiz, M.D., *Department of Psychiatry, 12 de Octubre Hospital, Rafael Calvo 30, Madrid 28010, Spain;* Juan F. Artaloytia, Ainhua Garibi, Jose A. Perez, Ana Pascual, Tomas Palomo

Summary:

Objective: To study the clinical characteristics of a large sample of late-onset psychosis, its evolution, onset of post-psychotic depression, and the response to treatment.

Method: Sample: 66 outpatients in a general hospital's catchment area in Madrid (Spain) fulfilling Howard et al.'s criteria for very-late onset (60 years or older) schizophrenia-like psychosis.

Minimum follow-up: one year. 76% females. Mean age: 68 (±9) Mean length of the episode 24 months (±33).

Results: Delusional type: Persecutory: 70%, Jealousy: 18%, Reference (9%) Partition: 28%. Marked hallucinations; 40%, mainly auditory (80%), more frequent in women ($p < 0.05$). Post-psychotic depression: 27% (no sex differences). The psychotic illness is detected early in the younger group ($p < 0.05$). Neuroleptic treatment obtains symptom reductions in 95% but only a 32% of total remission with no sex differences. Most used first-choice neuroleptics were haloperidol (36%) thloridazine (27.3%) and risperidone (13,6%). First-choice antidepressants were tricyclics and SSRIs in similar proportion and achieve symptom reduction in 94%, and a total remission in 57%.

Conclusions: Our findings are in general accordance with other series of late-onset schizophrenia and demonstrate the usefulness of this diagnostic category. Post-psychotic depression is frequent. Response to modern pharmacotherapy is good and better than previously described.

NR302 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Clinical Patterns of Spousal Homicide or Suicide in Older Persons

Donna Cohen, Ph.D., *Aging/Mental Health Department, University of South Florida, 13301 Bruce B. Downs Blvd., Tampa, FL 33612-3899;* Carl Eisdorfer, M.D.

Summary:

Objective: To identify and clarify the clinical characteristics and patterns of spousal/consortial (S/C) homicide-suicide (HS) in older persons.

Method: A total of 41 HSs, where the perpetrator was 55 yrs. or older, were identified from 1988–1997 in three medical examiner districts covering six entire counties in west central Florida. A total of 250 variables were coded and analyzed from medical examiner and law enforcement reports using a published protocol (Cohen et al., 1998). Dyadic deaths were classified using consensus criteria for three subtypes: dependent-protective, aggressive, and symbiotic. Funded by a Retirement Research Foundation grant.

Results: All perpetrators were male; 49% were the dependent-protective type, 29% the aggressive type, 20% the symbiotic type, and 2% could not be classified. The perpetrators were older than victims, with the greatest age difference in the aggressive HSs (68.2 vs. 58.5 yrs). The average ages of the dependent-protective perpetrators and victims (83.8 vs. 80.6 yrs) were greater than the symbiotic dyads (76.3 vs. 72.5 yrs). The perpetrators and victims in all three groups differed in health status, life stressors, and marital and psychosocial circumstances. Common features were perceptions by the older men of an unacceptable threat to the relationship and the unwilling and unknowing role of the female victims.

Conclusion: The results have important implications for assessment and interventions by clinicians. The clinical patterns merit research to detect, intervene, and prevent HS.

NR303 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Verbal and Physical Aggression in Poor Outcome: Geriatric Schizophrenia

Christopher R. Bowie, M.A., *Department of Psychology, Hofstra University, 324 Post Avenue, #10K, Westbury, NY 11590;* Patrick J. Moriarty, M.A., Philip D. Harvey, Ph.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Kenneth L. Davis, M.D.

Summary:

Aggression is prevalent in both schizophrenia and dementing conditions. This study examined the role of cognitive functioning, adaptive functioning, and symptomatology in predicting aggression in geriatric schizophrenic patients. Subjects resided in either a state institution or a nursing home. They were assessed with a comprehensive neuropsychological assessment battery, and rated with the Positive and Negative Syndrome Scale, Social Adaptive Functions Scale, and Overt Aggression Scale. The prevalence of aggressiveness in the past week in this geriatric sample of schizophrenic patients (37%) was similar to previous studies examining aggressiveness in acutely hospitalized younger patients. Negative symptom severity was predictive of physical aggression in the hospitalized group ($F(1, 54) = 8.83$, $p = .004$, $R^2 = .141$). In the nursing home group, positive symptom severity was predictive of verbal aggression ($F(1, 110) = 11.02$, $p = .001$, $R^2 = .091$) and self-care ability was predictive of physical aggression ($F(1, 110) = 4.10$, $p = .045$, $R^2 = .036$). Although clinically rated impulse control deficit was more common in the hospitalized patients, the two groups did not differ on rate of overt aggression. Thus, non-aggressive episodes of impulsive behavior may be qualitatively different from aggressiveness, yet still a barrier to discharge.

NR304 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

A Successful Regional Memory Screening Day for Community-Dwelling Elders

Janet M. Lawrence, M.D., *Geriatric Department, McLean Hospital, 115 Mill Street, Belmont, MA 02478;* Donald A. Davidoff, Ph.D., Debra Katt-Lloyd, B.S., Michelle D. Auerbach, M.S.

Summary:

Objective: To investigate if a large-scale, community-based memory screening program would be successful in identifying individuals with a high probability of dementia.

Method: A total of 494 individuals out of 787 attendees (63%) were screened with the Seven Minute Screen™ at 10 sites throughout New England on 10/29/1999. Subjects were recruited through the media. All sites conformed to a standardized format of an educational lecture, followed by individual screenings with locally trained staff. Subjects were informed of results. Those with high/retest scores were advised to seek diagnostic evaluation and encouraged to have results sent to their PCP.

Results: A total of 76 (15%) scored a high probability of dementia, 17 scored retest (3%). Feedback from participants indicated a high level of satisfaction with the process.

Conclusions: A memory screening day may allow detection of significant numbers of individuals previously unknown to have cognitive problems. With development of memory-enhancing and progression-slowing therapies and strategies to increase quality of life, early identification of dementia is crucial. Additional benefits include reassurance of those passing the screen and increased community awareness.

NR305 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Somatic Distress of the Mentally Ill and Its Relationship to Personality Disorders

Peter Manu, M.D., *Hillside Hospital Medical Svcs, 75-79 263rd Street, Glen Oaks, NY 11004;* Norert Schmitz, M.D., Norbert Hartkamp, M.D., Wolfgang Tress, M.D., Matthias Franz, M.D.

Summary:

Objective: Personality disorders are often invoked by clinicians as a contributing factor to the severity of physical complaints of psychiatric patients, but the scientific support for this association is scant. This study was designed to determine the relationship between somatic distress and the presence of personality pathology in individuals with well-defined psychiatric disorders.

Method: We analyzed 1437 consecutive referrals to an academic psychosomatic outpatient unit. Standardized psychometric and clinical evaluations were used to diagnose personality (P), depressive (D), anxiety (A), and somatoform (S) disorders. The assessment of somatic distress was based on the self-rating of the severity of 14 somatic experiences (SE) during the week preceding the evaluation.

Results: Compared with D (N = 324), A (N = 216) and S (N = 209), patients with P (N = 392) indicated the lowest severity of somatic distress (p = .001). Patients with the comorbid associations D + P (N = 130) and A + P (N = 79) had experienced milder somatic distress than those with D or A alone (p = .007). In contrast, patients with S + P (N = 78) had been more severely distressed than those with S (p = .02). Fatigue, back pain, nausea, and palpitations were among the five most severe SE in all of the seven diagnostic groups.

Conclusions: Personality pathology may contribute significantly to the physical illness experience of patients with medically unexplained symptoms who are not clinically anxious or depressed.

NR306 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Fatigue and Personality Pathology in the Mentally Ill

Peter Manu, M.D.,*Hillside Hospital Medical Svcs, 75-79 263rd Street, Glen Oaks, NY 11004;* Norert Schmitz, M.D., Norbert Hartkamp, M.D., Wolfgang Tress, M.D., Matthias Franz, M.D.

Summary:

Objective: Psychiatric disorders and abnormal personality traits are commonly identified in patients complaining of fatigue, most of whom can be diagnosed to have depressive (D), anxiety (A), somatoform (S) or eating (E) disorders. This study was designed to determine the relationship between the prevalence of severe fatigue and the presence of personality pathology in individuals with these psychiatric disorders.

Method: We analyzed 1197 referrals to an academic psychosomatic medicine outpatient unit. All patients underwent highly structured standardized psychometric and clinical assessments which allowed the categorical classification into D, A, S, and E groups. Within each group, the self-scored severity of fatigue experienced during the week preceding the evaluation was compared for patients with and without personality disorders (P).

Results: The one-week prevalence of severe fatigue was 38% in D (N = 324) and 45% in D + P (N = 139), p = NS; 29% in A (N = 216) and 29% in A + P (N = 79), p = NS; 33% in E (N = 99) and 32% in E + P (N = 53), p = NS; and 20% in S (N = 209) and 34% in S + P (N = 78), p < .01. The difference in fatigue severity was +5% for D + P vs D (p = NS), +1% for A + P vs A (p = NS), −2% for E + P vs E (p = NS) and 32% for S + P vs S (p < .01). The greater severity of fatigue had a significant contribution to the difference in the 14-item index of somatic distress only for S vs S + P (p = .03).

Conclusions: Severe fatigue may be a marker of personality pathology in patients with unexplained somatic complaints who do not suffer from depressive, anxiety, or eating disorders.

NR307 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Traumatic Events and BPD

Julia A. Golier, M.D., *Department of Psychiatry, Mt. Sinai-Bronx VAMC, 130 W. Kingsbridge Rd, #116A, Bronx, NY 10468;* Rachel Yehuda, Ph.D., Eres Bar-Tal, B.A., Vivian Mitropoulou, M.A., Antonia S. New, M.D., Larry J. Siever, M.D.

Summary:

Background/Methods: Trauma in general and childhood trauma in particular have been reported to be very prevalent in patients with borderline personality disorder (BPD) but it remains unclear whether this is a unique feature of this personality disorder. To investigate this question, we compared the frequency of lifetime trauma exposure in BPDs with other personality disorders (OPD) using a semi-structured, clinician-administered interview (The Trauma History Questionnaire as developed and validated by Green, et al.) One hundred and twelve patients with a DSM-III-R personality disorder were interviewed. The interviewers inquired about a number of traumatic life events including crime-related events, general events (e.g., accidents, illness, natural disasters), and physical/sexual events and recorded the age and number of each occurrence.

Results: 45 patients (26M/19F; age 36.5 ± 8.2) met criteria for BPD and 67 (48M/19F; age 38.3 ± 9.6) met criteria for OPDs. Trauma was quite prevalent among these patients occurring in the overwhelming majority. However, the prevalence of trauma BPD patients (97%) was not significantly different than that of OPD patients (90%) (X^2 = .8, p = ns). However, specific types of trauma were more common in BPD. In particular, BPD patients were more likely to have been sexually abused (44% vs. 20%; X^2 = 5.9, df1, p < .02) and physically assaulted (47% vs. 27%; X^2 = 3.8, df1, p < .05). The groups did not differ in the prevalence of crime events, general disaster events, or witnessing of traumatic events. BPDs were not significantly more likely than OPDs to have been exposed to trauma in childhood (35% vs. 26%, respectively) or in adolescence (53% vs. 36%, respectively). Further characterization of the sexual abuse in BPDs shows that the median age for sexual abuse in the sample was 15 years (range 7 to 34 years). BPDs were more likely to have attempted suicide than OPDs (40% vs 6%; X^2 = 17.6, df1, p = ns) and patients with a history of sexual abuse were also more likely to have history of suicide attempts (out of 22 patients with suicide history; 14 also had a sexual abuse history- or 63%; X^2 = 12.4, df1, p = <.001). These results suggest that a lifetime history of trauma is prevalent in the majority of subjects with personality disorders. Among patients with personality disorder, those with BPD were no more likely to have been traumatized in general and no more likely to have been traumatized during childhood, but were more likely to have been sexually abused.

NR308 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Memory Function in Holocaust Survivors with PTSD

Julia A. Golier, M.D., *Department of Psychiatry, Mt. Sinai-Bronx VAMC, 130 W. Kingsbridge Rd, #116A, Bronx, NY 10468;* Rachel Yehuda, Ph.D., Sonia Lupien, Ph.D., Robert A. Grossman, M.D., Philip D. Harvey, Ph.D.

Summary:

Impairments in verbal memory may underlie some of the symptoms in PTSD; however, their nature, specificity, and interaction with aging have yet to be fully elucidated. To explore these issues, we compared Holocaust survivors with PTSD (N = 28) with Holocaust survivors without PTSD (N = 15) and nonpsychiatric comparison subjects (N = 27) on measures of explicit and implicit memory using neutral and trauma-related stimuli. The groups, which did not differ in age (mean 67.7 ± 6.3 years) or gender distribution (61.5% female), performed differently on a test of explicit memory, the paired-associates task, both when the word pairs were related (F(2,66) = 5.5; p = 0.06) and unrelated (F(2,66) = 4.3; p = 0.017). By post hoc testing the PTSD group performed significantly worse than the nonpsychiatric comparison subjects. Regression coefficients of performance on age, covaried for reading score, differed among the groups for both related (F(2,63) = 4.1; p = 0.02) and unrelated (F(2,62) = 4.0, p = 0.02) words. The differences were largely due to more negative significant regression coefficients in the PTSD group. When trauma words were used, the PTSD group showed a significantly greater facilitation of recall than the non-PTSD or nonpsychiatric group (F(2,66) = 7.4; p = 0.001). In con-

trast, the groups did not differ in implicit memory as assessed by a word-stem completion task regardless of whether the previously presented words were neutral or trauma-related. These findings suggest that PTSD in Holocaust survivors is associated with impairment in hippocampal-dependent memory function and a greater facilitation of memory from trauma-relevant stimuli. The greater decline in performance with age among PTSD subjects raises the possibility that there is an acceleration of age-associated memory decline in this disorder, which if confirmed, would have wide-ranging implications for the assessment and treatment of older trauma survivors.

NR309 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Factor Analysis of DSM-IV BPD Criteria

Charles A. Sanislow, Ph.D., *Department of Psychiatry, Yale University, 184 Liberty St., New Haven, CT 06519;* Carlos M. Grilo, Ph.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To examine the factor structure of the DSM-IV borderline personality disorder Criteria in a carefully diagnosed treatment-seeking study group aged 18–45.

Method: As part of the multi-site Collaborative Longitudinal Personality Disorders Study (CLPS), 668 subjects were assessed using semi-structured diagnostic interviews. Axis II criteria were assessed using the Diagnostic Interview for Personality Disorders-IV. All interviews were conducted by masters or doctoral level clinicians trained to reliable standards. Exploratory factor analysis was utilized to identify latent structure of DSM-IV BPD criteria.

Results: Overall, the BPD diagnosis had an internal consistency of 0.86 (Cronbach's alpha). Exploratory factor analysis revealed the following three factors that accounted for a total of 64.8% of the variance (variances for the factors, and factor loadings for the items are shown in parentheses): "Disturbed Self" (47.6%) was composed of the "identity disturbance" (.686), "chronic emptiness" (.827), and "stress-related paranoid ideation" (.616) items; "Impaired Relatedness" (9.3%) was composed of the "abandonment" (.801) and "unstable relationships" (.700) criteria; and "Poor Regulation" (7.8%) composed of the "impulsivity" (.872) "suicidal/self-mutilative behavior" (.492) "affective instability" (.509) and "inappropriate anger" (.545) criteria.

Conclusion: These findings may help to outline central components of BPD and inform treatment plans by identifying subsets of criteria that may be more or less responsive to different treatment interventions. It may be that the different factors exhibit differential stability, and follow-up studies of our sample will explore this.

NR310 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Pathological Dissociation in BPD

Marianne Goodman, M.D., *Department of Psychiatry, Mt. Sinai-Bronx VA, 130 West Kingsbridge Rd, #116A, Bronx NY 10468;* Harold W. Koenigsberg, M.D., Lawrence Sprung, B.A., Antonia S. New, M.D., Vivian Mitropoulou, M.A., Larry J. Siever, M.D.

Summary:

Borderline personality disorder (BPD) is a debilitating illness affecting 2% to 3% of the population and has a 10% suicide rate. Understanding the factors that influence the more pathologic behaviors of suicide and self-mutilation are critical for treatment and prevention. Evidence from our group indicates that pathological dissociation may be one of these factors. Dissociation is the disruption of usually integrated functions of consciousness, memory, identity and perception and measurable with scales such as the Dissociative Experiences Scale (DES). Based on the DES, a dissociation taxon (DES-T) has been developed that reliably identifies individuals with pathological dissociation. The literature notes that childhood trauma is an important etiology of pathological dissociation, however more recent work investigates genetic influences.

To explore the role of childhood trauma and genetics on pathological dissociation in BPD, we examined pilot data on 95 patients with personality disorders. BPD diagnosis was significantly associated with DES-T membership, and DES-T membership was significantly associated with a suicide attempt history. Surprisingly, there were no significant associations between pathological dissociation and trauma history as measured by the Childhood Trauma Questionnaire in BPD. Serotonergic genetic data were analyzed in a subset of these patients (n = 50). Significant associations between the "UU" allele of tryptophan hydroxylase and DES-T was found (X^2 = 8.5 df = 2 p < .02). Additionally, the "C" allele of the serotonin 1B receptor was associated with DES scores over 30 (X^2 = 7.67 df = 2 p < 03). In summary, we found significant pathological dissociation in BPD which seems unrelated to childhood traumatic experiences. Our preliminary genetic findings on all personality disorders suggest that genetic factors may influence pathological dissociation.

NR311 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Caudate and Ventricular Volume in Neuroleptic-Naïve Schizotypal Personality Disorder

James J. Levitt, M.D., *Department of Psychiatry, Brockton VAMC, 940 Belmont Street, #116A, Brockton, MA 02301;* Robert W. McCarley, M.D., Aleksandra Ciszewski, B.A., Chandlee C. Dickey, M.D., Ron Kikinis, M.D., Ferenc A. Jolesz, M.D., Martha E. Shenton, Ph.D.

Summary:

Objective: A growing appreciation has emerged for the role of the basal ganglia in cognitive as well as in motor functioning. Anatomically, both motor and "cognitive" circuits exist that connect the frontal lobe to subcortical structures. Three such circuits originate in prefrontal regions believed important for higher cognitive functions, and topographically innervate the head of the caudate nucleus and nucleus accumbens forming starting and ending points for prefrontal "cognitive" cortical-basal ganglia circuits. Pathology in any of the core components of these circuits, such as in the caudate nucleus, may result in similar neurobehavioral syndromes. Neuroleptic medication, however, affects the size of the caudate nucleus, though reduced caudate volume reported in first-episode schizophrenia supports intrinsic pathology. For this reason, schizotypal personality disorder (SPD) subjects offer an ideal group for the measurement of the caudate as they are genetically related to schizophrenia but do not require neuroleptic treatment because of their less severe symptoms.

Method: We have thus chosen to measure the caudate nucleus, and the contiguous lateral ventricles, in 14 right-handed male SPDs, who have had no prior neuroleptic exposure, and 15 normal controls (NCLs), who were age, parental SES-, handedness- and sex-matched to the SPD subjects. MRI scans were obtained on a 1.5 Tesla magnet. For the measurement of specific regions of interest higher spatial resolution SPGR images (1.5 × .9375 × .9375 mm voxels) were used. For whole brain measurements, used to correct for head size, a spin echo double echo MR sequence with 3 mm axial contiguous slices was obtained; then reformatted and co-registered to 1.5 mm SPGR coronal obtained images; the resulting image was then segmented using Wells' expectation-maximization segmentation protocol.

Results: Repeated measures ANCOVA (with ICC and age as covariates) yielded a significant main effect for diagnosis (F = 6.37, df = 1,27, p < 0.02). Follow-up t-tests showed that right, left and total absolute caudate volume was smaller in SPD than in NCLs (4.14 v. 4.77 ml, p < 0.05; 4.07 v. 4.68 ml, p = 0.13; 8.21 v. 9.45 ml, p < 0.01). In addition, we measured that portion of the

lateral ventricles contiguous to the caudate nuclei. This revealed no differences in right and left contiguous ventricle relative volume in SPD subjects compared with normal controls (0.33 vs. 0.37%, p = 0.58; 0.33 vs. 0.39%, p = 0.38), suggesting that smaller caudate size in SPD is not associated with enlarged lateral ventricles.

Conclusion: These data are consistent with reduced caudate volume in first-episode schizophrenia studies and suggest that there may also be intrinsic pathology in the caudate nucleus in the schizophrenia spectrum population of SPD.

NR312 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Efficacy of Quetiapine Versus Haloperidol and Placebo in the Short-Term Treatment of Acute Schizophrenia

S. Charles Schulz, M.D., *Department of Psychiatry, University of Minnesota, 2450 Riverside Avenue, Minneapolis, MN 55454-1495;* Martin Jones, M.S., Emma Westhead, M.S., Paul P. Yeung, M.D.

Summary:

Background: The efficacy of quetiapine in relieving the positive and negative symptoms of schizophrenia has been demonstrated in a number of controlled and open-label extension studies.

Objectives: To compare the efficacy of quetiapine with existing treatment options, a meta-analysis was performed on data from four studies in which quetiapine was compared with haloperidol and placebo in the short-term treatment of acute schizophrenia.

Methods: The proportion of patients who experienced a clinically relevant response to treatment (≥40% reduction in the Brief Psychiatric Rating Scale (0–6) score from baseline to endpoint) was calculated for each treatment, within each trial. The homogeneity of treatment effects across studies was assessed. The combined odds ratio (OR) and associated 95% confidence interval were calculated, with an OR >1 indicating superiority of quetiapine over haloperidol or placebo.

Results: The response rates in the individual trials ranged from 26% to 43% for quetiapine, 19% to 47% for haloperidol, and 6% to 26% for placebo. There was no indication of heterogeneity of treatment effect between trials (p = 0.183). The combined OR for quetiapine vs placebo was 2.31 (95% CI 1.50, 3.56; p < 0.001), and for quetiapine vs haloperidol was 1.32 (95% CI 1.04, 1.68; p = 0.020).

Conclusions: In the short-term treatment of acute schizophrenia, quetiapine is significantly superior to haloperidol and placebo in terms of clinically relevant response rates. This would suggest that quetiapine is a first-choice antipsychotic. Serequel® is a trademark, the property of Zeneoa Ltd.

NR313 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Cannabis Use and Schizotypy in Healthy Students

Patrick Dumas, M.D., *Hopital Vinatier, 95 Boulevard Pinel, Bron F-69677, France;* Sebastien Bouafia, M.D., Mohamed Saoud, Ph.D., Christel Gutknecht, Jean Dalery, M.D., Thierry D'Amato, Ph.D.

Summary:

Many reports have evidenced links between cannabis use and schizophrenia and most psychiatrists acknowledge cannabis use increases risk factors in schizophrenia. In addition, it has been shown that schizotypal personality disorder [SPD], or even some SPD traits, may be a clinical expression of vulnerability to schizophrenia called "schizotypy". The evidence that cannabis use and schizotypy both constitute risk factors for the later development of schizophrenia asks the question of their relationships. The aim of the present study was to examine the association between cannabis use and SPD traits in young healthy French individuals. For this purpose, we have recruited 232 students, aged from 18 to 25 years old who have completed the Raine's Schizotypal Personality Questionnaire [SPQ] and four of the Psychiosis Proneness Scales developed by Chapman and colleagues [Magical Ideation Scale: MIS; Perceptual Aberration Scale: PAS; Revised Physical Anhedonia Scale: PhA; and Revised Social Anhedonia-Scale: SA]. Subjects were divided into three groups according to cannabis use: Never-Users [NU]; Past or Occasional-Users [POU] and Regular Users [RU]. By the mean of a two-way mixed effects model, we observed higher scores for RU or POU compared to NU at SPQ and MIS scales after adjustment for potential confounding factors. These results indicate that cannabis use is associated with categorial SPD and more precisely with the clinical positive dimension of this disorder. Such a relationship could be interpreted either as a single co-occurrence or as a real inter-dependence of these two phenomena. In order to clarify this question, further longitudinal studies on schizophrenia risk factors should include both an evaluation of cannabis use and the study of SPD traits.

NR314 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Three-Factor Structure of Self-Report Schizotypy

Patrick Dumas, M.D., *Hopital Vinatier, 95 Boulevard Pinel, Bron F-69677, France;* Mohamed Saoud, Ph.D., Sebastien Bouafia, M.D., Christel Gutknecht, Jean Dalery, M.D., Thierry D'Amato, Ph.D.

Summary:

Objective: It is now well established that schizotypal personality disorder [SPD], or even some SPD traits, may be a clinical expression of an underlying vulnerability to schizophrenia called "schizotypy". Many self-report scales have been proposed to measure schizotypy in nonclinical samples. The present study aimed to explore the factorial structure of schizotypy by the mean of responses to five such scales from young healthy individuals.

Method: For this purpose, we have recruited 232 French university students, aged 18 to 25 years old, who have completed the Raine's Schizotypal Personality Questionnaire [SPQ] and four of the Chapman and Chapman Scales [Magical Ideation Scale; Perceptual Aberration Scale; Revised Physical Anhedonia Scale and Revised Social Anhedonia Scale]. A Principal Component Analysis [PCA] was carried out on scores at each items to examine the factorial structure of schizotypy in this sample.

Results: PCA evidenced a three-factor model of schizotypy reflecting "positive or cognitive-perceptual", "negative or social-interpersonal," and "disorganization" latent factors.

Conclusions: Schizotypy, as assessed by these scales, is a multidimensional construct composed by at least three dimensions in this nonclinical sample. This factorial structure is similar to those of schizophrenia symptoms which raise the hypothesis of a continuum between normality and schizophrenia via SPD. These results replicate previous works on the topic with the same scales in other countries.

NR315 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Use of Paroxetine in Aggressive Personalities

Giampaolo La Malfa, M.D., *University of Florence, Viale Morgagni 85, Florence 50134, Italy;* Marco Bertelli, Michele Conte, Pierluigi Cabras, M.D.

Summary:

Objective: to verify the efficacy of the treatment with paroxetine vs placebo in reducing clinically differentiated kinds of aggressive behaviour in people with personality disorders (PD).

Methods: Thirty-two aggressive outpatients with DSM-IV diagnosis of a cluster B personality disorder and no axis I comorbidity had a four-week, single-blind treatment with placebo. During the

first week aggressivity was assessed trough Global Aggression Scale (GAS), Social Dysfunction and Aggression Scale (SDAS), and Past Feelings and Acts of Violence Scale (PFAV). Afterwards, patients were divided in two groups by kind of aggressivity using the Predatory—Affective Aggression Scale (PAAS). In both groups paroxetine was gruadual increased up to 40 mg/day. Each month for six months patients were again assessed as above. The Dosage Record and Treatment Emergent Symptom (DOTES) was used to assess side effects after placebo and paroxetine periods.

Results: If compared with placebo, paroxetine is associated with a statistically significant score reduction of all the three scales used. It is more effective on affective than predatory aggressivity. DOTES scores after paroxetine did not significantly differ from the ones after placebo.

NR316 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Combined Dialectical-Behavior Therapy and Fluoxetine Pharmacotherapy in Patients with BPD: Is There an Addictive Effect?

Elizabeth B. Simpson, M.D., *Department of Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906;* Karen J. Rosen, M.D., Teri B. Pearlstein, M.D., Ellen Costello, Ph.D., Shirley Yen, Ph.D., Ann Begin, Ph.D.

Summary:

Despite the frequent use of medication in the treatment of borderline personality disorder (BPD), there is a striking paucity of systematic pharmacologic studies in BPD, most of which have been open or uncontrolled trials. Studies in BPD have reported the efficacy of selective serotonin reuptake inhibitors (SSRIs) in reducing symptomatology accompanying BPD such as aggression, rage, self injury, suicidality, affective instability, and impulsivity. The psychosocial treatment Dialectical Behavior Therapy (DBT) has emerged as a specific treatment for BPD patients and appears to reduce suicidal behavior, psychiatric hospitalizations, and rates of treatment dropout. While studies indicate that SSRIs may be promising in the treatment of BPD, there are no controlled studies which adequately control for psychosocial treatment.

The purpose of this study was to examine whether the use of combined DBT and fluoxetine provides an additive effect in the treatment of BPD by comparing the efficacy of combined DBT and fluoxetine versus DBT and placebo in reducing scores on measures of depression, anger, aggression, suicidal ideation, and parasuicidal behavior.

This presentation describes the results of a 12-week, randomized, double-blind study of 20 women who met criteria for BPD as assessed by the Structured Clinical Interview for DSM-IV, Axis II, BPD (SCID-II, BPD) and consented to discontinue current psychiatric medications. All 20 subjects received DBT and were randomized to receive either fluoxetine (40 mg/day) or placebo. Pretreatment and posttreatment measures were obtained using the Beck Depression Inventory (BDI), State Trait Anxiety Scores (STAI), Speilberger Anger Expression Inventory (STAXI), Dissociative Experiences Scale (DES), Overt Aggression Scale (OAS), Self-Injury Questionnaire(SIQ) and clinician rated Global Assessment Scale (GAS).

Repeated measures ANOVA revealed no significant pre-post differences between groups. However, paired sample t-tests within each group indicated significant differences between pre- and post-treatment scores on the BDI ($t(10) = 5.44$, $p < .001$) and the GAS ($t(9) = -5.48$, $p < .001$) and near significant decreases in self report anxiety ($t(10) = 3.34$, $p < .008$) and dissociation ($t(10) = 3.42$, $p < .007$) in the placebo group. There were no significant differences between pre- and post-treatment scores on any of the measures for those in the fluoxetine group. No significant differences in self injury were found in either group (fluoxetine: Wilcoxon $Z = -.27$, $p = .79$; placebo: Wilcoxon $Z = -1.61$, $p = .11$).

While the number of subjects in the study was small, our findings indicate that, when psychosocial treatment (DBT) was controlled, fluoxetine was not beneficial in reducing several symptoms of BPD as compared with placebo. At this present time it may be premature to make treatment recommendations regarding pharmacologic guidelines for BPD.

NR317 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Sertraline in Premenstrual Dysphoric Disorder Patients on Oral Contraceptives

Ellen W. Freeman, Ph.D., *Dept. of OBGYN/Psychiatry, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104;* Stephen J. Sondheimer, M.D., Beatriz Garcia-Espana, M.A.

Summary:

Objective: The results of a previous study (Freeman et al., 1999) were re-analyzed to determine whether the efficacy of sertraline in the treatment of severe premenstrual syndrome or DSM-IV premenstrual dysphoric disorder (PMDD) was altered by concomitant use of oral contraceptives (OCs).

Method: Patients underwent three cycles of prospective screening before being randomized to three cycles of double-blind, parallel-group treatment with either sertraline, desipramine, or placebo. Outcome measures included a 17-item daily symptom report (DSR).

Results: There was no difference in the DSR total scores at baseline for patients on ($N = 44$) vs. not-on ($n = 123$) OCs (161 ± 52 vs. 162 ± 64, respectively; $p = 0.09$), or for any of the 5 DSR factor scores. At LOCF endpoint, the DSR total score for the sertraline group was 71 ± 54 for patients on OCs, and 84 ± 78 for patients not-on OCs ($t = 0.63$; $p = 0.53$). Comparison of responder rates found no differences between patients on vs. not-on OCs for any of the 3 treatment groups. More detailed analyses of the outcome data will be presented as well as differences in tolerability between the two groups.

Conclusion: The results of the current study provide the first placebo-controlled evidence that the efficacy of sertraline in treating severe PMS/PMDD is maintained when OCs are used.

NR318 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Fluoxetine Improves Social Functioning in Women with Premenstrual Dysphoric Disorder

Meir Steiner, M.D., *Department of Psychiatry, McMaster University, 50 Charlton Ave E/St. Joseph's Hamilton, ON L8N 4A6, Canada;* Rajinder A. Judge, M.D., Eileen Brown, Ph.D., Julia Dillon, Pharm.D.

Summary:

Objective: A previously reported, placebo-controlled, multi-site trial found fluoxetine effective in mediating PMDD mood symptoms; these data are now used to determine fluoxetine's effectiveness on social functioning in women with PMDD. Though cyclical mood disturbance is the pathognomonic feature of PMDD, impairment of social functioning frequently contributes to the severity of presentation.

Methods: Social functioning was assessed in 320 PMDD patients who were randomized to fluoxetine 20mg/day, fluoxetine 60 mg/day, or placebo. Symptoms were assessed by social impairment subtotals of the patient-rated and clinician-rated Premenstrual Tension Syndrome Scale (PMTS-P, PMTS-C). Items rated on the PMTS-P subtotal were: avoid social commitments, avoid family, cancel scheduled social activities, difficulty completing house/job routine, more accidents in daily housework/job, stopped

seeing best friends, and physical symptoms severe: unable to function. Outcome measures were change from mean baseline luteal phase scores to mean treated luteal phase scores.

Results: Fluoxetine treatment (20 and 60 mg/day) statistically significantly improved social functioning compared with placebo treatment when measured on the PMTS-P and PMTS-C social impairment subtotals (all analyses significant; $p < .05$). For all comparisons, 20 mg/day and 60 mg/day doses were not significantly different.

Conclusion: Fluoxetine treatment was statistically significantly superior to placebo in improving frequently reported PMDD associated social functioning as measured by derived social impairment subtotals of the PMTS-P and PMTS-C.

NR319 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

A Two-Year Follow-Up Study of Personality Dysfunction in High School Students

Yueqin Huang, M.D., *Dept. of Preventive Medicine, Beijing Medical University, 38 Xue Yuan Road, Beijing 100083, China;* Lihong Shi, M.D., Guizhi Zhang, Shumei Yun, M.D.

Summary:

Objective: To observe dynamic changes of personality development and personality dysfunction with age in adolescents.

Method: In the two-year follow-up study, 379 students (male 137, female 242) in three high schools selected by cluster sampling with representative in urban Beijing were investigated twice in 1997 and 1999 by Personality Diagnostic Questionnaire-revised (PDQ-R).

Results: The means of total PDQ-R were 23.9 ± 7.4 in 1997 and 22.8 ± 7.3 in 1999. When compared with 1997, the score of antisocial increased and that of dependent decreased significantly in males; the scores of antisocial, histrionic, avoidant, and paranoid increased, and those of dependent and schizoid decreased significantly in female in 1999 ($p < 0.05$). The positive rate of total PDQ-R scores in two years was 22.4%. Fifty-one percent of students with a positive score in 1997 became normal in 1999, and 6% of students with a negative score in 1997 became abnormal in 1999.

Conclusions: The PDQ-R score dynamically changes with age in adolescent. A half of high school students with personality dysfunction could improve. It indicates that personality dysfunction in adolescents can be partially corrected spontaneously without psychiatric treatment.

NR320 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Assessing Premenstrual Symptom Severity

Rebecca Robinson, M.S., *Health Outcome Department, Eli Lilly and Company, Lilly Corporate Center, DC1850, Indianapolis, IN 46285;* Ralph W. Swindle, M.D.

Summary:

Objective: To understand premenstrual symptomatology and treatment-seeking behaviors we examined three measurement approaches for premenstrual symptoms, their relationship to social functioning interference, and the role of symptom severity in a broader model of help-seeking for premenstrual symptomatology.

Methods: A sample of 1022 menstruating women (age 18-45) completed a telephone eligibility screening followed by a written questionnaire that measured the effect of premenstrual symptom severity on functioning, and treatment seeking behavior.

Results: Symptom severity measures were strongly inter-correlated: range .60 to .78 ($p < .001$), and were correlated with impairment in social and occupational functioning: range .44 to .77 (all $p < .001$). A global self-report measure identified 4.9% of women with severe symptoms, whereas a DSM-IV adapted approach identified 11.3% with premenstrual dysphoric disorder (PMDD). Treatment seeking was predicted by older age, recurrent symptoms in most cycles, greater self-reported symptom severity, greater overall use of healthcare services, and less negative attitudes toward "premenstrual syndrome" (all $p < .05$).

Conclusion: Women under-identify the severity of their premenstrual symptoms despite the fact that these symptoms interfere with social and occupational functioning. Women are also reluctant to seek treatment for even severe symptoms due to attitudinal barriers. These findings support the use of brief screening/diagnostic tools to improve the diagnosis of PMDD.

NR321 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Plasma Tryptophan Availability and Pathological Gambling

Rita Prieto, M.D., *Department of Psychiatry, Hospital Ramon Y Cajal-Alcala Universit, Crt. Colmenar, km. 9,1, Madrid 28034, Spain;* Angela Ibanez, M.D., Carlos Blanco, M.D., Jeronimo Saiz-Ruiz, M.D.

Summary:

Objective: Pathological gambling is classified as an impulse control disorder. A serotonergic deficit has been postulated in the pathogenesis of the disorder. Tryptophan is the precursor of brain serotonin and it competes with large neutral amino acids (LNNA) to enter into central nervous system.

Method: We studied 40 pathological gamblers seeking treatment in an outpatient unit, and 40 healthy controls matched by age and sex. We analyzed free and total tryptophan concentrations, and free and total large neutral aminoacids (LNNA).

Results: The free tryptophan concentration was 5.94 micromol/l in gamblers and 6.99 in volunteers ($t = -2.14$; $df = 39$; $p = 0.039$), and the free tryptophan/free LNNA ratio was 0.011 in gamblers and 0.013 in controls ($t = -1.15$; $df = 39$; $p = 0.034$). Total tryptophan concentration was 44,94 micromol/l in gamblers and 47.68 in controls and the total tryptophan/total LNNA ratio was 0.082 in gamblers and 0.080 in controls ($p>0.05$).

Conclusions: Free tryptophan and free tryptophan concentrations to free LNNA ratio were significantly decreased in pathological gamblers in comparison to normal controls. These findings are in agreement with the hypothesis that postulates a serotonergic dysfunction in the pathogenesis of pathological gambling.

NR322 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Elevated Peripheral Mu Opioid Receptor Densities Among Heroin Abusers

Ashwin A. Patkar, M.D., *Department of Psychiatry, T. Jefferson Medical College, 1201 Chestnut Street, Ste 1519, Philadelphia, PA 19107;* Allen R. Zeiger, Ph.D., Allan Lundy, Ph.D., Stephen P. Weinstein, Ph.D., Kenneth M. Certa, M.D.

Summary:

Objective: Opioid receptors in humans have been reported to be present on blood cells, such as monocytes, granulocytes, T-lymphocytes, and erythrocytes. Evidence indicating that opioid receptor densities on granulocytes from opiate abusers are elevated prompted us to confirm these findings and extend them to other blood cell types.

Method: Using heparinized blood enriched for white blood cells from six opioid abusers and four controls, we employed a flow cytometry assay using a rabbit antibody to the neuronal mu opioid receptor and a phycoerythrin-tagged anti-rabbit immunoglobulin.

Results: The opioid-dependent group had a mean blood cell fluorescence that was 44% higher than the control group. Examination of blood cell populations showed that all four cell types had mu opioid receptors and that the mu receptor densities on cells

from the opiate abusers were not elevated equally. Elevation was highest for glycophorin A-positive erythrocytes, helper and cytotoxic T-lymphocytes, and a cell population of unusual size that was more common in blood from opiate abusers than controls and least for monocytes and granulocytes.

Conclusions: The results are clinically important. Firstly, they suggest that chronic opiate use increases mu opioid receptors on certain blood cells. Secondly, opiate exposure seems to have different effects on mu opioid receptor regulation by different cell types. Thirdly, the presence of cells of unusual size suggests that blood trafficking may be altered among opiate abusers. Finally, since some cells, which show altered mu opioid receptor densities among opiate abusers regulate immune function, chronic opiate use may be responsible for impairment of immune activity, a hypothesis that we plan to investigate.

NR323 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Recognizing and Processing of Facial Expression in Acute First-Episode Psychosis

Minna K. Valkonen-Korhonen, M.D., *Department of Psychiatry, Kuopio University, P O Box 1777, Kuopio, FI 70211, Finland;* Ina Tarkka, Ph.D., Jan Kremlacek, M.S.C., Ari Paakkonen, Ph.D., Johannes Lehtonen, M.D., Jari Karhu, Ph.D.

Summary:

Background: Schizophrenics have behavioral deficits in recognizing facial expressions. Face-specific brain-responses have been identified in normal subjects.

Subjects: Eighteen never-medicated patients (14 females, age 16–47 years) were studied in acute psychosis (PANSS scores 106 [99–120]) and compared with 19 healthy controls (16 females, age (19–43 years).

Methods: A classical oddball paradigm was used with human faces as visual stimuli and happy expressions as targets. 64-channel continuous electroencephalogram was recorded and the event-related responses (ERPs) averaged off-line. Curry and BESA software was used for the cortex reconstruction and for calculation of the current source density maps and source locations.

Results: Patients missed more targets than controls. There was no difference in the early visual detection of stimuli around 92 ms. The ERPs at 145 and 230 ms, concerning stimulus-specific processing, were significantly larger in patients and the distribution of the activity was more unilateral. The higher the amplitudes the better the behavioral score. The patient-subgroup with the amplitudes resembling controls closest performed worst in recognizing task.

Conclusions: We observed striking neuronal hyperactivity during face-specific responses in first-episode psychosis. At the early phase of a psychotic illness it may have a compensatory role in an effort to maintain perceptual integration and social functioning.

NR324 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

The Next Generation SSRIs: A Comparison of the Transporter Binding Profile of R-Fluoxetine and S-Citalopram (LU 26-054)

Michael J. Owens, Ph.D., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322;* David L. Knight, B.S.

Summary:

Objective: Single isomers of SSRIs citalopram (*S*-citalopram) and fluoxetine (*R*-fluoxetine) are under development. For citalopram, the biological effects are predominantly mediated by its S-enantiomer, as the *R*-enantiomer is much less active for inhibiting serotonin (5-HT) transport. In contrast, both enantiomers of fluoxetine contribute to its biological activity. However, *S*-fluoxetine and its metabolite have significantly longer half-lives than *R*-fluoxetine and are potent inhibitors of P4502D6, resulting in an increased risk of drug interactions. Use of a single isomer should result in lower doses and/or an improved safety profile. In this study the potency and selectivity of *S*-citalopram and *R*-fluoxetine were assessed at the cloned human serotonin (hSERT), norepinephrine (hNET) and dopamine (hDAT) transporters.

Methods: Membranes prepared from cells expressing the human monoamine transporters were prepared. Twelve point competition curves spanning 10^{-13} – $10^{-4.5}$ mol/L of the competing SSRI were performed in triplicate.

Results: Mean results from 3–4 separate curves are shown:

	human SERT K_i (nmol/L)[a]	human NET K_i (nmol/L)[a]	human DAT K_i (nmol/L)[a]
S-Citalopram	1.13 ± 0.10	7841 ± 998	27410 ± 3107
R-Fluoxetine	1.38 ± 0.07	410 ± 59	3097 ± 268

[a]geometric mean ± SE

	Relative Selectivity (hSERT vs. hNET)	Relative Selectivity (hSERT vs. hDAT)
S-Citalopram	6939	24257
R-Fluoxetine	297	2244

Conclusions: Both *S*-citalopram and *R*-fluoxetine potently and selectively bind to the hSERT. However, *S*-citalopram is more selective than *R*-fluoxetine at the hSERT (~23 and 11 fold more selective for the hSERT vs the hNET and the hDAT, respectively). Whether the greater selectivity of *S*-citalopram for the hSERT contributes to a superior clinical profile for this agent remains to be seen.

NR325 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Human Monoamine Transporter Binding Profile of the SSRIs

Michael J. Owens, Ph.D., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322;* David L. Knight, B.S.

Summary:

Objective: The potency and selectivity with which the SSRIs bind to the monoamine transporters can theoretically predict both clinical efficacy and side effects. In the present study, we compared the binding affinity (K_i) of the currently marketed SSRIs at the human serotonin (hSERT), norepinephrine (hNET) and dopamine (hDAT) transporters.

Method: Membranes prepared from cells expressing the human monoamine transporters were prepared. Twelve point competition curves spanning 10^{-13} – $10^{-4.5}$ mol/L of the competing SSRI were performed in triplicate.

Results: Mean results from three to four separate curves are shown below:

	human SERT K_i (nmol/L)[a]	human NET K_i (nmol/L)[a]	human DAT K_i (nmol/L)[a]	Selectivity hSERT > hNET	Selectivity hSERT > hDAT
Citalopram	1.58 ± 0.12	6190 ± 818	16540 ± 3795	3917	10468
Fluoxetine	1.10 ± 0.01	599 ± 99	3764 ± 106	544	3422
Fluovoxamine	2.30 ± 0.19	1427 ± 141	16790 ± 2201	620	7300
Paroxetine	0.10 ± 0.01	45 ± 3	268 ± 8	450	2680
Sertraline	0.26 ± 0.02	714 ± 37	22 ± 1	2746	85

[a]geometric mean ± SE

Conclusions: All compounds tested were selective and had high affinity for the hSERT. Paroxetine and sertraline displayed moderate affinities for the hNET and hDAT, respectively. Citalopram showed the greatest selectivity and paroxetine the greatest potency for the hSERT. How the high selectivity of citalopram for the hSERT contributes to the favorable clinical profile of this compound is unclear.

NR326 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Cortisol Secretion in Women with Temporomandibular Disorder and Depression

Ania Korszun, M.D., *Adult Dental Health/Psychological Med., University of Wales- College of Medicine, Meath Park, Cardiff CF4 4XY, United Kingdom;* Elizabeth A. Young, M.D., Emily Dawson, B.S., Christine Brucksch, B.S., N. Cary Engelberg, M.D., Leslie Crofford, M.D.

Summary:

Temporomandibular disorders (TMD) are a common cause of chronic facial pain. They are associated with the occurrence of environmental stressors and have a high comorbidity with depression and fibromyalgia (FM), a stress-related condition of generalized myalgia. Abnormal cortisol secretion has been reported in both depression and fibromyalgia. We studied cortisol secretion in 14 women with muscular TMD, four with and 10 without comorbid depression, compared with matched normal controls, as well as 22 women with FM and 26 depressed women. All subjects were acclimatized to the General Clinical Research Center overnight and, on the following morning, an in-dwelling intravenous catheter was placed. Serial blood samples were obtained every 10 minutes for 24 hours and plasma cortisol was determined by radioimmunoassay.

There was a highly significant increase in daytime cortisol ($p = 0.004$), in women with TMD, both with and without depression, compared to controls. This pattern was similar to that observed in women with fibromyalgia, although the magnitude of the effect was greater in TMD. Depressed women, without comorbid TMD, showed a different pattern of cortisol secretion with a slight increase in cortisol levels throughout the 24 hour period. These data indicate that patients with FM and TMD show abnormal cortisol secretion distinct from that seen in depression.

NR327 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Phospholipid Metabolism in Frontal Lobe of Schizophrenia Patients

Juliana Yacubian, M.D., *Department of Psychiatry, Sao Paulo University, Rua Ovidio Pires de Campos S/N, Sao Paulo, SP 05403-010, Brazil;* Claudio C. Campi, M.D., Candida C. Pires, M.A., Mariella Ometto, M.A., Giovanni G. Cerri, M.D., Wagner F. Gattaz, Ph.D.

Summary:

Objective: To study alterations of the metabolism of phospholipid and high-energy phosphates in the frontal lobe of schizophrenics using ^{31}phosphorus magnetic resonance spectroscopy (^{31}P-MRS).

Methods: We studied 23 patients who satisfied diagnostic criteria for schizophrenia according to the Structured Clinical Interview for DSM-IV and 20 normal controls. Using ^{31}P-MRS, we measured the level of substances related to phospholipid metabolism (phosphomonoesters and phosphodiesters) and high-energy phosphates (phosphocreatine, inorganic phosphate, alpha-, beta-, and gama-adenosine triphosphate) in the frontal lobe of patients and controls. Patients were evaluated using the Brief Psychiatric Rating Scale (BPRS) and the Negative Symptom Rating Scale (NSRS). Neurocognitive performance was assessed using the Wisconsin Card Sorting Test, Stroop Test, and the Wechsler Adult Intelligence Scale (WAIS).

Results: There was a significant decrease ($p < 0.05$) of the level of phosphodiesters (PDE) in the frontal lobe of schizophrenic patients compared with controls. In schizophrenics, a negative correlation was found between the level of high-energy phosphates and neurocognitive performance.

Conclusion: Our results suggest that patients with schizophrenia have an alteration of membrane metabolism and energetic demand in the frontal lobe. These preliminary findings contrast with previous literature data that suggested an increase of PDE in schizophrenics.

NR328 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

QEEG Effects of Maintenance Clozapine Therapy in Chronic Schizophrenia Patients

Duncan J. Macrimmon, *Research Department, Hamilton Psychiatric Institute, 100 West 5th Street, Hamilton, ON L8L 2B3, Canada;* Susan J. Adams, M.D., Donald W. Brunet, M.D., Margarita Criollo, M.D., Howard Galin, Ph.D., James S. Lawson, Ph.D.

Summary:

Objective: To evaluate QEEG in chronic treatment resistant schizophrenic patients before and after Clozapine (CLZ) and whether there is a correlation between clinical change and QEEG findings.

Method: Eyes closed QEEG data (10/20–20 channels referenced to linked ears) are collected from 41 patients while on conventional antipsychotic medications and after approximately six months of CLZ. Abnormalities of individual patient topographic maps are determined by a congruence test using a pool of 477 healthy controls. A retrospective chart based review documented symptoms pre- and post-Clozapine.

Results: Aggregated congruence abnormalities of patients were greater than expected both before and after Clozapine but there was no change in the degree of abnormality. The clinical response did not correlate with: pre-, post- or pre-post abnormality. Differences between average maps were found for all frequency bands particularly for alpha, which showed increased activity frontally. Average delta, theta, and beta1 spectral power increased while beta3 decreased. There were no average map differences between the 20 most improved compared to the 21 less improved patients.

Conclusions: Maintenance CLZ produces QEEG changes that are different from conventional agents. While these effects could reflect CLZ's unique actions they do not appear to be directly related to clinical benefit.

NR329 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Dopamine Depletion in Schizophrenia: A SPECT Imaging Study

Lakshmi N.P. Voruganti, M.D., *850 Highbury Avenue, London, ON N6A 4H1, Canada;* Piotr Slomka, Ph.D., Pamela Zabel, M.S.C., Adel Mattar, M.D., A. George Awad, M.D., Giuseppe Costa, B.S.C.

Summary:

Objective: To identify inter-individual and intra-individual variations in striatal dopaminergic function, and examine their implications for predicting response to antipsychotic drug therapy in schizophrenia.

Methods: In this pilot study, drug-free schizophrenic patients ($n = 10$) were administered alpha-methyl paratyrosine (AMPT) to

induce dopamine depletion, and ^{123}I-IBZM SPECT scans were performed to measure D_2 receptor binding potentials, as an index of synaptic dopaminergic activity [Laruelle et al, 1997]. Patients' subjective responses to AMPT, and later response to antipsychotic drugs were monitored with standardized rating scales.

Results: The sequence of changes during the AMPT administration were consistent, characterized by lowered arousal, activity and mood in the first 24 hours, followed by the onset of akathisia and early extra-pyramidal symptoms towards the end of 48 hours. D_2 receptor binding ratios ranged between 4% and 35% among various subjects, and correlated significantly ($r = 0.78$, $p < 0.05$) with the time of onset dysphoria and akathisia, i.e., subjects with lower binding ratios were prone to develop early adverse effects, and responded unfavourably to treatment.

Conclusions: Synaptic dopamine may not be consistently elevated among all patients, and across all stages of psychosis, raising questions about the uniform use of dopaminergic blocking drugs in treating schizophrenia.

NR330 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Clozapine-Induced Obsessive-Compulsive Symptoms in Schizophrenia

Lakshmi N.P. Voruganti, M.D., *850 Highbury Avenue, London, ON N6A 4H1, Canada;* Chris Tremblay, R.N., Mustaq Khan, Ph.D.

Summary:

Objective: To examine clozapine's role in inducing/exacerbating obsessive-compulsive symptoms in schizophrenia.

Methods: Two matched groups of subjects receiving either clozapine (n = 50) or conventional antipsychotic drugs (n = 50) for the treatment of schizophrenia, were administered Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Leyton's Obsessional Inventory (LOI) to examine the prevalence of obsessive-compulsive symptoms. Severity of psychosis, depression and quality of life were simultaneously evaluated.

Results: The prevalence of obsessive compulsive traits (derived from LOI) was equal among the two groups (about 8.5%), but individuals receiving clozapine were at a significantly higher risk of developing obsessive compulsive symptoms (26% with clozapine, and 3.5% with others) after the initiation of antipsychotic drug therapy. The emergence of OC symptoms did significantly compromise the subjects' quality of life, but the symptoms responded well to concomitant administration of SSRIs, l-tryptophan or lamotrigine.

Conclusions: Earlier reports of increased incidence of OC symptoms among clozapine treated patients is confirmed in this cohort, raising speculations about the pathophysiological mechanisms of clozapine induced OC symptoms, especially the role of glutamate and serotonin in schizophrenia.

NR331 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Selective Modulation of Long-Term Plasticity by 5HT

Claus Normann, M.D., *Department of Psychiatry, University of Freiburg, Hauptstr 5, Freiburg 79104, Germany;* Joerg Walden, M.D., Joseph Bischofberger, Ph.D.

Summary:

Objective: To assess the modulation of different forms of synaptic long-term plasticity by 5-HT, a neurotransmitter involved in the pathophysiology of depression and the mode of action of selective serotonin reuptake inhibitors (SSRIs).

Methods: Patch-clamp experiments were performed on hippocampal slices of young adult rats and associative and conventional paradigms for the induction of long-term plasticity were used. For long-term depression (LTD), a postsynaptic action potential was asynchronously paired with a EPSP evoked by presynaptic Schaffer collateral stimulation.

Results: The associative LTD induction protocol resulted in a robust LTD of more than 50%. This was completely blocked by 1 mM 5-HT. This effect is mediated by the activation of the 5-HT_{1A}-receptor, a membrane-bound G-protein and the inhibition of calcium-influx via N-type channels. The long-term potentiation (LTP) is not impaired by 5-HT.

Conclusions: 5-HT inhibits LTD without affecting LTP, thus shifting a neural network to a more potentiated computational state. The synapses are protected from depotentiation and depression as long as 5-HT is present. Apart from being a model for learning and memory, long-term plasticity might be involved in emotional regulation and the pathophysiological and therapeutic role of 5-HT in affective states might be mediated by ist modulation of synaptic plasticity.

NR332 Tuesday, May 16, 12:00 p.m.-2:00 p.m.

Testing the Valeance Theory of Emotions Using Direct Noninvasive Brain Stimulation in Patients with GAD

Naresh P. Emmanuel, M.D., *Department of Psychiatry, Medical University of South Carolina, 67 President Street, p o box 250861, Charleston, SC 29425;* Mark S. George, M.D., R. Bruce Lydiard, M.D., James C. Ballenger, M.D., George W. Arana, M.D., Jeffrey P. Loberbaum, M.D., Olga Mintzer, M.D., Rebecca Kapp, R.N., Marsha Crawford, R.N., Alex Morton, Pharm.D., Michael R. Johnson, M.D., Sarah W. Book, M.D., Mark B. Hamner, M.D., Ziad H. Nahas, M.D.

Summary:

One version of the Valence Theory of Emotions holds that the right prefrontal cortex mediates negative emotions (e.g. anxiety) and the left prefrontal cortex mediates positive emotions (e.g. happiness). Repetitive transcranial magnetic stimulation (rTMS) is a technique for temporarily and non-invasively either exciting or inhibiting underlying superficial cortex. Some have speculated that high frequency rTMS (20 Hz) may be excitatory whereas low frequency rTMS (1 Hz) may be inhibitory. Here, we wondered whether rTMS might be used to test the valence theory of emotions. Specifically, we wondered if (1) over right prefrontal cortex, high frequency rTMS would increase and low frequency rTMS would decrease negative affect and (2) over left prefrontal cortex, high frequency rTMS would increase while low frequency rTMS would decrease positive affect. To test this theory, as part of a Generalized Anxiety Disorder (GAD) rTMS experiment, six GAD subjects were stimulated at motor threshold intensity with sham, right, and left high frequency, and right and left low frequency lateral orbitofrontal rTMS sessions over five different days in a single-blind, random order. Subjects self-rated their response using the positive and negative affect schedules (PANAS) before and 0, 20, 40, 60, and 240 minutes after rTMS. Time-points during the hour following stimulation by site and frequency were averaged and expressed as a ratio to that day's baseline rating. Confirming the hypothesis, compared with placebo, right prefrontal high frequency rTMS significantly increased negative affect ($p = 0.04$). In contrast, however, there was also a trend for left prefrontal high frequency rTMS to increase negative affect as well ($p = 0.08$). Moreover, low frequency stimulation of either hemisphere also non-significantly increased negative affect. There was no significant or even trend change in positive affect at any site or frequency. These results failed to find changes in affect by hemisphere and frequency consistent with pre-study hypotheses. This small study highlights the potential for using TMS to test regional neuroanatomic theories of emotion regulation. Caveats and confounds of this approach include pain with stimulation, probable bilateral effects of unilateral stimulation, and uncertainty about

whether different frequencies of stimulation truly have opposite effects on cortex and resultant behavior.

NR333 Tuesday, May 16, 12:00 p.m.-2:00 p.m.
B-Casomorphin, Schizophrenia and Autism

Zhongjie Sun, M.D., *University of Florida-Medical, Box 100274, Gainsville, FL 32610;* Robert Cade, M.D.

Summary:

Objective: The objective of this study is to determine the possible role of β-casomorphine-7 (β-CM7), whose concentration is significantly elevated in urine, blood, and CSF of schizophrenic and autistic patients, in the pathogenesis of schizophrenia and autism.

Method: In the first experiment, the induction of an immediate early gene, Fos, was used to map brain regions activated by intravenous infusion of different doses (5, 10 and 30 μg/kg) of β-CM7. The second experiment was designed to determine whether β-CM7 causes behavioral changes in rats.

Results: β-CM7 at different doses induced moderate to strong Fos expression in the nucleus accumbens, caudate putamen, ventral tegmental area, median raphe nucleus, and orbitofrontal, prefrontal, parietal, temporal, occipital, and entorhinal cortex. All of the above areas have been shown to be altered either functionally or anatomically in patients with schizophrenia, and most have been shown to function abnormally in autism. β-CM7 caused behavioral abnormalities (restlessness, violent running, reduced sound response, absent social interaction, hyperdefensiveness, etc.) in rats, which are behaviors found frequently in schizophrenia and autism.

Conclusions: β-CM7, a casein-derived exorphin, appears to play a role in the pathogenesis of schizophrenia and autism.

NR334 Tuesday, May 16, 12:00 p.m.-2:00 p.m.
Sertraline and Fluoxetine Treatment of OCD

Arun V. Ravindran, M.D., *Department of Psychiatry, Univ of Otta Royal Ottawa Hosp, 1145 Carling Avenue, Ottawa, ON K12 7K4, Canada;* Richard Bergeron, M.D., Vratislav Hadrava, M.D., Yves Choput, M.D., Elliot M. Goldner, M.D., Richard P. Swinson, M.D., Michael A. Van Ameringen, M.D.

Summary:

Objective: To evaluate the comparative efficacy and tolerability of sertraline versus fluoxetine in the treatment of obsessive compulsive disorder (OCD).

Methods: One hundred fifty adult, non-depressed outpatients with DSM-IV OCD from 11 Canadian centers were randomized double-blind to either sertraline (77) or fluoxetine (73) for 24 weeks following one week single blind placebo run-in. The initial daily dosage of sertraline was 50 mg and that of fluoxetine 20 mg with increases of 50 mg/day or 20 mg/day, respectively, every two weeks permitted after the fourth week of treatment. Primary efficacy assessments were the Yale-Browne Obsessive-Compulsive Scale, National Institute of Mental Health Obsessive-Compulsive Rating and Clinical Global impressions Scale of Severity.

Results: Seventy-six and 72 patients receiving sertraline and fluoxetine, respectively, were included in ITT analysis (total 148). Fifty-five (72%) sertraline-and 51 (71%) fluoxetine-treated patients completed the study. There was no significant differences between the groups in baseline measures and demographics. At endpoint, on all efficacy measures both compounds showed significant treatment effect ($p < 0.001$) compared to baseline values (e.g. Y-BOCS, baseline to week 24, sertraline: 25 ± 5 to 13 ± 8, fluoxetine; 26 ± 5 to 15 ± 8) with significant improvement starting as early as second week. However, on several measures including Y-BOCS and CGI-S, sertraline presented significantly greater response at several assessments points between visits four to 12 weeks. As well, at week 12, the distribution by severity was significantly different between groups with higher number of sertraline-treated patients being rated with CGI-S mild to normal (sertraline:49% vs fluoxetine:25%, $p = 0.007$).

Both treatments were well tolerated with no overall significant difference in the frequency of total or serious adverse events with some differences noted in the individual adverse event profile.

Conclusion: The study demonstrated that both sertraline and fluoxetine are effective and well tolerated in the long-term treatment of OCD. There is some evidence suggesting that sertraline induce improvement at an earlier time point.

NR335 Tuesday, May 16, 3:00 p.m.-5:00 p.m.
Fluvoxamine in OCD Schizophrenia

Pinkhas Sirota, M.D., *Abarbanel Mental Health Center, 15 Keren Kayemet, #6A, Bat-Yam 59100, Israel;* Ilya Reznik, M.D.

Summary:

Background: Obsessive compulsive related disorders are frequent comorbidities of schizophrenia. Previous studies have shown that some schizophrenic patients improved when serotonin reuptake blockers were added to their standard neuroleptic regimen.

Objective: To evaluate the efficacy of a combination of a selective serotonin reuptake inhibitor (fluvoxamine) with standard neuroleptics in treatment of obsessive compulsive symptomatology in schizophrenic patients as compared with neuroleptic-only therapy.

Methods: Thirty inpatients who met DSM-IV criteria for schizophrenia and had prominent obsessive compulsive symptoms were divided randomly into two groups. Fourteen patients were treated with conventional neuroleptics and fluvoxamine (Favoxil) in doses of 100–200 mg/day for eight weeks. Sixteen patients comprised a control group and received only their previous therapeutic neuroleptic therapy. The patients were assessed by Y-BOCS, PANSS, and CGI at baseline and endpoint. Side effects were assessed weekly. The data were analyzed using ANOVA and two tailed t-test.

Results: Considerable reduction in PANSS (34.3%) and Y-BOCS (29.4%) scoring was noted, CGI decreased moderately in both groups. Statistically significant differences ($p < 0.05$) between delta's of almost all parameters and subscores were observed. None of the patients showed an acute exacerbation at the endpoint of the study. Side effects were mild and easily tolerated in most patients.

Conclusions: This randomized controlled study reveals that coadministration of fluvoxamine, a selective serotonin reputake blocker, and neuroleptics in schizophrenic patients with obsessive compulsive symptoms was associated with specific improvements of these symptoms and probably augmented the efficacy of neuroleptics in these patients. Thus, the use of a SSRI in schizophrenic patients with OC symptoms is warranted and safe. Other implications of the findings, including general safety of combined pharmacotherapy and use of new antipsychotic medications are also discussed.

NR336 Tuesday, May 16, 3:00 p.m.-5:00 p.m.
Do Classic and Mixed Manic Episodes Run True?

Scott W. Woods, M.D., *Department of Psychiatry, Yale University, 34 Park Street, Room B38, New Haven, CT 06519;* C. Bruce Baker, M.D.

Summary:

The possible greater efficacy of lithium relative to divalproex in classic manic episodes and other evidence for differential treatment response in mania episodes vs. mixed episodes raise the

possibility that manic episodes and mixed episodes may run true over time.

Methods: We queried our management information system for all patients at our CMHC who had one or more diagnoses entered into the system of 296.4× (manic episode, M), 296.5× (bipolar depressed episode), or 296.6× (mixed episode, X) from 8/1/89 to 8/1/99, yielding 4,988 diagnostic entries in 1,449 patients. If the manic episode vs. mixed episode distinction did not run true over time, the statistic M/M + X within individuals would be expected to be normally distributed.

Results: M/M + X was not normally distributed in any analysis (example analysis in subjects for whom M + X > 2, K − S (Lilliefors) = .18, p = .0000). On inspection, M/M + X distributions took bimodal patterns with modes at 0 (all mixed) and 1 (all manic).

Discussion: Despite methodologic limitations, the suggestion of a pattern of diagnostic stability over time for classic and mixed mania episodes strengthens the need for research investigating treatment effectiveness separately in these episode subtypes.

NR337 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Weight and Metabolic Changes with Clozapine and Olanzapine

Daniel E. Casey, M.D., *Department of Psychiatry, Portland VA Medical Center, 3710 SW Veterans Hospital Road, Portland, OR 97201*

Summary:

Rationale: Atypical antipsychotic drugs have become the standard of care for treating acute and chronic psychoses. These new medicines have the benefits of better efficacy and far fewer side effects of extrapyramidal syndromes and tardive dyskinesia. However, some of these agents can cause weight gain.

Objective: To assess the prevalence and magnitude of weight changes in a real-life setting, a retrospective chart review of patients receiving clozapine or olanzapine for four months or more was conducted.

Methods: Changes in weight, body mass index (BMI), and measures of carbohydrate metabolism (fasting glucose) were assessed. All patients were treated in the Portland, Oregon VA Mental Health Division: 29 received clozapine and 136 received olanzapine. Patients were only included if they had paired (pretreatment and during treatment) values on a variable.

Results: Mean length of treatment with clozapine was 3.6 years and with olanzapine was 1.4 years. Using > 7% above baseline weight as the threshold of weight gain as an adverse effect (FDA definition), 69% of patients on clozapine met this criterion, as did 50% of the olanzapine-treated patients. Weight increased from 172 to 198 pounds (15%) during clozapine and from 188 to 204 pounds (8.5%) during olanzapine. BMI increased from 25.23 to 29.35 (16%) during clozapine and from 28.08 to 30.80 (9.7%) on olanzapine. For both drugs, neither weight gain nor BMI change was correlated with age, gender, dose, duration of treatment, or starting weight. Glucose levels also showed increases. In the clozapine group six out of 16 patients (38%) with normal pretreatment fasting glucose levels had elevated fasting glucose levels during treatment. In the olanzapine group seven out of 39 (18%) converted from normal to abnormal fasting glucose during treatment.

Conclusion: These data confirm that weight gain can be a clinically significant issue with some atypical antipsychotics and may increase the risk for weight-related medical illnesses such as diabetes mellitus.

NR338 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Effect of Olanzapine and Other Antipsychotics on Human Cardiac Ion Channel Blocking

William Crumb, Ph.D., *Zenas Technologies, 5896 Fleur de Ris Drive, New Orleans, LA 70124;* Charles M. Beasley, Jr., M.D., Alan F. Breier, M.D., Anna Thornton, Pharm.D.

Summary:

The use of a number of the members of the antipsychotic class of drugs has been associated with arrhythmias. The mechanism underlying these arrhythmias is most likely block of one or more cardiac ion channels. Experiments were therefore undertaken to evaluate the blockade by six antipsychotics (thioridazine, pimozide, haloperidol, clozapine, risperidone, and olanzapine) of the human cardiac sodium channel (I_{Na}) and four human cardiac potassium channels (I_{to}, I_{sus}, I_{Kl}, HERG) using the whole-cell patch clamp technique. These ion channels play a crucial role in cardiac conduction and repolarization. Fifty percent blockade (IC_{50}) of I_{Na}, I_{to}, I_{sus}, I_{Kl} was achieved by concentrations of these drugs in excess of 1 μM and in the case of olanzapine by concentrations exceeding 100μM. Such concentrations are substantially in excess of free drug concentrations achieved following therapeutic administration. In contrast, HERG was blocked with nM affinity with IC_{50} values ranging from 28nM—181nM, olanzapine having the highest IC_{50}. Taking into consideration the concentration of free drug, those members of this class of drugs more frequently associated with arrhythmias were found to produce a more profound block of HERG over a relevant concentration range. Thioridazine, haloperidol, and clozapine produced up to a 50% reduction in HERG current amplitude over a therapeutic concentration range, while olanzapine, pimozide, and risperidone produced less than a 10%-15% reduction of HERG current amplitude, even at the highest predicted therapeutic concentration. In conclusion, it is likely that block of HERG may contribute to the arrhythmias observed with this class of agents and may help to differentiate those agents more likely to be arrhythmogenic.

NR339 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Study of First-Episode Psychosis As an Early Intervention Strategy in Mexico

Ana Fresan, M.D., *Clinical Research Division, Psychiatric Institute of Mexico, Calz. Mexico-Xochimilco 101, Mexico City 14370, Mexico;* Rogelio Apiquian, M.D., Rosa E. Ulloa, M.D., Humberto Nicolini, Ph.D., Christina Loyzaga, M.D.

Summary:

Objectives: To examine a) the demographic and clinical characteristics, as well as comorbidity with substance abuse; b) the pathways to care; c) the premorbid functioning, and d) personality traits in a group of Mexican patients on their first psychotic episode at the moment of admission.

Method: 41 patients with nonaffective psychosis and 22 patients with affective psychosis were evaluated in a cross-sectional and descriptive study. Diagnoses were made with rating scales for psychotic symptoms, affective symptoms, movement disorders, premorbid functioning, and social functioning. Personality traits were examined with Cloninger's Temperament and Character Inventory (TCI).

Results: Age of onset of psychosis was 27+/−10 y.o. Duration of untreated psychosis (DUP) was 60+/−75 weeks. 26 (41.3%) patients had comorbid substance abuse, mainly alcohol (32%) 27 (43%) patients contacted first with a psychiatrist. Premorbid functioning was poor, in general and worse in patients with nonaffective psychosis. Psychosocial functioning was poor, particularly in the occupational area. Patients showed higher scores in harm avoidance and self-trascendence TCI temperament dimensions,

as well as lower scores in self-directedness TCI character dimension.

Conclusion: This is the first report of a first psychotic episode in Mexico and Latin America. The findings were consistent with previous first-episode studies. Patients showed a long DUP, which leads to perform early-detection programs focused in prodromic phases.

NR340 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Alpha-2 Agonists Enhance Cognition of Schizophrenia Patients in Combination with Atypical But Not Typical Neuroleptics

Joseph I. Friedman, M.D., *Department of Psychiatry, Mt. Sinai Hospital-School of Medicine, Box 1230, One Gustave Levy Place, New York, NY 10029;* David Adler, M.D., Humberto D. Temporini, M.D., Philip D. Harvey, Ph.D., Eileen M. Kemether, M.D., Kenneth L. Davis, M.D.

Summary:

Background: Although the significance of dopaminergic inputs with relation to PFC mediated cognitive functions has been extensively studied, noradrenergic inputs also have an importance influence. The alpha-2 noradrenergic agonist clonidine has previously been shown to improve PFC mediated cognitive functions in schizophrenic patients. Guanfacine, a selective alpha-2a agonist (Uhlen et al. 1995) also improves PFC cognitive functions, but without the significant adverse effects associated with clonidine (i.e., sedation, hypotension). Therefore, a double-blind, placebo-controlled trial of guanfacine adjunctive treatment to neuroleptic medication was conducted to test the efficacy of guanfacine in ameliorating some of the cognitive impairment in schizophrenia.

Methods: A total of 40 schizophrenic subjects receiving neuroleptic treatment were randomized to a four-week trial of guanfacine 2 mg per day or placebo adjunctive treatment. Subjects were assessed with an extensive cognitive battery, psychiatric and medical assessments.

Results: Overall, there was no significant effect of guanfacine treatment on cognitive test performance. However, when neuroleptic status was considered, a cognitive enhancing effect became apparent. Risperidone treatment was associated with an average improvement of five words on serial verbal learning ($t = 2.75$, $p = .01$), whereas treatment with typical neuroleptics was associated with an average 1.6 word improvement ($t = .81$, $p = .4$). In addition, risperidone treatment was associated with an average improvement on CPT signal detection index (D-prime) to 1.03 ($t = 2.47$, $p = .02$), whereas treatment with typicals was associated with an average increase in D-prime to 0.35 ($t = .1$, $p = .9$). The combination of risperidone and guanfacine produced an average 40 second improvement on Trails B performance ($t = 2.7$, $p = .02$), a 3.1 point improvement on the spatial working memory task ($t = 2.3$, $p < .05$), and a 55 msec decrease on CPT reaction time ($t = 2.04$, $p = .08$).

Conclusions: These data provide preliminary evidence for the effectiveness and safety of the alpha 2a agonist guanfacine as adjunctive treatment to risperidone for the treatment of cognitive dysfunction in schizophrenia.

NR341 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The PERSIST-Study: A Clinical Comparative Study of Atypical Neuroleptics in the Treatment of Schizophrenia

Christian Perro, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20251, Germany;* Martin Lambert, M.D., Steffen Moritz, Ph.D., Michael Krausz, Ph.D., Dieter Naber, M.D.

Summary:

Objective: Because of the necessity of long-term treatment in schizophrenia, an optimal initial therapy is of major importance. Newer antipsychotic agents appear to show better tolerability and efficacy but few comparative studies of the new antipsychotics has been done.

Method: We started a prospective clinical study (PERSIST-project) in the treatment of schizophrenia. The effectiveness of atypical agents (risperidone, zotepin, olanzapine, sertindole, and amisulprid) was compared with regard to psychopathology, compliance, quality of life, neuropsychology and comorbidity.

Results: 103 patients (66% men, 40% first episode patients, age 32 +/– 11 yrs.) were included. Psychopathology (PANSS) on admission was similar in all groups. First episode patients scored slightly lower than those with multiple rehospitalizations. All examined antipsychotics showed a good clinical response in first- and multiple-episode patients and differed only in the spectrum of side effects. The hospital stay of first-episode patients was shorter and the symptom scores were less severe than those of multiepisode patients.

Conclusion: All examined antipsychotic agents showed similar response in the treatment of schizophrenia in first- and multi-episode patients, even in the acute phase. There was little evidence for subgroups of responders to the different antipsychotics with regard to psychopathology.

NR342 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Cognitive Effects of Risperidone and Olanzapine in Patients with Schizophrenia or Schizoaffective Disorder

Philip D. Harvey, Ph.D., *Department of Psychiatry, Mt. Sinai Medical Center, 1 Gustave L. Levy Place, Box 1230, New York, NY 10029*

Summary:

Background: Novel antipsychotic medications have been reported to enhance cognition in patients with schizophrenia, in contrast to the negligible effects of conventional medications. In this study, the relative cognitive enhancing effects of risperidone and olanzapine, the two most commonly used of the newer medications, were compared.

Methods: Three hundred seventy-seven outpatients with schizophrenia or schizoaffective disorder were randomized to eight weeks of double-blind treatment with 2–6 mg/day of risperidone or 5–20 mg/day of olanzapine. The patients were rated with assessments of clinical symptoms and side effects (reported separately) and with a cognitive functioning battery examining secondary and working memory, vigilance, visuomotor speed, executive functioning, and verbal fluency.

Results: Statistically significant improvements from baseline functioning for patients treated with risperidone ($n > 116$, n's vary by the test) were detected at eight weeks for total learning over five trials on the California Verbal Learning Test (CVLT), Wisconsin Card Sorting Test (WCST) categories completed, and WCST total errors. Olanzapine ($n > 125$, n's vary by the test) improved performance on Trail Making Test part B, CVLT total learning, and the CPT. There were no statistically significant differences between the two medications in the extent of cognitive enhancement on any of the measures.

Implications: Risperidone treatment enhances cognitive functions that are known to be correlated with functional outcome in schizophrenia. In contrast to a small number of reports based on small sample sizes with different dosing schedules, there was no evidence of superiority of olanzapine to risperidone in enhancing any aspect of cognitive functioning. These findings replicate several previously published studies of cognitive change with risperidone treatment, using a larger sample size, more representative

samples of patients with schizophrenia, and double-blind methodology. Given these findings, differential cognitive benefits may play a lesser role than other efficacy and safety factors when choosing among atypical antipsychotics.

NR343 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Long-Term Cognitive Effects of Risperidone Treatment in Schizophrenia

Philip D. Harvey, Ph.D., *Department of Psychiatry, Mt. Sinai Medical Center, 1 Gustave L. Levy Place, Box 1230, New York, NY 10029*

Summary:

Background: Cognitive enhancement has been demonstrated with novel antipsychotic medications. The duration of these studies has been quite shor and there is no information avaialable about the long-term cognitive-enhancing efects of these medications.

Methods: Three hundred sixty-seven clinically stable, community-dwelling patients with schizophrenia were randomized to one year's treatment with risperidone or haloperidol. The patients were examined at 16 and 52 weeks after baseline with assessment of clinical symptoms and cognitive functioning. Rates of relapse were also examined.

Results: 121 subjects completed the 52-week protocol, while 25% of the risperidone patients and 40% of the haloperidol patients relapsed ($p < .01$). Total learning on the California Verbal Learning Test was the one aspect of cognitive functioning that was significantly enhanced by treatment with risperidone at both 16 and 52 weeks ($p < .05$). At 52 weeks, 45% of the patients treated with risperidone improved by more than 0.5 SD on this index of learning efficiency, resulting in their having scores in the clinically normal range at the end of the study.

Implications: In addition to preventing relapse in stable patients with more efficiency than haloperidol, risperidone improved memory performance as well. This improvement was clinically as well as statistically significant, indicating that risperidone treatment improves certain aspects of cognitive functioning even in patients who are selected for the absence of notable clinical symptoms.

NR344 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Improvement in Cognition Following a Switch to Open-Label Ziprasidone in Outpatients with Schizophrenia Treated with Conventional Antipsychotics, Olanzapine or Risperidone

Philip D. Harvey, Ph.D., *Department of Psychiatry, Mt. Sinai Medical Center, 1 Gustave L. Levy Place, Box 1230, New York, NY 10029;* Herbert Y. Meltzer, M.D., Steven J. Romano, M.D.

Summary:

Objective: Newer antipsychotic medications, in contrast to conventional compounds, have been reported to enhance cognitive functions in patients with schizophrenia. The ability of ziprasidone, a novel agent with a unique pharmacological profile, to improve cognitive functions was assessed in stable outpatients switched to ziprasidone due to lack of efficacy or intolerability of previous treatment.

Methods: Patients were randomized to a one of three dosing schedules and switched to ziprasidone 40–160 mg/day from conventional antipsychotics ($n = 93$), olanzapine ($n = 88$), and risperidone ($n = 41$) in three separate multicenter trials. Patients were assessed before switching and following six weeks of ziprasidone treatment with a cognitive assessment battery including specific tests of working and secondary memory, vigilance, visuo-motor speed, verbal fluency, and executive functioning.

Results: Patients switched to ziprasidone manifested wide-ranging improvements in cognitive functioning. Significant improvements were seen in all domains tested, including verbal fluency, learning and memory, executive functioning, and attention and vigilance ($p < 0.05$).

Conclusions: Treatment with ziprasidone enhanced cognitive functioning in patients with schizophrenia. These findings suggest that patients requiring a change in antipsychotic therapy may experience benefits in cognitive functioning following a switch to ziprasidone.

NR345 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Efficacy of Aripiprazole in Psychotic Disorders: Comparison with Haloperidol and Placebo

John M. Kane, M.D., *Department of Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004-1150;* Gary Ingenito, M.D., Mirza Ali, M.D.

Summary:

Objective: To compare the efficacy of aripiprazole, a novel agent in development for the treatment of symptoms associated with psychotic disorders, haloperidol and placebo in patients with schizophrenia or schizoaffective disorders.

Methods: Double-blind, four-week study comparing two doses of aripiprazole (15 mg; 30 mg), haloperidol (10mg) and placebo in over 400 hospitalized patients with acute relapse of schizophrenia or schizoaffective disorder (DSM-IV diagnosis).

Results: Both doses of aripiprazole and haloperidol were significantly more effective than placebo (change in PANSS-total, BPRS-total, LOCF; $p < 0.01$). Responder rates (30% decrease from baseline in PANSS-total at last visit) for both aripiprazole doses were significantly better than for placebo ($p < 0.05$), but did not differ significantly between haloperidol and placebo ($p > 0.1$). Aripiprazole was well tolerated; fewer patients discontinued treatment due to adverse events than with placebo or haloperidol. Aripiprazole-treated subjects showed no clinically meaningful increases in QTc prolongation and had comparable extrapyramidal symptomatology to subjects receiving placebo. In aripiprazole-treated patients, the mean change in plasma prolactin levels was comparable to placebo and less than haloperidol, while the incidence of clinically significant weight gain was less than with haloperidol.

Conclusions: This study clearly demonstrates the clinical efficacy and tolerability of aripiprazole and suggests it may be an important future therapeutic option.

NR346 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Tardive Dyskinesia in Chinese and Malays

Siow A. Chong, M.B., *Woodbridge Hospital, 10 Buangkok View, Singapore 539747, Singapore;* Rathi Mahendran, M.B., David Machin, Ph.D., Hong-Choon Chua, M.B., Gordon Parker, Ph.D., John M. Kane, M.D.

Summary:

Objective: We sought to establish the point prevalence of tardive dyskinesia among Chinese and Malay patients with schizophrenia hospitalised in a Singapore state mental institute and to examine for any association of tardive dyskinesia (TD) with neuroleptic-induced extrapyramidal side effects, age, gender, duration of neuroleptic treatment, and exposure to anticholinergic medications.

Method: Dyskinesia was assessed by the Abnormal Involuntary Movement Scale, while extrapyramidal side effects (EPSE) were assessed by the Simpson-Angus Rating Scale by raters who were blind to the clinical and medical histories.

Results: Of the 602 patients, 537 (89.2%) were Chinese and 65 (10.8%) were Malays. Using criteria proposed by Schooler and

Kane, the rates of TD were 40.6% for Chinese and 29.0% for Malays, higher than previously reported for Chinese subjects. Older age, lower current neuroleptic dose, and higher Simpson-Angus scores for parkinsonism were significantly associated with TD. Multivariate analysis did not show a significant difference in TD prevalence rate in the two races.

Conclusions: We conclude that suggested differences in inter-ethnic vulnerability for developing TD between Chinese and Malays are unlikely to exist and that any variation in prevalence is more likely to be determined by differences in duration of exposure and dose levels of neuroleptic drugs.

NR347 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Rapid Reduction in Hyperprolactiremia

Bruce J. Kinon, M.D., *Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285;* Bruce R. Basson, M.S., Jeff Wang, M.S., Sandra K. Malcolm, B.S., Virginia L. Stauffer, Pharm. D.

Summary:

Objective: To determine whether serum prolactin (PRL) levels were reduced in patients switched to treatment with olanzapine during a three-week clinical trial that studied the medication switching phenomenon.

Method: This multi-site study was designed to compare strategies for switching patients from previous antipsychotics to olanzapine. Outpatients with a diagnosis of schizophrenia or schizoaffective disorder and with documented clinical stability while being treated with a conventional antipsychotic or risperidone were randomized to one of four medication switching paradigms. Patients completing the study had been on olanzapine 10 mg/day as monotherapy for one to three weeks. PRL data was collapsed across all 4 switching groups.

Results: Baseline and endpoint serum PRL were obtained in 176 out of 209 patients. The prevalence of hyperprolactinemia among patients previously taking conventional antipsychotics ($n = 131$) dropped from 36% to 13% after three weeks of the study ($p < 0.001$). For those previously on risperidone ($n = 45$), the prevalence dropped from 76% to 22% after three weeks of the study ($p < 0.001$). For patients switched from conventional antipsychotics, mean serum PRL dropped from 24.01 ± 24.31 ng/ml to 13.68 ± 14.67 ng/ml ($p < 0.001$); for those switched from risperidone, levels decreased from 48.80 ± 38.14 ng/ml to 16.54 ± 17.51 ng/ml ($p < 0.001$).

Conclusions: Stable outpatients who switch to olanzapine from conventional antipsychotics or risperidone may demonstrate a significant reduction in prevalence of hyperprolactinemia and a reduction in mean serum PRL over a three-week switching process.

NR348 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Ziprasidone's Effect on Anxiety in a Group of Outpatients with Stable Schizophrenia

Nina R. Schooler, Ph.D., *Psychiatric Research Dept, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004;* Cynthia O. Siu, Ph.D.

Summary:

Objective: Nearly 50% of patients with schizophrenia have comorbid anxiety disorders. Ziprasidone's unique pharmacological profile, including 5HT1A agonism and 5HT and NE reuptake inhibition, may confer anxiolytic properties. An exploratory analysis was conducted to evaluate improvement in anxiety in outpatients with stable schizophrenia, as standard scales assessing psychosis do not adequately address anxiety. Stable outpatients were selected to reduce the influence of acute psychosis.

Methods: Patients on conventional antipsychotics ($n = 93$), olanzapine ($n = 88$), and ripseridone ($n = 41$) were randomized to one of three dosing schedules and received ziprasidone 40–160 mg/day in three six-week, open-label trials. Anxiety was measured by the PANSS anxiety item (G2; 1, absent, to 7, extreme). Analysis of patients with moderate or greater (≥4) anxiety, as well as analysis of those with at least minimal anxiety (≥2), was conducted. Other symptom items were analyzed to address the specificity of potential treatment effects.

Results: In patients with moderate or greater baseline anxiety, significant improvement in the PANSS anxiety item was observed ($p < 0.05$) independent of changes in depression or somatic concern. Significant improvement was also seen in the group of patients with at least minimal baseline anxiety ($p < 0.05$).

Conclusions: Improvement in the PANSS anxiety item, separate from changes in depression and somatic concern, was observed. In view of the prevalence of anxiety symptoms in schizophrenia, controlled trials using anxiety scales validated in this population are necessary to further evaluate ziprasidone's anxiolytic potential.

NR349 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Quality of Life and Well-Being of Schizophrenia Patients Under New Drug Treatment

Anne Karow, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20246, Germany;* Steffen Moritz, Ph.D., Michael Krausz, Ph.D., Martin Lambert, M.D., Dieter Naber, M.D.

Summary:

Subjective quality of life (QoL) and well-being are increasingly emphasized in the treatment of schizophrenia. The PERSIST-Project, treatment program and research project, assesses QoL, psychopathology and side effects during treatment of 100 schizophrenic patients by different atypical neuroleptics (amisulpride, clozapine, olanzapine, risperidone or zotepine). QoL, psychopathology, and side effects were measured at the beginning of neuroleptic therapy, shortly before discharge, after six months, and after one year by different QoL instruments (Alltagsleben, MLDL, SF-36, SWN), psychopathology (PANSS) and side effects (UKU). Patients rated their QoL significantly higher at the time of discharge from inpatient treatment compared with the beginning of treatment. Psychopathology, side effects, and subjective rating of QoL were not significantly correlated. At the six-months follow-up there was less change in rating of QoL compared to time of discharge. Psychotic symptoms seem to have very little influence on the rating of QoL. So both QoL and psychopathology should be measured independently. The assessment of QoL may be a valuable addition in the measurement of outcome in the treatment of schizophrenia.

NR350 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Negative Symptoms, Cognitive Dysfunction and Disability in Schizophrenia: Evidence of an

Mark Ast, Ph.D., *Psychiatric Rehabilitation, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004;* Stefanie Berns, Ph.D., Judith Jaeger, Ph.D., Pal Czobor, Ph.D., Stephen Panopoulos, M.A.

Summary:

Objective: In schizophrenia, disability in independent life functioning has been associated with both negative symptoms and cognitive deficits. Because cognitive deficits and negative symptoms are themselves associated, we wanted to clarify whether each alone contributes to disability or whether both impaired cognitive performance and disability might be the consequences of negative symptoms.

Method: Subjects with SCID-DSM-IV schizophrenia (N = 81) or schizoaffective disorder (N = 62) received a neuropsychological battery following hospital discharge. Symptomatology and disability were assessed longitudinally (≤18 months). Symptoms were rated using PANSS, and disability was rated using the Multidimensional Scale of Independent Functioning.

Results: Negative symptoms are associated with disability independent of impaired cognitive performance and deficits in such cognitive factors as memory span, working memory, and language are associated with disability independent of negative symptoms. With respect to disability, significant interactions are observed between negative symptoms and memory span ($p = .008$) and working memory ($p = .05$), with a trend for language ($p = .09$). Cognitive deficits are associated with disability in subjects with low but not high levels of negative symptoms.

Conclusion: Negative symptoms and cognitive deficits independently contribute to disability and may interact to produce more severe functional consequences than either alone. Effective rehabilitation efforts must recognize and address both.

NR351 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Interaction Gender Differences in the Disability of Schizophrenia

Mark Ast, Ph.D., *Psychiatric Rehabilation, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004;* Judith Jaeger, Ph.D., Stefanie Berns, Ph.D.

Summary:

Objective: Women with schizophrenia have been reported to have a less severe form of the disorder as a group than their male counterparts with respect to symptoms and disability. We sought to determine whether this finding would be replicated in a sample of outpatients with schizophrenia males and females being followed in the community after discharge from an acute hospitalization.

Method: 87 male and 56 female patients with schizophrenia or schizoaffective disorder (SCID DSM-IV) were recruited within six months following discharge into the community from a psychiatric hospitalization and received follow-up (≤18 months) assessments for symptomatology and disability in life functioning (LF). Symptomatology was rated using the PANSS and LF was measured by the overall global rating of the Multidimensional Scale of Independent Functioning (MSIF-OG).

Results: Males and females were not significantly different from one another on PANSS positive, negative, or general scores or on BPRS factors. Nevertheless, females achieved a significantly higher level of LF than males ($p < .0008$). LF was unrelated to age, years ill, education, or diagnosis.

Conclusion: Among patients recently discharged from a hospitalization for acute exacerbation, females were significantly less disabled in spite of there being no discernable gender differences in psychopathology.

NR352 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Gender, Cognition and Disability in Schizophrenia: Evidence of an Interaction

Judith Jaeger, Ph.D., *Psychiatric Rehabilation Department, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004;* Mark Ast, Ph.D., Stefanie Berns, Ph.D., Pal Czobor, Ph.D., Ann-Marie Donovan, M.A.

Summary:

Objective: It has been consistently observed in schizophrenia that: a) neuropsychological deficits are associated with disability in life functioning (LF) and b) females suffer less disability than males. This study investigated gender differences in the association between neuropsychological deficits and LF.

Method: 143 subjects (61% male) with SCID-DSM-IV schizophrenia (57%) or schizoaffective disorder were administered a comprehensive neuropsychological test battery at baseline (within six months of hospital discharge) and LF assessments longitudinally (up to 18 months). LF was measured by the overall global rating of the Multidimensional Scale of Independent Functioning (MSIF-OG) which ranges from (normal) to 7 (severely disabled).

Results: LF was unrelated to age, years ill, education, or diagnosis. Females achieved a higher level of LF than males ($p < .0008$), a difference that remained after accounting for neuropsychological performance. There were significant interactions, with respect to LF outcome, between gender and two neuropsychological domains: working memory ($p = .007$) and ideational fluency ($p = .02$)). These domains were significantly correlated with LF in females ($r = .51$, $p = .0001$ and $r = .40$, $p = .002$) but not males ($r = -.05$, $p = .64$ and $r = .17$, $p = .12$).

Conclusion: Cognitive deficits in schizophrenia may affect the genders differently with respect to disability. Rehabilitative interventions targeting cognitive deficits should consider gender specific strategies for maximum efficacy.

NR353 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Summer Birth and the Deficit Syndrome of Schizophrenia

Brian Kirkpatrick, M.D., *Department of Psychiatry, MD Psychiatric Residential Center, PO Box 21247, Baltimore, MD 21228-0747;* Erick L. Messias, M.D.

Summary:

Background: An association between the deficit syndrome and summer birth, in contrast to the winter birth risk factor associated with schizophrenia, was previously reported.

Aims: To test this association, we examined data from three population-based studies approximating treated-incidence samples of psychosis (Spain, England, and Ireland), and two population-based prevalence studies (Scotland and the U.S. Data sets developed by D Castle, RM Murray, C Kelly, RG McCreadie, D Walsh, KS Kendler, S Herrera, J Vazquez-Barquero.

Method: Patients were categorized into deficit and nondeficit groups using the Proxy for the Deficit Syndrome, and the association with summer birth tested using logistic regression.

Results: Results from four of the datasets largely supported the association of summer birth and the deficit syndrome (values for p for each definition):

	June/July/August	June/July	July/August	May-August	# deficit patients
Spain	<.02	<.08	<.04	<.003	22
England	<.08	.36	<.03	<.005	46
Scotland	<.03	<.04	<.03	<.06	50
US	<.01	<.003	.10	.01	77

In the Irish study (N = 22) there was no association with summer birth.

Conclusions: These results provide some confirmation for an association between summer birth and the deficit syndrome; the effect size appears to be greater than for the winter birth association, which may apply to the nondeficit form of schizophrenia only.

NR354 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

High Diabetes Frequency in Schizophrenia and Bipolar Disorder

Henry A. Nasrallah, M.D., *Department of Psychiatry, University of Mississippi, 1500 E. Woodrow Wilson Drive, Jackson, MS 39216;* Thantween S. White, Mary Robbins

Summary:

Several studies have reported an elevated frequency of diabetes mellitus (DM) in manic patients, up to three times the general population DM rate of 3.3%. Recent reports have also indicated that DM may develop in schizophrenia or schizoaffective patients treated with some atypical antipsychotics. Although weight gain is blamed for the emergence of DM in patients with psychosis, some cases of DM were *not* associated with weight gain, suggesting a possible susceptibility to DM in psychotic patients. We hypothesized that all psychotic disorders may be associated with elevated levels of DM, and we report the following confirmatory study.

All patients carrying a diagnosis of bipolar disorder (N = 276), schizoaffective disorder (N = 128), or schizophrenia (N = 351) who were being followed at our VA medical center were reviewed for a comorbid diagnosis and treatment for DM. The mean age for the three groups was 53, 50, and 51 years, respectively, and 96% of the patients were male. The proportion of DM was found to be very high in all three groups of psychotic patients (24.6% of bipolars, 25.8% of schizoaffective, and 41.0% of schizophrenics). Additional clinical data are being analyzed.

These data suggest that DM is highly prevalent in all psychotic patients. Several possible factors may be involved in this comorbidity of DM with psychosis including 1) possible genetic linkage of the two disorders, 2) antipsychotic-induced weight gain could lead to Type II DM, 3) hypercortisolemia in psychotic disorders is common and may contribute to hyperglycemia. These data emphasize the need to screen for DM in psychotic patients at the onset of the illness and to implement measures to prevent the emergence of DM, which may complicate treatment and lead to early mortality in patients with psychotic disorders.

NR355 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Button Pressing Distorts P300 Topography

Dean F. Salisbury, Ph.D., *Department of Psychiatry, Harvard Med/McLean Hospital, 115 Mill Street, NBG21, Belmont, MA 02478;* Martha E. Shenton, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: This study examined the contamination of P300 by movement-related potentials. P300 has been reported to show left-lateralized reductions in schizophrenia, but this asymmetry has not been found by all. There exists some debate in the literature about its presence. Most studies finding a P300 asymmetry had subjects perform a silent count of target stimuli, but most that did not used button presses, suggesting that response mode may be a salient difference.

Method: ERPs were recorded while subjects pressed a button to target tones (15% of trials, 1.5 kHz) among standard tones (1.0 kHz), while they silently counted target tones, and while they pressed a button to 100% 1.5 kHz tones. A motor contamination correction waveform was constructed by matching reaction times between the 100% target and button-press oddball tasks. This correction waveform was subtracted from the button-press task. Additionally, a simulation comparing data from schizophrenia subjects and the button-press and corrected data of normal subjects was performed.

Results: Button pressing altered P300 topography over the contralateral hemisphere relative to silent counting. The correction procedure restored normal topography. When P300 from the schizophrenia group was compared with the controls P300 on the button-press task, a group asymmetry interaction at T3 and T4 did not attain significance. By contrast, the corrected P300 data did show a significant group reversal of asymmetry.

Conclusions: A small diminution of the normal left greater than right P300 asymmetry over temporal sites caused by button pressing may be sufficiently large to interfere with the detection of a group reversal of P300 lateral temporal asymmetry. Contamination of P300 by button pressing is a real and prevalent confound on topography.

NR356 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Iloperidone: Atypicality Through the Alpha2C-Adrenoceptor Blockade? A Comparative Analysis

Hans O. Kalkman, Ph.D., *S360-405, Novartis Pharmaceuticals, Research Nervous System, Basle CH-4002, Switzerland;* E. Loetscher, Ph.D.

Summary:

Objective: The α_2-adrenoceptor is attracting increasing attention as an important site in terms of atypicality (Herberg et al, 1995; Reynolds 1998). This study aimed to determine the potencies of the antipsychotics clozapine, risperidone, olanzapine, haloperidol, melperone, setoperone, quetiapine, iloperidone, and the two major human metabolites of iloperidone (P88-8991 and P95-12113) in blocking α_{2C}-adrenoceptors. Yohimbine, a potent α_2-adrenoceptor antagonist, was used as a comparator.

Methods: Cells were transfected with a cAMP-responsive element-driven luciferase reporter gene and the recombinant human α_{2C}-adrenoceptor or dopamine D_{2A} receptor. The cells were incubated for four hours with combinations of antagonist and noradrenaline (α_{2C}-adrenoceptors) or antagonist and dopamine (D_{2A} receptors). At the end of the incubation, luciferase activity was determined.

Results: Yohimbine and iloperidone were the most potent α_{2C}-adrenoceptor antagonists (pK_B 8.48 and 7.83, respectively), and haloperidol and olanzapine were the most potent D_{2A} receptor antagonists (pK_B 8.73 and 8.36, respectively). Of the antipsychotics (with the exception of one of the iloperidone metabolites), clozapine had the highest α_{2C}:D_{2A} selectivity.

Conclusions: Evidence from this study supports the hypothesis that α_{2C}-adrenoceptor blockade raises noradrenaline and dopamine levels in the prefrontal cortex, thus contributing to the atypical profile of an antipsychotic drug.

NR357 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Receptor Profile of Two Metabolites of Iloperidone

Hans O. Kalkman, Ph.D., *S360-405, Novartis Pharmaceuticals, Research Nervous System, Basle CH-4002, Switzerland;* N. Subramanian, Ph.D.

Summary:

Introduction: Iloperidone, a new antipsychotic agent in development, has a balanced, broad spectrum antagonism at dopamine, serotonin, and noradrenaline α_{2C} receptors (Kongsamut et al, 1996; Kalkman et al, in preparation). This activity is expected to translate into improved antipsychotic efficacy with a favorable tolerability profile.

Objective: To determine the cross-reactivity of P88-8991 and P95-12113, the two human metabolites of iloperidone, at various receptors.

Methods: Radioligand binding assays were used to calculate pK_i values across a broad spectrum of receptors.

Results: The P88-8991 metabolite displayed high affinity (pK_i > 7.7) at α_1, α_{2C}, D_2, and $5HT_{2A}$ receptors, moderate affinity (pK_i 6.5 – 7.7) at $5HT_{2C}$ receptors, and weak affinity (pK_i < 6.5) at α_{2A} $5HT_{1A}$, and $5HT_6$ receptors. In comparison, the P95-12113 metabolite had high affinity at $5HT_{2A}$ receptors, and weak to moderate affinity at α_1, α_{2C}, D_2, $5HT_6$ receptors. Compared with the parent compound, both metabolites had a weaker affinity for all the receptors tested.

Conclusions: It is not known if either of the metabolites contribute to the *in vivo* efficacy and tolerability profile of iloperidone. However, the affinity of P88-8991 for the α_1, α_{2C}, D_2, and $5HT_{2A}$ receptors is thought likely to contribute to the antipsychotic profile of iloperidone. The blockade of α_{2C} and $5HT_{2A}$ receptors may also contribute to the tolerability profile.

NR358 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Benefits of Ziprasidone in Stable Outpatients with Schizophrenia Switched from Conventional Antipsychotics, Olanzapine, or Risperidone

George M. Simpson, M.D., *Department of Psychiatry, LAC/ USMC Medical Center, 1937 Hospital Place, Grad Hall, Los Angeles, CA 90033;* Steven G. Potkin, M.D., Peter J. Weiden, M.D., Richard L. O'Sullivan, M.D.

Summary:

Objective: Three six-week, multicenter, randomized, open-label, parallel group trials evaluated outcome in stable outpatient with schizophrenia following a switch from conventional antipsychotics (n = 93), olanzapine (n = 88), and risperidone (n = 41).

Methods: Patients were randomized in each trial to a variety of dosing schedules and received ziprasidone 40–160 mg/day. Reasons for switching were related to desire for enhanced efficacy and/or tolerability of previous treatment. Assessments included PANSS and CGI-S. Significance of mean change from baseline was tested by paired t-test. Safety assessments included laboratory, vital signs, treatment emergent adverse events, and specific movement disorder measures.

Results: Significant improvement was observed on PANSS total, PANSS positive subscale, and PANSS negative subscale scores for each group (except PANSS positive subscale for patients switched from risperidone) ($p < 0.05$). Significant improvement on the CGI-S was also observed for patients switched from conventionals and olanzapine ($p < 0.05$). Various dosing schedules for switching to ziprasidone were all effective and well tolerated.

Conclusions: Ziprasidone was well tolerated and resulted in improvement in multiple measures of psychopathology, including positive and negative symptoms, as well as overall status. Thus, some patients may experience enhancement in antipsychotic control following a switch to ziprasidone.

NR359 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Improvement in Indices of Health Status in Outpatients with Schizophrenia Following a Switch to Ziprasidone from Conventional Antipsychotics, Olanzapine or Risperidone

David G. Daniel, M.D., *Clinical Studies Limited, 6066 Leesburg Pike, 6th floor, Falls Church, VA 22041;* Petter Weiden, M.D., Richard L. O'Sullivan, M.D.

Summary:

Objective: Newer antipsychotics offer improved side-effect burden, especially regarding EPS. Other clinically significant side effects, though, may accompany some treatments. Indices of health status were assessed following a switch to ziprasidone from conventional antipsychotics, olanzapine, and risperidone.

Methods: Three six-week, randomized, open-label trials evaluated outcome in stable schizophrenics following a switch from conventional antipsychotics (n = 93), olanzapine (n = 88), and risperidone (n = 41). Patients were randomized in each trial to one of three dosing schedules and received ziprasidone 40-160 mg/day. Assessments (non-fasting), obtained at baseline and study completion, included total cholesterol, triglycerides, prolactin, weight, and height. Body mass index (BMI; kg/m2) was calculated.

Results: A significant improvement in total cholesterol and triglycerides was noted for patients switched from olanzapine and risperidone ($p < 0.05$). A significant decrease in prolactin was observed for patients switched from conventionals and risperidone ($p < 0.05$). For patients switched from olanzapine, a significant reduction in weight (mean change 1.71 kg) and BMI was observed ($p < 0.05$).

Conclusions: Short-term ziprasidone treatment was associated with significant improvement in several important indices of health status in patients switched from conventionals, olanzapine, and risperidone. A decrease in weight in patients switched from olanzapine is consistent with ziprasidone's weight-neutral profile. Findings are encouraging and should be replicated in larger controlled trials.

NR360 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Factor Structure for Positive and Negative Symptoms in South-African Xhosa Patients with Schizophrenia

Robin A. Emsley, M.D., *Department of Psychiatry, University Stellenbosch, PO Box 19063, Tygerberg 7505, South Africa;* Dana J. Niehaus, M.B., N. Irene Mbanga, R.N., Dan J. Stein, M.B., Claudine Laurent, M.D., Piet P. Oosthuizen, M.D., Stephan J. Maritz, Ph.D.

Summary:

Objective: Most studies investigating the symptom dimensions of schizophrenia utilizing the Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS) favor a three-factor model. This study investigates the factor structure of both the global and individual items of the SANS and SAPS in a large sample of South African Xhosa patients with schizophrenia.

Method: A total of 422 subjects participated. Both principal components and factor analytical procedures were applied.

Results: For the global items, a two-factor solution representing positive and negative symptoms accounted for 59.9% of the variance. However, a five-factor solution, after exclusion of the items attention and alogia, was consistent with the three-dimensional model of negative, psychotic, and disorganized factors. Analysis of the individual items yielded a five-factor solution representing diminished expression, disordered relating, psychosis, disorganization, and bizarre behaviour.

Conclusions: Our findings are very similar to those in other parts of the world, providing evidence that the factor structure for the symptoms of schizophrenia is relatively resistant to cultural influences. This is particularly true for negative symptoms.

NR361 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Effects of Nicotine Smoking on Brain Stem Auditory Evoked Potentials in Positive and Negative Symptoms of Schizophrenia

Ahmed A.R. Mubarak, M.D., *Department of Neuropsychiatry, Tanta University, 27 Darb El-Ebshihi, Tanta GHR 31111, Egypt;* Adel A. Badawy, M.S.C.

Summary:

Objectives: Studying brain-stem auditory evoked potentials BAEPs and comparing the specific waves in smokers versus nonsmokers in both positive and negative schizophrenia symptoms may elucidate the role of smoking in information processing, which may explain the basis of some schizophrenic symptoms.

Methods: BAEPs were recorded in 40 schizophrenic patients; 20 had predominantly positive symptoms (10 smokers and 10 nonsmokers), and 20 had predominantly negative symptoms (10 smokers and 10 nonsmokers). The severity of positive and negative symptoms was assessed by scale of assessment of positive symptoms

(SAPS) and scale of assessment of negative symptoms (SANS).

Results: Comparing the smokers with the nonsmokers positive symptoms group, we found no significant difference in the scores of SAPS. However BAEPs studies showed statistical significance in amplitude difference between 1st-5th waves and in interpeak latency between 1st-5th and 3rd-5th waves on the right side. The negative symptoms group showed significant increase of alogia, summary, composite scores of SANS among smokers but no significant difference between smokers and nonsmokers in the BAEPs studies.

Conclusion: The abnormal BAEPs in the positive symptoms smokers could imply disturbed information processing particularly on the right side, which may be implicated in the pathogenesis of positive symptoms. On the other hand, the high score of negative symptoms among smokers may suggest some role of nicotine in aggravating negative symptoms.

NR362 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Homicide and T102C of 5HT-2A Receptor Gene Polymorphism in Male Schizophrenia

Chee Ik-Sueng, M.D., *Department of Psychiatry, Chungnam University, 640 Taesa-Dong, Chung-Ku, Tarjon 301-721, Korea;* Shin Suk-Chui, M.D., Wang Seong-Keun, M.D., Shin Yun-O, M.D., Lee Sun-Woo, M.D., Shin Yong-Jae, M.D., Kim Young-Lan, M.D.

Summary:

Objective: Serotonergic activity has been related to impulsivity and aggression in psychiatric patients, including those with schizophrenia. Some researchers had reported that T102C of 5-HT2A receptor gene polymorphism may play an important roles in the development of schizophrenia. The authors examined the association of homicide and T102C among murderers with schizophrenia, patients with schizophrenia, and normal male controls to investigate the possible contribution of T102C to homicide in schizophrenia.

Method: The subjects were 105 murderers with schizophrenia, 86 patients with schizophrenia, and 102 normal controls, and all of them were male. Using polymerase chain reaction, T102C of 5-HT2A receptor gene polymorphism was analyzed. For a comparison of T102C genotypes and allele frequencies among murderers with schizophrenia, patients with schizophrenia, and normal controls, X^2-test was performed.

Results: (1) There were no differences in genotype and allele frequencies of T102C among murderers with schizophrenia, patients with schizophrenia, and normal controls. (2) The genotype of T102C between murderers with schizophrenia (T/T;35, T/C;57, C/C;13) and patients with schizophrenia (T/T;41, T/C;30 C/C;15) was statistically different ($X^2 = 7.177$, df = 2, p = 0.028), and allele frequencies were not different ($X^2 = 0.869$, df = 1, p = 0.351).

Conclusion: Although replication studies are necessary, these results suggest that T102C genotype may be associated with homicide in male schizophrenia.

NR363 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Substance Abuse in Schizophrenia and Impulsivity

Alain Dervaux, M.D., *Department of Psychiatry, Hopital Sainte Anne, DispMoreaudetours 1 RueCabanis, Paris F75014, France;* Franck J. Bayle, M.D., Xavier Laqueille, M.D., Marie C. Bourdel, M.D., Michele Leborgne, M.D., Jean-Pierre Olie, M.D., Marie O. Krebs, Ph.D.

Summary:

Objective: The objectives of this study were to compare impulsivity, sensation seeking, and anhedonia in a sample of schizophrenic patients with and without lifetime substance abuse or dependence.

Method: The "psychoactive substance use disorder" section of the Composite International Diagnostic Interview (CIDI) was used for the DSM-III-R diagnosis of abuse of or dependence on the following substances: alcohol, cannabis, amphetamines, sedatives, opioids, cocaine, hallucinogens, phencyclidine, inhalants. The Positive and Negative Syndrome Scale, the Barratt Impulsivity Scale, the Zuckerman Seeking Sensation Scale, and the Chapman Physical Anhedonia Scale were used in 100 subjects meeting the DSM-III-R criteria for schizophrenia or schizoaffective disorder.

Results: 41% of the subjects in the study presented comorbidity of lifetime substance abuse or dependence, mainly involving alcohol and cannabis. Adjusted on the basis of age and sex, the mean scores for impulsivity and sensation seeking were higher in the group with psychoactive substance abuse or dependence than in the group with no history of addiction. There were no significant differences in the mean scores between the two groups for the physical anhedonia scale.

Conclusions: As in the general population, high levels of impulsivity and sensation seeking could be risk factors for substance abuse in schizophrenic patients.

NR364 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Donepezil Augmentation in Psychosis: fMRI Effects and Cognition

Samuel C. Risch, M.D., *Department of Psychiatry, Medical University of SC, 67 President Street, # 502N, Charleston, SC 29425;* Mark S. George, M.D., John S. Markowitz, Ph.D., John S. Mintzer, Ph.D., Ziad H. Nahas, M.D., Juliet Goldman, M.D., Michael D. Horner, Ph.D., Simmy Palecko, R.N., Susan R. McGurk, Ph.D., Cynthia Gilliard, B.S., Susan Owens, B.S., C. Lindsay DeVane, Ph.D., Scott D. Christie, M.D.

Summary:

Objectives: Neurocognitive impairments in multiple domains are common in schizophrenia and are powerful predictors of functional impairments and poorer quality of life. We report the results of an ongoing double-blind, placebo-controlled, randomized, crossover study of donepezil augmentation of both typical and atypical antipsychotics in stable outpatients with schizophrenia.

Method: To date, during the IRB-approved study protocol, six subjects have had serial measurements of psychosis, mood and multiple cognitive measures at baseline (BL), and then in a random order after three months of placebo, and after three months of donepezil (DP). Four of these subjects also received serial

echoplanar BOLD fMRI studies during a verbal fluency task (the Controlled Oral Word Association Test (COWAT) on a 1.5 Tesla scanner at the same timepoints.

Results: A within subjects ANOVA for TIME and DRUG (DP and PL) revealed that there was significant improvement on DP for neuropsychological tasks of verbal fluency ($p = 0.07$) and attention ($p = 0.03$). The serial fMRI data in four subjects were spatially normalized in Talairach space (Statistical Parametric Mapping) and then analyzed as a group. At all three time points during the verbal fluency task compared with rest, there was significant activation in the occipital cortex and posterior cingulate ($p < 0.001$, extent threshold $p < 0.05$ for all imaging results). These posterior brain areas were the only areas of significant activation during the PL condition. However, during the DP condition there was also activation in the right dorsolateral prefrontal cortex as well as the anterior cingulate. Thus, uniquely while on DP augmentation, the schizophrenia subjects had a more normal pattern of activation of prefrontal cortex and cingulate.

NR365 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

An Overview of the Efficacy and Safety of Rapid-Acting Intramuscular Ziprasidone

Dan L. Zimbroff, M.D., *Department of Behavioral Med., Lomalin Dame Medical Center, 710 Barton Road, Redlands, CA 92373;* David G. Daniel, M.D., Shlomo Brook, M.D., Karen R. Reeves, M.D.

Summary:

Objective: To review results from clinical trials with intramuscular (IM) ziprasidone.

Method: Two 24-h, randomized, double-blind trials assessed ziprasidone IM 10 mg ($n = 63$) and 20 mg ($n = 41$) versus respective 2 mg dose groups ($n = 54$ and 38) in acute agitation and psychosis. Two open-label, seven-day trials ($n = 438$) with fixed- and flexible-dose ziprasidone IM and haloperidol IM for up to three days, and in the transition to oral treatment (≤Day 7).

Results: Ziprasidone IM 10 mg and 20 mg produced rapid, significant, dose-related reductions in symptoms of agitation. Decreased mean Behavioural Assessment Rating Scale (BARS™) scores were seen at 15 minutes after the first dose of ziprasidone IM 20 mg, and were significant compared with ineffective 2 mg doses at 30 minutes ($P < 0.01$). PANSS agitation items scores were significantly lower at 4 h post-dose with ziprasidone IM 20 mg ($P < 0.05$), and no extrapyramidal syndrome (EPS) or acute dystonia was seen. Reductions in BPRS total, BPRS agitation items, and CGI-S scores with flexible-dose ziprasidone IM were significantly greater compared with haloperidol IM ($P < 0.05$), and ziprasidone IM was associated with a substantially lower incidence of movement disorders. Both efficacy and tolerability were maintained during and after the transition from IM to oral ziprasidone treatment.

Conclusion: Ziprasidone IM is rapid and effective in reducing acute agitation and offers tolerability advantages over haloperidol IM, particularly with regard to movement disorders.

NR366 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

5HT Receptor Dysfunction in Schizophrenia

Myung A. Lee, M.D., *Psychiatry, Vanderbilt University, 1601 23rd Avenue South Ste 306, Nashville, TN 37212;* Herbert Y. Meltzer, M.D.

Summary:

Objective: To evaluate serotonin $(5\text{-HT})_{1a}$ function in patients with schizophrenia (SCH) by administration of ipsapirone (IPS), a 5-HT_{1a} partial agonist.

Method: Patients with SCH (DSM-III-R)(N = 38;29M) and normal controls (N = 31;20M) were administered IPS, 0.5 mg/kg, p.o or placebo in random order. Blood samples for the plasma cortisol level and body temperature were obtained from 30 minutes before to 180 minutes after the drug administration.

Results: Female controls had markedly greater increases in cortisol to IPS than male controls. The placebo-adjusted increase in plasma cortisol was significantly blunted in female SCH compared with female controls ($p = 0.01$). The male SCH did not differ from the female SCH or male controls. There were no significant differences in the temperature response in males and females or between schizophrenics and controls. The placebo-adjusted IPS-induced increase in cortisol was significantly correlated with negative symptoms ($r = -0.47$, $N = 26$, $p = 0.01$) and Verbal Memory—Delayed Recall ($r = -0.40$, $N = 25$, $p = 0.05$).

Conclusions: 5-HT_{1a} receptors play an important role in the regulation of prefrontal cortical dopaminergic, cholinergic, and serotonergic function. Previous studies have shown increased density of 5-HT_{1a} receptors in specific brain areas from patients with SCH. The 5-HT_{1a} partial agonist tandospirone has been reported to improve verbal memory in patients with SCH. Our results add to the evidence that $5HT_{1a}$ function is abnormal in patients with SCH. The inverse correlations of the IPS-induced increase in cortisol with negative symptoms and verbal memory are consistent with the view that 5-HT_{1a} receptor function is diminished in prefrontal cortex in SCH.

NR367 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Subcortical Dopamine Activity in Schizotypal Personality Disorder

Harold W. Koenigsberg, M.D., *Department of Psychiatry, Mount Sinai-Bronx VAMC, 130 West Kingsbridge Rd, #116A, Bronx, NY 10468;* Marianne Goodman, M.D., Vivian Mitropoulou, M.A., Antonia S. New, M.D., Larry J. Siever, M.D.

Summary:

2 deoxyglucose (2-DG) is an analog of glucose and inhibits intracellular glucose metabolism. By reducing cortical metabolic activity, 2-DG induces a "stress" paradigm for frontal cortex. Plasma homovanillic acid (pHVA) has been used as a marker of dopaminergic responsiveness to 2-DG and has been shown to be increased in response to 2-DG in schizophrenic patients compared to normal controls. We have pilot data on 13 patients with schizotypal personality disorder (SPD, a schizophrenia spectrum disorder) and eight normal control subjects participating in a double-blind-placebo controlled paradigm of 40 mg/kg of 2-DG/placebo administered as a bolus infusion over 10min. Two blood samples were obtained prior to drug administration (baseline) and then at 1/2 intervals starting at +15 and ending at +135 minutes post infusion. The pHVA percent change on the drug day was 27% from baseline for normal controls and 14% for the SPD patients (for comparison 54% in SZ in a similar paradigm). These data provide preliminary support for our hypothesis that SPD patients demonstrate reduced dopaminergic activation compared to normal controls following a prefrontal stress in contrast to schizophrenic patients who demonstrate increased responses.

NR368 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Schizotypal Personality

Harold W. Koenigsberg, M.D., *Department of Psychiatry, Mount Sinai-Bronx VAMC, 130 West Kingsbridge Rd, #116A, Bronx, NY 10468;* Marianne Goodman, M.D., Vivian Mitropoulou, M.A., Antonia S. New, M.D., Larry J. Siever, M.D.

Summary:

Schizotypal personality disorder (SPD) shares phenomenologic, genetic, and biologic features with schizophrenia, yet SPD patients do not develop the long-term psychoses associated with schizophrenia. SPD patients manifest the so-called negative or deficit symptoms, which include excessive social anxiety, eccentric appearance and behavior, no close friends, impoverished speech, and inappropriate or constricted affect also seen in schizophrenia as well as cognitive impairments in visuospatial memory, sustained attention, and verbal learning at a somewhat less severe level than are seen in schizophrenia. Treatment with risperidone, a $5HT_2$ and dopamine D_2 blocking agent, holds particular promise in the treatment of SPD. Unlike traditional antipsychotics, risperidone targets the deficit or negative symptoms of schizophrenia and so would be expected to target these symptoms in SPD as well. SPD patients are often particularly sensitive to neuroleptic side effects and could be expected to tolerate risperidone better than traditional neuroleptics. Because of the absence of the more severe psychotic symptoms, we hypothesized that SPD patients would respond to lower doses of risperidone than typically employed in the treatment of schizophrenia. We report on a double-blind placebo controlled nine-week study of the treatment of SPD patients with low doses of risperidone. Following a two-week placebo wash out, patients were randomized into the nine-week trial. Risperidone was administered according to a step-wise increasing dose schedule to a maximum of 2 mg per day. Among 14 SPD patients studied thus far, four of seven patients on active drug and nine of seven patients on placebo were responders in the last week of the trial, where response is defined as a 30% or greater improvement over baseline on the positive or negative symptom scales of the PANSS (Pearson $\chi 2 = 5.600$, df = 1, p = .02). Data on cognitive change will also be presented. These data will be updated with findings form additional subjects.

NR369 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Impact of Schizophrenia on Health-Related Quality of Life

Michael B. Durkin, M.S., *Janssen Pharmaceuticals, 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200;* William S. Edell, Ph.D., Samir H. Mody, Pharm. D., Bryan E. Adams, Ph.D., Ed A. Repp, M.B.A.

Summary:

Objective: To evaluate the impact of schizophrenia versus other chronic conditions on health-related quality of life (HRQL).

Methods: All schizophrenic patients completing the SF-36 survey who were admitted to adult (n = 233) or geropsychiatric (n = 380) inpatient units in hospitals using the CQI+^{sm} Outcomes Measurement System were selected. Randomly generated observations were drawn from the general US population SF-36 data to construct cohorts matching the schizophrenia sample in distribution of age and gender. Comparisons were also made with three disease cohorts: hypertension, congestive heart failure (CHF), and diabetes. All comparisons employed independent samples t-tests.

Results: Schizophrenic patients had significantly lower scores ($p < .001$) on virtually all HRQL domains when compared with the general US population and to patients with hypertension or diabetes. Schizophrenics scored lower ($p < .001$) on mental health domains when compared with CHF patients. In terms of physical health (i.e., Physical Functioning, Role-Physical, and General Health), adult schizophrenics scored higher than CHF patients ($p < .05$), while geriatric schizophrenics were similar to CHF patients in those domains.

Conclusions: Schizophrenia's association with lower HRQL extends beyond mental health to physical health status. The physical health status of schizophrenics is more impaired than that observed in patients with diabetes and hypertension, and is comparable to patients with CHF.

NR370 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Relative Risk Estimates of Eye-Tracking Dysfunction in Siblings of Patients with Schizophrenia

Christopher J. Case, B.A., *CBDB, NIH/NIMH, Bldg 10, Room 4S239, Bethesda, MD 20814-9296;* Jonathan B. Strauss, B.S., Robert J. Nicolson, M.D., Daniel W. Hommer, M.D., Daniel R. Weinberger, M.D., Michael F. Egan, M.D.

Summary:

Objective: Eye tracking dysfunction (ETD) is frequently seen in patients with schizophrenia and their siblings and is a candidate intermediate phenotype for genetic studies. We sought to assess relative risk (λ), a measure of heritability, in a large sample of patients and siblings using two control groups ascertained by different recruitment methods.

Methods: Smooth pursuit was qualitatively assessed on 112 patients, 192 siblings, and two control groups using infrared oculography (16.67°/sec). Control group A (from NIH volunteer office) consisted of 44 subjects; control group B (ascertained via newspaper ads) consisted of 33 subjects.

Results: No differences were found between patients (mean = 2.50), siblings (mean = 2.35), and control group A (mean = 2.24). Compared with group B (mean = 1.96), however, both patients and siblings performed worse. Relative risk was moderate (λ = 2.8). Pooling control groups gave similar results ($\lambda = 2.5$). Control groups were similar with respect to age and ethnicity.

Conclusion: While ETD appeared moderately heritable in families of patients with schizophrenia, magnitude of relative risk was critically dependent on control group used. Because systematic ascertainment is typically not possible, future studies of neurobiological phenotypes should consider using large cohorts of controls gathered through several ascertainment strategies to assess relative risk.

NR371 Tuesday, May 16, 3:00 p.m.–5:00 p.m.

Olanzapine Treatment of Patients with Schizophrenia and Comorbid Substance Abuse

Kimberly H. Littrell, N.P., *The Promedica Research Center, 3758 Lavista Road, Suite 100, Tucker, GA 30084-5648;* Craig G. Johnson, M.D., Carol D. Peabody, M.S., Nicole M. Hilligoss, M.S.

Summary:

Background: Research suggests that nearly half of all patients with schizophrenia concurrently abuse substances. However, despite the high prevalence rate, effective treatment of these comorbid conditions has eluded mental health professionals for decades. Clozapine has been reported to be effective in the treatment of patients dually diagnosed with schizophrenia and substance use disorders. Preliminary data from animal studies and case reports indicate that olanzapine may also be helpful in this difficult-to-treat population.

Objective: To evaluate the efficacy and safety of olanzapine in patients with schizophrenia and comorbid substance use disorders.

Method: Thirty patients with schizophrenia or schizoaffective disorder who also met DSM-IV criteria for substance abuse or dependence (21 ♂, 9 ♀) were treated in a 12-month prospective, open-label olanzapine trial. All patients were receiving conventional antipsychotic medications at entry. Patients were evaluated with efficacy and safety measures at baseline and monthly thereafter including the PANSS, Schizophrenia/Substance Abuse Interview Schedule (SSAS), Herth Hope Index, AIMS, Barnes Akathisia

Scale, Simpson Angus Scale, laboratory assays, vital signs, and weights.

Results: Improvements in all efficacy variables were observed. PANSS data was analyzed using ANOVA and t-test at baseline, 6 months, and 12 months. Statistically significant improvement ($p < .05$) in psychopathology from baseline to endpoint: PANSS Total (BL = 87, 32% mean decrease), PANSS Positive (BL = 29, 31% mean decrease), PANSS Negative (BL = 22, 41% mean decrease), and PANSS General (BL = 37, 33% mean decrease). T-test results indicated statistically significant changes in PANSS scores occurred in the first six months of treatment. Patients' level of hope increased 54% from baseline to endpoint. Significant reductions in extrapyramidal symptoms were also noted. Twenty-one patients (14 ♂, 7 ♀) remained substance free during the study period. Nine patients (7 ♂, 2 ♀) used either alcohol or marijuana during the study period, but at significantly lower frequencies than prior to enrollment. Findings from the SSAS revealed that the effects of olanzapine on decreasing substance abuse fell into three main categories: 1) improvement in dysphoria and depression (88.9%), 2) improvement in negative symptoms (77.8%), and 3) improvement in positive symptoms (55.5%).

Conclusion: Our results indicate that improvements in psychopathology and hopefulness associated with olanzapine treatment, along with reduced side effects, may contribute to abstinence and sobriety among dually-diagnosed patients.

NR372 Tuesday, May 16, 3:00 p.m.–5:00 p.m.

Clozapine, Diabetes, Weight Gain and Lipid Abnormalities

David C. Henderson, M.D., *Department of Psychiatry, Massachusetts General Hospital, 25 Staniford Street, Boston, MA 02114;* Enrico Cagliero, M.D., Colin Gray, Rima A. Nasrallah, B.S., Doug L. Hayden, M.A., David A. Schoenfeld, Ph.D., Donald C. Goff, M.D.

Summary:

Objective: The goal of this five-year naturalistic study was to examine, in clozapine patients, the incidence of treatment-emergent diabetes mellitus in relation to other factors including weight gain, lipid abnormalities, age, clozapine dose, and treatment with valproate.

Method: Data were collected from the medical records, including age, gender, race, diagnosis, family history of diabetes, and age at clozapine initiation. Clozapine dose, use of valproate, and laboratory results were recorded at six-month intervals.

Results: The mean age at the time of clozapine initiation of the 82 patients studied was 36.4 years (SD 7.8) and twenty-two (27%) were women. Seventy-five (91%) were Caucasian, three (4%) African American, three (4%) Hispanic, and one (1%) Asian. The baseline weight was 175.5 lb. (SD 34.0) and BMI was 26.9 Kg/m^2 (SD 5.0). Thirty of 82 patients (36.6%) were diagnosed with diabetes during the five-year follow-up. Weight gain, valproate, and clozapine total daily dose were not significant risk factors for developing diabetes mellitus. Patients experienced significant weight gain that continued until approximately month 46. There was a nonsignificant increase in total serum cholesterol and a significant increase in serum triglyceride levels.

Conclusions: These results support the hypothesis that patients treated with clozapine appear to be at greater risk for developing diabetes and experience significant weight gain and lipid abnormalities.

NR373 Tuesday, May 16, 3:00 p.m.–5:00 p.m.

The Impact of Untreated Psychosis in Mexican Patients with First-Episode Psychosis

Rogelio Apiquian, M.D., *Clinical Research Division, Psychiatric Institute of Mexico, Calz. Mexico-Xochimilco 101, Mexico City 14370, Mexico;* Rosa E. Ulloa, M.D., Ana Fresan, M.D., Humberto Nicolini, Ph.D., Christina Loyzaga, M.D.

Summary:

Objective: To examine the effects of duration of untreated psychosis (DUP) in patients with first psychotic episode.

Methods: We recruited and assessed during a six-month period 23 patients with affective and 49 patients with nonaffective psychosis. Psychotic symptoms were evaluated with PANSS and psychosocial functioning with a specific scale. We divided the sample in patients with short DUP (< 6 months) and patients with long DUP (LDUP) (> 6 months).

Results: Mean age of the sample was 28 +/– 9 years, 54% were male, mean DUP was 56 +/– 71 weeks. Patients with LDUP (n = 35, 48.6%) were more frequently unemployed (48.6% vs. 27.0%, $\times 2 = 3.5$, $p = 0.05$). At baseline the LDUP group showed a poorer functioning in occupational (4.5 vs. 3.9, $t = 2.1$, $p = 0.03$), familiar (2.8 vs. 2.2, $t = 2.4$, $p = 0.01$), social (3.5 vs. 3.0, $t = 2.1$, $p = 0.03$) and economic (3.7 vs. 3.2, $t = 2.2$, $p = 0.02$) areas. There were no differences in symptom severity between groups. At the sixth month, LDUP group showed higher scores in positive (13.0 vs 9.1, $F = 7.0$ (1,70) $p = 0.01$), negative (14.6 vs. 11.4, $F = 4.4$ (1,70), $p + 0.04$), general (31.1 vs. 24.3, $F = 9.9$ (1,70), $p = 0.003$) and total PANSS (58.8 vs. 44.9, $F = 9.3$ (1,70), $p = 0.003$). They also showed a poorer familiar functioning (2.6 vs. 1.7, $F = 11.8$ (1,70), $p = 0.001$).

Conclusions: Patients with LDUP showed poor functioning and reduced recuperation in psychotic symptoms. Long DUP could be a poor-prognosis predictor.

NR374 Tuesday, May 16, 3:00 p.m.–5:00 p.m.

The Role of Cognitive Functioning in Vocational Outcome in Schizophrenia

Susan R. McGurk, Ph.D., *Department of Psychiatry, Mount Sinai, 998 Crooked Hill Rd, #81-102, West Brentwood, NY 11717;* Christopher R. Bowie, M.A., Joseph I. Friedman, M.D., Michael Parrella, Ph.D., Leonard White, Ph.D., Philip D. Harvey, Ph.D., Kenneth L. Davis, M.D.

Summary:

Cognitive functioning, specifically secondary memory and executive functioning, more so than positive symptoms, appears to be a major determinant of employment and the ability to benefit from psychiatric rehabilitation in patients with schizophrenia. A recent study evaluating the relationship between cognitive functioning and work status in patients with schizophrenia demonstrated that patients who were unemployed or who were working part-time performed significantly worse on cognitive measures and received significantly more vocational rehabilitation than patients who were full-time employed (McGurk and Meltzer, in press). The goal of the present study is to determine prospectively predictors of success in competitive employment in outpatients with schizophrenia in a state hospital mental health system. Patients included in the study are those who express an interest in competitive employment to vocational counselors. They are evaluated on measures of clinical symptoms and cognitive functioning. Length of participation in vocational rehabilitation and work history will also be evaluated.

Thus far, it was found that patients in supported employment (N=10) had better cognitive functioning, but did not differ on clinical symptom severity, compared with patients who were unemployed (N=14). Additionally, employed patients were more likely to be receiving an atypical antipsychotic (clozapine, risperidone, olanzapine) ($X2 = 3.6$, $p < 0.05$), whereas unemployed patients were more likely to be receiving conventional antipsychotic treatment. Patients will be followed to assess determinants of success in rehabilitation and employment placements.

NR375 Tuesday, May 16, 3:00 p.m.–5:00 p.m.

Atypical Antipsychotics: Evolving Therapeutic Indications

Peter F. Buckley, M.D., *Department of Psychiatry, Case Western Reserve Univ., 11100 Euclid Avenue HPV5080, Cleveland, OH 44106;* Del D. Miller, M.D., Beth Singer, B.A., Karl Donenwirth, M.S.

Summary:

We are witnessing a period of rapid change in the pharmacotherapy of schizophrenia, as evidenced by the replacement of conventional antipsychotics by novel antipsychotics as the drugs of choice for first episode and maintenance therapy. More recently, use of novel antipsychotics has also expanded to beyond schizophrenia with potential efficacy in agitation/aggression, suicidality, and movement disorders, which are features of other nonpsychotic psychiatric and neuropsychiatric disorders. To address this burgeoning clinical interest in a manner complementary to prescription use data, we sampled the perceptions and clinical experience across general and specialist psychiatrists in two U.S. states. Among 284 respondents, 97% had used risperidone, 93% olanzapine, 71% quetiapine, and 66% clozapine in their clinical practice. The overwhelming majority of respondents (96%) favored the use of novel antipsychotics as first-line treatments for schizophrenia. Additionally, respondents considered these drugs to be of therapeutic value in dementia (94% of respondents), autism (78%), developmental delay/mental retardation (78%), and personality disorders (75%). The most frequently cited drawbacks to the expanding clinical use and profile of novel antipsychotics were cost, weight gain, and the current lack of a long-acting intramuscular preparation. These findings confirm and extend the impression gained from prescription data of an increase and broad shift in the use of novel antipsychotics.

NR376 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Neuroscience Sweepstakes in Schizophrenia Research

R. W. Heinrichs, Ph.D., *Department of Psychology, York University, 4700 Keele Street, Toronto, ON M3J 1P3, Canada;* Stephanie McDermid, B.A., Lara Davidson, M.A.

Summary:

Objective: To assess quantitatively the strength and consistency of evidence on neurobiological and neurobehavioral differences between schizophrenia patients and healthy people.

Method: Fifty research literatures spanning the years 1980–1999 were synthesized using meta-analytic techniques. The English language neuroscience literature was searched using Medline. Articles were included in the database if they reported findings that were convertible to effect sizes (Cohen's *d*). The literatures included cognition, psychophysiology, regional brain volume, metabolism and blood flow, studies of post mortem neurotransmitter receptor binding, birth and development.

Results: The most powerful individual literatures include the P50 potential (d = 1.54) and verbal memory (d = 1.41), while the weakest include excess winter births in the schizophrenia population (d= .05) and abnormal dopamine metabolite in cerebrospinal fluid (d = 0). The majority of neuroimaging literatures yield intermediate effect sizes. Across research domains neurocognitive performance yields significantly larger effects than neurobiology. In addition, 40% of the biological findings have confidence intervals for the mean that include zero.

Conclusions: Cognitive brain function is more sensitive than neuroanatomy, neurophysiology, neurochemistry or neurodevelopment to schizophrenic illness. Schizophrenia is a high-level disturbance of the working brain and requires new models and paradigms.

NR377 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Neurocognitive Subtype in Schizophrenia

Stephanie McDermid, B.A., *Department of Psychology, York University, 4700 Keele Street, Toronto, ON M3J 1P3, Canada;* R. W. Heinrichs, Ph.D.

Summary:

Two puzzling aspects of schizophrenia are its heterogeneity and the apparent independence between neurocognitive performance and positive symptoms. Yet brain regions like the left medial temporal area are implicated in both verbal memory processes and in symptoms like delusions and hallucinations. Here we present evidence that verbal memory impairment distinguishes a subgroup of schizophrenia patients who also differ in symptom profile and illness adjustment. Using the California Verbal Learning Test (CVLT), our schizophrenic patient sample was partitioned into memory-impaired and memory-unimpaired groups, each with n = 16 patients that were matched for age, sex, IQ, and CPZ equivalent daily dose. These groups were then administered the Brief Psychiatric Rating Scale (BPRS) and the Sickness Impact Profile (SIP). Results indicate that the memory-impaired group demonstrate significantly more positive symptoms and experience a significantly poorer quality of life than their memory-unimpaired counterparts. This finding supports the idea that there are different kinds of schizophrenic illness and that neurocognitive measures are a valid means of parsing what is still studied as a single disease state. A case study is presented for illustration.

NR378 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

A Six-Year Follow-Up Study of Cognitive and Functional Decline Across the Life Span of Patients with Chronic Schizophrenia

Thomas Coleman, M.A., *Neuroscience, Pilgrim Psych Ctr Bldg 81, Ward 102, 998 Crooked Hill Rd, Brentwood, NY 11717;* Joseph I. Friedman, M.D., Philip D. Harvey, Ph.D., Christopher R. Bowie, M.A., Patrick J. Moriarty, M.A., Michael Parrella, Ph.D., Leonard White, Ph.D., David Adler, M.D., Kenneth L. Davis, M.D.

Summary:

Background: We have previously demonstrated substantial risk of cognitive and functional decline among geriatric poor-outcome schizophrenic patients over a 60 month follow-up (Friedman et al, 1998). Clearly this is not a linear process. Recent studies demonstrate the stability of neuropsychological deficits early in the course of schizophrenia (Gold et al. 1999; Hoff et al, 1999). Therefore, the nature and timing of the progressive cognitive decline observed in some schizophrenic patients following the onset of illness and prior to senium requires elucidation.

Methods: The schizophrenic subjects received index assessments in the hospital with a variety of clinical and cognitive assessments. Reassessments were performed approximately 6 years later. These patients were compared to a sample of healthy control subjects and AD patients who had served as participants in a large scale study of the characteristics of patients with Alzheimer's disease, the CERAD project.

Results: Cognitive and functional decline (defined by our CDR criteria) was not encountered in the schizophrenic group until age 65, at which point the incidence of decline grew with increasing age. Comparison of the incidence of six year cognitive decline by CDR for the schizophrenic subjects with age matched normal controls and Alzheimer's patients demonstrated significant differences between the groups. Analysis of the Mini Mental State Examination data by multifactorial ANOVA demonstrated a significant age x diagnosis interaction (F = 5.12, df = 6,201) on MMSE decline over 6 years. Planned comparisons using the simple effects test demonstrated that only the schizophrenic subjects expe-

rienced a significant effect of aging on MMSE decline (F = 4.14, df = 3,66 p = 01).

Conclusions: These data provide the basis for the following conclusions. 1. The severity of cognitive decline observed in geriatric poor outcome schizophrenic patients does not extend to younger patients with an equally poor prognosis. 2. The cognitive decline observed in younger poor outcome schizophrenic patients is subtle and requires many years to detect. 3. The cognitive decline observed in poor outcome geriatric schizophrenic patients is not the result of normal aging. 4. The cognitive decline observed in poor outcome geriatric schizophrenic patients is not the result of Alzheimer's disease.

NR379 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Dissolution Profile and Safety of Olanzapine Orally Disintergrating Tablet in Patients with Schizophrenia

Cindy C. Taylor, Ph.D., *Lilly Research Labs, Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46285;* Barry Jones, M.D., P. Chue

Summary:

The safety and efficacy benefits of olanzapine may not be fully realized in patients with schizophrenia unable or unwilling to swallow traditional olanzapine tablets. One solution is an orally-disintegrating olanzapine tablet that dissolves on contact with saliva. In this open-label study, 11 outpatients (6 male, 5 female; mean age 32.5 years) meeting DSM-IV criteria for schizophrenia, schizophreniform disorder, or schizoaffective disorder were stabilized on olanzapine tablets (5 to 20 mg/day) for a minimum of one week, then transferred to the same dose of the olanzapine orally-disintegrating tablet for 7 days (mean dose = 12.7 mg/day). At each daily visit, visual assessments were made for elapsed time to initial disintegration (every 15 seconds) and complete disintegration (every 1 minute following start of disintegration) of the olanzapine orally-disintegrating tablet. Treatment-emergent adverse events were collected at completion of the study. In most cases, the tablet had begun to dissolve by 15 seconds, with a mean time to initial disintegration of 15.78 seconds, and a mean time to complete disintegration of 0.97 minutes. All 11 of the patients completing the study stated that this was an acceptable form of the medication. All vital signs and clinical laboratory tests were within the normal range, and no serious adverse events were reported. Three patients reported non-serious clinically significant adverse events during the study (asthenia, purpuric rash, headache, depression, and insomnia). In conclusion, the olanzapine orally-disintegrating tablet is practical and safe for use in patients that are unable or unwilling to take traditional oral olanzapine tablets.

NR380 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Efficacy of Olanzapine Combined with Mood Stabilizers in the Treatment of Bipolar Disorder

Mauricio F. Tohen, M.D., *MC 541, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;* Thomas G. Jacobs, M.A., Tricia M. Meyers, M.S., Richard C. Risser, M.S., Elizabeth L. Keeter, R.N., Peter D. Breier, M.D.

Summary:

Objective: To determine the efficacy of olanzapine vs. placebo when each is added to mood-stabilizer therapy.

Methods: Patients in a bipolar I manic or mixed episode (n = 344) were randomized into a 6-week double-blind study, during which they received either olanzapine (5–20 mg/day) or placebo, concomitant with mood-stabilizer (valproate, 50–125 μg/mL serum conc., or lithium, 0.6–1.2 mEq/L serum conc.).

Results: Olanzapine-treatment improved patients' YMRS total scores significantly more than did placebo (–13.11 vs. –9.10, p = .003). Separation from placebo was significant by the first time-point at Week 1. Response rates (≥50% improvement on YMRS) were also significantly higher with olanzapine (67.7% vs. 44.7%, $p < .001$). In patients presenting with depressive symptoms (DSM-IV diagnosis of mixed episode and baseline HAMD-21 score ≥20), olanzapine improved HAMD-21 scores by 10.31 points, compared with 1.57 for placebo ($p < .001$), and response rates (≥50% reduction of HAMD-21) were 43.1% for olanzapine and 9.5% for placebo (p = .006). Extrapyramidal symptoms (Simpson—Angus, Barnes, AIMS) were not significantly changed from baseline to endpoint. Treatment-emergent symptoms that were significantly higher for olanzapine patients included somnolence, dry mouth, weight gain, increased appetite, and tremor (all incidences ≥10%), and speech disorder (6.6%).

Conclusion: These data suggest that olanzapine is effective, safe, and well-tolerated for augmentation therapy of both manic and depressive symptoms associated with bipolar I manic or mixed episodes.

NR381 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Clozapine in Patients Nonresponsive or Intolerant to Standard Acceptable Treatment for Schizophrenia

Martin Dossenbach, *Eli Lilly GESMBH, Barichgasse 40–42, Wien A-1030, Austria;* I. Bitter, M. Slabber, J. Pretorius, G.Y. Bartko, Z. Banics, F. Martenyi

Summary:

Objective: The primary intent of this study was to compare the efficacy and safety of olanzapine versus clozapine in schizophrenic patients having failed to adequately respond to standard acceptable antipsychotic medication, or because of intolerable side effects caused by the medication.

Method: This was a randomized, double-blind, parallel study of 150 patients meeting diagnosis criteria for schizophrenia according to the DSM-IV, and who were non-responsive or intolerant of standard acceptable antipsychotic therapy. The double-blind study period was 18 weeks in duration.

Results: At the 18 week endpoint (LOCF), no statistically significant differences between olanzapine and clozapine were found with any efficacy measure used: BPRS total, positive, negative, or PANSS total, positive, negative, and general psychopathology. Regarding EPS, no statistically significant differences in parkinsonism, akathisia, and dyskinesia were noted.

Conclusion: Olanzapine demonstrated similar efficacy and safety to clozapine among treatment resistant schizophrenic patients.

NR382 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Predictive Value of Early Anti-anxiety Effect on the Acute-Antipsychotic Outcome: A Comparison of Fluphenazine and Olanzapine

Martenyi Ferenc, *Eli Lilly GESMBH, Barichgasse 40–42, Wien A-1030, Austria;* Martin Dossenbach, M. Jakovljevic, S. Metcalfe

Summary:

Anxiety symptoms are common during the course of schizophrenia. Generalized anxiety symptoms were observed by Kraepelin in 24.5% of his dementia praecox sample in 1908 (Jablensky et al 1993). The prevalence of comorbid anxiety in patients with schizophrenia is reported to range from 13 to 25%.

In a 6-week, double blind study that compared olanzapine to fluphenazine in the treatment of patients with schizophrenia

PANSS total score was the primary efficacy variable. In this study, olanzapine was numerically superior to fluphenazine on the PANSS total score, -39.9 versus -27.9, respectively (p = 0.080) (Jakovljevic et al, 1999). As a secondary efficacy variable the Hamilton Anxiety Rating Scale (HAMA) was also measured. At the 6-week endpoint olanzapine had a statistically significantly greater response on the HAMA than fluphenazine (-9.8 versus -5.8, respectively; p = 0.048). Additional analyses were completed to determine if there was any correlation between the HAMA response and overall PANSS response. Patients with ≤20% (non-responsive), or who demonstrated a 20%, 30%, or 40% improvement on the HAMA after the first week of olanzapine treatment showed improvement on the PANSS total score at week 6 of 31.8, 53.6, 56.3, and 63, respectively. The differences in the long-term antipsychotic effects between olanzapine patients with no early antianxiety effect (≤20%) and antianxiety effects of 20%, 30% and 40% were significant for the 20% and 40% improvement patient group (p = 0.012 and 0.0001 and close to significant for the 30% improvement group 0.077 respectively. There was no predictive value of early antianxiety effect on the 6-week antipsychotic effect in the fluphenazine treatment group.

Antianxiety effect of olanzapine could be a predictor of the acute antipsychotic effect.

NR383 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Mirtazepine Treatment of Negative Schizophrenia

Michael Berk, M.D., *Department of Psychiatry, Wits Medical School, 7 York Road, Parktown, Johannesburg 2193, South Africa;* Camelia Ichim, M.D., Shlomo Brook, M.D.

Summary:

The negative symptoms of schizophrenia remain a major clinical challenge. Mirtazapine is an antidepressant with antagonist properties at 5HT2a, 5HT3 and alpha 2 receptors as well as indirect 5HT1a agonist effects. Many of these pharmacological actions have clinical or preclinical evidence of efficacy in schizophrenia. This study was a 6 week randomised placebo controlled trial of mirtzepine add on to haloperidol 5mg in the treatment of 30 patients with DSM-IV schizophrenia. The primary finding of the trial was a 42% reduction in PANNS negative symptom scores in the mirtazepine group compared to placebo (mirtazepine 13.9, SD 1.56; placebo 23.9, SD1.56; p = 0.000, F = 20.31; DF = 1) The PANNS total scores, CGI severity and improvement scales in addition showed superiority of mirtazepine over placebo. There was no difference between the groups on the HAMD scale, suggesting that the improvement in negative symptoms was not an artifact of mood improvement. These results suggest a potential role for mirtazepine in the negative symptoms of schizophrenia.

NR384 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Relationship Between Inadequate Physical Healthcare and Poor Mental Health Among Individuals with Schizophrenia

James M. Russell, M.D., *Department of Psychiatry, University of Texas, 301 University Blvd Route 0197, Galveston, TX 77555-0197;* Joan A. Mackell, Ph.D.

Summary:

Objective: To study whether "inadequate" physical healthcare is associated with poor mental health.

Methods: In September 1999, 504 caregivers of people with schizophrenia completed self-administered questionnaires about those under their care. "Inadequate" physical healthcare was defined as not receiving two of the following exams: dental within twelve months, eye within twenty-four months, or physical with twelve months. The analysis included only participants with all three data points (n = 260, 52%). Information about current psychiatric status and quality of life was also collected.

Results: Inadequate care was received by 30% (n = 77) of respondents. The groups did not differ by age, gender, or race. Almost all (98%) used antipsychotics. Similar mental healthcare utilization was also reported. However, those in the inadequate physical healthcare group had lower quality of life (p < 0.001), more positive and negative psychotic symptoms (p < 0.05), no structured daily activity (56% v. 34%, p < 0.01), and more alcohol and drug abuse (12% v. 6%, p = 0.08).

Only 25% of caregivers in the inadequate group believed that their doctor cared about their patients' physical health. They were also more likely to rate both physical (46% v. 18%, p < 0.001) and mental healthcare (39% v. 23%, p = 0.01) as fair or poor.

Conclusion: Despite similar use of mental healthcare services, individuals receiving inadequate physical healthcare are more ill, both mentally and physically, than those who receive adequate physical healthcare.

NR385 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Early Psychosis: Duration of Untreated Psychosis Predicts Outcome

Katherine A. Black, M.D., *6-Lane, Qeii Hospital, 5909 Jubliee Road, halifax, NS B3H 2E2, Canada;* Lynn Peters, M.D., Qing Rui, David Whitehorn, Ph.D., Lili C. Kopala, M.D.

Summary:

Objective: For patients first presenting with psychosis the duration of untreated psychosis (DUP) varies widely. We studied DUP and its association with outcomes in patients referred to an early psychosis program.

Methods: DUP was determined for 21 patients with no previous treatment for psychosis by use of a retrospective structured interview. PANSS and GAF ratings were completed at baseline and 6 month follow-up. For analysis, patients were placed into a short DUP (n = 10) and long DUP (n = 11) group using the median DUP (60.7 weeks) as a dividing point.

Results: At baseline the two groups did not differ significantly on positive symptoms or total PANSS ratings. There was a trend towards more severe negative symptoms in the long DUP group. The long DUP group had a significantly higher mean rating for the passive/apathetic social withdrawal item of the PANSS. At 6 month follow-up the long DUP group was significantly more symptomatic on positive symptom and total PANSS scores. Significantly more long DUP patients had enduring positive psychosis symptoms.

Conclusions: The results confirm the wide range of DUP among patients referred to an early psychosis program and support the association of long DUP with poorer clinical outcome.

NR386 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Auditory P3 and Personality Traits in Schizophrenia

Ronald J. Gurrera, M.D., *Department of Psychiatry, Brockton DVAMC, 940 Belmont Street, # 116A, Brockton, MA 02301;* Margaret Niznikiewicz, Ph.D., Ileana Berman, M.D., Paul G. Nestor, Ph.D., Christopher Allen, B.A., Martha E. Shenton, Ph.D., Christopher Dodd

Summary:

Objective: To explore the relationship between auditory P3 event-related cortical potential amplitude and major personality dimensions in individuals with schizophrenia.

Method: Subjects (8M, 3F; mean age ±SD = 38.9 ±8.0) were medicated, met DSM-IV criteria for chronic schizophrenia, and gave written informed consent. P3 responses to a standard auditory oddball paradigm were recorded with a 64 channel geodesic

net. After data were digitally referenced to the common average and subjected to artifact rejection and filtering protocols, peak P3 amplitude (highest voltage in 275–550 msec post-stimulus window) was measured at each lead. The NEO Five-Factor Inventory (Costa & McCrae, 1991) was used to assess five personality domains: neuroticism, extroversion, openness, agreeableness, and conscientiousness. Pearson correlations between NEO scale scores and P3 amplitudes were computed in an initial exploratory analysis; all correlations with a significance level ≤.05 were then entered into a principal components factor analysis that included NEO scores.

Results: P3 amplitude at 18 leads was significantly correlated with one or more NEO scales. The first factor had an eigenvalue of 7.83 and accounted for 34.0% of the variance. This factor contained the highest loadings for neuroticism (–.784) and conscientiousness (.845), and high loadings (range .507 to .736) from four leads concentrated in the left temporal region; the highest loading on this factor (.908) was for a left frontotemporal lead. Only one right hemisphere lead, also in the temporal region, had a substantial loading (.580) on this factor.

Conclusion: P3 amplitude decrements are associated with subsequent poor personality functioning (Squires-Wheeler et al, 1993). Individuals with schizophrenia score lower on neuroticism, and higher on conscientiousness, than healthy controls (Gurrera et al, 2000). These preliminary results suggest that left temporal lobe P3 deficits in schizophrenia may be associated with deviant personality trait scores. The present study is in progress and will include a normal control group.

NR387 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

EEG Abnormalities and Antipsychotics

Franca Centorrino, M.D., *No. Belknap 3, McLean Hospital, 115 Mill Street, Belmont, MA 02478;* Margaret Tuttle, B.A., Won-Myong Bahk, M.D., Matthew J. Albert, B.A., Bruce Price, M.D., Ross J. Baldessarini, M.D.

Summary:

Background: Clozapine is associated with electroencephalographic (EEG) abnormalities and a dose-dependent risk of epileptic seizures. Much less is known about the EEG effects of newer antipsychotic agents.

Methods: EEG results were scored for abnormality (0–3 scale), blind to diagnosis and treatment in 330 psychiatrically hospitalized patients, comparing those treated with various antipsychotics and untreated controls. Drug-type and dose as well as clinical factors, comorbidity, and use of other drugs were evaluated for associations with EEG abnormalities by bivariate analyses, and suggestive associations further evaluated by logistic regression.

Results: Marked differences were found between specific antipsychotics and drug-types. Low-potency atypical antipsychotics carried the highest EEG risk (36.7%), followed by high-potency atypicals (25.8%), low-potency typical agents (16.7%), and high-potency neuroleptics (14.6%). As expected, subjects not on antipsychotics carried the least risk of EEG abnormalities (13.3%). Other factors found significantly associated with abnormal EEG were hypertension, use of lithium, and age >40. Substance use comorbidity and benzodiazepine cotreatment lowered risk. Unassociated were daily dose (mg/kg), duration of antipsychotic treatment, sex, psychiatric diagnosis and treatment-responsiveness.

Conclusions: EEG abnormalities were strongly associated with atypical antipsychotics, particularly clozapine and olanzapine, and with comorbid hypertension and older age.

NR388 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Weight, Cholesterol and Glucose in the Treatment of Patients with the Newer Antipsychotics

Franca Centorrino, M.D., *No. Belknap 3, McLean Hospital, 115 Mill Street, Belmont, MA 02478;* Edward Rivera, M.D., Matthew J. Albert, B.A., Giuseppa Drago-Ferrante, M.D., Ross J. Baldessarini, M.D.

Summary:

Objective: To compare blood cholesterol, glucose, liver function assays and weight in patients treated with clozapine (CLZ), risperidone (RSP), and olanzapine (ONZ).

Method: Medical records of 44 patients with psychotic disorders, treated for ≥6 months with CLZ (N = 15), RSP (N = 15), and ONZ (N = 14), were reviewed.

Results: All three antipsychotics increased cholesterol significantly: CLZ (median = 218 mg/mL) > RSP (median = 157 mg/mL, p = .0045) ≥ ONZ (median = 180 mg/mL, p = 0.046). High cholesterol was correlated with high glucose (p = 0.023), and high glucose with increased weight (p = 0.035). Weight was greater in patients on CLZ and ONZ compared to RSP (p = 0.0092 and 0.0010 respectively). There was a significant association between lower weight and older age (p = 0.0352), and a trend toward lower cholesterol with older age. No correlation was found between abnormal cholesterol or glucose levels and psychiatric diagnosis or co-treatment with other psychotropic agents.

Conclusion: Both CLZ and ONZ increased cholesterol and blood glucose in association with greater weight than RSP. The correlation of increased weight, cholesterol and glucose with higher morbidity and mortality reported in the medical literature warrants closely monitoring patients for changes of cholesterol and glucose. Clinicians should also counsel patients on healthy diet and exercise to minimize/prevent weight gain.

NR389 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Implications of Antipsychotic Treatment Patterns on Health Outcomes in Schizophrenia

Luella M. Engelhart, M.A., *Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560;* Carmela Janagap, Richard E. White, Ph.D., Margaret Rothman, Ph.D.

Summary:

Objective: It is recommended that treatment of acute schizophrenia episodes include daily antipsychotic medication for 6 weeks at doses within the range of 300–1000 chlorpromazine equivalents. We assessed the impact of continuous therapy (CT), intermittent therapy (IT), or low-exposure therapy (LT) on quality of life in the usual care setting for patients with schizophrenia.

Methods: Data on prescribed and dispensed medications, assessments of quality of life, symptoms, and hospitalizations from a one-year, naturalistic, randomized clinical trial were analyzed. Of 546 patients who completed the study, 159 were treated with CT (≥90% of study days on drug), 248 with IT (<90% and >50% days on drug, and intermittent use), and 139 with LT (≤50% days on drug). Patients were further classified as receiving monotherapy or polytherapy. SF-36 Mental Component Scores (MCS) and risk of relapse were compared for each group using regression models.

Results: Relative to LT, patients treated with CT or IT had better MCS at one year (both p ≤ 0.01). Risk of relapse was lower for patients receiving CT (OR = 0.33, p < 0.01) and IT (OR = 0.78, p = 0.43), relative to LT. There were no differences in MCS for patients treated with monotherapy or polytherapy; however, patients receiving monotherapy had a 69% lower risk of relapse (p < 0.01).

Conclusions: These results suggest a high proportion of patients in usual care do not receive optimal maintenance therapy following

acute relapse. Continuous therapy was associated with better quality of life and relapse prevention than other patterns of treatment, and monotherapy reduced patients' risk of relapse.

NR390 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Atypical Antipsychotic-Induced Diabetes Mellitus

Naveed Iqbal, M.D., *Department of Psychiatry, Montifiore Medical Center, 111 East 210th Street, Bronx, NY 10467;* Raquel L. Oldan, M.D., Gordon Baird, M.D., Bruce J. Schwartz, M.D., Leyla Baloy, Bharat Bhagoji, M.D., Mohammad S. Simjee, M.D.

Summary:

Methods: We reviewed the medical records of all patients with a DSM IV diagnosis of Schizophrenia admitted at Kingsboro Psychiatric Center in New York, and who were referred to the medical/endocrinology consultation service at this hospital, for evaluation and treatment of new onset Diabetes Mellitus secondary to treatment with atypical Antipsychotic medications. Nine patients were recorded to have developed new onset Diabetes Mellitus over a two year period. Eight patients were on Olanzapine, and one patient had received Clozapine. Two of the patients on Olanzapine had also developed ketoacidosis. One of the patients who had developed ketoacidosis, became euglycemic when treatment was changed from Olanzapine to Risperdal.

Conclusions: The nine case reports will be presented with details of the psychiatric and medical treatment, as well as patient clinical characteristics. The high prevalence of new onset Diabetes Mellitus with or without weight gain and the development of ketoacidosis in schizophrenic patients treated with some of the atypical Antipsychotic medications will be discussed. The need for early detection, comprehensive weight management strategies and adequate and alternative treatment strategies for patients developing Diabetes Mellitus secondary to some of the atypical Antipsychotics will be reviewed and discussed.

NR391 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Evaluating the Cognitive Deficits in Schizophrenia

Shin-Min Lee, M.D., *Military Psychiatric Center, No 60 Hsin-Min Road, Pei-Tou, Taipei 112, Taiwan;* Shay-Yun Kuo, M.S., Mei-Chun Wang, M.S., Yue-Cune Chang, M.D., Hsin-Jung Lo, B.S., Ming Chang, M.D.

Summary:

Objective: Cognitive deficits are a core and endure feature of the psychopathology of schizophrenia. This study is designed to evaluate the cognitive dysfunction in neuroleptic-naïve schizophrenics and normal control subjects by Wisconsin Card Sorting Test (WCST) and Maze task paradigm. The relationship between the WCST and Maze task paradigm is analyzed.

Method: We included 103 male normal control subjects and 17 age-matched male neuroleptic-naïve schizophrenics in this study. WCST and Maze test were applied to evaluate the executive function in these subjects. A statistical method for analyzing longitudinal data, named Generalized Estimating Equation (GEE) method, was used to explore the relationship between the WCST and Maze test.

Results: The cruising velocities, both in the simple and complex mazes of normal subjects and schizophrenics, were significantly ($p < 0.001$) correlated to the Categories score of the WCST. And the velocities of the simple mazes were also significantly ($p < 0.01$) related to the Learn-to-learn score of the WCST while the velocities of the complex mazes were possibly ($p = 0.08$) related.

Conclusions: Our results indicate that the Maze task paradigm in evaluating the executive function of the schizophrenic and normal subjects is highly associated with the WCST. And the analysis of Maze-solving behavior is a valuable tool for the study of cognitive dysfunction in schizophrenia.

NR392 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Are Clinical Ratings of Cognitive Dysfunction in Schizophrenia Valid?

Nehal Vadhan, M.A., *Department of Psychology, Hemostead, NY 11549;* Brett R. Goldberg, B.A., James C.Y. Chou, M.D., Philip D. Harvey, Ph.D., Mark R. Serper, Ph.D.

Summary:

Objective: Recently, increased attention has been given to clinician based ratings of cognitive dysfunction in schizophrenia. A few studies have been conducted, for example, examining the factorial structure of the Positive and Negative Symptom Scale (PANSS) cognitive rating items. Even less examination has been given to the Attention subscale on the Scale for the Assessment of Negative Symptoms (SANS). No study to date has examined the validity of clinically rated measures of cognitive dysfunction.

Method: We compared the SANS clinician rated assessment of patients' attentional ability to well established cognitive performance measures of attentional dysfunction. Performance based measures of attention included the continuous performance test (CPT) and the digit span distraction test (DSDT). Subjects included 35 DSM-IV diagnosed schizophrenic patients. Independent raters completed the clinical and cognitive assessments. Additionally all raters were blind to the purpose of the study.

Results: SANS attention factor showed good concurrent validity with both CPT ($r = .78$) and DSDT ($r = .87$).

Conclusions: Clinical ratings of attentional functioning in schizophrenia appears to have adequate concurrent validity. Discussion will focus on the utility of clinician based ratings of cognitive dysfunction in schizophrenia.

NR393 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Cardiac Performance and Abnormalities in Anorexia Nervosa Patients

Carla E. Ramacciottii, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56126, Italy;* Ombretta Biadi, M.D., Elisabetta Coli, M.D., Roberta Rossini, M.D., Lucia Polese, M.D., Mario Mariani, M.D., Giovanni B. Cassano, M.D.

Summary:

Either muscle dysfunction or arrhythmias have been claimed as a possible cause of sudden death in Anorexia Nervosa (AN) patients. The aim of the present study was to assess the resting and exercise-related cardiac performance in a sample of malnourished subjects with AN. Ten subjects with a DSM-IV diagnosis of AN (age 23± 7 yrs; BMI 13.7 ± 1.1 Kg/m^2) and ten healthy constitutionally thin women (BMI 19 Kg/m^2) of similar age and physical activity level, underwent the study protocol. The cardiovascular assessment was comprehensive of: electrocardiogram; arterial blood pressure; M-mode echocardiographic examination; 2D Doppler echocardiography; oxigen consumption (VO_2); Head-up tilting test and bicycle "breath to breath" ergometer (CPX) to examine cardiopulmonar function. AN patients showed a smaller left ventricular mass ($p < .001$), longer ventricular outflow time ($p < .01$) and lower deceleration time ($p < 05$) than healthy subjects; mitral valve motion and anatomic abnormalities were also more frequent in AN patients. The CPX examination reveals a significantly higher heart rate ($p < .005$), workload ($p < .01$), lower VO_2 VO_{2MAX} ($p < .05$) and anaerobic threshold ($p < .01$) in AN patients compared to the control group. The results of our study underline the impairment of the cardiac function in Anorexia Nervosa patients. The reduced oxigen consumption could be related to a

lower energy expenditure, thus allowing the patient to maintain overactivity level notwithstanding the malnutrition.

NR394 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Survey of Epidemiological Factors Associated with Adolescent Obesity

Sandra L. Straffen, R.N., *Cleveland Clinic Foundation, 9500 Euclid Avenue, P78, Cleveland, OH 44195;* Gabrielle Taylor, M.D., Kathleen S. Franco-Bronson, M.D., Rebecka Peebles, M.D., Ellen Rome, M.D.

Summary:

Primary objective of this research is to examine gender-specific demographics, comorbid medical and psychiatric conditions, attitudes and behavioral practices among obese adolescent males and females. It has been purported but not extensively reviewed that gender specific characteristics may be influential in the outcome of treatment interventions. To further elucidate these predominant characteristics, intended subjects were randomly identified through individuals seeking care at the Cleveland Clinic Foundation, exhibiting a nonpathologic cause for their obesity and a BMI above the 90th percentile. Procedures consisted of retrospective chart reviews and the completion of a series of standardized questionnaires. A normal weight comparison group completed these forms to control for or further suggest any gender specific or weight related correlations. This subject pool consists of 100 individuals per subject group: obese female adolescents, control females, obese male adolescents, control males. Significant variances were found between obese adolescents and control groups in the areas of sexual activity ($p < 0.05$), pregnancy ($p < 0.05$). The incidence of various medical conditions, such as cholelithiasis, hyperlipidemia, and hypercholesterolemia, was significantly higher in the obese. Obese females acknowledged more sexual activity than all other groups ($p < 0.001$). Further research is indicated to explore learned behaviors, self-concept, or organic gender differences as well as treatment options in obese adolescents.

NR395 WITHDRAWN

NR396 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

New Intravenous Pharmacology for Refractory Agitation

Michael R. Miller, M.D., *Department of Psychiatry, Salem Hospital, 1127 Oak Street SE, Salem, OR 97301;* Margaret Bennington-Davis, M.D.

Summary:

Objective: To suggest the effectiveness of intravenous valproate in the treatment of agitation in delirious or psychotic patients in a general hospital setting.

Background: Valproate is an anticonvulsant effective in psychiatric conditions including bipolar disorder & agitation in dementia. This report describes experience with IV valproate in a general hospital setting.

Method: Pharmacy identified 13 cases in one year where Depacon was used in patients in ventilators, with swallowing impairment, or unable to cooperate with oral medication. Retrospective chart review examined patterns of diagnostic indications, responses, dosing, and side effects. [Funded by Abbott Laboratories]

Results: Depacon was used for delirium & agitation (7 cases), seizure disorders (4), & agitated psychosis (2). It supplemented or replaced traditional medical treatments for agitation such as IV Haldol, Inapsine, morphine, & benzodiazepines, allowing dose reductions in 72% of cases. In 3/7 refractory cases of delirium, Depacon facilitated swift clearing of mental status, often shortening ICU/IMCU stays. Loading doses at greater than manufacturer's recommendation (>250 mg) were tolerated with no limiting side effects. Depacon was well tolerated in patients with a multiplicity of medical problems (CAD/CHF, pneumonia/ARDS, PUD/GI bleed, post-surgery, recent CVA, brain tumors, alcoholism with dementia, & autoimmune disorders). Side effects included sedation, nausea/vomiting, & decreased Dilantin levels. No patients had significant hematological or hepatic changes.

Conclusion: This series found Depacon to be rapidly effective & well tolerated in otherwise refractory agitation. It may be a valuable new option in the treatment of agitated, medically ill patients. Controlled trials with larger populations are needed to determine safety, clinical indications, & the most effective loading/maintenance doses.

NR397 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Eating Behavior Items in Young Adult Twins

Carol A. Beresford, M.D., *Department of Psychiatry, Children's Hospital, 1056 East 19th Avenue, Denver, CO 80218;* John K. Hewitt, Ph.D., Thomas P. Beresford, M.D.

Summary:

Objectives: we previously studied seven eating behavior items in a mixed gender sample of adolescent twins and found that four of the items were associated with drinking behavior. In the present study we hypothesized that all seven items would characterize a sample of young adult females disproportionately.

Method: we conducted an analysis by gender of seven eating behavior items endorsed on a questionnaire in a sample of 909 twins from our state registry. Subject ages ranged from 18 to 30; 602 were female and 307 male. The response frequencies for each item were analyzed using chi Square tests in two-by-two tables.

Results: all seven items differentiated females from males (six at $p < 0.001$) with consistently higher frequencies among females. They were: eating in secret (16.9%), feeling fat (61.8%), finding it hard to stop eating (32.1%, $p < 0.01$), thinking about thinness (40.4%), purging (5.3%), eating to relieve stress (28.2%), and not eating to relieve stress (38.4%).

Conclusion: eating behavior items consistently characterized the young adult females versus males and were more consistent among young adult females than adolescent females. This suggests a relation between age and eating behavior that may have a bearing on alcohol use behavior in women.

NR398 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Prevalence of Eating Disorders in Navarra, Spain: Epidemiological Survey of 4,962 Adolescents

Pilar Gual, M.D., *Department of Psychiatry, University Clinic, APDO 4209, Pamplona, NA 31080, Spain;* Miguel A. Martinez-Gonzalez, M.D., Francisca Lahortiga, Ph.D., Marta Perez-Gaspar, M.D., Cesar A. Soutullo, M.D., Salvador Cervera-Enguix, M.D.

Summary:

Objective: Our goal was to assess the prevalence of eating disorders (ED) in Navarran adolescents. Navarra is a Northern-Spanish Autonomous Region the size of Connecticut with a population of 550,000. There are no epidemiological studies of ED in Navarra, available studies in other Spanish regions have not selected representative samples.[1,2]

Method: Using a multistage random sampling (town-school-classroom) with all schools in Navarra as sampling frame, we selected 6,143 adolescents. After informed consent was obtained

from parents, 4,962 (87%) of 6,143 adolescents (2,862 girls, 2,100 boys), ages 12-21, received the Eating Attitudes Test (EAT-40) questionaire.[3] Adolescents who had an EAT score >30 received clinical interviews by a psychiatrist to evaluate the presence or absence of DSM-IV ED. We used consensus diagnostic conferences for borderline cases.

Results: The prevalence of any ED in adolescent girls was 4.1% (95% CI: 3.5-4.9): AN: 0.31% (95% CI: 0.14-0.59), BN: 0.76% (95% CI: 0.48-1.16), and ED-NOS (3.1%, [95% CI: 2.47–3.77]).

Discussion: Adolescent girls in Navarra suffer from ED with a prevalence similar to that found in other Spanish studies in Madrid (AN: 0.7%, BN: 1.2%),[1] and Zaragoza (AN: 0.14%, BN: 0.55%, NOS: 3.8%)[2] and also the U.S.A. (AN: 0.5–1%, BN: 1–3%)

NR399 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Interpersonal Psychotherapy in Resistant Obese Patients

Virginie Rouch, M.D., *Department of Psychiatry, Casselardit, Hopital de Casselardit, Toulouse 31059, France;* Laurent J. Schmitt, M.D., Henri Sztulman, M.D., Frederic Sanguignol, M.D., Stephanie Ruffie, M.D.

Summary:

Objective: This preliminary study investigates the impact of brief interpersonal psychotherapy in resistant obese patients. Focusing on grief, interpersonal disputes, role transitions or interpersonal deficits, may improve various dimensions of eating disorders and therapeutic alliance.

Method: 19 resistant obese patients, BMI >39, mean age years, were randomly compared to 19 obese subjects similar in age, BMI and who failed in reducting weight after three therapeutic programs. Both groups followed the same program: exercise, dietetary reduction, educative measures. The first group received eight interpersonal psychotherapy sessions over 3 weeks. Evaluation was performed at the beginning and at week 3 using: Eating Disorder Inventory, Beck Depression Inventory (BDI) and helping alliance scale of Luborsky.

Results: Both groups significantly improved for BDI or helping alliance at the end of the program. Weight decrease was not significantly different between the two groups. Two dimensions were significantly improved, $P > 0.05$, ineffectiveness and interpersonal distrust.

Discussion: IPT allows a reduction of feelings of ineffectiveness and interpersonal distrust. Improving these dimensions encourages better interpersonal functioning and social relations. The outcome, however, did not concern weight reduction directly. Further study is necessary to evaluate the impact of IPT in association with other treatments in programs for resistant obese subjects.

NR400 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Patterns of Symptom Change for Three Types of Treatment Responses to Nefazodone

Madhukar H. Trivedi, M.D., *Department of Psychiatry, Univ TX Southwestern Med Ctr., 5959 Harry Hines Blvd, #600, Dallas, TX 75235-9101;* Bruce D. Grannemann, M.A., Susan F. Mahadi, M.Ed.

Summary:

Objective: While extensive work suggests that the Hamilton Rating Scale for Depression (HRSD) can be divided into symptom clusters, relatively little work explores the patterns of change in the symptom clusters during treatment. This paper investigates the utility of using subscales of symptoms on the HRSD to define the pattern of treatment response to nefazodone.

Method: Using principal component analysis, the HRSD was divided into 4 symptom clusters (mood, sleep, appetite, and anxiety). Data for 996 patients with major depressive disorder, who participated in a 12 week acute phase study with nefazodone, were used for a post hoc analysis of changes in symptom cluster scores. Patients were divided into three groups: early, late, and non-responders.

Results: Mood and sleep clusters follow the overall pattern of the HRSD total score. However, the appetite cluster was unrelated to the pattern of response to treatment. More importantly, non-responders exhibit a rebound in the sleep cluster between weeks 3 and 4, and no further improvement in the mood cluster which distinguishes them from late responders.

Conclusions: Monitoring changes in symptom clusters provides a means to differentiate late responders from nonresponders.

NR401 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Effect of Venlafaxine Extended Release on Diabetic Neuropathic Pain

Nadia R. Kunz, Pharm. D., *Wyeth-Ayerst, 145 King of Prussia Road, Radnor, PA 19087;* Richard Entsuah, Ph.D., Veeraindar Goli, M.D., Richard L. Rudolph, M.D., Marc Cantillon, M.D.

Summary:

Objective: The current study evaluated the efficacy, safety, and tolerability of venlafaxine extended release (XR)[4] as a treatment for painful diabetic neuropathy (DN).

Background: The tricyclic antidepressants have demonstrated efficacy in treating the often-severe DN pain by enhancing synaptic levels of serotonin and norepinephrine. Venlafaxine XR is a newer antidepressant that selectively inhibits the reuptake of serotonin and norepinephrine.

Methods: 244 patients were randomized to treatment with venlafaxine XR 75 mg or 150–225 mg, or placebo for ≤6 weeks. The primary efficacy variables were pain intensity and pain relief scales, and secondary efficacy variables were Patient Global Rating of Pain Relief and Clinical Global Impressions (CGI) scale (Severity of Illness and Global Improvement items).

Results: As measured by the primary efficacy variables, venlafaxine XR 150–225 mg resulted in significantly ($P < 0.05$) lower pain intensity (weeks 4–6) than venlafaxine XR 75 mg and placebo, and significantly ($P < 0.05$) greater pain relief (weeks 2–6) than placebo. Venlafaxine XR 75 mg differed statistically from placebo only on pain relief at weeks 2, 3, and 5. On the secondary measures, similar results were obtained on Patient Global Rating of Pain Relief and CGI-Severity of Illness and Global Improvement. On CGI-Global Improvement, statistical superiority ($P < 0.05$) over placebo was also demonstrated for venlafaxine XR 150–225 mg. Since the presence of depression was an exclusion criterion, symptom improvement can only be attributed to an analgesic, rather than antidepressant, effect. Consistent with its labeling, the most common adverse event associated with venlafaxine XR was nausea.

Conclusion: The demonstrated efficacy and favorable safety-tolerability profile of venlafaxine XR in the amelioration of DN pain suggests that this antidepressant should be considered for the analgesic needs of this patient population.

[4]Effexor XR®

NR402 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Comorbid Mental Health Symptoms, Impaired Role Functioning and Nonpsychiatric Health Care Costs in an HMO

Enid M. Hunkeler, M.A., *Research Division, Kaiser Permanente, 3505 Broadway, 7th floor, Oakland, CA 94611;* William D. Spector, Ph.D.

Summary:

We examined the relationship between co-morbid mental health symptoms (depression, acute anxiety, chronic anxiety, panic attacks, trouble controlling rage and violent impulses), role functioning and non-psychiatric medical care costs in an HMO. We analyzed telephone and administrative data on a random sample of 10,000 stably insured Health Plan members. About 24% of respondents reported at least one symptom. Acute anxiety (17%) was most prevalent followed by trouble controlling rage and violent impulses (8.5%), depression (7.5%) chronic anxiety (5.9%) and panic attacks (4.9%). Almost 5% reported deteriorated work, family and/or social functioning due to emotional problems. A strong relationship was found between the number of mental health symptoms, impaired work, family and/or social functioning and non-psychiatric health care costs during the year after the interview. After adjusting for sociodemographics, and prior medical treatments, the mean costs of non-psychiatric medical care were: $1,948 for respondents with neither mental health symptoms nor functional impairment, and $3,906 for those with 5 symptoms and deteriorated work, family and social functioning. Co-morbid acute anxiety and depression were the symptoms most affecting costs. Integrated health care programs may be more cost-effective if they identify and treat patients with both co-morbid mental health symptoms and impaired social role functioning.

NR403 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Clinical and Economic Outcomes with Olanzapine

Douglas Del Paggio, Pharm.D., *Office of the Medical Director, Alameda CO BHCS, 2000 Embarcadero Cove, Ste 400, Oakland, CA 94606;* Jeanette Logan, Pharm.D., Patrick Finley, Pharm.D.

Summary:

High acquisition costs have inspired research efforts to analyze the apparent cost and clinical effectiveness of atypical antipsychotics. Authors measured the outcomes of 189 subjects started on olanzapine within a large urban county behavioral health department.

The subjects were primarily male (63.5%) with an average age of 33.9 years. Fifty-six subjects remained on olanzapine for a full year (i.e., responders) and 22 switched to other antipsychotics. Subgroup analysis revealed that responders had alower total PANSS score at baseline and were more likely to have a diagnosis of thought disorder ($p = 0.039$). Responders demonstrated a significant reduction in total PANSS scores (17.3%) and negative subscale PANSS scores (17.7%) at six month follow-up. Hospital costs, crisis costs and crisis visits decreased significantly during the one year follow-up period (intent-to-treat; $n = 78$; $p = 0.0466$, 0.0086 and 0.0217, respectively) and median medication costs increased significantly ($1,539 per patient). Overall, total resource utilization increased from $10,956 per patient to $11,020 ($64) following olanzapine initiation, or by $5 per patient per month.

In conclusion, olanzapine was associated with favorable clinical outcomes, and total resource utilization rose insignificantly in the captured population. Future integration of functional outcomes may further address cost effectiveness issues.

NR404 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

New Approaches for Rating Belief About Depression

Larry G. Onate, *Department of Psychiatry, AHSC, 1501 North Campbell Avenue, Tucson, AZ 85724-5002;* Pedro L. Delgado, M.D., Rachel E. Manber, Ph.D., John J.B. Allen, Ph.D., Sabrina Hitt, Cynthia A. McGahuey, B.S., Mona Mort, Ph.D.

Summary:

Beliefs about illness shape a person's attitudes and behaviours to illness. These impact compliance. The concept of "personal models of illness" has been applied to understanding a person's beliefs about the causes, consequences and treatments for some medical illnesses, but to date, it has not been applied to depression.

Methods: To assess perceptions of depression in depressed patients, we developed the Perception of Illness about Depression Scale (PIDS). It evaluates 89 variables in 3 different categories: causes of depression, meaning of depression, and remedies for their depression. The PIDS was administered to 92 unmedicated depressed (DSM-IV) patients (29 men, 63 women; age 19–64 yrs.) about to enter one of two clinical trials. Data were analysed using a factor analysis.

Results: 36.5% of the variance regarding a person's perception of the possible causes of depression was explained by three components relating to external (e.g. life circumstances), internal (e.g. personal flaws), or physical (e.g. poor sleep) causes. 58% of the variance regarding consequences of/attitudes towards depression was explained by two components: a hopelessness/pessimistic component (I will always be depressed) and a positive/optimistic component (I have a new challenge). Beliefs about the cause of depression strongly influenced a person's beliefs about what should constitute an effective treatment. A detailed analysis of patterns, beliefs and concepts of illness will be presented.

Conclusions: There is considerable variability in the beliefs and attitudes about depression, even in a relatively homogeneous group of depressed patients who have been recruited into clinical trials. Understanding patterns of beliefs and attitudes about the cause of depression can be used to predict expectations regarding the effectiveness of different treatments for depression. Better understanding the specific beliefs and attitudes that a person has about depression may help to focus psychoeducational efforts aimed at enhancing treatment compliance.

NR405 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Retrospective One-Year Review of the Outcomes of Atypical Antipsychotic Use at Central Texas Veterans Health Care System

William R. Clark, Pharm.D., *Department of Pharmacology, Central Texas Veterans Administration, 4800 Memorial Drive, Waco, TX 76711;* Jennifer L. Defilippi, Pharm.D.

Summary:

Objective: Assess differences in outcome among atypical antipsychotics in clinical use.

Methods: Retrospective chart review of patient exposures to atypical antipsychotic agents over a one year period at the Central Texas Veterans Health Care System. Each exposure was evaluated for outcome, average and maximum doses, duration of therapy, concomitant medications, and previous atypical antipsychotic therapy. Positive outcomes included: discharge from hospital; current inpatient use; or short term use with symptom resolution. Negative outcomes included: discontinuation due to lack of efficacy or adverse event; lost to follow-up after initial prescription; or death. Medication noncompliance was considered a third outcome.

Results: Interim analysis revealed: positive outcome rates of: risperidone 61%; olanzapine 65%; quetiapine 59%; negative outcome rates of: risperidone 29%; olanzapine 21%; quetiapine 26%. Medication noncompliance rates were: risperidone 10%; olanzapine 14%; quetiapine 15%. Additional antipsychotics were used with 8.5% of risperidone, 7.4% of olanzapine and 20% of quetiapine exposures. However, 19% of quetiapine use occurred after nonresponse to other atypical agents compared to 10% of risperidone and 11% of olanzapine exposures. Cost of therapy with a positive

outcome: risperidone $112/month, olanzapine $230/month, quetiapine $144/month.

Conclusions: Positive and negative outcomes were similar among the atypical antipsychotics. Higher rates of additional antipsychotic use with quetiapine may be related to use in more refractory patients.

NR406 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Seizure Threshold in ECT: Differences Between Instruments

Worrawat Chanpattana, M.D., *Department of Psychiatry, Srinakharinwirot University, 681 Samsen Dusit, Bangkok 10300, Thailand;* Wanchai Buppanharun, M.D., Somchai Chakrabhand, M.D.

Summary:

The determination of seizure threshold can help guide the selection of the stimulus dosage in electroconvulsive therapy (ECT); however, this threshold is subject to a variety of influences. We measured the effect of the selection of ECT instrument on initial seizure threshold by titration in 88 patients. Treatment was given with the MECTA SRI or the Thymatron DGx instrument, by random assignment. Measured seizure thresholds were higher with the MECTA instrument than the Thymatron instrument in 79% of patients ($p < 0.0001$), and were on average 61% higher ($p < 0.0001$). Because greater side-effects may follow higher stimulus dosages, these differences have potential clinical implications. Moreover, when different ECT instruments are used on the same patient, corresponding adjustment of the stimulus dosage may be needed.

NR407 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Drugs and Post-ECT Course in Catatonic Depression

Conrad M. Swartz, M.D., *Department of Psychiatry, Southern IL University, P O Box 19642, Springfield, IL 62794-9642;* Vicki Morrow, M.D., Lara Surles, M.D., J Frank James, M.D.

Summary:

Objective: Medication influence on post hospitalization outcome of major depressive disorder with catatonic features treated by ECT is unknown. We assessed this effect.

Method: We interviewed the patient or knowledgeable close relative 3 to 7 years after treatment with ECT for major depression with catatonic features, in a university inpatient program, during a particular 4-year period. The 19 patients were all for whom we could obtain followup. Asymmetric bilateral brief-pulse ECT was used exclusively.

Results: 77% of the 13 patients discharged on antimelancholic medications had good outcome, compared to 0 of the other 6 patients ($z = 2.874$, $p = 0.0041$); age was not significant. Antimelancholic medications were lithium, tricyclics, buproprion, and venlafaxine. The other group received SSRIs (3 patients), clozapine, diazepam, or trazodone. The antimelancholics group had no deaths but the other group had 3 deaths. For most patients the informant did not identify catatonia or depression; rather "don't know" or another disorder was mentioned. Two patients for whom ECT produced remission from catatonia denied such benefit.

Conclusions: Patients who receive antimelancholic medication after ECT for catatonic depression have fewer rehospitalizations and better outcome. These results provide no basis for SSRI usage after ECT. Past catatonic depression is not reliably identified by informant interview, nor is good ECT response excluded.

NR408 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Impact of Victimization on Inpatient Treatment

Robert M. Vidaver, M.D., *Department of Psychiatry, Dartmouth Medical School, 36 Clinton Street, Concord, NH 03301;* Michelle P. Salyers, Ph.D., Kim T. Mueser, Ph.D., Stanley D. Rosenberg, Ph.D.

Summary:

Objective: Recent studies report high levels of violent victimization among people with severe mental illness (SMI) (1). Traumatic experiences (lifetime) in SMI clients are related to both to the severity of psychiatric symptoms and service utilization (2), but the direction of these causal relationships remains unclear.

Method: We examined *prospectively* the impact of recent victimization on 139 clients meeting diagnostic criteria for SMI. Consecutive, consenting admissions to a state hospital were assessed for trauma history, recent exposure to interpersonal violence, psychiatric symptoms, and recent hospitalizations. Clients were then followed for 12 months to determine total hospital days, re-hospitalization, self-harming and violent behavior, symptom severity and treatment adherence while in hospital.

Results: Recent exposure to violence was common, with 40% of clients suffering severe assaults within the year prior to admission. Recent victimization was associated with histories of childhood abuse, substance use disorder and recent arrests. Prospectively, recent victimization was associated symptoms of irritability, medication non-compliance (17% vs. 8%), and incidents of assaultiveness (46% vs. 28%) during inpatient treatment, but not with length nor number of hospitalizations over the following year.

Conclusions: Recent victimization appears to negatively impact symptoms and treatment participation in persons with SMI requiring acute inpatient services.

NR409 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Risperidone and 9-Hydroxy Risperidone Concentrations Are Not Dependent on Age or Creatinine Clearance Among Elderly Subjects

Robert A. Sweet, M.D., *Department of Psychiatry, University of Pittsburgh, 3811 Ohara Street, Room 1234, Pittsburgh, PA 15213-2593;* RaeAnn Maxwell, Ph.D., Benoit H. Mulsant, M.D., Jules Rosen, M.D., Margaret A. Kirshner, B.A., Kari B. Kastango, M.S., Bruce G. Pollock, M.D.

Summary:

Objective: Risperidone (R) is extensively metabolized to an active metabolite, 9-hydroxyrisperidone (9-OH), which is dependent on renal clearance. R and 9-OH clearances are reduced in the elderly when compared to young subjects. Hypothesis: Among elderly subjects, R and 9-OH clearance would further decline with increasing age and decreasing creatinine clearance (CrCl).

Methods: Twenty geriatric inpatients evaluated in a naturalistic setting with regards to total daily R dose (TD) and dosing interval (DI). Baseline CrCl over 8 hours and radioimmunoassay of R and 9-OH steady state concentrations were determined. Multiple linear regression was used to examine the impact of age, weight, CrCl, TD and DI on concentrations of R, 9-OH, their sum and the ratio of 9-OH/R.

Results: Mean TD was 1.3 ± .73 mg. Mean Age was 76.4 ± 9yrs (range 55–91). Mean CrCl was 55.43 ± 32.8ml/min/1.73sq.m (17.0–141.88ml/min/1.73sq.m). Steady-state R and 9-OH concentrations were 4.14 ± 5.3ng/ml and 9.1 ± 6.3ng/ml, respectively. Concentrations of R, 9-OH, their sum and 9-OH/R did not correlate with any of the independent variables.

Conclusions: Among elderly subjects, R and 9-OH clearance do not decline with increasing age or declining CrCl. Accumulation of 9-OH may not be as great as expected.

NR410 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Reducing the Use of Restraint and Seclusion in the Acute Inpatient Psychiatric Setting

Ilana Iacobovici, M.D., *Department of Psychiatry, University of Maryland Medical School, 701 West Pratt Street, 4th floor, Baltimore, MD 21201;* Jill A. RachBeisel, M.D.

Summary:

Objective: The use of restraint and seclusion (R&S) has come under critical review by local and national agencies with the expectation that serious efforts to reduce or eliminate such use is made. This study examines factors influencing the use of R&S and strategies implemented to reduce its use.

Methods: Standardized training on managing aggressive behavior was provided to all inpatient staff including a patient/family education module. Data were collected on all R&S events on 4 psychiatric units, including one latency age unit, during a 6 month period.

Results: Of 196 episodes of R&S 81% involved male patients 60% of whom were on voluntary status. 54% were children under 10 years of age. 76% of patients/families received the educational module at admission. Substance abuse disorders were identified in 8%(n = 14) with only 1.6%(n = 3) intoxicated at the time of R& S. While 97% of the patients had a prn medication for agitation ordered, only 23% of the patients received medicine within 60 minutes prior to R&S and 29% during or immediately following R&S. Less restrictive interventions such as verbal de-escalation, time-outs, medication and activity distraction were tried in 97% of the cases before R&S was implemented. Staffing patterns were not found to be a significant influence on the use of R&S.

Conclusions: This study demonstrates that admission status, substance abuse and staffing patterns had little influence on the use of R&S where as gender and age may play a more important role. Despite staff's ability to incorporate a variety of less restrictive interventions, more effective strategies such as timeliness of medication are needed. Further correlations will be presented.

NR411 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Long-Term Impact of an Intensive Subunit on Acuity

Eric S. Cole, Ph.D., *Delaware Psychiatric Center, 1901 North Dupont Highway, New Castle, DE 19720;* Cheryl K. Cantrell, M.D., Deborah E. Boyer, B.A.

Summary:

Objective: We have previously reported that establishing a high acuity subunit within a chronic psychiatric ward can have an immediate impact on acuity indicators like prn medications and seclusions. This study examines the longer term impact of such a subunit.

Method: Data on seclusion and prn medications were collected on 27 continuously hospitalized patients for one year before and two years after the opening (January, 1997) of the Intensive Treatment Module (ITM) and compared using the chi test.

Results: Total unit seclusions dropped between 1996 and 1998 (252 to 86, p = 1E-12),with a dramatic reduction for the ITM patients in 1996–97 (224 to 99) and for the non-ITM patients in 1997–98 (30 to 6). Total prn medication use increased from 1996 to 1998 (2554 to 3334, p = 4E-12); however, prn use in ITM patients increased steadily, while use in non-ITM patients decreased overall with the lowest use in 1997. The difference in pattern of prn medication use was highly significant (ITM: 827 to 2080 vs non-ITM: 1727 to 1254, p = 3E-115).

Conclusions: The high acuity subunit continued to be associated with significant changes in major indicators of acuity over a two year period. The pattern of prn medication utilization requires further investigation.

NR412 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Reasons for Discontinuation and Switching of SSRIs

Scott Bull, Pharm.D., *Research Department, Kaiser Permanente, 3505 Broadway, 7th floor, Oakland, CA 94611-5714;* Francois Collin, Enid M. Hunkeler, M.A.

Summary:

The purpose of this study was to investigate reasons for switching and discontinuation of Serotonin Selective Re-uptake Inhibitors (SSRIs) approximately 3 and 6 months after initiating treatment. Telephone surveys were conducted with 674 patients at The Kaiser Permanente Northern California Medical Care Program who were started on fluoxetine or paroxetine for the treatment of a new or recurrent case of depression. Thirty-eight (5.6%) patients switched and 190 (28.2%) of the patients discontinued their antidepressant within the first 4 months. An additional 31.0% of study members discontinued their antidepressant late (5–7 months after starting treatment). The most frequently reported reasons for discontinuation were "No Longer Depressed" (15.3%) and "No Improvement" (13.6%). "Drowsiness/Fatigue" (10.5%) was the most common side effect for discontinuing treatment early and "Sexual Dysfunction" (10.2%) was most frequently reported side effect for switching antidepressants or discontinuing treatment late. Patients who said they also received counceling or who recalled being told how to take their medication were nearly twice as likely to continue antidepressants for 4 months. (Odds Ratio = 1.96 and 1.89 respectively). Side effects account for approximately 1/3 of SSRI discontinuations. Good medication taking instructions and/or psychosocial support may prolong medication use.

NR413 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Care of Persons with Schizophrenia on Medicare

Lisa B. Dixon, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, Room 476, Baltimore, MD 21201;* Alan Lyles, Sc.D., Corey B. Smith, M.A., Jeffrey S. Hoch, Mavreen Fahey, M.L.A., Leticia T. Postrado, Ph.D., Anthony F. Lehman, M.D.

Summary:

Objectives: This study describes the predictors of the use and cost of ambulatory services by Medicare recipients with schizophrenia.

Methods: The Medicare claims of a 5% random sample of all individuals in the United States with at least one schizophrenia diagnosis on a Medicare claim during 1991 were examined. Multivariate analyses assessed the impact of race, age, gender, and Medicaid co-insurance on the use and cost of any ambulatory service, individual therapy, psychiatric somatotherapy, group therapy, and family therapy.

Results: Nearly 25% of the Medicare sample (N = 12,440) had no filed claim for an ambulatory mental health service. The average total number of visits was 7.9 ± 21 visits/year. Individual therapy was used most frequently (M = 5.0 ± 14 visits/year) with little use of family and group therapy. The average cost of care for those who received any service was $470 ± 1028/year. Of persons less than 65 years old, Whites were 1.46 times more likely than African-Americans to receive any ambulatory service (95% CI = 1.17-1.84). Persons 65 or older were also less likely to receive any service (CI = 0.36-0.44). Costs of care were also lower for African-Americans and older people.

Conclusions: This study suggests substantial under-utilization of appropriate ambulatory services by Medicare beneficiaries with schizophrenia, especially African-Americans.

NR414 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Determinants of Psychotherapy Among Antidepressant Recipients

Thomas W. Croghan, M.D., *Drop Code 1850, Eli Lilly and Company, Lilly Corporate Centre, Indianapolis, IN 46285;* Regina L.H. Powers, Ph.D., Thomas J. Kniesner, Ph.D.

Summary:

Objective: To determine the correlates of psychotherapy among antidepressant recipients in the SSRI era.

Method: Using insurance claims data for antidepressant users with employer provided insurance, we used sample selection models to determine the number of psychotherapy visits in the 12 months following initiation of antidepressant treatment. Explanatory variables included provider choice, demographic characteristics, pre-period costs and use of psychotherapy for non-depression reasons, and certain characteristics of the health plan, including use of utilization management, employee assistance programs, and the level of coinsurance.

Results: Significant predictors of psychotherapy use during the post-treatment period included choice of a mental specialty provider relative to a primary care provider, either a psychiatrist (OR = 2.43) or a non-physician mental health specialist (OR = 1.39); use of case or utilization management (OR = 0.874); major depression (OR = 1.37); use of anxiolytics (OR = 1.02); prior period psychotherapy (OR = 1.33); and high medical utilization in the pre-period (OR = 1.32).

Conclusion: Antidepressant recipients initially treated in primary care plans with utilization management receive less psychotherapy than others. The effects on mental health status remain to be determined.

NR415 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Predictors of Use of Atypical Antipsychotic Medications in a Veterans Population

Teresa J. Hudson, Pharm.D., *HSR&D, Veterans Administration, 2200 Fort Roots Dr. Bldg 58, North Little Rock, AR 72114;* Weiwei Feng, Ph.D., Mark Austen, M.S., Richard R. Owen, M.D.

Summary:

Objective: Novel antipsychotic medications have several advantages over traditional agents in the treatment of schizophrenia. Little is known about factors that affect prescribing of novel agents. This study examines variation in novel antipsychotic prescribing at 13 VA Medical Centers from six Veterans Integrated Service Networks (VISNs).

Methods: Using automated data, we identified 695 patients with an outpatient prescription for antipsychotic medicatin following their last discharge with a diagnosis of schizophrenia in 1997. Most patients (667) of the 695 subjects were male. Approximately 45% were African American, 48% white, and 6% Hispanic. Mean age was 48.6 (range 22–89).

Results: Novel antipsychotics were prescribed for 49.1 of the subjects, with significant variation among the facilities ($x^2 = 28.6$, df = 12, P = 0.005) and VISNs studied ($x^2 = 11.3$, df = 5, P = 0.046). White patients were more likely than non-whites to receive novel antipsychotics (OR = 1.664, P = 0.0002) controlling for martial status, gender, age, and facility.

Conclusions: Although nearly half of patients with schizophrenia are receiving novel antipsychotics in this sample, the variation among facilities and networks as well as by ethnicity suggests that prescribing practices for these agents could be improved. Further research is needed to determine the factors that influence these practices.

NR416 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Lifetime Cost of Bipolar Disorder in the U.S.: An Estimate Based on Incidence and Course of

Charles E. Begley, Ph.D., *School of Philosophy, University of Texas, 1200 Herman-Pressler, Houston, TX 77030;* John F. Annegers, Ph.D., Alan C. Swann, M.D., Christopher Lewis, B.S., Sharon Coan, M.S., William B. Schnapp, Ph.D., Lynda Bryant-Comstock, M.P.H.

Summary:

Objective: A cost model was developed to provide estimates of the present value of total and per case lifetime costs for 1998 incident cases of bipolar disorder in the US.

Methods: Age- and sex-specific incidence rates for bipolar disorder were estimated by simulating rates that are consistent with existing prevalence surveys. The courses of illness of incident cases were estimated for six prognostic groups based on the frequency and duration of acute episodes. Direct mental health service costs were estimated for acute episodes, recovery, and maintenance treatment. Excess health service costs were added to the mental health service costs. Projected indirect costs were estimated based on data from the National Comorbidity Survey. Additional direct and indirect costs associated with excess alcohol and drug abuse were estimated based on data obtained from the literature.

Results: The total lifetime cost of all persons with onset of bipolar disorder in 1998 is estimated at $22.8 billion. Average cost per case was $238,976, with a range from $12,690 for single manic episode to $454,456 for non-responsive/chronic.

Conclusion: The model suggests substantial cost differences between bipolar patients with stable and non-progressive disease and the more severe cases whose conditions deteriorate over time. This difference underscores the importance of achieving a stable outcome to limit the economic outlay of severe bipolar patients.

NR417 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Illness
Effect of Provider Choice on Treatment and Treatment Adequacy Among Depressed Patients

Thomas J. Kniesner, Ph.D., *Center for Policy Research, Syracuse University, 426 Eggers Hall, Syracuse, NY 13244-1020;* Regina L.H. Powers, Ph.D., Thomas W. Croghan, M.D.

Summary:

Objective: To understand the effect of provider choice on subsequent treatment choices and the adequacy of that treatment.

Method: Using insurance claims data for a population of depressed persons, we estimated multivariate models of the likelihood of receiving any treatment, the type of treatment received (psychotherapy-only, medication-only, or combination), and the adequacy of that treatment. Explanatory variables included provider choice (primary care provider, psychiatrist, psychologist, or other mental health specialist); characteristics of depression symptoms and severity; and demographic characteristics.

Results: Persons diagnosed as depressed by psychiatrists were most likely to receive any treatment, while those diagnosed by psychologists and other non-physician mental health specialists were least likely to receive treatment. Among those treated, those diagnosed by primary care physicians tended to receive medication-only treatment. Those diagnosed by other providers, including psychiatrists, tended to receive psychotherapy only. A sizable minority of persons diagnosed by psychiatrists received combination treatment. Once treated, the majority of depressed persons received adequate care, independent of provider type.

Conclusion: There are substantial differences in the likelihood of receiving any care depending on choice of initial provider. How-

ever, provider type had little effect of the adequacy of treatment once it was initiated.

NR418 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

SSRI Usage Patterns As Risk Factors for Hospitalization

Reinee E. Sheffield, Pharm.D., *Research Department, PCS Health Systems, 9501 East Shea Blvd, MC034, Scottsdale, AZ 85260;* Anthony T. Losasso, Ph.D., Chistopher Young, Ph.D., Karen D. Way, Ph.D.

Summary:

Objective: To estimate the risk of hospitalization associated with fluoxetine, paroxetine, and sertraline antidepressant usage patterns in a Midwestern health maintenance organization.

Method: Multiple logistic regression analysis of retrospective, longitudinal pharmacy and medical claims for newly treated patients between June 1996 and June 1997 (N = 592).

Results: Paroxetine use was a significant risk factor for unstable usage patterns, discontinuation (OR: 2.007, $p < 0.01$) and switching/augmentation (OR: 1.865, $0.05 < p \leq 0.10$) compared to fluoxetine. Sertraline use predicted discontinuation (OR: 1.445, $0.05 < p \leq 0.10$, vs. fluoxetine). Compared to stable-use patients initiated on fluoxetine, the combinations of switching/augmentation and paroxetine (OR: 5.852, $0.01 < p \leq 0.05$) or sertraline (OR: 9.471, $p < 0.01$) significantly predicted hospitalization, but not stable-use and sertraline (OR: 0.303, $0.05 < p \leq 0.10$). The combination of sertraline and early discontinuation predicted hospitalization (OR: 3.477, $0.05 < p \leq 0.10$).

Conclusions: Paroxetine and sertraline use may be significant risk factors for unstable usage patterns compared to fluoxetine. Paroxetine or sertraline initiation among patients exhibiting unstable usage patterns may increase the risk of hospitalization compared to fluoxetine initiation among stable-use patients. Sertraline initiation among stable-use patients may lower the risk of hospitalization.

NR419 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Concordance with Dose Recommendations of Schizophrenia Guidelines in Veterans Administration Facilities

Weiwei Feng, Ph.D., HSR&D, *Veterans Administration, 2200 Fort Roots Drive Bldg 58, North Little Rock, AR 72114;* Teresa J. Hudson, Pharm.D., Mark Austen, M.S., Richard R. Owen, M.D.

Summary:

Objective: The American Psychiatric Association, the Veterans Administration, and others have developed and disseminated evidence-based recommendations for treatment of schizophrenia. This study evaluates concordance with antipsychotic dose recommendations guidelines in 13 VA Medical Centers in 6 Veterans Integrated Service Networks (VISNs).

Methods: We identified patients with schizophrenia who received and outpatient prescription for antipsychotic medication following their last discharge in fiscal year 1997. Due to lack of dosage information, we excluded patients prescribed depot medications. Most (667) of the 695 veterans were male. Mean age was 48.6 years. Approximately 45% were African American, 48% white, and 6% Hispanic.

Results: About 75% of the patients were prescribed guideline-concordant antipsychotic doses according to VA guidelines versus 54% with the APA guideline. There was no significant difference in demographic variables (age, race, marital status) between the groups who met the guideline and who failed. Among VISNs or medical facilities within a VISN, no significant difference in concordance was found.

Conclusions: The higher concordance rates with VA guidelines are due to difference in the recommended dose ranges as compared to the APA guidelines. More research is needed to determine predictors of guideline concordance and to determine the impact of prescribing practices on patient outcomes.

NR420 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Differences in Medication Adherence Between Users of Conventional and Atypical Antipsychotics in a Large State Medicaid Program

Joseph Menzin, Ph.D., *Boston Health Ec., 5 Suburban Park Drive, Billerica, MA 01821;* Luke Boulanger, M.A., Mark Friedman, M.D., Joan A. Mackell, Ph.D., John Lloyd

Summary:

Objective: This study assessed differences in treatment patterns and medication adherence between users of conventional and atypical antipsychotics in clinical practice.

Method: Administrative claims for a 10% random sample of California Medicaid ("Medi-Cal") recipients was used. We identified outpatients 18+ years of age with schizophrenia or schizoaffective disorder initiating monotherapy with conventional antipsychotics (C), risperidone (R), or olanzapine (O) in the first 3 months of 1997, following the elimination of prior authorization for atypical antipsychotics. Dosing, concomitant medications, treatment switching, and adherence, measured by persistence (i.e., "covered days"), were evaluated over 1 year. Multivariate methods were used to adjust for differences between groups in potential confounding factors.

Results: A total of 298 patients on C (93), R (63), and O (142) met study inclusion criteria. The groups were similar demographically (mean age: 42 years, 54% male). The final daily doses (mg) (mean $\pm$ SD) for R and O were 4.8 ± 3.6 and 14.3 ± 7.5, respectively. Compared to patients prescribed C, those prescribed R and O were at least two-thirds less likely both to switch antipsychotics (adjusted odds ratios 0.35 and 0.24 respectively; both $p < 0.05$), and to have anticholinergics added (adjusted odds ratios 0.33 and 0.16 respectively; both $p < 0.05$). Persistence with all antipsychotics was approximately 60% regardless of whether patients started treatment with C, R, or O.

Conclusions: Compared to conventional medications, the use of atypical antipsychotics is associated with significantly less therapy switching, and a reduced use of anticholinergics. However, patients were without any antipsychotic medications a substantial portion of the year, highlighting a need for improved therapies in the management of schizophrenia.

NR421 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Factors Affecting Supply of Mental Health Care Services

Jong I. Park, M.D., *Department of Psychiatry, University of Ulsan, 388-1 Poongnap-Dong, Songpa-Gu, Seoul 138-040, Korea;* Jin Pyo Hong, M.D., Yoon Kim, M.D., Tong W. Suh, M.D., Chang J. Suh, Ph.D.

Summary:

Objective: The purpose of the study is to investigate the factors affecting adequate provision of mental health care services to the psychiatric patients in mental hospitals.

Method: Five hundreds and seventy-five psychiatric patients chosen by the stratified random sampling in six hospitals in Korea; three from mental hospitals and three general hospitals, were investigated about mental health care services provided for one week. The variables for the study are as follows: doctor interviews,

nursing care, group therapy, medication, and miscellaneous services which are transformed into virtual financial cost using Korean Resource Based Relative Value Scale points. Severity of psychiatric symptoms were assessed by RAI-MH(Resident Assessment Instrument-Mental Health).

Results: When the Medicaid was compared to the Health Insurance in mental hospitals, the relative ratio of services was sixty-seven percent. Mental hospitals compared to general hospitals under Health Insurance, it was only 31%. The longer the hospitalization, the lesser services the patient received in all hospitals. The difference was insignificant by age and diagnosis group. Moderate correlation was observed between severity of psychiatric symptoms and services only in mental hospitals under Health Insurance.

Conclusions: The significant factors affecting supply of mental health care services in Korean mental hospitals were duration of hospitalization, type of hospital, type of reimbursement.

NR422 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Antidepressant Use Patterns in a Naturalistic Setting

Brent Hale, R.Ph., *Eli Lilly and Company/ DC4025, Lilly Technology Center South, Indianapolis, In 46285;* Ryan Tierney, B.S., Catherine A. Melfi, Ph.D., William Signa, M.S., Thomas W. Croghan, M.D.

Summary:

Objective: To examine the comparative use patterns of initial prescriptions for antidepressants (citalopram, fluoxetine, paroxetine, sertraline, venlafaxine, venlafaxine XR) in a naturalistic setting.

Methods: A total of 240,604 patients with prescription claims were followed for one year to analyze length of therapy, switching, and titration rates.

Results: There was differentiation among products in drug utilization patterns. The majority of antidepressant recipients did not receive six months of continuous treatment. Receipt of fluoxetine was associated with the longest length of therapy (139.9 days), and receipt of citalopram was associated with shortest length of therapy (113.2 days) ($p < 0.0001$). Venlafaxine recipients were most likely to switch antidepressants (22.6%), and fluoxetine recipients were least likely to switch (7.5%) ($p < 0.0001$). Among continuous users, venlafaxine XR patients were most likely to titrate (44%), and venlafaxine were least likely to titrate (22.3%).

Conclusion: Fluoxetine remains the medication most associated with achieving an adequate course of treatment. The impact of use patterns on both clinical and economic outcomes cannot be ignored nor can one drug be expected to treat all patients.

NR423 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Dosing of Conventional Antipsychotics in Severely Ill Veterans with Schizophrenia: Opportunities for Improvement

Marcia T. Valenstein, M.D., *HSR & D, VAMC, p o box 130170, Ann Arbor, MI 48113-0170;* Frederic C. Blow, Ph.D., Richard R. Owen, Jr., M.D., Laurel A. Copeland, M.P.H., Stephanie Visnic, M.S.

Summary:

Background: Schizophrenia is a devastating and costly illness. Unfortunately, treatments for schizophrenia often do not reflect research based findings. Since the 1980s, research and review articles have recommended the use of moderate doses of conventional antipsychotics (between 300 and 1,000 mg chlorpromazine equivalents (CPZE)). We describe antipsychotic doses prescribed for a large cohort of severely ill schizophrenic veterans between 1991–1995 and examine the relationship between doses and patient characteristics.

Methods: 935 veterans with schizophrenia on oral conventional antipsychotics were enrolled in the study between January 9, 1991 and December 19, 1995. At enrollment, clinicians listed patients' current medications and doses and completed a 19-item Brief Psychiatric Rating Scale (BPRS). Antipsychotic doses and the relationship between doses and patient characteristics are described.

Results: Approximately half (52%) of these patients were receiving doses of conventional antipsychotics between 300–1,000 CPZE; 20% were receiving doses below and 28% doses above this range. Younger patients and African-Americans were more likely to receive high doses. Approximately 16% of patients receiving doses below 300 mg and 37% of patients receiving doses over 1,000 mg CPZE had BPRS scores greater than 30 (items rated on a 0–6 scale).

Conclusions: Only half of these severely ill patients were receiving recommended doses of conventional antipsychotics. A significant minority were receiving low doses despite continuing psychotic symptoms or high doses despite doubtful incremental efficacy and the availability of atypical agents. Clinicians were more likely to use high doses in symptomatic patients, younger patients, and African Americans.

NR424 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Should We Screen for Depression in Primary Care Settings? A Decision Analysis

Marcia T. Valenstein, M.D., *HSR & D, VAMC, p o box 130170, Ann Arbor, MI 48113-0170;* Sandeep Vijan, M.D., John Zeber, M.H.A., Kathryn Boehm, M.D., Amna Buttar, M.D.

Summary:

Background: Depressive disorders are common in primary care, cause substantial disability, but often remain undiagnosed. Depression screening is one strategy for increasing detection.

Methods: We developed a semi-Markov model to examine lifetime costs and benefits of periodic or one-time screening for cohorts of 20, 40, or 60 year old primary care patients. Parameter estimates were drawn from the published literature and analyses conducted from the perspective of a single healthcare payer.

Results: In the base case, annual depression screening had an incremental cost-utility (C/U) ratio of $225,759/QALY gained compared to usual care. Opportunistic screening had a higher C/U ratio but one-time screening had a C/U ratio of only $48,866/QALY gained. Estimated C/U ratios were sensitive to several parameters including utilities assigned to health states with MDD, MDD prevalence, costs of screening, treatment initiation once MDD is diagnosed, and remission rates with treatment. Sensitivity analyses indicated that 3 or more parameters in the base case must be changed to decrease the C/U ratio of *annual* screening below $50,000/QALY but a change in only one model parameter would increase the C/U ratio of *one-time* screening above $50,000/QALY.

Conclusions: Annual or periodic screening for depression is unlikely to be a cost-effective intervention in primary care unless substantial improvements are also made in the quality and effectiveness of depression treatment. One-time screening for depression should be considered even with current treatment practices.

NR425 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Program Leaders' Attitudes and Beliefs About Clinical Practice Guidelines for Addiction Treatment

Mark L. Willenbring, M.D., *Mental Health Department, VA Medical Center, 1 Veterans Drive, Minneapolis, MN 55417;* Dan Kivlahan, Ph.D., Michael Grillo

Summary:

Objective: To guide implementation of the new VA clinical practice guideline (CPGL) for the management of substance use disorders, program leaders were surveyed about attitudes and beliefs about CPGLs in general and in addiction treatment.

Method: Mail survey of addiction treatment program leaders.

Results: In the first wave of surveys, 58/96 (60%) were returned. Respondents were familiar with VA and ASAM guidelines. They were positive towards CPGLs, but were concerned about their use in disciplinary proceedings and loss of clinician autonomy. Perceived barriers to implementation were insufficient staff time and administrative support and insufficient training. Staff training and easy access to the guideline in the clinical setting were seen as helpful implementation strategies. Although 85% rated naltrexone effective, only 28% of programs offered it; 40% identified pharmacy restrictions as a barrier. Other newer evidence-based therapies were not well understood.

Conclusion: VA addiction program leaders are knowledgeable and supportive of CPGLs. However, they will need consultation, training, and support for successful CPGL implementation. Staff need to be convinced of the guideline's utility and evidence supporting newer treatments. Concerns about staff time, lack of administrative support, and clinician autonomy must be addressed.

NR426 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Generalizability of Antidepresssant Efficacy Trials: Results from an Outpatient Practice

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905;* Michael A. Posternak, M.D.

Summary:

Introduction: The majority of individuals who apply to enroll in an antidepressant efficacy trial do not qualify due to various exclusion criteria. It is unclear how much these exclusion criteria impact on response rates. We examined the outcomes of outpatients treated for major depression in routine clinical practice who were initiated on an antidepressant, and compared response rates of those patients who would qualify for an antidepressant trial with those who would not.

Method: Seventy-four psychiatric outpatients with a principal diagnosis of major depressive disorder as determined by the Structured Clinical Interview for DSM-IV (SCID) were initiated on an antidepressant according to standard clinical practice. Prospective ratings using the Clinical Global Impression-Improvement (CGI) scale were made. Patients were considered to have had a positive response if they achieved a CGI score of 1 (very much improved) or 2 (much improved) following an adequate trial.

Results: Using the least restrictive inclusion criteria, 33/56 (58.9%) and 13/18 (72.2%) of patients who would and would not qualify respectively for an antidepressant trial, responded. Using the most restrictive inclusion criteria, 4/7 (57.1%), and 42/67 (62.7%), responded.

Conclusions: Our results suggest that antidepressants are as effective in those patients who would not be included in an antidepressant trial as those who would be. This supports the generalizability of standard antidepressant efficacy studies.

NR427 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

An Outcomes Measure: The Multidimensional Assessment of Symptoms and Psychosocial Functioning (MASP)

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905;* Jill I. Mattia, Ph.D.

Summary:

Objective: The goal of this project is to develop a multidimensional, modular, self-report questionnaire that evaluates the course and outcome of psychiatric treatment for the most common DSM-IV Axis I disorders seen in outpatient psychiatry settings. The reliability and validity of the scale is described.

Methods: The Multidimensional Assessment of Symptoms and Psychosocial Functioning (MASP) is a self-administered questionnaire that assesses the most common DSM-IV disorders presenting in mental health outpatient settings. A series of 522 psychiatric outpatients completed the MASP immediately before or after their intake evaluation. One hundred and eighty-six patients completed a booklet of questionnaires that included established measures of the same symptom domains of the MASP, and 177 patients completed the MASP a second time within a week of the initial administration.

Results: The MASP subscales achieved good-excellent levels of internal consistency (15 of the 16 subscales had an alpha coefficient of .90 or above; mean alpha coefficient = .94). The individual MASP items correlated more highly with their own subscale than other subscales (mean item-parent subscale correlation = .70; mean item-other subscale correlation = .27). The mean of the test-retest reliability coefficients was .86. The MASP subscales were much more highly correlated with established measures of the same symptom domain (mean r = .70), than with measures of other types of psychopathology (mean r = .27). Subscale scores were significantly associated with blind psychiatric diagnoses.

Conclusions: The MASP is a reliable and valid measure of the severity of the most common DSM-IV disorders. Because it is modular disorder specific subscales can be administered as appropriate, and ongoing outcome evaluation can be incorporated into routine clinical outpatient practice without disruption.

NR428 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Pathological Gambling in Psychiatric Outpatients: Prevalence, Comorbidity, Demographics and Clinical Correlates

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905;* Jill I. Mattia, Ph.D.

Summary:

Background: Studies of the prevalence of PG in psychiatric and substance abusing patients suggest that the disorder is not rare. Most studies have been of substance abusers in treatment, and the rate of PG has been found to be many times higher than the rate found in epidemiological surveys. In the only study of PG in a heterogeneous sample of patients, Lesieur and Blume (1990) found that 6.7% of 105 psychiatric inpatients were pathological gamblers. We are not aware of any study of the prevalence of PG in an outpatient sample using DSM-IV diagnostic criteria.

Method: In the present study 749 psychiatric outpatients were evaluated with a semi-structured diagnostic interview that included a module to diagnose DSM-IV PG.

Results: Eighteen (2.3%) patients had a lifetime history of DSM-IV PG. Five patients had current PG (0.9%), and 13 (1.4%) had a past diagnosis. No patient had PG as their principal diagnosis. All five patients with current PG wanted treatment to address their gambling problem. Compared to the patients without PG, the patients with PG were significantly more often male and nonwhite. There were no differences between patients with and without PG in marital status, age, or education. The patients with PG were not diagnosed with significantly more current DSM-IV Axis I disorders (3.2 ± 1.9 vs. 2.6 ± 1.6, $t = 1.51$, n.s). Looking at the specific disorders, the gamblers were more frequently diagnosed with bipolar I disorder, social and specific phobia.

Conclusions: Our results suggest that PG is relatively rare in general psychiatric outpatient settings. Less than 1% of patients met current DSM-IV criteria for PG, and approximately 2% had a lifetime history of PG. Although PG was not the principal diagnosis in any patient, those patients with the disorder wanted treated to address their gambling problem. Reasons why the prevalence rate was low will be discussed.

NR429 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Depression in a Diabetes Disease Management Program

Alan C. Regenberg, B.A., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Philadelphia, PA 19104;* Tina L. Harralson, Ph.D., Maureen Disbot, R.N., Catherine J. Datto, M.D., Ira R. Katz, M.D., Joseph J. Gallo, M.D.

Summary:

Objective: The purpose of this report is to examine the association between depression and correlates that have been related to diabetic maintenance.

Method: This sample includes 1414 persons (mean age = 62.5 years; range = 20 to 90 years) who were referred to a diabetes disease management program by their primary care physicians. Participants were contacted by telephone and interviewed regarding their mental and physical health.

Results: DSM-IV criteria were used to construct three groups: those meeting criteria for major depressive episode (MDE; 5%), minor depression (4%), and those not meeting criteria (91%). Those meeting criterion for MDE were found to be significantly younger than persons with minor depression (mean difference = 7 years younger) or those not meeting criterion for depression (mean difference = 10 years younger). Body mass index was greater for persons with MDE (34.7) as compared to persons not meeting the depression criterion (30.5). Groups did not differ on how often they checked their blood sugar, however, persons with MDE reported greater maximum blood sugar levels compared to the minor depression group (mean difference = 56.4 mg/dL) and to the no depression group (mean difference = 68.4 mg/dL). HgbA1c levels did not differ among the groups.

Conclusion: In this sample, MDE was associated with greater BMI, higher maximum blood sugar, and younger age. This suggests a relationship between major depression and poorer diabetic maintenance. More research is needed to determine whether depression impairs the ability to manage diabetes or whether depression is associated with a more severe form of diabetes.

NR430 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

The Use of Administrative Data to Assess Quality of Care for Bipolar Disorder in a Large Staff-Model HMO

Jurgen Unutzer, M.D., *Department of Psychiatry, UCLA NPI, 10920 Wilshire Boulevard, Suite 300, Los Angeles, CA 90024;* Gregory E. Simon, M.D., Wayne J. Katon, M.D.

Summary:

We examined patterns of care for 1,246 adults treated for bipolar disorder in a large health maintenance organization. Computerized pharmacy, laboratory, and visit data were used to assess: continuity and dosing of treatment with mood stabilizers, laboratory monitoring for adverse effects and therapeutic serum levels, and frequency of follow-up visits.

83% of our 1,246 subjects filled a mood stabilizer prescription during the one-year study period, and doses were within recommended ranges 80% of the time. Over 75% of the patients on mood stabilizers had at least one apparent interruption in medication use. Approximately half of the long-term users of mood stabilizers had at least one 7-month period without a recorded blood level and approximately half had a similar period without monitoring for adverse medication effects. 58% of the 116 subjects discharged from a psychiatric hospitalization had a visit with a psychiatrist or a psychiatric nurse practitioner within 30 days. 68% of those discontinuing mood stabilizer treatment made a mental health visit within 90 days. Our findings demonstrate the feasibility of using administrative data systems for population-based quality of care assessment and suggest opportunities for improving the care of bipolar patients.

NR431 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Deviant Sexual Arousal in Pedophilia: A PET Study

Igor I. Galynker, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Ave at 16th St, 6 Karpas, New York, NY 10003;* Yelena Itskovich, M.D., Konstantin Nikiforov, M.D., Erik Klein, B.A., Sara Acker, B.A., John Matochik, Ph.D., Edyth London, Ph.D.

Summary:

Background: Pedophilia is a disorder characterized by sexual molestation of children. Such behavior poses serious to the well-being of children and the society at large. However, neither the etiology nor neuroanatomical substrates of pedophilia are known. Whether pedophilic sexual arousal is in itself abnormal beyond the deviant choice of object is also unknown.

Method: We obtained sexual histories and investigated sexual arousal and regional cerebral glucose metabolism (rCMRglc) in heterosexual male pedophiles and healthy controls using positron emission tomography (PET) under three experimental conditions: 1) a neutral stimulus, 2) a pedophilic sexual stimulus, 3) an adult sexual stimulus (all stimuli were audiotapes). Measures of sexual arousal and rCMRglc were compared across stimulus conditions and across groups.

Results: Pedophiles (n = 20) had overwhelmingly higher incidence of preadolescent sexual contact with older partners compared to controls (n = 23) (62% vs. 5%). Pedophiles (n = 5) had much longer periods of sexual arousal than controls (n = 5) with the neutral stimulus (180 sec vs 0 sec), with the pedophilic stimulus (720 sec vs 55 sec.), and at baseline (no stimulus, 120 sec vs. 21 sec). On PET under the neutral stimulus, pedophiles as compared to controls had decreased rCMRglc in the right temporal cortex ($p < .05$), the left lateral parietal cortex ($p < .02$), and the left ventral superior frontal cortex ($p < .02$). In pedophiles but not controls, activation with pedophilic sexual stimulus (compared to neutral stimulus) was associated with decreased rCMRglc in those areas, as was previously reported for female subjects reexperiencing histories of sexual abuse.

Conclusions: Pedophiles have deviant sexual arousal: they are hypersexual relative to controls both at baseline and in response to pedophilic sexual stimuli. Pedophiles have high incidence of preadolescent sexual contact. Moreover, their rCMRglc patterns under neutral conditions and when activated with audiotapes of pedophilic sexual contact are similar to those observed in PTSD. These findings have etiological and treatment implications which will be discussed.

NR432 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

SPECT in the Diagnosis of Catatonia

Igor I. Galynker, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Ave at 16th St, 6 Karpas, New York, NY 10003;* Richard Goldfarb, M.D., Milica Stefanovic, M.D., Shelevaya Tamara, M.D., Lilia Katsovich, M.D., Thomas Moesse, B.A.

Summary:

Background: Catatonia is a neuropsychiatric syndrome characterized by dramatic changes in the nature and intensity of psychomotor activity. We previously reported reduced regional cerebral blood flow (rCBF) in a patient with catatonia observed by single photon emission computer tomography (SPECT) (Galynker et al, J Nucl Med 1997;38:251–254). Clinically, catatonia is often difficult to differentiate from idiopathic and neuroleptic-induced parkinsonism. This presentation explores the usefulness of SPECT in the diagnosis and treatment monitoring of catatonia.

Method: Five cases in which catatonia was a significant feature of psychiatric illness and presented difficulties in differential diagnosis are discussed. In each, a ^{99m}Tc-HMPAO SPECT scan was obtained to aid in diagnosis and was repeated after the patient improved clinically. Distinctive features of their clinical presentation, differential diagnosis, pharmacotherapy, and follow-up are presented. Radiological features of catatonia on a SPECT scan and possible guidelines for clinical use of SPECT are discussed.

Results: In all five cases, patients had clinical features of catatonia which were either missed or confused with parkinsonism or dementia. The SPECT scans of all patients were abnormal and had a characteristic appearance of vascular insufficiency not corresponding to vascular supply. Parietal and temporal cortex were affected in all subjects, motor cortex in three subjects. Decreased perfusion in the motor cortex was the single most striking feature. All patients were treated either pharmacologically or with ECT and improved clinically. The repeat SPECT scans obtained upon their clinical improvement showed normalization of rCBF.

Conclusions: Cerebral perfusion scintigraphy appears to be useful for diagnosis and treatment monitoring in patients with neuropsychiatric symptoms suggestive of catatonia. In the presence of appropriate clinical correlates, the radiological appearance of vascular insufficiency which does not correspond to vascular supply in parietal, temporal, and especially posterior frontal (motor) cortex are consistent with. If controlled prospective studies confirm our observations, this would constitute the first radiological diagnostic procedure used in psychiatry.

NR433 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Is Pedophilia an Impulsive Aggressive Disorder?

Lisa J. Cohen, Ph.D., *Department of Psychiatry, Beth Israel Medical Center, 6 Karpas, First Ave at 16th St, New York, NY 10003;* Igor I. Galynker, M.D., Yelena Itskovich, M.D., Erik Klein, B.A., Sara Acker, B.A., Sean Murphy, B.A., Ken Cullen, M.S.W.

Summary:

Within the last decade, a growing body of literature on impulsive-aggressive disorders suggests a framework within which to investigate pedophilia. Impulsive-aggressive disorders are characterized by a failure to inhibit repetitive, aggressive behavior that is pleasurable in the short run but harmful in the long run and would be comorbid with high rates of Cluster B axis II disorders. As part of a comprehensive study, 20 male pedophiles, 23 demographically matched non-patient controls, and 13 depressed male inpatients were compared on measures of neuropsychological and personality functioning.

Methods: Subjects were administered a battery of neuropsychological tests assessing frontal-lobe related executive function and two questionnaires assessing DSM axis II disorders (MCMI-2, SCID II for DSM IV Questionnaire). Data was analyzed by MANOVA, follow-up univariate f-tests, and Bonferroni paired contrasts.

Results: Pedophiles did not differ from non-patient controls on most measures of executive function. In contrast pedophiles differed greatly from non-patient controls on most measures of personality impairment. While pedophiles exceeded controls on 2 out of 5 Cluster B scales (Antisocial and Borderline), elevated scores on Cluster A and Cluster C scales were more notable. In contrast to MDD patients, however, pedophiles had higher Cluster B scores and were less anxious and depressed.

Conclusions: Male pedophiles exhibited severe, pervasive and specific personality impairment. While they exhibited impulsive features, this did not stand out as a primary characteristic. Moreover, the lack of impairment in executive functions is inconsistent with the impulsive-aggressive literature. Pedophilia may not be well characterized as an impulsive-aggressive disorder.

NR434 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Personality in Pedophiles and Two Control Groups

Lisa J. Cohen, Ph.D., *Department of Psychiatry, Beth Israel Medical Center, 6 Karpas, First Ave at 16th St, New York, NY 10003;* Igor I. Galynker, M.D., Sara Acker, B.A., Yelena Itskovich, M.D., Erik Klein, B.A., Mandy Rosenfeld, Ken Cullen, M.S.W.

Summary:

Background: Although there is ample documentation of the detrimental effects of childhood sexual abuse, there is surprisingly little clinical research on adults who sexually abuse children. This study assesses the specificity of personality impairment in male pedophiles compared to male psychiatric inpatients with major depression (MDD) and healthy male controls.

Methods: Pedophiles (n = 21) were recruited from CAP associates, an outpatient facility specializing in treatment of sexual offenders. Depressed males (n = 13) were recruited from an inpatient psychiatric unit at Beth Israel Medical Center. Normal control subjects (n = 23) were recruited through newspaper advertisements. All subjects were assessed with personality questionnaires, including the Millon Clinical Multi-Axial Inventory-2 (MCMI-2), the Dimensional Assessment of Personality Impairment (DAPI-Q), and the Temperament and Character Inventory (TCI). Data was analyzed by MANOVA, follow-up univariate f-tests, and Tukey-HSD paired contrasts.

Results: Both pedophiles and MDD inpatients demonstrated significant and pervasive personality impairment in all three measures, compared to controls. On MCMI-2, pedophiles were less dysthymic and anxious than MDD patients, but more obsessive-compulsive, narcissistic, histrionic, and delusional. Pedophiles, but not MDD patients, were also more antisocial and passive-aggressive than controls.

Conclusion: It appears that pedophiles may have a specific profile of personality impairment, which can be distinguished from personality impairment in other psychiatric conditions.

NR435 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

An Open-Label Trial of Sildenafil to Reverse Antidepressant-Induced Sexual Dysfunction in Women

Albert N. Bayer, M.D., *31700 W 13 Mile Rd Ste 107, Farmington Hills, MI 48334-2170*

Summary:

Background: Sexual dysfunction is a common, and often underrecognized, adverse event associated with antidepressant medication use. Multiple strategies have been proposed for the management of antidepressant-induced sexual dysfunction, but scientific evidence supporting their use is relatively lacking. Sildenafil has been approved for the treatment of erectile dysfunction in males. This study evaluates the efficacy of sildenafil for the treatment of antidepressant-induced sexual dysfunction in women, a novel application for this agent.

Method: 21 adult female patients with major depression (DSM IV criteria) who described treatment-emergent sexual dysfunction were evaluated with a clinical interview, the Hamilton Rating Scale for Depression (HAM-D), and the Arizona Sexual Experiences Scale (ASEX). Al subjects were prescribed sildenafil 50 mg. prior to sexual activity and the clinical interview, HAM-D, and ASEX were repeated at follow-up.

Results: Subjects demonstrated statistically significant ($P < 0.001$) reduction in both the ASEX and HAM-D scores, indicating improvement of sexual dysfunction and depressive symptomatology. Clinical, subjective reports were equally robust.

Conclusions: Sildenafil represents an efficacious, well-tolerated agent for use in the management of antidepressant-induced sexual dysfunction in females.

NR436 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Behavioral and Psychological Symptoms in Institutionalized and Noninstitutionalized Demented Subjects

Adrian Sapetti, M.D., *Department of Psychiatry, C. Medico Darwin, Avenida Cordoba 5782, Buenos Aires 1414, Argentina;* Marcos D. Sehinkman, M.D.

Summary:

Objectives: this multicentre open study evaluated efficacy and safety of risperidone in the treatment of behavioral and psychological symptoms in institutionalized and non-institutionalized demented subjects, as well as side effects occurrence.

Methods: open study with a duration of 12 treatment weeks per patient with a total of 61 institutionalized and non-institutionalized demented subjects. Visual Analogue Scales were used for subject's caregiver and physician's provided information (clinical and psychiatric evaluations). Initial dose was 0.25 mg b.i.d. oral solution, allowing adjustments by increments of 0.25 mg per day up to a maximum dose of 2 mg/day (study's maximum dose).

Results: risperidone showed efficacy with great safety profile for behavioral and psychological symptoms in demented patients receiving a mean dose of 1 mg/day oral solution, with low occurrence of side effects/EPS and well-tolerated by patients and their families.

Conclusions: positive correlation between administration of risperidone in low doses (mean dose 1 mg/day), behavioral and psychological symptoms improvement and acceptation from physicians.

NR437 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Response to Sildenafil by Patients with Erectile Dysfunction Related to the Presence of Major Risk Factors

Adrian Sapetti, M.D., *Department of Psychiatry, C. Medico Darwin, Avenida Cordoba 5782, Buenos Aires 1414, Argentina;* Enrique Comesana-Diaz, M.D.

Summary:

Objective: 8 weeks, open label, naturalistic study in patients with ED, to evaluate efficacy of sildenafil in relation with presence of MRF.

Method: 94 male patients were included, 18 years older and above, who were diagnosed ED with more than 6 months of evolution. Primary efficacy tool: Questions 3 and 4 of the IIEF 15, establishing a cut-off point at 4 of the score. For the efficacy analysis, the sample was divided into 3 subgroups: A (no RF), B (1 RF), C (2 or more RF). Descriptive statistical analysis was performed, followed by nonparametric test (Wilcoxon Signed Rank Test), and Chi square/Exact Fisher Test for proportion comparison.

Results: Group A: 100% responders (score 4 or more for questions 3 and 4 of IIEF), group B: 85.7% and group C: 78.9%. A vs B: p = 4.61837E-03; A vs C: p = 1.843259 E-05; B vs C: p = 0.3944836.

Conclusions: There is a statistical significant relation between response to sildenafil and presence of RF. It is required, then, the correction of RF in order to improve response to sildenafil without increasing doses.

NR438 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Treatment of Paraphilia and Sexual Aggressive Impulsiveness with the Luteinizing Hormone Releasing Hormone (LHRH-Agonist) Eeuprolide Acetate

Peer Briken, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, hamburg 20246, Germany;* Evangelia Nika, M.D., Professor Wolfgang Berner

Summary:

Up to now there are no published results of therapy of paraphilia (Pedophilia, Sadism) and sexual aggressive impulsiveness with LHRH-(luteinizing hormone-releasing hormone) Agonists in the Germanspeaking countries. We describe 11 patients which were treated with the LHRH-Agonist Leuprolide Acetate in a period of 12 months. The patients showed no tendency of sexuell aggressive behaviour and reported an evident reduction of penile erection, ejaculation, masturbation, sexual deviant impulsiveness and phantasies. In combination with other treatments LHRH-Agonists seem to be a very promising alternative to cyproterone acetate and its possible carcinogene effects.

NR439 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Frontal Changes Predict Response Durability/Speed

Ian A. Cook, M.D., *Department of Psychiatry, UCLA, 760 Westwood Plaza, Rm 37-426, Los Angeles, CA 90024-1759;* Andrew F. Leuchter, M.D., Elise Witte, Ph.D., William F. Stubbeman, M.D.

Summary:

Background: The early physiologic changes associated with clinical response to antidepressants are incompletely characterized. Quantitative EEG cordance has found pretreatment variation in depression. We explored its use in detecting changes associated with treatment.

Methods: 51 unipolar depressed adults completed a treatment trial using, either fluoxetine or venlafaxine vs placebo in double-masked controlled protocols. Subjects were comparable between trials. Cordance was measured at pretreatment baseline, after 48 hours on drug/placebo, and after 1 week. Change from baseline was calculated for prefrontal cortex electrodes. "Responders" showed a decrease in HAM-D to ≤10 (≥17 at intake).

Results: Prefrontal cordance decreased significantly at 48 hours and 1 week for medication responders; this was not observed in medication nonresponders, placebo responders, or placebo nonresponders. A consistent decrease in cordance at both times was associated with significantly faster improvement, more complete response, and increased probability of response.

Conclusions: Decreases in prefrontal cordance occur rapidly in responders to antidepressants with both serotonergic and mixed mechanisms, as early as 48 hours. Early and consistent prefrontal changes characterize patients who will have a rapid and complete response. The prefrontal region appears to mediate response to medications with different mechanisms. Cordance may have clinical applicability as a physiologic predictor of response.

NR440 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Switching from Fluoxetine to Reboxetine: An Efficacy and Safety Study in Depressed Patients Resistant to Fluoxetine

Maurizio Fava, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC 812, Boston, MA 02114;* Patrick J. McGrath, M.D., Wang-Pui Sheu, M.A., Monica Froeschke, R.N., Saeeduddin Ahmed, M.D.

Summary:

The aim of our study was to assess both the efficacy and tolerability of switching depressed patients who have failed to respond to the SSRI fluoxetine to the selective norepinephrine uptake inhibitor reboxetine.

Methods: This ongoing study involves the enrollment of patients with major depressive disorder (MDD) who have not responded to at least 6–12 weeks of fluoxetine treatment, with 3 weeks prior to switching at a minimum dose of 40 mg/day. This study consists of an 8-week open-label treatment phase (data from which are reported here) and a 24-week placebo controlled discontinuation phase, which is in progress. Patients are switched without a washout from fluoxetine to reboxetine 4 mg b.i.d., with the possibility of increasing the dose to 10 mg/day after 4 weeks of treatment. Efficacy measures include the 25-item HAM-D and the CGI Severity and Improvement Scales. Spontaneously reported adverse events (AEs) are systematically assessed at each visit of the study. These AEs are divided into two groups to account for the possibility of initial drug-drug interactions due to the persistence of fluoxetine and norfluoxetine blood levels in the subjects on reboxetine: those AEs that emerge and remit during the first four weeks of reboxetine treatment and those AEs that emerge during the first four weeks and persist after that.

Results: Thus far, we have enrolled 80 outpatients with MDD (mean age 45.5 yrs, 56 women) into the study. We have observed a statistically significant reduction in HAM-D-25 scores between baseline and week 4 ($p < .0001$), baseline and week 8 (completers, $p < .0001$), and baseline and last observation carried forward ($p < .0001$). The most common AEs during the first 4 weeks of the study were: headache, dry mouth, insomnia, constipation, dizziness, and diaphoresis. AEs decreased in frequency after the initial 4 weeks of treatment.

From these preliminary data, it appears that switching depressed patients from fluoxetine to reboxetine is effective and well-tolerated for patients resistant to fluoxetine.

NR441 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

A Validation Study of a Computerized Management System for the Diagnosis and Treatment of Depression

Maurizio Fava, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC 812, Boston, MA 02114;* Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., James M. Russell, M.D., Michael O'Boyle, M.D., Angela Camilleri, M.P.H., Wilma M. Harrison, M.D.

Summary:

Several studies have shown that major depressive disorder (MDD) is often under-recognized and under-treated in primary care. A computerized Depression Clinical Management System (D-CMS) has been developed to help primary care physicians diagnose depression and determine which patients are suitable for management in primary care and when referral to a mental health professional should be considered. The purpose of the study was to assess the validity of the D-CMS by evaluating its agreement with independent "expert clinician" diagnostic assessments and management recommendations.

Methods: 202 primary care patients (146 women; mean age: 45 years) who either screened positive (n = 156) or negative (n = 46) for depression on a 3-item screening checklist were randomly assigned to one of three sequences in which they underwent two "expert" clinical interviews (one structured and one unstructured) and were also administered the computerized D-CMS, all within the same day. The degree of agreement (κ) between D-CMS and the other two interviews in terms of diagnosis of DSM-III-R MDD and of comorbid psychiatric conditions, and treatment recommendation was estimated. The structured clinical interview (SCID) was considered the "gold standard."

Results: The κ between the D-CMS and the SCID for diagnosis of MDD (0.67) was comparable to the κ between the unstructured interview and the SCID for diagnosis of MDD (0.66). The κ between the D-CMS and the SCID for treatment recommendation (0.69) was actually slightly higher than the κ between the unstructured interview and the SCID (0.58). However, the κ between the D-CMS and the SCID for diagnosis of comorbid psychiatric disorders (0.35) was markedly lower than the κ between the unstructured interview and the SCID (0.72).

Conclusions: Since a previous study (Williams et al, 1992) has reported an inter-rater κ of 0.64 for major depression when all interviewers used the same instrument (SCID) in five academic centers, our findings of κs of 0.67 and 0.69 for MDD diagnosis and treatment recommendation between the D-CMS and the SCID suggest that the D-CMS is a promising tool for the diagnosis and management recommendation for MDD in primary care. However, reliability was not high for diagnosing psychiatric comorbidity.

NR442 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Efficacy of Quetiapine and Risperidone Against Depressive Symptoms in Outpatients with Psychotic Disorders

Martha Sajatovic, M.D., *345 Timberidge Trail, Gates Mills, OH 44040;* Jamie A. Mullen, M.D., Dennis Sweitzer, Ph.D.

Summary:

Objective: To assess the efficacy of quetiapine and risperidone in treating depressive symptoms in outpatients with psychoses

Method: In a 4-month open-label trial, quetiapine and risperidone were compared for efficacy in treating depressive symptoms in 751 adults with psychoses. Patients were diagnosed with primary psychotic disorders or primary mood disorders with psychotic features, and were randomized in a 3:1 ratio (quetiapine: risperidone). Assessments included Hamilton Rating Scale for Depression (HAMD); Clinical Global Impression; and Positive and Negative Syndrome Scale.

Results: Both quetiapine and risperidone produced improvements in HAMD scores, but quetiapine produced a greater improvements (–44.6% vs –34.4%, $p = 0.0015$). In patients with mood disorders and a high baseline HAMD (≥20), quetiapine produced a greater reduction in HAMD (–47.9% vs –34.2%, $p = 0.0042$). For patients with moderate HAMD baselines (10 to <20) both drugs were equally effective.

Conclusion: Both quetiapine and risperidone were effective in treating depressive symptoms in patients with primary psychotic disorders and mood disorders with psychotic features. Quetiapine produced a statistically significantly greater effect in patients with higher initial HAMD scores than risperidone.

NR443 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Sexual Function and Satisfaction in the Treatment of Chronic Depression with Nefazodone, Psychotherapy and Their Combination

John M. Zajecka, M.D., *Department of Psychiatry, Rush-Presbyterian Medical Ctr, 1725 West Harrison St., #955,*

Chicago, IL 60612; David L. Dunner, M.D., Robert M.A. Hirschfeld, M.D., Susan G. Kornstein, M.D., Philip T. Ninan, M.D., A. John Rush, M.D., Michael E. Thase, M.D.

Summary:

Objective: Antidepressants are often associated with negative effects on sexual function and satisfaction, potentially impacting compliance and treatment outcome, an issue both clinicians and patients are reluctant to discuss. This is the first study to systematically assess the impact of antidepressant therapy compared to psychotherapy on sexual functioning in patients with chronic major depressive disorder (CMDD).

Method: Outpatients with CMDD (n = 681) were randomized to 12-weeks of nefazodone, Cognitive Behavioral Analysis System of Psychotherapy (CBASP), or combined nefazodone/CBASP (COMB). Sexual functioning was assessed using the Modified Rush Sexual Inventory, a validated self-rated scale.

Results: From baseline to week 12, statistically significant improvement in sexual functioning was evident across all groups. Controlling for gender and change in depressive symptoms, COMB (mean change = 14.9 ± 29) yielded significantly ($p < .006$) greater improvement in overall sexual satisfaction than CBASP (mean change = 2.6 ± 27). The nefazodone alone group (mean change = 6.9 ± 28) was not significantly different from CBASP alone. Across all treatments, the frequency of initiating sexual activity improved in both males (mean change = 6.3 ± 29) and females (7.8 ± 23) as did improvement in sexual satisfaction: males (mean change = 7.4 ± 28) and females (8.5 ± 29). No statistically significant worsening of sexual function was observed among treatment groups. Gender differences and improvement in specific areas of sexual functioning will be described.

Conclusion: The results suggest that, unlike many antidepressants, nefazodone is not associated with sexual side effects but rather leads to improvement in sexual functioning relative to improvement in depressive symptoms, particularly when combined with psychotherapy in patients with CMDD.

NR444 Tuesday, May 16, 3:00 p.m.-5:00 p.m.

Change in Health-Related Quality of Life in Patients with Schizophrenia Taking Antipsychotic Agents

William S. Edell, Ph.D., *Horizon Mental Health Management, 1500 Waters Ridge Drive, Lewisville, TX 75057-6011;* Michael B. Durkin, M.S., Samir H. Mody, Pharm.D., Bryan E. Adams, Ph.D., Richard E. White, Ph.D., Alec Z. Qiu, M.S.

Summary:

Objective: To examine change in health-related quality of life (HRQL) from inpatient admission to follow-up of adult and geriatric patients with schizophrenia treated with antipsychotic agents.

Method: Data were obtained from the CQI+^{8m} Outcomes Measurement System, an ORYX (JCAHO) accepted performance improvement system, which tracks patients admitted to adult and geriatric psychiatric inpatient programs in over 100 general hospitals across 35 states. Health status was measured by the SF-36 at admission and three months (geriatric) or six months (adult) post-discharge follow-up. All patients with schizophrenia who were taking conventional or atypical antipsychotic agents and completed the SF-36 at admission and follow-up (n = 75) were included. Atypical antipsychotic agents included clozapine, olanzapine, quetiapine, and risperidone.

Results: Improvement in HRQL was associated with antipsychotic usage on a majority of SF-36 scales examined. Largest improvements were found on Role Physical ($p < .001$), Role Emotional ($p < .001$), Social Functioning ($p < .001$), and Mental Health ($p < .01$).

Conclusions: Marked improvement in diverse aspects of HRQL among schizophrenic patients treated with either conventional or atypical antipsychotic agents supports the humanistic value of antipsychotic medications beyond simple symptom amelioration.

NR445 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Depression and Methamphetamine and Cocaine Dependence

Steven L. Batki, M.D., *Department of Psychiatry, SUNY Upstate Medical, 750 East Adams Street, Syracuse, NY 13210;* Julia D. Moon, Mark V. Bradley, Kevin Delucchi, Ph.D., David F. Hersh, M.D., Scott B. Smolar, D.O., Matilda M. Mengis, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to compare the prevalence and severity of depression in patients with methamphetamine and cocaine dependence, and to assess the clinical correlates of depression in stimulant abusers.

Summary:

Objective: To describe and compare the prevalence and severity of depression in methamphetamine (MA) and cocaine (COC) dependent research participants, and to assess clinical correlates of depression.

Method: Preliminary analyses were performed on a total N of 213 subjects (Ss) who made up two separate cohorts in trials of fluoxetine treatment of COC or MA dependence. A total of 149 Ss were in the COC cohort and 64 were in the MA cohort. Cohorts were compared on two measures of depression and on a number of other variables.

Results: While both cohorts had similar proportions of men and women, they differed significantly on most other salient characteristics. MA subjects were younger (mean age 35 vs. 39 yrs, p = .0003); more likely to be white (MA 73% white vs. COC 70% African American, p = .0001); and more likely to be gay or bisexual (MA 45% vs. COC 22%, p = .0016). Education level was higher in the MA Ss (14 vs 13 yrs). Significantly more MA than COC Ss were employed full time (MA 53% vs. COC 28%, p = .0006). ASI employment and alcohol severity were worse in the COC group. Mean (±SD) Beck Depression Inventory scores at intake were 17.1 (±9.9) for the MA cohort and 14.5 (±7.8) for the COC group (p = NS). SCID diagnosis of current major depressive disorder was found in 35 (23.5%) of COC Ss, and in 10 (15.6%) MA Ss (chi square 1.66, p = 0.197).

Conclusion: While cocaine-dependent Ss differed significantly from MA-dependent Ss on a number of demographic variables, and appeared more impaired in employment and alcohol severity, the average severity of depressive symptoms did not differ significantly between the two cohorts, and methamphetamine subjects were about as likely to meet criteria for current Major Depressive Disorder as were cocaine subjects.

References:

1. Kosten TR, Markou A, Koob GF: Depression and stimulant dependence: neurobiology and pharmacotherapy. J Nerv Ment Dis 1998; 186(12): 737–45
2. Markou A, Kosten TR, Koob GF: Neurobiological similarities in depression and drug dependence: a self-medication hypothesis. Neuropsychopharmacology 1998; 18(3): 135–74

NR446 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Genome Wide Scan of BPD: Parent-of-Origin Effect

Melvin G. McInnis, M.D., *Department of Psychiatry, John Hopkins University, 600 North Wolfe Street, Meyer 4-141, Baltimore, MD 21287-7463;* Francis J. McMahon, M.D., Sylvia G. Simpson, M.D., Dean F. MacKinnon, M.D., Tsuo H. Lan, M.D., James B. Potash, M.D., J. Raymond DePaulo, Jr., M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the complexity of the inheritance of BP disorder and possible role of the sex of the affected parent in the inheritance of bipolar disorder.

Summary:

We have ascertained 65 multiplex bipolar pedigrees through a treated BPI proband and two affected first-degree relatives, now genotyped at 10 cM intervals throughout the genome. There are 605 interviewed and genotyped subjects, of whom 129 are bipolar I (BPI), 99 bipolar II (BPII), 71 recurrent unipolar depression (RUP), and seven schizoaffective-manic (SA-M). The mean age of onset for the BPI subjects was 21.6 +/– 11.9 years, for BP II was 22.6 +/– 10.5 years, for RUP 26.8 +/– 11.5 years, and for SA-M was 22.2 +/– 12.3 years. We analyzed the total sample and then partitioned according to the sex of the affected parent; there were 23 "paternal" and 34 "maternal" pedigrees. Analytic methods included multipoint parametric and nonparametic analyses (GENEHUNTER) and IBD analysis (single point) of affected sib pair (SIBPAL and simIBD). Our results suggested strongest evidence for susceptibility loci in three regions: at 2p13 – NPL = 2.33 (p = 0.007); HLOD = 1.53; 8q24 – NPL = 2.7 (p = 0.005) HLOD = 2.2, and 18q21 – NPL = 2.7 P = 0.003), HLOD = 2.05. The increased allele sharing on 2p and 18q were primarily in the paternal pedigrees, while the findings on 8q24 were primarily in the maternal pedigrees. Based on these results, we conclude that some of the inherited susceptibility to bipolar disorder may depend on the sex of the parent transmitting the disease.

References:

1. McMahon FJ, Hopkins PJ Xu J, McInnis MG, et al: Linkage of bipolar affective disorder to chromosome 18 markers in a new pedigree series. (*American Journal of Human Genetics* 1997; 61: 1397–1404
2. Stine OC, Xu J, Koskela R, McMahon FJ, et al: (1995). Evidence for linkage of bipolar disorder to chromsome 18 with a parent-of-origin effect. American Journal of Human Genetics 1995; 57: 1384–1394

NR447 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Baseline Cerebral Glucose Metabolism Compared with Other Potential Divalproex Response Markers

Terence A. Ketter, M.D., *Department of Psychiatry, Stanford University Sch of Med, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723;* Po W. Wang, M.D., Claudia M. Santosa, M.A., Debbie L. Tate, Connie M. Strong, M.S., Nadia Sachs, M.Eng.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that baseline medication-free cerebral glucose metabolism and lithium response may be robust markers of divalproex response, unlike other biological parameters such as the magnetic resonance spectroscopy metabolites NAA, choline, and myo-inositol; plasma GABA and glutamate; and clinical parameters such as personality, temperament, and creativity ratings.

Summary:

Objective: To compare baseline cerebral glucose metabolism (CMRglu) with other potential divalproex response markers.

Method: Twenty-eight bipolar disorder patients were evaluated with clinical and baseline (medication-free) biological measures, which were compared with divalproex Clinical Global Impression-Improvement (CGI-I) ratings.

Results: Ten of 28 (36%) patients (mean age 30.8, 8F/2M, 3BPI/7BPII) were divalproex responders, and 18/28 (64%) (mean age 35.2, 12F/6M, 8BPI/10BPII) nonresponders. Controlling for age and gender effects, divalproex CGI-I correlated robustly with baseline resting globally normalized medial frontal gyrus (MFG) CMRglu ($r = 0.94$, $N = 16$, $df = 12$, $p < 0.0001$); and lithium CGI-I ($r = 0.83$, $N = 12$, $df = 8$, $p = 0.002$); but *not* with baseline dorsolateral prefrontal N-Acetylaspartate, choline, or myo-Inositol (max = 0.18, N = 22, df = 8, p = NS); baseline plasma GABA or glutamate (rmax = 0.31, N = 12, df = 8, p = NS); or personality (NEO), temperament (TCI, ATS), or creativity ratings (rmin = –0.48, N = 12, df = 8, p = NS).

Conclusion: Further study is needed to explore these preliminary findings that divalproex response is related to baseline MFG CMRglu and lithium CGI-I, but *not* to several other clinical and biological measures.

References:

1. Ketter TA, Kimbrell TA, George MS, Willis MW, et al: Baseline cerebral hypermetabolism associated with carbamazepine response, and hypometabolism with nimodipine response in mood disorders. Biol Psychiatry 1999; 46(15): 1364–74
2. Petty F, Rush AJ, Davis JM, Calabrese JR, et al: Plasma GABA predicts acute response to divalproex in mania. Biol Psychiatry 1996; 39: 278–284

NR448 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Efficacy of Nurse Tele-Health Care As an Augmentation to SSRI Treatment of Depression in Primary Care

Enid M. Hunkeler, M.A., *Research Division, Kaiser Permanente, 3505 Broadway, 7th floor, Oakland, CA 94611;* William A. Hargreaves, Ph.D., Joel Meresman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand a new model for treating depression in primary care that: (1) reduces depressive symptoms, (2) improves functioning, and (3) increases patient satisfaction. The new model involves primary care nurses, trained and supervised by a psychologist, delivering telehealth care to depressed patients on SSRIs.

Summary:

Quality of depression treatment in primary care has been criticized. At Kaiser Permanente, an HMO, we found that a program of structured telephone follow-up contacts by trained primary care nurse enhances the effectiveness of SSRI treatment for depression without increasing costs. We randomized 303 patients to usual care (SSRI plus counseling), or nurse telehealth care and assessed them at baseline, six weeks, and six months using the Hamilton Rating Scale for Depression (HDRS), Beck Depression Inventory (BDI), SF-36, and a treatment satisfaction scale. Patients given nurse telehealth care were more likely to experience a 50% improvement on the HDRS at both six weeks (50% vs. 37%, P = .01) and six months (P = .002), on the BDI at six months (P = .02), and on the SF-12 for mental functioning at six weeks (45.79% vs. 42.87%, P = .01). Patient satisfaction with treatment also substantially improved with telehealth care. A telephone intervention by primary care nurses improves treatment outcomes for depressed patients treated in primary care. This intervention fits well within primary care, and its large-scale application should be explored.

References:

1. Sturm R, Wells KB: How can care for depression become more cost-effective? JAMA 1995; 273(1): 51–58
2. Brown C, Schulberg H: The efficacy of psychosocial treatments in primary care: a review of randomized clinical trials. General Hospital Psychiatry 1995; 17: 414–424

NR449 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Rapid Antidepressant Response with ECT

Mustafa M. Husain, M.D., *Department of Psychiatry, University of Texas Southwestern Med, 5161 Harry Hines Boulevard, Dallas, TX 75232;* Hilary Berstein, L.C.S.W., Melanie Biggs, Ph.D., Keith Rasmussen, M.D., Thomas J. Carmody, Ph.D., A. John Rush, M.D., Rebecca S. Knapp, M.D., Max Fink, M.D., Charles H. Kellner, M.D., Teresa A. Rummans, M.D., Kevin A. O'Connor, M.D., Georgios Petrides, M.D., Mark D. Beale, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand that ECT works rapidly as an antidepressant treatment.

Summary:

Objectives: To determine when symptomatic response and remission occur during acute treatment with ECT, and to evaluate early symptom change as a predictor of ultimate benefit.

Methods: In an ongoing, NIMH-funded, multicenter, randomized trial evaluating the relative efficacy of continuation ECT vs pharmacotherapy (li plus nortrip), 269 patients with major depression have received an index course of bilateral, moderately suprathreshold ECT. HAM-D (24-item) ratings were obtained three times per week, following each ECT. For these analyses, we defined response as ≥50% reduction in HAM-D and remission as a final HAM-D score of ≤8. The percentage of patients who were responders/remitters was calculated after each ECT.

Results: Cumulative response rates were 30.6% after two ECT, 66.4% after four ECT, 80.2% after six ECT, and 89.6% after 10 ECT. Of those who ultimately responded, only 1.2% did so after 10 ECT. Of the 243 responders, 76.1% ultimately remitted. The average number of ECT from response to remission was 2.5 (SD = 2.4). Among patients who achieved a 30% reduction in HAM-D after three ECT, 87.2% ultimately responded.

Conclusion: Speed of antidepressant response to ECT is rapid, and, in fact, more rapid than that typically reported for antidepressant medications. Early symptom reduction is a good predictor of ultimate response to ECT.

References:

1. Derivan AT: Antidepressants: Can we determine how quickly they work? Issues from the literature. Psychopharmacology Bulletin 1995; 31: 23–28

NR450 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Mania Improvement During Olanzapine Treatment Is Unaffected by Outcome of Previous Mood-Stabilizer Therapy

Robert W. Baker, M.D., *US Medical, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285;* Mauricio F. Tohen, M.D., Denai R. Milton, M.S., Virginia L. Stauffer, Pharm.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: (demonstrate, recognize, diagnose, treat . . .)

Summary:

Background: Olanzapine is effective for the treatment of acute bipolar mania. (Tohen et al., 1999). It is clinically relevant whether olanzapine utility is limited to those patients who also respond to older mood stabilizers.

Methods: This four-week, double-blind, placebo-controlled trial studied olanzapine 5–20 mg/day for hospitalized subjects in acute manic or mixed bipolar episodes. The primary outcome variable was change in the Young-Mania Rating Scale (Y-MRS) total score. We investigated whether prospectively identified recent failure to respond to other mood stabilizers predicted response to olanzapine.

Results: Y-MRS improvement for subjects treated with olanzapine (n = 55) was 14.78 (baseline: 28.76) vs. 8.13 for those on placebo (n = 60, baseline: 29.43, p < .001). Olanzapine-treated subjects with poor response to most recent lithium exposure (n = 24) had mean Y-MRS improvement of 15.88; those with poor response to most recent valproate exposure (n = 21) had mean Y-MRS improvement of 14.67. Categorization of subjects based on response to other mood stabilizers did not demonstrate significant differences in Y-MRS change from baseline.

Conclusions: Olanzapine worked well for patients who also benefit from valproate or lithium. Its positive effects are undiminished in non-responders to these older agents. Therefore, olanzapine appears to be a non-redundant addition to the roster of effective mood stabilizers for mania.

References:

1. Bowden CL, Brugger AM, Swann AC, et al.: Efficacy of divalproex vs. lithium and placebo in the treatment of mania. JAMA 1994; 271: 918–924

2. Tohen M, Sanger TM, Tollefson GD, et al.: Olanzapine versus placebo in the treatment of acute mania. Am J Psychiatry 1999; 156: 702–209

NR451 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Excellent Response Frequency of Venlafaxine

Charles B. Nemeroff, M.D., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322;* Marc Cantillon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the superiority of venlafaxine over fluoxetine and placebo to attain both response and remission in outpatients diagnosed with depression.

Summary:

Objectives: To evaluate the efficacy (including "remission" by HAM-D) and tolerability of venlafaxine and fluoxetine in depressed outpatients.

Methods: This was a six-week, double-blind, randomized, placebo-controlled, flexible dose comparison of venlafaxine and fluoxetine. The dose of venlafaxine was 37.5 mg qd from days 1 to 4 and 75 mg qd (37.5 mg bid) from days 5 to 14. The dose could be increased to 150 mg qd (75 mg bid) on day 15 and 225 mg qd (112.5 mg bid) on day 29, if clinically indicated. The fluoxetine dose was 20 mg qd from days 1 to 14, with an increase to 40 mg qd on day 15 and 60 mg qd on day 29, if clinically indicated. An intent-to-treat analysis of efficacy was based on HAM-D total and depressed mood item MADRS, and CGI scale at weeks 1, 2, 3, 4, and 6. Remission on HAM-D was defined by a score ≤8.

Results: A total of 308 patients were randomized and 297 patients (96 venlafaxine, 100 fluoxetine, 101 placebo) were included in the efficacy analysis. Sixty-seven patients discontinued (24 venlafaxine, 19 fluoxetine, 24 placebo). Results are shown in Tables 1 and 2.

Table 1. Frequency of response

	HAM-D Response	MADRS Response	CGI Response
Placebo Freq (n = 101)	39 (39%)	35 (35%)	39 (39%)
Fluoxetine Freq (n = 100)	44 (44%)	44 (44%)	53 (53%)
Venlafaxine Freq (n = 96)	54 (56%)	53 (55%)	62 (65%)
p-values*			
Overall	.040	.015	.001
V vs P	.013	.004	.001
V vs F	.086	.117	.100
F vs P	.438	.175	.041

*Chi-square for all p-values

Table 2. Achievement of remission (HAM-D) ≤8) at week 6

Venlafaxine	Fluoxetine	Placebo
27/69 = 39%	24/66 = 36%	16/66 = 24%

Venlafaxine superiority over fluoxetine was noted for the three outcome variables, although differences between the groups were not statistically significant. The incidence of adverse events ≥10% and ≥2× placebo for venlafaxine were nausea, sweating, dizziness, vomiting, anxiety, constipation, and fatigue; for fluoxetine they were nausea and fatigue.

Conclusions: These preliminary data indicate that venlafaxine and fluoxetine were significantly more effective than placebo for the treatment of depression.

References:

1. Dierick M, Ravizza L, Realini R, Martin A: A double-blind comparison of venlafaxine and fluoxetine for treatment of major depression in outpatients. Prog Neuro-Psychopharmacol Biol Psychiatr 1996; 20: 57–71
2. Tylee A, Beaumont G, Bowden MW, Reynolds A: A double-blind, randomized, 12-week comparison study of the safety and efficacy of venlafaxine and fluoxetine in moderate to severe major depression in general practice. Primary Care Psychiatry 1997; 3: 51–58

NR452 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Predictors of Response to Treatment Among Outpatients Resistant to Fluoxetine 20 mg/Day

Jonathan E. Alpert, M.D., *Department of Psychiatry, Massachusetts General Hospital, WAC-815, 15 Parkman Street, Boston, MA 02114;* Jerrold F. Rosenbaum, M.D., Andrew A. Nierenberg, M.D., Johanna A. Gordon, B.A., Karen E. Kelly, B.A., Andrea C. Hutchins, B.A., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will become familiar with the relationship between certain clinical variables and treatment outcomes in patients who had initially failed to respond to eight weeks of treatment with fluoxetine 20mg/day.

Summary:

Objective: We examined potential predictors of response to adjunctive treatment strategies among a cohort of outpatients with major depressive disorder (MDD) who had responded inadequately to fluoxetine and were then treated with higher dose fluoxetine, fluoxetine plus lithium, or fluoxetine plus desipramine.

Method: We identified 99 adults with MDD (49.5% female; mean age: 41.6 ± 10.7) who were either partial (48%) or non-responders (52%) to eight weeks of prospective treatment with fluoxetine 20 mg/day. These patients were randomized to four weeks of double-blind treatment with higher-dose fluoxetine (40–60 mg/day), fluoxetine plus lithium (300–600 mg/day), or fluoxetine plus desipramine (25–50 mg/day). We found that *response rates* across the three groups did not differ significantly (high-dose fluoxetine 38%, fluoxetine plus lithium 27%, fluoxetine plus desipramine 34%). In the present analysis, we compared responders vs. non-responders to double-blind treatment across demographic and clinical dimensions including comorbidity, depressive subtype, and depression history. Significance was set at $p \leq 0.01$.

Results: Response to double-blind treatment was not predicted by melancholic or atypical depressive subtypes, baseline depression severity, duration of current MDD or number of lifetime MDD episodes, comorbid borderline personality disorder, current or lifetime anxiety or eating disorder, or past history of alcohol or substance abuse/dependence. *Response rates* did not vary significantly according to current age or gender or marital, educational or employment status. There was a trend for responders to have had an earlier age of onset of MDD (23.1 +/– 10.8 vs. 29.6 +/– 13.5 years; F = 5.7, df = 1; $p < 0.02$).

Conclusion: Approximately one-third of patients who had failed to respond to eight weeks of fluoxetine treatment did respond to either a higher dose of fluoxetine or fluoxetine adjuncts, but standard clinical variables (except perhaps age of onset) did not predict response.

References:

1. Fava M, Davidson KG: Definition and epidemiology of treatment-resistant depression. Psychiatric Clinics of North America. 1996; 19(2): 179–200
2. Fava M, Rosenbaum J, McGrath P, et al: Lithium and tricyclic augmentation of fluoxetine treatment for resistant major depression. Am J Psychiatry 1994; 15(9): 1372–1374

NR453 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Transcranial Magnetic Stimulation in Major Depression: High Frequency Repetitive Transcranial Magnetic Stimulation Increases Cortical Excitability

Fumiko Maeda, M.D., *Department of Neurology, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, KS452, Boston, MA 02215;* Julian P. Keenan, Ph.D., Robert J. Birnbaum, M.D., Stefanie Freund, M.D., Alvaro Pascual-Leone, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to understand the possible mechanism of the antidepressant effect of TMS.

Summary:

Objectives: In recent years, there has been an increasing interest toward repetitive transcranial magnetic stimulation (rTMS) as a potential treatment tool for major depressive disorder (MDD). Most past rTMS studies have relied on the clinical outcome. We attempted to examine possible neurophysiological correlates.

Method: We studied 18 medication-free patients with medication-refractory MDD. The severity of depression and bihemispheric motor cortical excitability (MCE) using paired-pulse TMS, were examined before and after delivering nine days of 10Hz rTMS to the left dorsolateral prefrontal cortex (LDLPFC).

Results: As a group, the patients showed a significant increase in left MCE from rTMS treatment whereas there was no significant change in the right hemisphere. The responders (5/18) had a significantly decreased left MCE at baseline as compared with the non-responders (13/18), which then became symmetrical post-rTMS treatment. However, non-responders had a greater interhemispheric asymmetry post-rTMS treatment.

Conclusions: TMS may be a useful tool not only for the treatment of MDD, but for elucidating the underlying pathophysiology. TMS parameters presumed to increase MCE might exert antidepressant effects if applied to the hemisphere with reduced MCE. Findings of abnormalities in MCE may have predictive value for eventual treatment outcome.

References:

1. Maeda F, Keenan J, Pascual-Leone A: Interhemispheric asymmetry of motor cortical excitability measured by transcranial magnetic stimulation in major depression. (submitted)
2. Shajahan PM, Glabus MF, Jenkins JA, Ebmeier KP: Postexercise motor evoked potentials in depressed patients, recovered depressed patients, and controls. Neurology 1999; 53: 644–646

NR454 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Cortisol Concentrations in Breast Milk of Women with Major Depression

Mary T. Cox, Ph.D., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Atlanta, GA 30322;* Zachary N. Stowe, M.D., Amy L. Hostetter, B.A., Clayton Ramsey, B.A., Kevan Sternberg, B.S., Jim Ritchie, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have a better understanding of the potential impact of neuroendocrine changes of mood disorders on breast milk and breastfeeding infants of depressed mothers.

Summary:

The benefits of breastfeeding are well documented, and >50% of women plan to breastfeed. Many of these women may experience mood and anxiety disorders in the postpartum period. Treatment planning for these women includes a comprehensive risk/benefit assessment. Typically, nursing infant exposure to medication is of greatest concern. However, nursing infant exposure to the neuroendocrine alterations of maternal mood disorders via breast milk is an uninvestigated area. Twenty-six women treated for major depression submitted 360 milk samples for measurement of cortisol, IgA, and IgM at various times during the treatment course. Concurrently, the Perceived Stress Scale (PSS) and Beck Depression Inventory (BDI) scales were completed.

Cortisol levels in the breast milk ranged from <0.01 to 1.56 ug/dL. There was a significant time dependent excretion of cortisol into breast milk by a third order polynomial ($R = 0.48$, $F = 16.435$, $df = 3,170$, $p < 0.001$). PSS and BDI scores did not directly correlate with peak breast milk cortisol concentrations. However, subjects ($n = 4$) with the highest PSS and BDI also had higher peak milk cortisol, raising the possibility that the nursing infant of a depressed mother would be exposed to increased levels of cortisol, the impact of which is unknown.

References:

1. Weinberg MK, Tronick EZ: The impact of maternal psychiatric illness on infant development. J Clin Psychiatry 1998; 59(supp 2):53–61
2. Plotsky PM, Owens MJ, Nemeroff CB: Psychoneuroendocrinology of depression. Psychiatric Clinics of North America 1998; 21(2): 293–307

NR455 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Toward a Molecular Anatomy of Bipolar Affective Disorder

Francis J. McMahon, M.D., *Department of Psychiatry, University of Chicago, 924 East 57th Street, R012, Chicago, IL 60637;* Sylvia G. Simpson, M.D., J. Raymond DePaulo, Jr., M.D., Melvin G. McInnis, M.D., Dean F. MacKinnon, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should (1) understand molecular genetic approaches to psychiatric diagnosis, and (2) recognize clinical features of bipolar disorder that may predict specific genetic risk factors.

Summary:

Objective: An analysis of the relationship between clinical features and allele sharing could clarify the question of genetic linkage between bipolar affective disorder (BPAD) and chromosome 18q21-22.

Method: Families were ascertained through a proband with bipolar I (BPI), ≥1 affected sibling, and ≤1 affected parent. Subjects ($n = 586$) were interviewed by a psychiatrist, assigned a RDC diagnosis, and genotyped with 32 markets on chromosome 18q21–23 using automated methods.

Results: Exploratory analyses of the first 28 families showed that excess paternal allele-sharing on 18q21 was confined to pairs where one sibling was diagnosed with BPII disorder and the other with BPI or bipolar II (BPII). Prospective analyses of 30 additional families confirmed this finding. In the total sample, multipoint affected sib-pair linkage analysis produced a peak paternal lodscore of 1.53, but in the 15 families with at least one BPII-BPII sibling pair, the peak paternal lodscore was 4.67 on 18q22. Maternal lod scores were uniformly negative.

Conclusions: These findings, limited by the small number of families containing a BPII-BPII sibling pair, lend molecular support to the validity of BPII disorder, strengthen the evidence of linkage to 18q21–22, and suggest that BPII is more genetically homogenous than BPI in this sample.

References:

1. McMahon FJ, Hopkins PI, Xu J, McInnis MG, et al: Linkage of bipolar affective disorder to chromosome 18 markers in a new pedigree series. Am J Hum Genet 1997; 61: 1397–1404
2. McMahon FJ, Xu J, Stine O.C, Simpson SG et al: Clinical features of bipolar disorder linked to chromosome 18. New Research Abstract, 1996 annual meeting of the American Psychiatric Association, NY, NY

NR456 Wednesday, May 17, 9:00 a.m.-10:30 a.m.

Mirtazapine Relapse and Pattern of Acute Response

Andrew A. Nierenberg, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114-3117;* Charlotte Kremer, M.D., Megan M. Smith, B.A., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will understand the relationship between pattern of acute response to open-label mirtazapine and continuation treatment with either placebo or mirtazapine.

Summary:

Background: The need for continuation therapy is widely recognized for depressed patients who respond to antidepressants. This report examines the relationship between pattern of acute response and placebo-controlled continuation treatment with the novel antidepressant mirtazapine.

Methods: A total of 410 outpatients (56.1% female; mean age 39.5 ± 12.2 years; mean HAMD-17 score = 22.7 ± 3.6) were treated openly with mirtazapine (mean dose 30.6 mg) for eight to 12 weeks. Patients who responded acutely were randomized to continue on the same dose of mirtazapine or be switched to placebo. Responders were classified as: placebo-pattern responders (early responders and nonpersistent responders) and true drug-pattern responders (late and persistent responders) as per Quitkin and colleagues (1987).

Results: Of the placebo-pattern responders, 5/38 (13.2%) relapsed with continuation mirtrazapine, and 12/40 (30.0%) randomized to placebo relapsed ($p = 0.074$). Of the true drug-pattern responders, 10/40 (25.0%) relapsed with continuation mirtazapine, and 23/41 (56.1%) relapsed when switched to placebo ($p = 0.005$).

Conclusions: Among those with an acute phase placebo pattern of response there is no statistically significant difference in relapse rates between those who continue on either mirtazapine or placebo. Those with a true-drug pattern of response have a robust and statistically significant protective effect with continued mirtazapine compared to placebo substitution.

References:

1. Quitkin FM, Rabkin JD, Markowitz JM, et al: Use of pattern analysis to identify true drug response. Arch Gen Psych 1987; 44: 259–264
2. Stewart JW, Quitkin FM, McGrath PI, et al: Use of pattern analysis to predict differential relapse of remitted patients with major depression during 1 year of treatment with fluoxetine or placebo. Arch Gen Psych 1998; 55: 334–343

NR457 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Divalproex Treatment of Mania with Dementia

Pierre N. Tariot, M.D., *Department of Psychiatry, Monroe Community Hospital, 435 East Henrietta Road, Rochester, NY 14620;* Lon S. Schneider, M.D., Jacobo E. Mintzer, M.D., Andrew J. Cutler, M.D., Muriel R. Cunningham, M.Ed., James W. Thomas, M.S., Kenneth W. Sommerville, M.D.

Summary:

Objective: Divalproex sodium (DVPX) has been used to treat manic symptoms in other populations. This study tested the use in subjects with manic symptoms and dementia.

Methods: 172 elderly nursing home residents with dementia and manic symptoms were randomized to either DVPX or placebo treatment for 6 weeks. Study drug was initiated at 125 mg BID and titrated to a target dose of 20 mg/kg/day. Manic features, other behaviors, cognition, and safety were assessed weekly.

Results: The study was suspended prematurely because of tolerability considerations. There was no drug-placebo difference in BRMS, BPRS, or MMSE scores. There was significant improvement on the CMAI scores for agitation. The CGI score favored placebo. Nineteen (22%) DVPX subjects and 3 (4%) placebo subjects withdrew from the study because of adverse events. Somnolence, thrombocytopenia, anorexia, dehydration, and weight loss were increased in DVPX subjects. Subjects withdrew for adverse events after reaching or exceeding doses of approximately 15 mg/kg/day, chiefly from somnolence.

Conclusion: There were excessive side effects at DVPX doses above approximately 15 mg/kg/day, which may have contributed to the CGI results. However, significant improvement in agitation but not manic symptoms was noted. Further study of agitation at doses below 15 mg/kg/day is recommended.

NR458 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Thyroid Axis Dysfunction Is Related to Longitudinal Course of Depression

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 rue du 4eme RSM, 68250 Rouffach 00110, France;* M. Claude Mokrani, Ph.D., Paul Bailey, M.D., Marc-Antoine Crocq, M.D., Thanh S. Diep, M.D., Jean-Paul Macher, M.D.

Summary:

Objective: The aim of this study was to investigate whether dysfunction of the thyroid axis is related to clinical characteristics in major depression.

Methods: Thyrotropin (TSH) responses to 8 AM and 11 PM protirelin challenges (TRH, 200μg IV) were examined, on the same day, in 108 drug-free DSM-IV euthyroid major depressed inpatients. Twenty-six patients had a single major depressive episode; the remaining 82 patients were classified according to the course of recurrent episodes: 53 with full interepisode recovery, 29 without full interepisode recovery. Based on their TRH-TSH test responses, patients were also classified according to stage of thyroid axis dysfunction (stage 1: blunted ΔΔTSH alone [i.e. abnormally low difference between 11PM-ΔTSH and 8 AM-ΔTSH]; stage 2: combination of blunted ΔΔTSH and 11 PM-ΔTSH; stage 3: combination of blunted ΔΔTSH, 11 PM-ΔTSH and 8 AM-ΔTSH).

Results: The degree of thyroid dysfunction was moderate in patients with a single major depressive episode (no thyroid dysfunction: 35%; stage 1: 35%; stage 2: 27%; stage 3: 3%); intermediate in patients with full interepisode recovery (no thyroid dysfunction: 21%; stage 1: 45%; stage 2: 19%; stage 3: 15%); and marked in patients without full interepisode recovery (no thyroid dysfunction: 3%; stage 1: 24%; stage 2: 27%; stage 3: 46%) ($\chi^2 = 22.8$, df = 6, $p = 0.0008$). These differences could not be explained by differences in age, gender distribution, or severity or subtype of depression.

Conclusions: Our results suggest that level of thyroid axis dysfunction is related to longitudinal course of depression.

NR459 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Dopamine Function in Men with Bipolar Depression

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 rue du 4eme RSM, 68250 Rouffach 00110, France;* M. Claude Mokrani, Ph.D., Paul Bailey, M.D., Thanh S. Diep, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

Objective: Indirect observations suggest that dopamine function may be altered in some groups of depressed patients, notably in bipolar patients.

Methods: In order to obtain an indirect index of dopaminergic neurotransmission at the post-synaptic level, we evaluated the prolactin (PRL), growth hormone (GH), adrenocorticotropic hormone (ACTH), and cortisol responses to the dopamine agonist apomorphine (APO, 0.75 mg SC) in 65 drug-free DSM-IV male major depressed inpatients: 15 with bipolar depression (BD), 34 with unipolar depression (UD), 13 with a single major depressive episode (SMDE); compared with 15 age-matched hospitalized male controls (HC). We also examined, in the same subjects, PRL response to 8 AM and 11 PM protirelin challenges (TRH, 200 μg IV) and cortisol response to dexamethasone suppression test (DST, 1mg orally).

Results: No significant differences in basal and post-APO ACTH, cortisol, and GH values were found between controls and patients. However, BDs had lower APO-induced PRL suppression than HCs ($p < 0.002$), UDs ($p < 0.004$) and SMDEs ($p < 0.005$) (all p values corrected by Bonferroni's method for four pairwise comparisons). On the other hand, there was no difference in PRL response to TRH tests between controls and patients. Although post-DST cortisol values were higher in patients than in controls ($p < 0.05$), PRL values did not differ significantly between DST suppressors and nonsuppressors.

Conclusions: Taken together these results suggest that decreased APO-induced PRL suppression in male bipolar depressed patients is not due to deficiency of pituitary lactotrophs and/or increased HPA axis activity, but may reflect altered post-synaptic receptor sensitivity in the tuberoinfundibular dopamine system.

NR460 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Vagal Nerve Stimulation in Depression

Lauren B. Marangell, M.D., *Department of Psychiatry, Baylor College of Medicine, One Baylor Plaza, #110 D, Houston, TX 77030;* A. John Rush, M.D., Mark S. George, M.D., Harold A. Sackeim, Ph.D.

Summary:

Objective: Vagus nerve stimulation (VNS) is an approved therapy for treatment-resistant epilepsy. We examined the safety and potential antidepressant effects of VNS for treatment-resistant, major depressive episodes (MDEs).

Method: Adult outpatients (n = 30) with nonpsychotic, treatment-resistant, major depressive (n = 21) or bipolar I (n = 4) or II (n = 5) (depressed phase) disorder, whose current MDE was ≥2 years in duration or who had ≥4 MDEs in a lifetime, and who also had failed at least 2 robust medication trials in the current MDE were eligible. Each participant was either on stable antidepressant regimens or not taking antidepressants (n = 5). Vagus nerve stimulation was delivered by the NeuroCybernetic Prosthesis at a fixed dose (maximum comfortably-tolerated) for 8 weeks following a 2-week, single-blind, recovery period (no stimulation), and a 2 week stimulation adjustment period. The first 12 weeks following implantation are defined as the acute phase. Patients continue to be followed at monthly intervals to determine long-term safety and efficacy.

Results: At the end of the acute phase, 40% of the participants responded, defined as ≥50% reduction in $HRSD_{28}$. Longer-term data will be presented.

Conclusions: These positive open trial results in a severe, treatment-resistant patient group suggest that chronic VNS is a safe and effective treatment for a significant proportion of these patients.

NR461 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Treatment of Psychosocial Impairments in Major Depression

Robert M.A. Hirschfeld, M.D., *Psych & Behav. Science, Univ of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0188;* David L. Dunner, M.D., Gabor I. Keitner, M.D., Daniel N. Klein, Ph.D., Lorrin M. Koran, M.D., Susan G. Kornstein, M.D., John C. Markowitz, M.D.

Summary:

Objective: Pharmacotherapy has been shown to improve psychosocial functioning in patients with chronic depression, but no studies have yet compared pharmacological and psychosocial approaches. The present study compared the efficacy of nefazodone, and Cognitive Behavioral Analysis System of Psychotherapy (CBASP), with their combination in improving *psychosocial functioning* in chronically depressed patients.

Method: 681 outpatients with chronic depression were randomly assigned to 12 weeks of treatment with Nefazodone, Cognitive Behavioral Analysis System of Psychotherapy (CBASP), or Combined nefazodone and CBASP therapy (COMB). The primary efficacy measures of psychosocial functioning were obtained on SAS-SR, LIFE and MOS SF-36 scales. HAM-D total score was used as a measure of symptomatic improvements.

Results: Psychosocial functioning improved substantially between baseline and endpoint in all three treatment groups. At endpoint, COMB patients achieved significantly superior improvements compared with either monotherapy on the MOS SF-36 general health ($p < .005$), vitality ($p < .0001$) social functioning ($p < .0001$), role emotional ($p < .0001$), mental health ($p < .0001$), and cognitive functioning ($p < .0001$) subscales, on the SAS-SR overall score ($p < .0001$), and the LIFE impairment in employment, household duties, interpersonal relationships with children, and global assessment of satisfaction and recreation subscales. A comparison of symptomatic improvements (HAM-D total score) with psychosocial improvements (SAS-SR total score) revealed that a similar pattern was observed in the rate of improvements from baseline to weeks 4, 8, and 12 of treatment. However, the patients achieved more symptomatic than psychosocial improvements.

Conclusions: Impaired psychosocial functioning in patients with chronic depression improves with monotherapy of nefazodone or CBASP, and with their combination. However, combined nefazodone and psychotherapy treatment is superior to either monotherapy in improving psychosocial functioning.

NR462 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

A Placebo-Controlled Trial of St. John's Wort in Major Depression

Richard C. Shelton, M.D., *Department of Psychiatry, Vanderbilt University, 1500 21st Avenue South, #2200, Nashville, TN 37212;* David L. Dunner, M.D., Uriel Halbreich, M.D., Michael E. Thase, M.D., Robert M.A. Hirschfeld, M.D., Alan J. Gelenberg, M.D., Martin B. Keller, M.D.

Summary:

Objective: This double-blind, placebo-controlled multicenter study evaluated effectiveness of St. John's Wort (SJW) in persons with major depression of at least moderate severity.

Methods: 200 outpatients with major depression (SCID-DSM-IV) were recruited at 11 US university medical centers. Participants were healthy, free of psychotropic drugs at baseline, with a baseline 17-item Ham-D score ≥20. Subjects with a prior SJW treatment failure were excluded. They were randomly assigned to treatment with either a standard extract of SJW or placebo for 8 weeks used in many published studies (Lichtwehr LI-160). The dose of SJW extract was titrated to 900 mg./day and maintained for at least 4 weeks. If there was not an adequate response, the dose then was advanced to 1200 mg./day through the duration of the trial. Open antidepressant treatment followed for non-responders. Assessments included the Ham-D, Ham-A, BDI, and CGI.

Results: SJW was tolerated with few dropouts due to side effects. An interim analysis has shown that the response rate was low to SJW and placebo and not significantly different. The complete dataset will be presented.

Conclusions: The data suggest that SJW is no more effective than placebo in patients with major depression of at least moderate severity.

NR463 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Thyroid Hypofunction in Rapid-Cycling Bipolar Disorders

Laszlo Gyulai, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Philadelphia, PA 19104-2649;* Michael Bauer, M.D., Mark S. Bauer, M.D., Avital Cnaan, Ph.D., Peter C. Wybrow, M.D.

Summary:

Objective: Thyroid hormone deficiency has been suggested to play a key role in the development of a rapid cycling pattern in bipolar disorder. Using lithium carbonate as a physiologically and clinically relevant challenge paradigm to the hypothalamic-pituitary (HPT) axis, this study examined whether subjects with rapid cycling bipolar disorder (RC-BD) are particularly sensitive to the "antithyroid" properties of lithium. To our knowledge, this is the first prospective evaluation of the HPT in unmedicated RC-BP patients, compared to healthy controls under lithium challenge.

Methods: Hormones of the HPT axis and thyrotropin (TSH) response (ΔTSH_{max}) to thyrotropin-releasing-hormone (TRH) were studied in 20 medication-free subjects with RC-BD and compared to 20 age- and Sex-matched healthy control subjects. The same investigations were repeated after 4 weeks of treatment with lithium carbonate to maintain blood levels between 0.7 and 1.2 mEq/L.

Results: At baseline, the results of thyroid function tests including the TRH challenge test did not differ between RC-BD and healthy controls. Serum concentrations of total thyroxin (T4) significantly decreased, basal TSH and ΔTSH significantly increased in both RC-BD and in healthy controls after treatment with lithium. However, subjects with RC-BD had significantly higher ΔTSH after TRH stimulation than controls.

Conclusions: Subjects with RC-BD are quantitatively more susceptible to the thyroprivic effect of lithium compared to healthy

controls. Findings of this study may reconcile the divergent literature on whether patients with RC-BP do or do not have evidence of thyroid hypofunction and emphasize the important role of the HPT axis in the pathophysiology of rapid cycling bipolar affective disorder.

NR464 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Efficacy of Divalproex for Bipolar Depression

Laszlo Gyulai, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Philadelphia, PA 19104-2649;* Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Susan L. McElroy, M.D., Frederick Petty, M.D., Samuel C. Risch, M.D., Alan C. Swann, M.D.

Summary:

Objective: There have been no double-blind, placebo-controlled trials to examine the efficacy of anticonvulsants in the prevention of depressive episodes in bipolar patients. The Divalproex/Bipolar Study Group presented preliminary findings indicating that divalproex reduces depressive morbidity in bipolar patients. This presentation describes the effects of divalproex on dimensions of depressive morbidity over a 52-week treatment period.

Methods: A randomized, double-blind, parallel-group multicenter study of treatment was conducted over a 52-week maintenance period. Patients who met recovery criteria within 3 months of the onset (open phase) of an index manic episode (n = 372) were randomized to maintenance treatment with divalproex, lithium or placebo (PLA) in a 2:1:1 ratio. The outcome measures were premature discontinuation for depression, time to a depressive episode and average change from baseline in SADS-C subscale scores for depression.

Results: A higher percentage of patients on PLA discontinued treatment due to depression than those on divalproex; the same was true for patients on PLA plus SSRIs vs. on randomized divalproex plus SSRIs. Patients taking divalproex in the open phase relapsed earlier on randomized lithium than on randomized divalproex. Patients treated with randomized divalproex had less subsyndromal depressive symptoms than those receiving randomized PLA.

Conclusions: Divalproex-treated patients had less depressive morbidity during the randomized phase on most outcome measures than did PLA-treated patients. This effect appears related to baseline features of the illness.

NR465 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Anxiety Symptoms in the Treatment of Chronic Depression

Philip T. Ninan, M.D., *Department of Psychiatry, Emory University, 1841 Clifton Road, Room 401, Atlanta, GA 30329;* A. John Rush, M.D., Frances E. Borian, M.B.A., Susan G. Kornstein, M.D., John M. Zajecka, M.D., Michael E. Thase, M.D., Barbara O. Rothbaum, Ph.D.

Summary:

Objective: To evaluate symptoms of anxiety and their change with treatment in chronic depression.

Method: In a multi-center study, 681 outpatients with chronic major depression were randomly assigned to receive 12 weeks of cognitive behavioral analysis system of psychotherapy (CBASP), nefazodone, or a combination of CBASP and nefazodone (COMB). Symptoms of depression (HAM-D) and anxiety (HAM-A) were assessed at baseline and regularly during the 12 weeks of active treatment.

Results: For those who completed 12 weeks of treatment (n = 519), 52% of patients receiving CBASP, 55% receiving nefazodone, and 85% receiving COMB were responders based on HAM-D criteria. Correlation of total HAM-A scores with total HAM-D scores were 0.59 at baseline and increased to 0.79 at week 12. Patients who received COMB had a significantly greater reduction in total HAM-A scores during the last 4 weeks of treatment. Among the responders (n = 334), HAM-A scores were significantly lower at weeks 2, 3 and 4 for patients receiving nefazodone alone, compared to CBASP or COMB ($p < .05$), with no difference in HAM-A scores among the treatment groups in subsequent weeks.

Conclusion: In outpatients with chronic depression, anxiety symptoms are highly correlated with depressive symptoms and are reduced with treatment, most evident with COMB. Among the responders, the delivery of CBASP is associated with a slower rate of reduction in anxiety, even when combined with nefazodone, compared to nefazodone alone. The initiation of psychotherapy in patients with chronic depression responding to treatment, is associated with a slower rate of reduction in anxiety initially.

NR466 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Psychotic Versus Nonpsychotic Major Depression: Distinct Clinical Features

John D. Matthews, M.D., *Department of Psychiatry, Mass General Hospital, 15 Parkman Street, Warren 1220, Boston, MA 02114;* Christina M. Dording, M.D., Robert W. Irvin, M.D., Andrew A. Nierenberg, M.D., Kathryn A. Bottonari, B.A., Margarita L. Delgado, B.A., Megan M. Smith, B.A., Maurizio Fava, M.D.

Summary:

Objective: To compare clinical features (i.e., depressive subtype, severity of illness, and Axis I comorbidity) of patients with Major Depressive Disorder (MDD) with psychotic features with those of a matched group of patients with MDD without psychotic features.

Methods: We matched a population of 27 consecutive depressed patients with MDD with psychotic features with 27 patients with MDD without psychotic features based on age (19–68 years old, means of 40.0 years for psychotic patients and 39.8 years for non-psychotic patients) and gender (33.3% male and 66.7% female in both groups). We assessed psychiatric history, including age of first episode of Major Depression, number of depressive episodes, length of their current episode, number of hospitalizations and Axis I psychiatric diagnoses, by using the DSM-IV SCID at their initial screening visit for enrollment into an antidepressant treatment trial. In addition, subjects were evaluated using the Hamilton Depression Rating Scale (HAM-D) and the Clinical Global Impression (CGI) score.

Results: Patients with MDD who also have psychotic features are more likely to be of a melancholic subtype ($p < 0.001$) and are more likely to have a current diagnosis of both panic disorder ($p < 0.01$) and PTSD ($p < 0.05$) than non-psychotic patients with MDD. On the other hand, patients with nonpsychotic depression are more likely to have a comorbid diagnosis of specific phobia ($p < 0.05$) and dysthymia ($p < 0.05$) than patients with psychotic depression. Patients with MDD who also have psychotic features had also higher baseline Hamilton Depression Scores (28.0+/–4.7 versus 20.3+/–3.2, $p < 0.0001$) as well as initial higher CGIs (5.6+/–0.8 versus 4.3+/–0.71, $p < 0.0001$). No other significant differences were noted in terms of clinical features.

Conclusion: There are significant differences regarding psychiatric comorbidity, severity of illness, and depressive subtype between depressed patients with and without psychotic features. These findings support the view that MDD with psychotic features may be a distinct clinical entity from non-psychotic Major Depression.

NR467 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Sexual Energy Scale (SES): A Simple Valid Screening Tool for Measuring Sexual Dysfunction

Julia K. Warnock, M.D., *Department of Psychiatry, University of Oklahoma, 2808 South Sheridan, Suite 200, Tulsa, OK 74129-1014;* Anita L.H. Clayton, M.D., William R. Yates, M.D., J. Clark Bundren, M.D.

Summary:

Objectives: Sexual dysfunction (SD) is gaining increased attention as a public health concern. Laymann et al (1999) documented a 43% prevalence of SD in women and a 33% prevalence of SD in men. Progress in the research and treatment of SD is hampered by the lack of practical and valid psychometric instruments. The Sexual Energy Scale (SES) provides a simple, easy and objective means of assessing the patient's lost familiar experience of sexual desire and vital/sensual energy. The SES also measures changes in sexual function following an intervention. The scale is a visual analog model in which the patient rates their current sexual energy level on a scale of 1 to 10.

Design: To determine concurrent validity, the Changes in Sexual Functioning Questionnaire (CSFQ) and the SES were completed by a series of psychiatric patients (N = 17) who presented for treatment of medication induced SD. The CSFQ is a 32 item structured interview designed to measure illness and medicated-related changes in sexual functioning with reliable and valid psychometric properties.

Results: Figure 1 shows the correlation coefficients between the SES and the CSFQ and subscales.

Conclusions: The SES indicates good concurrent validity with the CSFQ. Discriminate validity is supported by the low correlation between the SES and the Hamilton Depression Scale. The SES can be used by clinicians as an easy valid tool in the assessment of SD.

NR468 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Depressive Mood Symptoms Associated with Ovarian Suppression

Julia K. Warnock, M.D., *Department of Psychiatry, University of Oklahoma, 2808 South Sheridan, Suite 200, Tulsa, OK 74129-1014;* J. Clark Bundren, M.D., David W. Morris, M.A.

Summary:

Objectives: GnRH agonist induced ovarian suppression has been noted to be an effective treatment for endometriosis. Evidence indicates that depressive symptoms may be precipitated in women during the course of GnRH agonist therapy. This randomized, prospective double-blind, placebo-controlled trial evaluated the hypothesis that patients requiring GnRH agonist therapy for endometriosis will have less depressive symptoms if they are treated with sertraline as compared to the placebo control group on GnRH agonist therapy.

Design: The subjects were 33 women with laparoscopically diagnosed endometriosis who were psychiatrically well and who were appropriate candidates for ovarian suppression with GnRH agonist therapy (leuprolide, 3.75 mg IM Q 28 days). Assessment instruments included the Hamilton Rating Scale for Depression (HRSD-21) and the Menopausal symptoms Index (MENSI) given at baseline and at months 1, 2, and 3.

Results: A Hotellings T^2 test for repeated measures analysis indicated a statistically significant ($p < 0.05$) between group difference across time for the HRDS-21 ($T^2 = 13.3$; $F(3,28) = 4.1$; $p = 0.02$) with the treatment group receiving sertraline manifesting significantly fewer depressive symptoms than the placebo control group. No significant between group differences were found in the MENSI scores across time ($T^2 = 6.9$; $F(3,26) = 2.1$; $p = 0.12$).

Conclusions: Ovarian suppression with GnRH agonist therapy is associated with an increase in depressive mood symptoms which can be treated with sertraline.

NR469 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Effects of Paroxetine and Mirtazapine on Driving

Ian Hindmarch, Ph.D., *H. P. R. U., Egerton Road, Guildford GU2 5XP, United Kingdom;* Fran M. Ridout, B.S.C.

Summary:

Objective: To assess the effects of paroxetine and mirtazepine on driving skills.

Method: 12 healthy volunteers received paroxetine 20 mg mane (5 days), mirtazepine 15 mg mane (2 days) then 15 mg b.i.d (2.5 days), mirtazepine 15 mg nocte (2 days) then 30 mg nocte (2 days) and placebo in a double blind balanced 4-way crossover study. Brake reaction time (BRT) was measured on days 0, 2 and 5 psychometric assessments including critical flicker fusion (CFF), choice reaction time (CRT), subjective measures of sedation (LARS) and sleep parameters (LSEQ) on days 1, 2, 3, 4 and 5.

Results: Paroxetine had no significant effect on BRT compared to placebo. Although subjective ratings of sleep quality and sedation were impaired, contemporaneous measures of CNS arousal (CFF) and reaction time showed significantly improved performance. Mirtazepine significantly impaired BRT (day 2) and both objective (CFF, CRT) and subjective (LARS, LSEQ) measures.

Conclusion: Paroxetine 20 mg/day has no psychomotor or behavioral toxicity [1] and has no negative impact on BRT. In contrast, mirtazepine, used here as a verum [2], significantly impaired performance on all measures confirming the sensitivity of the tests and the inadvisability of mirtazepine as a treatment for ambulant patients.

NR470 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Patients with Severe Depression May Benefit from Buspirone Augmentation of Selective SSRIs

Bjorn G. Appelberg, *Department of Psychiatry, Helsinki University, Lapinlahdentie Box 320, Fin-Helsinki Hyks, Finland;* Erkka Syvalahti, Timo Muhonen, Teuvo Koskinen, Hannu Naukkarinen, Olli-Pekka Mehtonen

Summary:

Case reports and open studies have reported augmentation with buspirone to be beneficial in depression refractory to treatment with selective serotonin re-uptake inhibitors (SSRI:s).

Method: 102 out-patients patients, who fulfilled DSM-IV criteria for a major depressive episode and who had failed to respond to minimum of 6 weeks treatment with either fluoxtine or citalopram were included in this double-blind, randomised placebo controlled study. After a single-blind placebo wash-in period of two weeks, while continuing their SSRI, the patients were randomised to adjunctive treatment with either buspirone 10–30 mg b.i.d. or placebo for 6 weeks. Patients were assessed using MADRS, CGI and visual analogue scales.

Results: After the first week of double-blind treatment there was a significantly greater reduction of the MADRS score in the buspirone group as compared to placebo ($p = 0.029$). At endpoint there was no significant difference between treatment groups as a whole, although patients with initially high MADRS-scores (>30) showed a significantly greater reduction of MADRS-score ($p = 0.044$) in the buspirone group.

Conclusion: Augmentation with buspirone may speed up the antidepressive response of patients refractory to treatment with fluoxetine or citalopram. Patients with severe depressive symptoms are those who are probably most prone to benefit from augmentation with buspirone.

NR471 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Dysphoric Mania and Suicide Risk

Jose de Leon, M.D., *Department of Psychiatry, University of Kentucky, 627 West 4th Street, MHRC 627, Lexington, KY 40508-1207;* Berta Lalaguna, M.D., Fernando Mosquera, M.D., Miguel Gutierrez, M.D., Blanca Fernandez de Corres, M.D., Jose L. Perez de Heredia, M.D., Ana Gonzalez-Pinto, M.D.

Summary:

Objective: Dysphoric mania appears to have a worse outcome than pure mania. Bipolar disorder is associated with a high suicide risk. This study attempts to establish whether dysphoric mania is associated with greater suicide risk in a sample of bipolar I patients from a catchment area in a Basque state, Alava (North of Spain)

Method: This catchment area includes 340,000 people. All acute psychiatric patients are admitted to one acute psychiatric unit located in a hospital of the National Health System in Spain. Between February of 1997, and September of 1998, all 86 patients who met DSM-IV criteria for manic episodes were included. Patients were assessed with the SCID-P, the PANSS, the Young scale for mania, the Hamilton depression scale (including a suicide risk rating), the Phillips premorbid scale, and the CGI. McElroy's criteria for dysphoric mania were used.

Results: Patients with dysphoric mania reported significantly more suicidal ideation (48%), than patients with pure mania (19%) (Chi square = 7.91; df = 1; p = 0.005). The frequency of history of suicide attempts was 30% in patients with dysphoric mania and 14% in patients without dysphoric mania (Chi square = 2,91; df = 1, p = 0.08).

Conclusions: As dysphoric mania may be associated with a higher risk of suicide, patients manifesting this type of mania need to be closely monitored.

NR472 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Effectiveness of Citalopram in the Prevention of Depression Recurrence in Elderly Patients

Rene Kylsner, *ICR Department, H. Lundbeck A/S, 9 Ottiliave J, Valby DK-2500, Denmark;* E. Pleidrup, M.D., H. L. Hansen, M.D., J. Bent-Hansen, M.D., D. Loldrup Poulsen, M.D., M. Lunde, H.E. Hopfner Petersen, M.S.C.

Summary:

Objectives: Major depression is often associated with a high degree of recurrence. Double-blind, placebo-controlled studies have demonstrated the effectiveness of citalopram, the most selective serotonin re-uptake inhibitor in clinical use, in the prevention of depressive relapse (1, 2).

The objective of the present study was to evaluate the effectiveness of citalopram in the prevention of recurrent depressive episodes in elderly patients.

Method: Elderly patients (≥65 years) meeting DSM-IV diagnostic criteria for major depression received 8–12 weeks of open treatment with citalopram in flexible doses (20–40 mg daily). Responders, defined by a total score <12 on the Montgomery-Asberg Depression Rating Scale (MADRS), received 12–16 weeks of continued treatment at their established effective dose. Patients who continued to respond were randomised to double-blind treatment for 48 weeks or longer with either continued citalopram or placebo. Depression recurrence was defined as a MADRS total score ≥22, confirmed 3–7 days later.

Result: A total of 121 patients (65–92 years) responding to citalopram were randomised to double-blind treatment. Survival analyses demonstrated that the rate of depression recurrence was statistically significantly lower ($p < 0.001$) in patients receiving citalopram maintenance therapy than in patients receiving placebo.

Conclusion: Long-term maintenance treatment with citalopram is effective in the prevention of depression recurrence in elderly patients.

NR473 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Childhood Emotional Trauma and Chronic PTSD in Adult Outpatients with Treatment-Resistant Depression

Marcia J. Kaplan, M.D., *Department of Psychiatry, University of Cincinnati, 222 Piedmont, Suite 8500, Cincinnati, OH 45219;* Nadya Klinetob, Ph.D.

Summary:

Objective: The intent of this study was to test the hypothesis that patients with treatment resistant depression are more likely than treatment responsive patients to suffer from sequelae of childhood trauma that may perpetuate depression despite adequate medication treatment.

Method: 20 subjects with treatment-resistant depression and 20 subjects with treatment-responsive depression were administered a structured interview and a battery of psychological tests to assess levels of current depression, confirm diagnosis, and quantify childhood trauma and presence of dissociative phenomena. Tests used include the Beck Depression Inventory, the Mini International Neuropsychiatric Interview, the Minnesota Multiphasic Personality Inventory-2, the Childhood Trauma Questionnaire, and the Trauma Symptom Inventory.

Results: Compared to treatment responders, the treatment resistant subjects were significantly more depressed, had significantly more co-morbid anxiety disorders, reported significantly greater levels of childhood emotional abuse, and experienced current-day sequelae of childhood emotional abuse.

Conclusion: The hypothesis was supported by these results. This study suggests that reported history of childhood emotional abuse and sequelae of that abuse may be associated with treatment resistance in depressed outpatients.

NR474 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Incongruent Psychotic Symptoms and Age of Onset in Bipolar Disorder

Jose L. Perez de Heredia, M.D., *Department of Psychiatry, Santiago Hospital, Olaguibel 29, Vitoria 01004, Spain;* Juan L. Figuerido, M.D., Miguel Gutierrez, M.D., Berta Lalaguna, M.D., Jesus Ezcurra, M.D., Jose de Leon, M.D., Ana Gonzalez-Pinto, M.D.

Summary:

Objective: Early onset in bipolar disorder may be associated with misdiagnosis and psychotic symptoms. This study attempts to establish the frequency of incongruent psychotic symptoms and their association with early onset in a sample of bipolar patients from a catchment area in a Basque state, Alava (North of Spain).

Method: This catchment area includes 340,000 people. Between February of 1994, and May of 1996, all 169 in-patients and outpatients diagnosed as DSM-IV bipolar I disorder in the state of Alava at the five outpatients community mental health centers, or at the Santiago Apostol Hospital were included. Patients were assessed with the SCID-P, the PANSS, the Young scale for mania, the Hamilton depression scale, the Phillips premorbid scale and the CGI. The families were interviewed, and all charts were reviewed to verify information.

Results: There were 73 (43%) patients with a history of incongruent psychotic symptoms. They had a significantly earlier onset of illness than those who did not have a history of psychotic incongruent symptoms ($p = 0.008$).

Conclusions: Incongruent psychotic symptoms appear to be more prevalent in early presentations of bipolar disorder.

NR475 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

What Can We Learn from Self-Assessment of Mania?

Elie G. Hantouche, M.D., *Department of Psychiatry, Pitie-Salpetriere, 47 BD de L'Hopital, Paris 75013, France;* Hagop S. Akiskal, M.D., Jean-Francois Allilaire, M.D., Jean-Michel Azorin, M.D., Marc L. Bourgeois, M.D., Daniel Sechter, Sylvie Lancrenon, Ph.D., Liliane Chatenet-Duchene, M.D.

Summary:

Objectives: This paper derives from the French national multisite collaborative study on the clinical epidemiology of mania (EPIMAN). In this report we focus on data obtained from a factor analysis of manic symptomatology as self-rated by 104 hospitalized manic patients.

Method: EPIMAN involves training 23 French psychiatrists in 4 different sites to rigorously apply a common protocol deriving from the criteria of DSM-IV, and McElroy et al; the use of such instruments as the Beigel-Murphy scale (Manic State Rating Scale, MSRS), the Ahearn-Carroll Multi-Visual Analogic Scale of Bipolarity (MVAS-BP, which includes 26 items), a modified HAM-D, and the Semi-Structured Interview for Evaluation of Affective Temperaments (based on Akiskal-Mallya). A principal component analysis (with varimax rotation) was conducted on the MVAS-BP and comparative and correlational analyses according to subcategorization of mania and to mutidimensionality in Carroll-Klein model of bipolarity.

Results: Before rotation, a major factor was identified (33% of variance) in which almost all the items ($n = 23$) were represented. After varimax rotation, seven interpretable and clinically relevant factors were isolated showing a good matching to manic symptomatology as listed in the DSM-IV: F1 "Elation-Inflated Self-esteem" (6 items), F2 "Hyperactivity" (8 items), F3 "Psychomotor Acceleration" (4 items), F4 "Anxious Dysphoria" (3 items), F5 "Interpersonal" (3 items), F6 "Sleep" (1 item) and F7 "Anger" (1 item). Further analyses showed:

1) the capability of the five major factors of MVAS-BP to separate individually (p highly significant for each) between Pure *versus* Dysphoric Mania (as categorized by the presence of at least 2 coexisting depressive symptoms);

2) correlations at a high significant level with the 4 dimensions of Carroll-Klein model of bipolarity: "Consummatory Reward" and F1 (r = 0,93), "Incentive Reward" with F2 (r = 0,84), "Psychomotor Regulation" with F3 (r = 0,85) and "Central Pain" with F4 (r = 0,84). F2 ("Activation") was significantly correlated ($r \geq 0,7$) with all dimensions of Carroll-Klein model.

Conclusions: Self-assessment of acute mania by using the Ahearn-Carroll MVAS-BP could be of help for screening the illness (obtaining the core symptoms of mania), recognizing and assessing mixed states (such as dysphoric mixed mania) and understanding the complexe phenomenology of mania.

NR476 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Long-Term Mirtazapine Versus Citalopram in Major Depression

Esa Leinonen, M.D., *Tampere University Hospital, Tampere 33521, Finland;* Jon Skarstein, M.D., Kirsten Behnke, Hans Agren, Ph.D., Albert J. Schutte, M.D.

Summary:

Objective: To compare the efficacy and tolerability of mirtazapine with citalopram in the long-term treatment of major depression.

Method: This was a multicentre, randomised, double-blind 16-week extension to an 8-week study. Patients with DSM-IV major depression and MADRS total score ≥22 received mirtazapine 15-60 mg/day or citalopram 20–60 mg/day for 8 weeks. Consenting patients responding to treatment (≥50% decrease in MADRS total score and total MADRS score ≤18) entered a 16-week extension period, on the same treatment regimen. The primary efficacy variable was change from baseline in MADRS total score.

Results: 109 mirtazapine and 117 citalopram patients entered the extension period. 104 mirtazapine and 103 citalopram patients completed the study. After 24 weeks of treatment, the change from baseline in MADRS score was 25.3 ± 5.9 and 24.6 ± 6.0 in the mirtazapine and citalopram treatment groups, respectively. Mirtazapine gave a significantly greater reduction in MADRS score than citalopram at week two (−10.83 versus −8.11, p = 0.002), three (−15.14 versus −12.86, p = 0.009), and four (−18.31 versus −15.65, p = 0.004) of the study. Similar numbers of generally mild adverse events occurred in each group (mirtazapine 74 patients, citalopram 87 patients).

Conclusions: Mirtazapine and citalopram are effective and well tolerated in the long-term treatment of major depression. Mirtazapine seems to have a faster onset of action than citalopram.

NR477 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Effects of Bupropion Sustained Release on Sexual Functioning

Lawrence A. Labbate, M.D., *Department of Psychiatry, Medical University of SC, VA Med Ctr/109 Bee Street #116, Charleston, SC 29401;* Peter S. Brodrick, M.D., Robert P. Nelson, M.D., George W. Arana, M.D., R. Bruce Lydiard, M.D.

Summary:

Objective: The purpose of this study was to evaluate the effects of bupropion SR on objective and subjective measures of sexual function in healthy men without psychiatric disorders.

Methods: Healthy males (N = 13, mean age 30) without psychiatric or medical illness completed a two week placebo-controlled, double-blind, crossover trial of bupropion SR, 300mg/d. Subjects had a one-week washout period between trials. Sexual function was measured using a validated, self-administered questionnaire and the RigiScan, an instrument measuring nocturnal penile tumescence and rigidity. Measurements were made at baseline, and at the end of placebo and bupropion trials.

Results: No differences were found in self-reported sexual function, number of nocturnal erections, total erection time, or penile rigidity in subjects taking bupropion compared to placebo or baseline conditions. There was no cross-over effect, and the order of bupropion or placebo did not affect the outcome. There were very few adverse effects from placebo or bupropion.

Conclusions: These findings support that bupropion does not have subjective adverse sexual side effects, and does not affect nocturnal erections in healthy males.

NR478 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Changes of Personality Traits During SSRI Treatment

Antoine Pelissolo, M.D., *Department of Psychiatry, Hospital F. Widal, 200 Rue du Faubourg St-Denis, Paris 75010, France;* Sylvie Troy, M.D., Jean-Pierre Lepine, M.D.

Summary:

Objectives: It has been shown that Harm Avoidance (HA) and Self-Directedness (SD), measured by the Temperament and Character Inventory (TCI), may be partially correlated to depressive measures, and may vary during antidepressant treatment. We aimed to explore if these changes can be influenced by the existence of a personality disorders.

Method: Seventy-nine out-patients with DSM-IV major depression were openly treated during 6 months with sertraline (50–200

mg/d). Patients completed the TCI before and after treatment. Thirty-two had an ICD-10 personality disorders (PD), and 47 did not. TCI variations after treatment of patients with PD were compared to those patients without PD.

Results: About 75% of patients were considered as responders after 6 months of treatment. Significant variations in TCI dimensions were observed only for HA and SD. PD patients experienced greater, although not significant, decreases in HA scores than patients without PD (3.2 vs 1.7; $p = 0.08$). Patients with and without PD exhibited the same improvement to SD scores (3.6 and 3.1 respectively; $p = 0.6$).

Conclusion: Most TCI personality dimensions are stable during 6 months of SSRI (sertraline) treatment, but HA and SD scores may fluctuate similarly in depressive patients with or without PD.

NR479 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Personality and Temperament in Bipolar Disorders

Courtney M. Rennicke, B.A., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723;* Connie M. Strong, M.S., Claudia M. Santosa, M.A., Nadia Sachs, M.Eng., Po W. Wang, M.D., Mirene E. Winsberg, M.D., Terence A. Ketter, M.D.

Summary:

Objective: To investigate personality and temperament in bipolar disorder patients and healthy controls.

Method: We obtained NEO Personality Inventory (NEO PI-R), Cloninger's Temperament and Character Inventory (TCI), and Akiskal's Affective Temperament Scale (ATS) in euthymic bipolar disorder outpatients (24F/10M, mean age 39.4) and healthy controls (19F/12M, mean age 35.9).

Results: Patients had 63% increased Neuroticism (NEO-N) on the NEO PI-R; 98% increased Harm Avoidance (TCI-HA) on the TCI; and 739% increased Cyclothymia (ATS-C) on the ATS. Controlling for age, gender, and diagnosis, NEO-N correlated with TCI-HA ($r = 0.687$) and ATS-C ($r = 0.622$); and TCI-HA correlated modestly with ATS-C ($r = .296$). Using a 99% confidence interval (mean $\pm$ 3 SD) of control data criterion provided better diagnostic categorization with ATS-C (86% correct), than with NEO-N (59% correct), or TCI-HA (54% correct) (Chi-square = 17.3, $p = 0.0002$).

Conclusion: Euthymic bipolar disorder patients had increased NEO-N, TCI-HA, and ATS-C. NEO-N correlated with TCI-HA and ATS-C, possibly due anxiety and lability commonalities, respectively, while TCI-HA correlated more modestly with ATS-C. ATS-C appeared the most closely related to diagnosis.

NR480 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Clinical Depression and the Dissociation Between Conscious and Unconscious Memory

Mustaq Khan, Ph.D., *Star Program, London Psychiatric, 850 Highbury Ave, p o box 5532, London, ON N6A 4H1, Canada;* Verinder Sharma, M.D., Shahe Kazarian, Ph.D.

Summary:

Objective: Conscious (explicit) recollection is typically better for participant-generated than for experimenter-provided study words. This effect is reversed when unconscious (implicit) memory is assessed. Such reversal is an example of a memory dissociation. Two experiments looked at the effect of clinical depression on this dissociation.

Method: Participants read visually presented words and guessed other words from letter clues. Explicit and implicit memory was compared among 27 university students and three inpatient groups: 27 patients with DSM-IV diagnosis of Major Depressive Disorder, including 14 with Bipolar I Depression; 9 with schizophrenia (Paranoid Type); and 9 with Major Depressive Disorder in full remission.

Results: In Experiment 1, depressed and remitted patients failed to show memory dissociation, whereas university students and schizophrenics did. In Experiment 2, the contributions of controlled and automatic influences on memory were investigated. Compared to university students, depressives appeared to have difficulty focussing attention on episodic memories, for they tended to treat automatic influences that produce feelings of familiarity as being similar to actual episodic experiences.

Conclusions: The results are consistent with prior research showing that depressives attend more to their own ruminative thoughts than to external events. The results also indicate that implicit memory procedures can reveal effects of depression on psychological functioning that are not revealed by traditional, conscious assessments of memory.

NR481 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Is Olanzapine a Mood Stabilizer?

Peter D. Feldman, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;* Mauricio F. Tohen, M.D., Thomas G. Jacobs, M.A., Verna Toma, B.S.C., Fan Zhang, Ph.D., Todd M. Sanger, Ph.D., Alan F. Breier, M.D.

Summary:

A double-blind, placebo-controlled 4-week study was conducted to provide additional information on efficacy and safety of olanzapine in the treatment of mania. Patients with a DSM-IV diagnosis of bipolar I disorder, manic or mixed, with or without psychotic features, were randomized to receive a dose range of 5, 10, 15, or 20 mg/day of olanzapine or placebo for a 4-week period. The mean modal dose of olanzapine was 16.4 mg/day.

Compared to placebo, olanzapine-treated patients had a statistically significantly greater mean improvement on the Y-MRS total score (−8.13 placebo vs −14.78 olanzapine, $p < .001$); statistical significance was evident within one week of olanzapine treatment and was maintained throughout the 4-week acute phase. Statistically significantly more olanzapine-treated patients responded (≥50% improvement on the Y-MRS total score) than did placebo-treated patients (64.8% vs 42.9%, respectively; $p = .023$). In addition, relative to placebo-treated patients, olanzapine-treated patients had a statistically significantly greater mean improvement on the HAMD-21 total score in patients presenting with depressive symptoms (−6.81 placebo vs −12.29 olanzapine, $p = .046$), CGI-BP Severity of Overall Illness score (−0.73 placebo vs −1.72 olanzapine, $p < .001$), and the PANSS total score (−7.43 placebo vs −21.19 olanzapine, $p < .001$). Olanzapine was generally well tolerated; only two patients discontinued due to adverse events (unintended pregnancy and rash) and there were no statistically significant differences on measures of parkinsonism or akathisia between olanzapine- and placebo-treated patients. Compared to placebo, olanzapine demonstrated superior efficacy and a favorable safety profile in the treatment of acute mania.

NR482 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Olanzapine in the Treatment of Juvenile Bipolar Disorder

Jean A. Frazier, M.D., *Department of Psychiatry, McLean Hospital, Belmont, MA 02178;* Joseph Biederman, M.D., Thomas G. Jacobs, M.A., Mauricio F. Tohen, M.D., Verna Toma, B.S.C., Peter D. Feldman, Ph.D., Michael A. Rater, M.D.

Summary:

Objective: Despite widespread use of antipsychotics in juveniles with bipolar disorder, few studies using these medications have been conducted in this patient population. The primary objective

of this study was to assess safety and efficacy in the novel antipsychotic olanzapine after up to 8 weeks of open-label treatment.

Methods: Twenty-three bipolar disorder patients (currently manic or mixed), ages 5 to 14, received olanzapine (dose range: 2.5–20 mg/day). Efficacy was assessed using the Young Mania Rating Scale (YMRS) as the primary measure. Response was defined *a priori* as ≥30% improvement from baseline to endpoint in YMRS total score and a CGI-BP mania score ≤3 at endpoint.

Results: A statistically significant mean change from baseline to endpoint in the YMRS was observed (−19.04 ± 9.21, $p < .001$), with a response rate of 60.9%. Of the 23 patients who received olanzapine, 22 (95.7%) completed. One patient discontinued due to an adverse event (depression). Extrapyramidal symptom measures were not statistically significantly different from baseline levels. However, significant increases were observed in weight (4.98 ± 2.32 kg, $p < .001$).

Conclusions: Olanzapine was an effective monotherapy for juvenile bipolar disorder. No serious clinically significant safety concerns attributable to olanzapine were observed. Further studies are warranted to confirm these findings.

NR483 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Safety and Efficacy of Lamotrigine for the Long-Term Treatment of Bipolar Depression

Russell Huffman, Ph.D., N and P Clinical Development, Glaxo Wellcome, p o box 13398, RTP, NC 27709-3398; David Rudd, Pharm.D., Eileen Monaghan, John A. Ascher, M.D., Gilda Womble, M.S., Charles L. Bowden, M.D., R. Bruce Lydiard, M.D.

Summary:

Objective: To evaluate the long-term safety and efficacy of lamotrigine, as monotherapy or adjunctive therapy, for the treatment of bipolar depression.

Methods: A one-year, open-label, flexible-dose continuation study (GW #604) was conducted in 124 subjects previously enrolled in a 7-week, double-blind, placebo-controlled study (GW #602).

Results: Subjects previously randomized to placebo showed statistically significant improvement throughout the study on HAMD-17, MADRS and CGI scales, and subjects previously randomized to lamotrigine maintained the statistically significant difference vs. placebo observed during the double-blind study. Lamotrigine was well tolerated at doses of up to 500mg/day, with 15% of subjects discontinued prematurely due to an adverse event. There were no serious rashes. Lamotrigine had no effect on clinical laboratory parameters.

Conclusion: This open-label study provides evidence that lamotrigine is safe as a long-term treatment for bipolar depression, and that lamotrigine's mood stabilizing effect is maintained for up to one year.

NR484 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Frontal Tests in Unipolar and Bipolar Depression

Janusz K. Rybakowski, M.D., *Adult Psychiatry Department, University of Medical Sciences, Szpitalna 27133, Poznan 60-572, Poland;* Alina Borkowska, Ph.D.

Summary:

The aim of the study was comparing patients with depression in the course of unipolar or bipolar mood disorders on Wechsler Adult Intelligence Scale (WAIS-R) and frontal lobe tests: Wisconsin Card Sorting Test (WCST), Trail Making Test, Stroop Test and Verbal Fluency Test. Patients were studied during acute depressive episode, before starting pharmacological treatment. Unipolar depression (UD) group comprised 30 patients (5 male, 25 female), mean age 40 ± 10 years, mean duration of illness 5 ± 5 years, mean intensity of depression on 17-item Hamilton Scale 23 ± 2 points. Bipolar depression (BD) group included 15 patients (7 male, 8 female, mean age 41 ± 10, mean duration of illness 7 ± 5 years, mean intensity of depression 23 ± 3 points. Both groups did not differ for total and verbal scale on WAIS-R, however the results of performance scale were significantly lower in BD. On all neuropsychological tests (except for non-perseverative errors in WCST) patients with BD performed significantly worse than UD patients. The results obtained suggest the difference in cognitive dysfunction connected with frontal lobe pathology between unipolar and bipolar depressed patients during acute episode. They may corroborate other findings pointing on more marked functional and structural brain abnormalities in bipolar depressed patients compared with unipolar ones.

NR485 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Response and Remission Rates in Different Subpopulations with Major Depression Administered Venlafaxine, SSRIs, or Placebo

Richard Entsuah, Ph.D., *Clinical Research and Develop., Wyeth-Ayerst Research, 145 King of Prussia Road, Radnor, PA 19087*

Summary:

Objective: To determine whether gender and age influence response and remission following treatment of major depression.

Method: A pooled analysis of a multicenter double-blind, placebo-controlled study where subjects (n = 2045), aged 18–80 years and meeting DSM-III-R or -IV criteria for moderate-severe depression, were randomized to receive venlafaxine (VEN), a selective serotonin reuptake inhibitor (SSRI; fluoxetine, paroxetine, or fluvoxamine), or placebo for 8 weeks. Depression was assessed using Hamilton Rating Scale for Depression (HAM-D). Response equaled ≥50% decrease in baseline HAM-D_{21} score. Remission equaled HAM-D_{17} score ≤7. Differences between VEN, SSRI, and placebo for gender and age subpopulations were determined using Fisher's exact test.

Results: Outcomes with each treatment were similar for all subpopulations. In both genders, VEN and SSRI remission rates were superior to placebo at week 8 (all $P < 0.05$); additionally, VEN had a higher remission rate than SSRIs in these subpopulations. With VEN, response was more rapid (week 2 vs placebo, $P < 0.02$); by week 8, response rates were higher (61–79%) than with SSRIs (51–62%) ($P \leq 0.01$).

Conclusions: These data may suggest that depressed patients of different genders and ages respond similarly to available pharmacotherapies. Moreover, a more rapid response and remission are likely with VEN.

NR486 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Lack of Gender Effects in Mood Response to Alpha-Methyl-Para-Tyrosine (AMPT)

Francisco A. Moreno, M.D., *Department of Psychiatry, Univ. of Arizona C.O.M., 1501 N Campbell Avenue, #70PC, Tucson, AZ 85724;* Cynthia A. McGahuey, B.S., Karen Bridges, Pedro L. Delgado, M.D.

Summary:

Although gender differences in the prevalence of depression are well known, the effects of gender on underlying mechanisms of illness and antidepressant action remain less clear. In a retrospective study (Moreno et al, 1998) SSRI-treated women were found to be more vulnerable than men to the depressogenic effects of acute plasma tryptophan (TRP) depletion. The present study

determines the effects of gender on the mood response to acute catecholamine depletion.

Methods: Data were analyzed in 61 subjects who underwent catecholamine depletion at the Arizona Health Sciences Center. Subjects had participated in a variety of studies utilizing alpha-methyl-para-tyrosine (AMPT) an inhibitor of tyrosine hydroxylase, the rate-limiting enzyme for the synthesis of catecholamines. Mood ratings were obtained once before and after and twice daily during 2 days of testing.

Results: 39% of subjects were men and 61% were women. ANOVA with repeated measures revealed that catecholamine depletion caused a significant increase in HAM-D score as demonstrated by the main effect of time ($F = 5.3$, $df = 4$, $p = .001$). Time x gender interaction was not significant ($F = 0.97$, $df = 4$, $p = .434$). There was no effect of age.

Implications: In contrast to the results of our prior study with TRP depletion, no gender differences were seen with catecholamine depletion, although the sample size is relatively small and there were different groups of subjects. The lack of gender difference during catecholamine depletion when contrasted to TRP depletion suggests that there may be more prominent gender differences in 5-HT function than catecholaminergic function. Further studies are needed to determine whether these differences relate to the neurotransmitter depletion test itself, or if they reflect true gender differences between the catecholaminergic and serotonergic pathways involved in the regulation of mood states.

NR487 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Emotional Blunting with SSRIs

Pedro L. Delgado, M.D., *Department of Psychiatry, Univ of AZ School of Medicine, 1501 N. Campbell Ave. Rm. 7303, Tucson, AZ 85724-2004;* Adam Opbroek, M.D., Cindy Laukes, M.A., Cynthia A. McGahuey, B.S., Alan J. Gelenberg, M.D., Francisco A. Moreno, M.D., Joanna Katsanis, Ph.D., Richard D. Lane, M.D., Mona Mort, Ph.D.

Summary:

Objective: Selective serotonin reuptake inhibitor (SSRI) antidepressants have become the first line drugs used for treatment of major depression due to their favourable safety profile and relative lack of serious side effects. However, up to 50% of patients taking SSRIs can develop sexual dysfunction. Some reports suggest that SSRIs can also cause blunting of other specific emotional responses (ability to cry).

Methods: To assess emotional blunting in SSRI-treated depressives, we developed an 18-item rating scale designed to assess specific aspects of normal emotional response: the Laukes Emotional Intensity Scale (LEIS). Each LEIS item is scored on a scale of 1 (a lot less) to 5 (a lot more), with a score of 3 being "the same as usual". Therefore, a score <54 reflects increasing degrees of emotional blunting and a score >54 reflects more emotionality. The LEIS was administered to 15 patients who were being recruited into a study of SSRI-induced sexual dysfunction. All patients were in remission from depression [Hamilton Depression (HAM-D) score <10] and were taking an SSRI. Subjects were asked to fill out the LEIS, the Arizona Sexual Experiences Scale (ASEX) and were assessed with the Ham-D. Eighteen healthy control subjects responded to the same rating scales.

Results: Total mean LEIS score for patients (39.4 + 8.0) were significantly lower than for controls (57.1 + 3.3) ($DF = 1,37$, $F = 93.2$, $p = 0.00$). Compared with controls, patients reported significantly ($p < .05$) less ability to cry, be irritated, care about others' feelings, feel sadness, have erotic dreams, be creative, feel surprise, feel angry, express their feelings, be worried by things or situations, and feel pleasure with and have interest in sex. Total score on the LEIS was correlated with total score on the ASEX but not the Ham-D.

Conclusions: 80% of patients with SSRI-induced sexual dysfunction also describe clinically significant blunting of several emotions. Emotional blunting may be an under-appreciated side effect of SSRIs that could contribute to treatment noncompliance or reduced quality of life.

NR488 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Mood Stabilization with Lamotrigine in Rapid-Cycling Bipolar Disorder: A Double-Blind, Placebo-Controlled Study

Paul Greene, *Glaxo Wellcome, 5 Moore Drive, Research Triangle, NC 27709;* Nancy L. Earl, M.D., John A. Ascher, M.D., Eileen Monaghan, Patricia Suppes, M.D., Charles L. Bowden, M.D., Joseph R. Calabrese, M.D.

Summary:

Objective: Early experience with lamotrigine (LTG) suggests particular utility in treating rapid cycling bipolar disorder. The double-blind, placebo-controlled phase of this study was conducted to evaluate the efficacy of lamotrigine in this patient population.

Methods: Study GW#614 enrolled 326 rapid cycling bipolar patients into an initial open-label stabilization phase. Subjects experiencing clinical response to LTG were discontinued from other medications and, if stable (HAMD-17 score <14 and Mania Rating Scale score of <12 for the last 2 weeks of the 8–12-week open phase) were subsequently randomized to monotherapy with LTG or placebo for 6 months.

Results: A total of 177 patients were entered into the controlled phase of the study. Forty-one percent LTG vs. 26% of PBO ($p < 0.05$) patients completed six months of randomized treatment without any additional clinical intervention. Survival analysis based on time from randomization to time of intervention suggested a 6-week difference in median survival in favor of LTG.

Conclusion: This study, the largest of its kind conducted to date, suggests that LTG is a useful alternative to other mood stabilizers in the maintenance treatment of patients with rapid cycling bipolar disorder.

NR489 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Controlled Studies of Lamotrigine in Unipolar Depression

John A. Ascher, M.D., *Glaxo Wellcome, 5 Moore Drive, Research Triangle, NC 27709;* Sharyn R. Batey, Pharm.D., Margaret Beaman, Kathleen Mitchell, Eileen Monaghan, Arifulla Khan, M.D., Peter D. Londborg, M.D.

Summary:

Objective: Lamotrigine, an established antiepileptic drug, has previously demonstrated efficacy in a controlled study of bipolar depression (Calabrese et al., 1999). Recent case reports also suggest utility in unipolar depression. Two studies were designed to further evaluate the antidepressant activity of lamotrigine in this population.

Methods: Study GW#613 enrolled a total 437 outpatients meeting DSM-IV criteria for Major Depressive Disorder with a HAM-D total score >20. Parallel treatments were placebo, lamotrigine (target 200mg/day) and desmethylimipramine (target 200mg/day) for 8 weeks. Study visits were conducted at least weekly and included efficacy (HAM-D, MADRS and CGI) and safety measures.

Study GW#20022 enrolled a total of 152 outpatients meeting entry criteria similar to study #613. Subjects were randomized to either lamotrigine (dose and titration similar to study #613) or placebo for 7 weeks of treatment.

Results: Lamotrigine displayed evidence of antidepressant activity in this patient population as evidenced by statistically signifi-

cant differences from placebo on key efficacy measures including HAM-D and CGI. The drug was well-tolerated at the doses studied.

Conclusion: Lamotrigine may represent an effective alternative to the use of traditional antidepressants in the treatment of unipolar depression.

NR490 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Mortality in Psychotic Depression

Meena Narayan, M.D., *Department of Psychiatry, Yale University, 184 Liberty Street, New Haven, CT 06519;* Joyce Chen, J. Douglas Bremner, M.D., J. Craig Nelson, M.D.

Summary:

Background: Major depression is associated with increased mortality. It is unclear if this high mortality in depressed subjects is related to the severity or the subtype of major depression. Since psychotic depression is a distinctly severe subtype of depression, we hypothesized that the mortality rate in patients with psychotic unipolar major depression will be greater than those with non-psychotic unipolar major depression.

Methods: 29 patients with unipolar psychotic depression and 67 patients with non-psychotic unipolar depression who required admission to Yale New Haven Hospital between 1976 and 1988 were selected. Subjects were chosen if their current age was > 60 years and if a standard DST was performed on admission. The number of patients dead or alive at the time of follow up was determined by a National Death Search Database and death certificates were obtained.

Results: 45% (13/29) of patients with psychotic depression had died at follow-up, in contrast to 21% (14/67 patients) of those with non-psychotic depression ($X^2 = 4.61$, df = 1, $p < 0.05$). A survival analysis and an analysis of covariance of age, sex, DST status and index of medical illness will be presented.

Conclusions: Patients with psychotic depression had higher mortality rates compared to those with non-psychotic major depression. The presence of psychotic symptoms may be an independent risk factor for death in depressed subjects.

NR491 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Topiramate in Chronic Civilian PTSD: An Open-Label Study of a Novel Treatment

Jeffrey L. Berlant, M.D., *Department of Psychiatry, University of Washington, 4477 Emerald, # A-300, Boise, ID 83706-2044*

Summary:

Objective: This poster will examine the clinical response to topiramate for the treatment of post-traumatic stress disorder (PTSD), based on the hypothesis of symptom generation from kindling of limbic nuclei after traumatic-event exposure.

Method: Outpatients who were diagnosed with PTSD involving civilian traumas were treated with topiramate monotherapy or as add-on therapy. Self-reports of partial and full resolution of Criterion B re-experiencing symptoms were completed by 35 adults, who had been symptomatic for an average of 18 years; 17 completed PCL-C instruments pre-treatment and at week 4.

Results: Topiramate suppressed nightmares in 79% and flashbacks in 85%, with full suppression in 75% of each. Partial improvement was evident in a median of 4 days, and were fully absent in median 8.0 days. Threshold dosage for partial response was 75 mg/day in 95% of patients and for full response ≤100 mg/day in 91%. Pre-and-post PCL-C adjusted-score reductions (49%) were highly significant ($p < 0.001$), with similar reductions in re-experiencing, avoidance, and hyperarousal criteria symptoms.

Conclusions: Topiramate appears to be effective as add-on or monotherapy in patients with PTSD exhibiting trauma-related nightmares or intrusive memories/flashbacks.

NR492 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Safety and Efficacy of Risperidone Versus Placebo As Add-On Therapy to Mood Stabilizers in the Treatment of the Manic Phase of Bipolar Disorder

Gary S. Sachs, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, 5th floor, Boston, MA 02114*

Summary:

Background: Early open-label studies suggest the atypical antipsychotic agent risperidone is safe and effective as add-on therapy for acute mania in bipolar disorder.

Methods: A randomized, controlled, double-blind, multicenter, Phase III trial compared add-on risperidone (1-6 mg/day), haloperidol (2–12 mg/day), or placebo with open-label lithium or valproate for the management of acute mania. The initial double-blind treatment phase lasted for 3 weeks; in a subsequent extension phase, patients received open label risperidone (0–6 mg/day) along with a mood stabilizer (lithium and/or valproate and/or carbamazepine) for 10 weeks. A total of 158 patients were randomized into the three groups. Adverse events were noted; primary efficacy was change from baseline on YMRS at endpoint.

Results: Preliminary analysis indicates statistically significant change in favor of risperidone ($p = 0.009$) on YMRS at endpoint (3 wks) as versus placebo; statistically significant change in favor of risperidone on CGI ($p = 0.002$) as versus placebo. The overall incidence of adverse events was similar in the placebo and risperidone groups; patients receiving haloperidol had greater EPS than placebo or risperidone.

Conclusions: The preliminary results of this study indicate that risperidone (1–6 mg/day) is safe and effective as add-on therapy to lithium or valproate for the treatment of acute bipolar mania.

NR493 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Systematic Treatment Enhancement Program for Bipolar Disorder

Gary S. Sachs, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, 5th floor, Boston, MA 02114;* Michael E. Thase, M.D., Leslie Leahy, Ph.D., Sara R. Gaughan, B.A., Phillip Lavori, Ph.D., Jennifer Conley, M.A., David J. Kupfer, M.D.

Summary:

Objective: The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) is a large NIMH sponsored clinical research effort designed to address public health issues related to effectiveness of treatment for bipolar disorder.

Method: STEP-BD uses a hybrid design to balance external and internal validity. The 20 STEP-BD clinical treatment centers utilize a common set of "model practice procedures" which form the basis of the STEP-BD disease management program. Subjects consent to participate in the open disease management program at study registration and clinical information is harvested from their medical record. A series of randomized study pathways with separate consents examine the outcome of specific treatment strategies at major clinical decision points over the course of bipolar illness. STEP-BD methods are compared to those of recent efficacy and effectiveness studies on various parameters related to validity and generalizability.

Results: STEP-BD generally favors external validity over internal validity but shares many features of efficacy trials.

Conclusions: Using standard outcome measures across randomized and nonrandomized study pathways STEP-BD provides a cost effective approach to an important but difficult to study patient population. The infrastructure is expandable to address additional clinical questions and open to collaborators seeking to address related scientific questions.

NR494 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Does Antidepressant Therapy Improve Cognition?

P. Murali Doraiswamy, M.D., *Department of Psychiatry, Duke University Medical Center, Box 3018, Durham, NC 27710;* K. Ranga R. Krishnan, M.D., Cathryn M. Clary, M.D.

Summary:

Objectives: Depression in late life is often associated with cognitive and psychomotor deficits, and may be a risk factor for subsequent dementia. In addition, depression is frequently comorbid with dementia. Despite these data, there is a relative paucity of well-controlled studies of adequate duration comparing different antidepressant strategies in elderly depressed patients with and without cognitive impairment. In this report, we used data from two multicenter trials to analyze the effects of antidepressant therapy on cognitive functioning in late life depression.

Methods: 446 subjects 60 years or older (75% ≥65 years), with DSM-III-R major depression participated in two randomized multicenter trials of 12 week duration. The first compared sertraline (range 50–100 mg) to fluoxetine (20–40 mg) and the second compared sertraline (range 50–150 mg) to nortriptyline (25–100 mg). Cognitive assessments included a Shopping List Task (SLT), a serial verbal learning task administered according to Buschke's selective reminding procedure, the Digit Symbol Substitution Test (DSST), and the Mini-Mental State Exam (MMSE). Two-way analysis of covariance was used to examine the effects of treatment.

Results/Conclusions: Sertraline and fluoxetine, and sertraline and nortriptyline were equally efficacious in reducing depressive symptoms in the primary efficacy analyses. The relationship between baseline depression severity and cognition will be presented. Despite similar overall antidepressant response, treatment with sertraline had more positive effects on verbal learning and recall as well as on visual tracking, coding and motor performance than nortriptyline ($p < 0.05$ for all comparisons). These data will be discussed in relation to the growing links between late-life depression and dementia.

NR495 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Interpersonal Sensitivity in Bipolar II: A 557-Case Study

Franco Benazzi, M.D., *Department of Psychiatry, NHS Forli, Via Pozzetto 17, Cervia, RA 48015, Italy*

Summary:

Objective: Affective temperaments (mainly cyclothymic temperament) are common in bipolar II disorder (Akiskal, 1996). Reported links with social phobia (Himmelhoch, 1998) suggest that social anxiety personality traits might also be common in bipolar II disorder. Aim of the study was to find the prevalence of interpersonal rejection sensitivity (a personality trait among DSM-IV atypical features) in bipolar II disorder compared with unipolar depression.

Method: 557 consecutive unipolar (major depressive/dysthymic disorders) and bipolar II disorder outpatients, presenting for major depressive episode treatment during the last two years, were interviewed by the author during the first visit with the Structured Clinical Interview for DSM-IV Axis I Disorders-Clinician Version, and the Global Assessment of Functioning Scale. DSM-IV text definition of interpersonal rejection sensitivity was followed. Often, family members or close friends supplemented the clinical information during the interview. Statistics were calculated with STATA 5 statistical software.

Results: Interpersonal rejection sensitivity was significantly more common in bipolar II than in unipolar patients (37.8% vs 20.5%, odds ratio 2.3, $p = 0.0000$). Sensitivity and specificity for bipolar II diagnosis were 37.8% and 79.4%.

Conclusions: Interpersonal sensitivity seems common in bipolar II disorder, and could be a clinical marker for its diagnosis, with high specificity.

NR496 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Female Depression and Menopause

Franco Benazzi, M.D., *Department of Psychiatry, NHS Forli, Via Pozzetto 17, Cervia, RA 48015, Italy*

Summary:

Objective: Menopause - depression association is unclear. Study aim was to compare female depression with onset before and after menopause, to find if endocrinological changes had impact on depression.

Methods: 512 consecutive unipolar bipolar I/II depressed outpatients interviewed with DSM-IV Structured Clinical Interview, Montgomery Asberg Depression Rating Scale, Global Assessment of Functioning scale, and divided in patients with depression / mania onset before 40, and after 40.

Results: Female depression with onset after 40 had significantly higher age / age at onset, shorter duration, fewer recurrences, fewer atypical features, fewer bipolar II, more unipolar, and less axis I comorbidity, than female depression with onset before 40. Male depression with onset after 40 had significantly higher / age at onset, shorter duration, fewer atypical features, and less axis I comorbidity, than male depression with onset before 40.

Conclusions: Female depression with onset after 40 had significantly more unipolar and fewer bipolar II patients, than female depression with onset before 40, a finding not observed in males. Different frequency of mood disorders, with partly different biology, suggests that biology of depression in menopause women may be different from that of non-menopause women. Differences may be related to endocrinology of menopause.

NR497 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

A Comparison of Three Self-Rating Scales for Acute Mania

Edward G. Altman, Psy.D., *Department of Psychiatry, Univ. of Illinois, ROOM 614-N, 1601 West Taylor Street., Chicago, IL 60612;* Donald Hedeker, Ph.D., James L. Peterson, B.S., John M. Davis, M.D.

Summary:

Objective: Three self-rating mania scales, The Internal State Scale (ISS), the Self-Report Manic Inventory (SRMI), and the Altman Self-Rating Mania Scale (ASRM), were compared together in a sample of acutely disturbed bipolar manic patients. The rationale was to evaluate their relative sensitivities for detecting acute mania, and, to provide objective criteria for their use in clinical and/or research settings.

Method: Forty-four adult inpatients with a diagnosis of bipolar disorder, manic or mixed, completed all three scales shortly after admission, and 31 patients completed them again after 4–6 weeks of pharmacotherapy. Patients were also rated by clinicians on the CARS-M at the same time:

Results: At baseline, scores on the ASRM and the ISS well-being subscale were significantly correlated with clinician-administered CARS-M scores. Post-treatment scores were significantly decreased for the ASRM, SRMI, and the ISS activation subscale. The sensitivities for each scale to correctly identify patients with acute symptoms was 45% for the ISS, 86% for the SRMI, and 93% for the ASRM. Self-rating scores were unrelated to patients' insight into their illness.

Conclusions: Overall, the ASRM and SRMI were more sensitive than the ISS for detecting acute symptomotology in patients with bipolar disorder. All three self-rating measures were sensitive to

treatment effects. However, the item content of the SRMI and the poor sensitivity of the ISS may limit their utility in inpatient settings. When considering all outcome measures together, the ASRM appears to offer some advantages over the others.

NR498 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Comorbidity of Headache and Depression in a Cohort of Patients with Mood Disorders

Sally J. Czaja, Ph.D., *Department of Psychiatry, NJ Medical School, 30 Bergen Street, Newark, NJ 07107-3000;* Donald S. Ciccone, Ph.D., Gerald S. Leventhal, Ph.D., Myron L. Pulier, M.D., Eric Anderson, Ph.D., Rhonda Matlack, M.A., Steven J. Schleifer, M.D.

Summary:

Objective: Recent studies show that many patients with major depression suffer from comorbid headache. The present study addresses the following questions: (1) How prevalent are headaches among patients with clinical depression?; (2) How much of the variance in headache frequency is explained by individual differences in mood?; (3) Do mental health services for depression serve to reduce headache frequency?

Method: Data were drawn from an existing archive of 672 consecutive adult outpatient referrals who met diagnostic criteria for mood disorder (single or recurrent major depression, dysthymia) and completed initial and follow-up questionnaires.

Results: At enrollment, 44% of females and 22% of males reported moderate to marked headache frequency in the past month, χ^2 (1) = 29.8, $p < .000$. After controlling for age, depression accounted for 15% of the variance in headache frequency for females and 9% of the variance for males. Corresponding F tests for ΔR^2 were 83.9 for females and 20.1 for males, both p's $< .000$. A repeated measures analysis of variance, with headache frequency as the dependent measure, revealed a significant gender-by-treatment interaction with females deriving more benefit from mental health services than males, $F(1,670) = 4.3$, $p < .05$. Moderate to marked headache frequency was reported by 30% of patients whose depression responded to treatment compared to 44% of non-responders, χ^2 (1) = 8.3, $p < .01$.

Conclusions: Headaches were more prevalent among females with mood disorders than males. Females responded better (reported fewer headaches) than males following treatment for depression. Overall, patients whose mood improved after treatment (responders) had fewer headaches than patients who did not improve.

NR499 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Treatment Effects of Medical Comorbidity on Late-Life Depression

David W. Oslin, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, room 790, Philadelphia, PA 19104;* Thomas R. Ten Have, Ph.D., Michael J. Kallan, M.S., William S. Edell, Ph.D.

Summary:

Previous studies have demonstrated a synchrony between major depression and physical disability in late life. However, there have been few studies that have been able to demonstrate clear effects of specific medical illnesses and the treatment of late life depression. A sample of 671 elderly patients who received inpatient treatment for depression was evaluated at entry into the hospital and 3 months after discharge. As previously reported, physical disability and the total number of medical illnesses were significantly related to change in depressive symptoms. Moreover, the presence of arthritis, circulatory problems, or a skin problem was related to a worse outcome. The effect of these problems was both statistically and clinically significant. After accounting for pretreatment disability, arthritis and skin problems continued to a predict a worse outcome. However, accounting for the residual disability after treatment mediated the effects of each of the diseases. The results of this study are supportive of the role that pain and vascular disease play in the development of depression in late life.

NR500 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Clinical, Humanistic and Economic Outcomes Associated with Long-Term Olanzapine Treatment of Mania

Madhan Namjoshi, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285;* Gopalan Rajamannar, Ph.D., Thomas G. Jacobs, M.A., Peter D. Feldman, Ph.D., Todd M. Sanger, Ph.D., Mauricio F. Tohen, M.D., Alan F. Breier, M.D.

Summary:

Objective: To determine the clinical, humanistic, and economic outcomes associated with a novel antipsychotic olanzapine in the treatment of mania.

Methods: Patients with a confirmed diagnosis of mania were randomized to either olanzapine (5–20mg) or placebo for 3 weeks, followed by a 49-week open label extension phase in which all patients were treated with olanzapine. The Young Mania Rating Scale (Y-MRS) and the Medical Outcomes Study Short Form 36 (SF-36) were used to assess changes in clinical and humanistic outcomes respectively.

Results: Patients experienced a statistically significant mean improvement in clinical symptoms over 49-weeks. Statistically significant improvements were seen in the scores on several dimensions of the SF-36 during the open label phase. When compared to the direct costs incurred by patients in the 52 weeks prior to the study, the patients saved a mean of $902.29 per month during the 49 weeks of olanzapine therapy.

Conclusion: Olanzapine has a positive impact on the clinical, humanistic, and economic outcomes in patients with mania, and could be considered a cost-effective treatment option for manic disorders.

NR501 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Economic Aspects of Nefazodone, Cognitive Behavioral Analysis System of Psychotherapy and Their Combination for the Treatment of Chronic Depression

James M. Russell, M.D., *Department of Psychiatry, University of Texas, 301 University Blvd Route 0197, Galveston, TX 77555-0197;* William H. Crown, Ph.D., Madhukar H. Trivedi, M.D., John C. Markowitz, M.D., Rachel E. Manber, Ph.D., Bruce A. Arnow, Ph.D., Frances E. Borian, M.B.A.

Summary:

Objective: Results from a recent trial suggest that combination of nefazodone and Cognitive Behavioral Analysis System of Psychotherapy (CBASP) is more efficacious than either modality alone in the treatment of chronic depression (Keller *et al.,* 1999). This preliminary analysis assesses economic aspects of these treatment alternatives.

Methods: Outcomes data from the 12-week acute phase of a 12-site trial investigating the therapeutic efficacy of nefazodone, CBASP, and their combination using symptom and functional metrics as well as medical claims cost data encompassing 1.4 million lives (MarketScan®, The MEDSTAT Group) are combined. Claims data are used to attribute costs to clinical interventions. Economic benefits of treatment are calculated by multiplying income and

proportional changes in functional capacity. Modified versions of the Social Adjustment Scale (SAS), SF-36, and L.I.F.E. are used to determine functional capacity.

Results: Work impairment improved significantly for all groups, but is greatest for combination therapy ($p < 0.02$). This pattern is also observed for the overall SAS score ($p < 0.001$). Baseline to week 4 differences in overall SAS demonstrate significantly greater improvement for nefazodone mono-therapy compared to CBASP mono-therapy ($p = 0.032$). Conservative estimates of mean direct treatment costs per patient, irrespective of response, are $770 (nefazodone), $1800 (CBASP), and $2500 (combination). Estimated mean direct treatment costs per acute responder are $1700 (nefazodone), $4000 (CBASP), and $3400 (combination).

Conclusions: Combination treatment is most efficacious. Direct treatment costs per acute responder are lowest for treatments using nefazodone. Further cost-effectiveness results incorporating variation in time-to-response, other direct costs, and economic benefits associated with treatment will also be presented.

NR502 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Impact of Depression and Perceived Stress on Obstetrical Complications

Claudia L. Baugh, B.A., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Ste 4003, Atlanta, GA 30322;* Kelley A. Calhoun, B.S., Kevan Sternberg, B.S., Donald J. Newport, M.D., *Zachary N. Stowe*, M.D.

Summary:

The impact of depression on obstetrical outcome remains an important facet of the risk benefit assessment in the treatment planning for mental illness during pregnancy. Previous studies have demonstrated that depressive symptoms in pregnancy may be associated with lower birth weight infants, small for gestational age, and pre-term delivery. Similarly stress and major adverse life events have been associated with poor prenatal care and a higher rate of obstetrical complications. However, the majority of these studies have been obtained from a lower socio-economic groups. The present study represents an attempt to isolate the potential effects of depression both 'state' and 'trait', as well as stress on obstetrical outcome. The study involved 334 pregnant women with a history of depression referred to the Emory University Pregnancy and Postpartum Mood Disorders Program. Of these women, 75 women completed >3 follow up visits across pregnancy and obstetrical records had arrived. The women (age 32.2 ± 4.7 years) represented a homogenous group of subjects with >90% married and all with a history of major depression (MDE). Group A consisted of women who remained euthymic (BDI < 9) through out pregnancy; Group B experienced mild to moderate depressive symptoms ($9 \leq BDI \leq 16$); and Group C experienced severe depressive symptoms during pregnancy (BDI > 16, 29 ± 9.0). A total of 34 obstetrical complications were identified and were equally distributed across the three groups. There were no alterations in serum estradiol (E2), progesterone (P), and prolactin between the three groups or associated with complications. Similarly, there was no association between obstetrical complications and peak BDI and/or peak PSS scores.

NR503 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

A Survey of Prescribing in the Treatment of Depression

Timothy J. Petersen, Ph.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman St., WACC 812, Boston, MA 02114;* Christina M. Dording, M.D., Rebecca A. Kornbluh, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Background: With the increasing number and type of antidepressants available to clinicians, there is a need to better understand current prescribing practices and to what degree these practices reflect research findings.

Objective: The purpose of this study was to examine prescribing practices in a sample of psychiatrists attending a psychopharmacology review course.

Method: 439 of 800 clinicians asked (55%) responded to a 15-item questionnaire that was given prior to beginning the review course. Items covered three major content areas: first line preferences in the treatment of certain depression, antidepressant agents most associated with certain side effects, and first line preferences in the treatment of certain depressive subtypes.

Results: 214 (49%) clinicians indicated a belief that one antidepressant type is more efficacious than others. Of these 214 clinicians, 103 (48%) indicated SSRIs as being most efficacious, while 53 (25%) indicated venlafaxine as being most efficacious. 378 (93%) clinicians indicated SSRIs as their first line treatment preference. Mirtazapine (56%) was endorsed as most likely to be associated with weight gain; fluoxetine (57%) with sexual dysfunction; paroxetine (48%) with a discontinuation syndrome; and fluoxetine (52%) with agitation. For the treatment of anxious, atypical and melancholic depression, SSRIs were the first choice of treatment (58%, 57%, and 57%), and for depression with prominent insomnia mirtazapine and nefazadone (31% and 27%, respectively) were the first choices of treatment.

Discussion: Despite the lack of evidence of a significant difference in efficacy between older and newer agents, clinicians perceive the newer agents to be more efficacious than the older drugs (TCAs and MAOIs), even in the melancholic and anxious depressive subtypes. Similarly, although sexual dysfunction and agitation appear to occur at similar rates with all the SSRIs, fluoxetine was perceived to be most likely to cause these side effects. The significance of these discrepancies between empirical evidence and clinicians' perceptions will be discussed.

NR504 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Medication Noncompliance in Bipolar Disorders

Joseph F. Goldberg, M.D., *Department of Psychiatry, Payne Whitney-NYPresbyterian, 525 East 68th Street, New York, NY 10021*

Summary:

Objective: Pharmacotherapy noncompliance arises in half or more of bipolar patients and contributes importantly to affective relapse, yet little is known about its etiologies and clinical correlates. We assessed patient attitudes toward different mood stabilizers and factors associated with high or low treatment compliance.

Method: 31 patients from the adult Bipolar Disorders Clinic of New York Presbyterian Hospital completed a survey of attitudes about thymoleptic drugs, side effects, and compliance patterns.

Results: Approximately 25% of patients missed ≥3 mood stabilizer doses/month, regardless of drug type. Over 80% of patients rated divalproex as effective, as did 63% regarding lithium and 64% regarding carbamazepine. Patients' rank ordering of factors influencing medication adherence included: 1) drug effectiveness, 2) side effects, 3) the desire not to take medications for mood, 4) the ability to take only 1 drug, and 5) cost. Significant side effects were perceived to be more common with lithium (41%) than divalproex (19%) or carbamazepine (0%) ($p < .05$). Noncompliance was associated with prior treatment nonresponses, psychosis when manic, and chronic polypharmacy ($p < .05$).

Conclusions: Noncompliance may arise in a significant minority of bipolar patients treated long-term in an academic medical center. For a majority of bipolar patients, mood stabilizer efficacy may supercede concerns about adverse effects or unwanted treatment consequences.

NR505 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Evolution of Polypharmacy in Bipolar Disorders

Joseph F. Goldberg, M.D., *Department of Psychiatry, Payne Whitney-NYPresbyterian, 525 East 68th Street, New York, NY 10021*

Summary:

Objective: Clinicians often prescribe polypharmaceutical regimens for bipolar patients, yet little empirical data exist on the use of multi-drug regimens in the course of routine treatment. We compared characteristics of bipolar patients receiving 1 vs. ≥2 mood stabilizers, and assessed their successive vs. simultaneous use.

Method: 37 patients were drawn from the Bipolar Disorders Clinic of New York Presbyterian Hospital. Lifetime medication histories were obtained by patient interviews with corroboration from hospital records.

Results: Lifetime, 54% of patients simultaneously took ≥2 mood stabilizers (i.e., lithium, divalproex, carbamazepine, gabapentin, lamotrigine, and/or topiramate) (mean = 2.6 ± 0.8 trials; mean # simultaneous mood stabilizers = 2.5 ± 0.4). Forty-three percent received their first 2 mood stabilizers simultaneously while 57% had successive trials. The average time from a 1st to 2nd mood stabilizer was longer (55.4 months) than the time from a 2nd to 3rd (20.5 months) or a 3rd to 4th (13.3 months) ($p < .05$). Concomitant mood stabilizers were added less often among patients taking divalproex (48%) than lithium (66%), and fewer subsequent mood stabilizers were added after beginning divalproex than lithium ($p < .05$). Mood stabilizers were used *simultaneously* more often than *successively* in patients with histories of psychotic mania or substance abuse, and longer durations of lifetime illness ($p < .05$).

Conclusions: Multiple mood stabilizers are used at some point for most bipolar patients, typically among those who are more severely ill, and later rather than earlier in the longitudinal course of illness. Prescribers may be inclined to switch mood stabilizers more quickly after each successive trial.

NR506 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Intermittent Luteal Phase Dosing of Sertraline Is Effective in Premenstrual Dysphoric Disorder

Uriel Halbreich, M.D., *Biobehavioral Department, University of Buffalo, 462 Grider Street, BB170, Buffalo, NY 14215-3098;* Richard Bergeron, M.D., Anna Stout, Ph.D., Ellen W. Freeman, Ph.D., Kimberly A. Yonkers, M.D., Teri B. Pearlstein, M.D., Wilma M. Harrison, M.D.

Summary:

Objective: SSRIs such as sertraline and fluoxetine have been shown to be effective in the treatment of Premenstrual Dysphoric Disorder (PMDD) in several placebo controlled trials with medication administered daily throughout the menstrual cycle[1,2]. Women seeking treatment for PMDD may prefer to restrict the use of medication to the luteal (symptomatic) phase of the menstrual cycle to avoid potential side effects during their symptom-free time each month. The purpose of this large, multicenter, placebo controlled study was to evaluate efficacy and tolerability of sertraline for PMDD when dosed only in the luteal phase of the menstrual cycle.

Method: 281 women with DSM IV defined PMDD were randomly assigned to luteal phase sertraline (50–100 mg daily) or placebo for 3 menstrual cycles after a single blind placebo lead-in period. Assessments included Daily Rating of Severity of Problems (DRSP), luteal phase Hamilton Depression Scale (HDRS), Social Adjustment Scale, and CGI-Sand/I each cycle.

Results: Sertraline was significantly superior to placebo for treatment of PMDD when dosed intermittently (luteal phase), as shown by the CGI-Sand/I change from baseline ($p < 0.001$ for each) and proportion of responders (CGI ≤ 2) [$p < 0.01$] and other ratings. Results will also be presented for daily ratings, HDRS, and psychosocial adjustment.

Conclusion: Sertraline was well tolerated and effective when dosed intermittently for PMDD.

NR507 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Long-Term Treatment of Depression with Bupropion Sustained Release

Karen L. Weihs, M.D., *Department of Psychiatry, G.W. University Medical Center, 2300 Eye Street NW, Washington, DC 20037;* Trisha Houser, B.A., Sharyn R. Batey, Pharm.D., John A. Ascher, M.D., Carolyn Bolden-Watson, Ph.D., Rafe M.J. Donahue, Ph.D., Alan Metz, M.D.

Summary:

Objective: To evaluate the safety and efficacy of bupropion sustained release (SR) for the long-term treatment of depression.

Methods: Eligible subjects were treated with bupropion SR (300mg/day) during an 8-week Open-Label Phase (OLP). Responders to treatment (Clinical Global Impressions Scale of Improvement of 1 or 2 for the 3 weeks prior to randomization) entered a 44-week randomized, placebo-controlled Double-Blind Phase (DBP).

Results: The majority of the approximately 800 subjects who entered the OLP were white (87%), female (68%), with an average age of 39 years, and a diagnosis of moderate recurrent depression. Over half of these subjects (52%) met criteria and entered the DBP. Mean HAMD scores for these subjects decreased from 24.1 at Baseline to 4.0 at the end of the OLP. Subjects entering the DBP were comparable to the overall population with respect to their demographic and psychiatric profiles. Bupropion SR was well tolerated; adverse events accounted for 9% and ≤2% of discontinuations from the OLP and DBP, respectively.

Conclusion: This is the first long-term treatment study of depression with bupropion SR; results indicate that long-term (maintenance) treatment with bupropion SR is well tolerated.

NR508 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Anxiety and Response to Bupropion Suspended Release or Sertraline

A. John Rush, M.D., *Department of Psychiatry, UT Southwestern Medical Center, 5323 Harry Hines Blvd, Ste 9086, Dallas, TX 75235-9070;* Madhukar H. Trivedi, M.D., Sharyn R. Batey, Pharm.D., Rafe M.J. Donahue, Ph.D., Thomas J. Carmody, Ph.D., Trisha Houser, B.A., John A. Ascher, M.D.

Summary:

Objective: To determine whether pretreatment anxiety levels in patients with major depressive disorder (MDD) were associated with preferential antidepressant response to bupropion sustained release (SR) or sertraline and to determine whether and when reductions in symptoms of anxiety occurred.

Methods: A *post hoc* analysis was conducted on a 16-week randomized, double-blind study comparing bupropion SR (n = 122) and sertraline (n = 126) in outpatients with MDD. Antidepressant response and clinically significant anxiolysis were defined by

≥50% reductions in baseline HAMD and HAMA scores, respectively.

Results: Bupropion-SR and sertraline had comparable antidepressant and anxiolytic activity according to reductions from baseline HAMD scores (−15.5 bupropion-SR; −16.3 sertraline) and HAMA scores (−9.8 bupropion-SR; −10.1 sertraline). Baseline anxiety levels did not differentiate responders to bupropion SR from responders to sertraline and were unrelated to antidepressant treatment response. Survival analyses failed to reveal significant between-drug differences in time to onset of anxiolysis, and ANOVAs failed to reveal significant differences in anxiety levels over the multiple time periods.

Conclusion: Bupropion-SR and sertraline had comparable antidepressant and anxiolytic activity. The results from this analysis emphasize the unreliability of selecting antidepressant agents based on levels of baseline anxiety or on anticipation of more rapid anxiolysis.

NR509 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Mood Stabilization with Lamotrigine in Rapid-Cycling Bipolar Disorder

Nancy L. Earl, M.D., *Glaxo Wellcome, 5 Moore Drive, Research Triangle, NC 27709;* Paul Greene, John A. Ascher, M.D., Chai-Ni Chang, Gary S. Sachs, M.D., Terence A. Ketter, M.D., Alan C. Swann, M.D.

Summary:

Objective: Lamotrigine (LTG), an established antiepileptic drug, is currently under investigation for the treatment of bipolar disorder. The open label phase of this study examined the efficacy of lamotrigine in stabilizing Bipolar I and II patients with a recent history of rapid cycling.

Methods: Study GW#614 enrolled 326 rapid cycling bipolar patients into an initial open-label stabilization phase, during which LTG was added to current treatment. Subjects experiencing clinical response were discontinued from other medications and, if stable (HAMD-17 score <14 and Mania Rating Scale score of <12 for the last 2 weeks of the 8–12-week open phase) were subsequently randomized to monotherapy with LTG or placebo for 6 months.

Results: The majority of patients enrolled were in a depressed episode at screening. Of the intent-to-treat sample enrolled, the rate of mood stabilization and randomization after LTG treatment was 56% with comparable efficacy across patients with differing polarities at study entry.

Conclusion: The open label data from this phase of the study suggest that LTG is effective in the stabilization of patients with rapid cycling bipolar disorder and may be a useful treatment alternative for these difficult to treat patients.

NR510 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

A Comparison of Atypical Antipsychotic Agents As an Adjunct to Mood Stabilizers in Rapid-Cycling Bipolar Disorder

Christina M. Demopulos, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, 5th floor, Boston, MA 02114;* S. Nassir Ghaemi, M.D., Aysegul Yildiz, M.D., Gabriele Sachs, M.D.

Summary:

Objectives: 1) To determine the overall treatment outcome of adjunctive atypical antipsychotics in rapid cycling bipolar disorder; and 2) To compare the treatment outcomes between adjunctive atypical antipsychotics, risperidone, quetiapine and olanzapine in rapid cycling bipolar disorder.

Methods: The charts of patients with rapid cycling bipolar disorder receiving atypical antipsychotic treatment were reviewed. Gender, age, bipolar type, history of first rank psychotic symptoms, type and duration of atypical antipsychotic (AAP) therapy and concomitant medication use at initiation of AAP were recorded. Clinical Global Impression and GAF scores were obtained at treatment baseline and endpoint and change in CGI and GAF was calculated.

Results: The percent of those taking risperidone, quetiapine or olanzapine was 44% (n = 11), 24% (n = 6) and 32% (n = 8) respectively. Mean duration and dosing respectively, for Risperidone was 23.6 ± 14.6 wks,; 1.96 ± .10 mg; Quetiapine 20.0 ± 17.4 wks, 162.5 mg ± 130.5 mg; Olanzapine 35.9 ± 27.7 wks, 14.7 mg ± 12.9 mg. The overall mean improvement in the CGI trended toward significance and in the GAF was significant (t-test; p = .10, p = .002 respectively). All three AAP agents were equally effective (anova; ΔCGI; p = .50; ΔGAF; p =. 42). Only 36% percent of cyclers had a history of psychosis.

Conclusion: These preliminary findings show that overall rapid cycling bipolar patients had an improvement in course with AAPs. Comparing AAPs, there were no significant differences in improvement between agents. Consistent with the literature this report suggests that a greater proportion of rapid cyclers do not have a history of significant psychotic symptoms. A larger sample population will be examined to determine the significance of these findings.

NR511 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Solar Eclipse Induces Rapid Mood Changes

Belso Nora, M.D., *National Institute of Psychiatry, huvosvolgyi Ut 116, Budapest 1021, Hungary;* Szili Ilona, Rihmer Zoltan, M.D., Mirnics Zsuzsa

Summary:

Objective: Mood changes of hospitalized and drug-treated inpatients with DSM IV diagnosis of major depression at the time of total Solar Eclipse (SE) (11. Aug. 1999.) in Hungary was investigated.

Hypothesis: the SE induces rapid mood changes in these patients.

Method: 14 inpatients (5 males, 9 females) who were diagnosed as mild or moderate major depression were included. The patients were rated three times: 24 hours before, at the time, and 24 hours after the SE (Zung Self Rating Depression Scale and 17-item version Hamilton Depression Rating Scale was made).

Results: While at the time of SE the patients reported subjective mood improvement on the Zung scale (mean scores: 57,1 *50,1* and 56,8 resp.) the objective evaluation of their mood showed a slight worsering (mean Hamilton scores: 21,0 *24,1* and *20,3 resp.*).

Conclusions: The objective worswering of depression may be relate to the light deprivation at an unusual time ("darkness at noon"), while the mild subjective improvement of the mood may be the reflection of a placebo response (positive expectations regarding to the SE).

Limitations: because of the small number of the patients, this study needs replication at the time of next total Solar Eclipse.

NR512 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Risperidone for Acute Mania: Focus on Safety

Charles L. Bowden, M.D., *Department of Psychiatry, University of TX Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7792;* Gary S. Sachs, M.D.

Summary:

Objectives: This poster will examine the safety of the atypical antipsychotic risperidone as add-on therapy for the management of bipolar disorder.

Methods: A randomized, controlled, double-blind three-week trial comparing the safety and efficacy of risperidone versus placebo added to either lithium or valproate for the management of acute mania in BD.

Results: The most common treatment emergent adverse events (TEAEs) of risperidone add-on treatment with either lithium or valproate included somnolence, headache, dyspepsia, EPS, dizziness, constipation, and tremor. Two of 52 patients (3.8%) receiving risperidone add-on therapy experienced serious TEAEs, including anxiety, tachycardia, and an increase in creatine phosphokinase. Four of 51 patients receiving placebo (7.8%) and 4 of 53 patients (7.5%) receiving haloperidol add-on therapy experienced serious TEAEs. None of the 52 patients receiving risperidone experienced an induction of mania during the double-blind trial.

Conclusions: Risperidone (1–6 mg/day) add-on therapy was statistically significantly more effective in reducing symptoms of mania than monotherapy of lithium or valproate ($p = 0.009$). Risperidone is a safe and effective agent when added to valproate or lithium for the acute treatment of BD.

NR513 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

A Single-Blind Trial Assessing the Effectiveness/ Efficacy of Fluoxetine Versus Sertraline for the Treatment of Major Depression

Rita A. Suri, M.D., *UCLA, 300 UCLA Medical Plaza, #2200, Los Angeles, CA 90095;* Lori L. Altshuler, M.D., Natasha Rasgon, M.D., Jeffrey Calcagno, M.D., Mark A. Frye, M.D., Michael J. Gitlin, M.D., Sun Hwang, M.D.

Summary:

Method: A randomized, single- blind, parallel- group study of 10 weeks duration comparing the efficacy of sertraline (50- 200 mg/day) and fluoxetine (20–40 mg/day) was conducted in 44 psychiatric outpatients with DSM- IV major depression. Primary efficacy measurements consisted of the 21- item Hamilton Rating Scale for depression and the Clinical Global Impression scale. A positive response was defined as remission (HAM- D score </ = 7 and a CGI score of </ = 2).

Results: Overall response rates at six weeks of treatment were 21% for sertraline 50 mg, 43% for sertraline 100 mg, and 31% for fluoxetine 20 mg. At four weeks of treatment, response rates were 0% for sertraline 50 mg, 46% for sertraline 100 mg, and 31% for fluoxetine 20 mg. For subjects with a doubling of antidepresant dose at week 6, response rates at week 10 (four weeks on increased dose) were 40% for sertraline 100 mg, 43% for sertraline 200 mg, and 55% for fluoxetine 40 mg.

Conclusions: Sertraline 50 mg, sertraline 100 mg, and fluoxetine 20 mg demonstrated response rates that were not significantly different ar six weeks of treatment. Subjects on sertraline 100 mg and fluoxetine 20 mg demonstrated an earlier response (some improved by four weeks), compared to subjects on sertraline 50 mg. Fpr patients without a positive response at six weeks, an increased antidepressant dose resulted in remission, when assessed four weeks later, for a substantial proportion of patients.

NR514 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

A Naturalistic Study of Mirtazapine in Mexican Psychiatric Practice

Herben J. Harmsen, M.D., *CNS Department, Organon Miexicana, CALZ DE CAMARONES 134, Mexico City, MX 02870, Mexico;* Ilse Van Hensbeek, M.D.

Summary:

Aim: To assess efficacy and tolerability of mirtazapine (30–60 mg/day) in depressed patients in an open-label non-comparative naturalistic study.

Methods: Depressed outpatients were included by psychiatrists and assessed at baseline and after 1, 2-3 and 6 weeks of treatment. Sexual functioning was assessed by ASEX and efficacy by CGI on the ITT group using the LOCF method. Treatment-emergent adverse events were registered. Descriptive statistics and the Wilcoxon test (for CGI and ASEX) were used.

Results: Out of 667 depressed patients, 94.7% was moderate to severely ill; furthermore, 84.6% suffered from sleep disturbances and 69.2% of sexually active patients (n = 343) showed sexual dysfunction at baseline. 39% of patients switched from another antidepressant because of lack of efficacy (78.8%) or due to adverse events (20.8%). The mean dose was 33.1 mg/day. In total, 19.6% of patients dropped out; only 8.5% because of adverse events and 0.7% due to lack of efficacy. Depressed mood as assessed on the CGI was very much or much improved at endpoint in 84.6% of patients. Mean score of severity of illness was significantly reduced from day 7 onwards ($p < 0.0001$). Adverse events reported with an incidence higher than or equal to 5% were somnolence (28.3%), weight increase (6.0%) and dry mouth (5.2%). Patients without sleep disturbances increased from 15.4% at baseline to 90% at study-endpoint. The number of patients with sexual dysfunction decreased from 69.2% at baseline to 25.9% after 6 weeks of treatment. The improvement was highly significant ($p < 0.0001$) on each factor of sexual functioning: drive, arousal, lubrication/erection, orgasm and satisfaction with orgasm.

Conclusions: mirtazapine is an effective and well-tolerated antidepressant with additional beneficial effects on sleepimprovement and sexual functioning.

NR515 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Primary Prevention of Schizophrenia

Ernest H. Friedman, M.D., *1831 Forest Hills Boulevard, East Cleveland, OH 44112-4313;* Gary G. Sanders, B.S., Diane A. Sedlak, B.A.

Summary:

Early antecedents of selective deficits in early-stage sensory processing in schizophrenia, a failure to support the entrainment of intrinsic gamma-frequency oscillators (40 Hz), are suggested by short-term laboratory experience demonstrating that adult female speech production is sufficient to influence infant speech production occurring in the silent intervals between the adult vocalizations on the order 3 seconds that is linked with increased coherence of gamma-band EEG activity that is associated with the execution of more complex tasks. Infant speech production involves linguistic processing and associative learning through increases in effective connectivity between distinct cortical systems. This hypothesis is supported by nongenomic transmission across generations of maternal behavior and stress responses beginning in the first week of life which is anticipated by the influence of maternal rhythms on the fetus. Therefore, early interventions to prevent neurocognitive defects (at least those of a sensory and perceptual nature) are needed to establish effective cortical oscillations during pregnancy. Running enhances neurogenesis, learning and long-term potentiation, and auditory feedback of rhythmic events promotes attention to temporal signals that highlight significant stimuli and may rejuvenate the brain. These strategies are facilitated by the remarkable neural plasticity that is inherent in reproduction itself and underlies subsequent behavioral changes, particularly those unique to late pregnancy and the postpartum period.

NR516 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Treatment of Bipolar Depression: Clinical and Economic Outcomes

Lynda Bryant-Comstock, *M.P.H., Global Health Outcomes, Glaxo Wellcome, 5 Moore Drive, p o box 13398, Research*

Triangle, NC 27514; Dell B. Mather, Todd A. Lee, Paul E. Keck, Jr., M.D., Hong Li, Ph.D., Sean D. Sullivan, Ph.D.

Summary:

Objectives: To estimate and compare the clinical and economic outcomes of treatment for bipolar patients experiencing an acute depressive episode.

Methods: A discrete-state transition model of bipolar disorder and its treatment was utilized for multiple simulation runs using 1000 patients over a 52-week period. The treatment algorithm, developed using consensus guidelines and expert panel opinion, models the use of lamotrigine, lithium, carbamazepine and divalproex alone or in combination, and three categories of adjunctive agents. Changes in primary and/or adjunctive medication occur as individuals transition between acute depression, continuation and prophylaxis.

Results: Eighty-nine percent of patients receiving lamotrigine as their initial agent completed the 52-week simulation compared with 83%, 73%, and 79% of patients treated with lithium, carbamazepine, and divalproex-initiated patients. The average annual cost per patient initiated on lamotrigine, lithium, carbamazepine, and divalproex was $7,398, $7,571, $8,610 and $8,854, respectively.

Conclusions: These data suggest that initial lamotrigine treatment for bipolar depression results in more patients remaining on treatment, reduction in the duration of acute episodes and lover average annual treatment costs compared with other agents.

NR517 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Predictive Factors of Chronic PTSD in a One-Year Follow-Up Study of Rape Victims

Jean-Michel Darves-Bornoz, M.D., *Clinique Psychiatrique Univ., Hospital Universitaire, Tours 37044, France;* Jean-Pierre Lepine, M.D., Marie Choquet, M.D., Andree Degiovanni, M.D., Philippe Gaillard, M.D.

Summary:

Objective: This study aimed to investigate the psychological disorders following rape as well as the course of Post-Traumatic Stress Disorder (PTSD), and to determine clinical factors predictive of chronic PTSD.

Methods: Seventy-three rape victims consecutively referred to a forensic center in Tours, France, were observed in a systematic follow-up study over one year following rape using structured interview schedules (ADIS, SI-PTSD, SCID-D and other sociodemographic and clinical questionnaires).

Results: The frequency of PTSD was massive (88% after 1 month, 71% after 3 months, 65% after 6 months, 58% after 1 year). First, the early disorders predicting PTSD one year after rape included somatoform and dissociative disorders, agoraphobia and specific phobias as well as depressive and gender identity disorders and alcohol abuse. In addition, through stepwise logistic regressions, the following features were found to be good models of prediction of chronic PTSD one year after rape: for the characteristics of the traumas, *intrafamily rape, being physically assaulted outside rape,* and *added physical violence during rape;* for the early psychological and behavioral attitudes, *low self-esteem, permanent feelings of emptiness* and *running away;* and for early mental disorders, *agoraphobia* and *depressive disorders.* Finally, among all these predictive factors, *added physical violence during rape, low self-esteem, permanent feelings of emptiness* and *agoraphobia* were shown to constitute a strong model of predictors.

Conclusion: People presenting features such as the predictive factors of chronic PTSD found in the study, should be asked about an history of rape and symptoms of PTSD, and treated with particular attention by health services.

NR518 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Treatment of Impulsive Aggression with Divalproex

Angela M. Hegarty, M.D., *245 Southlawn Avenue, North Great River, NY 11722*

Summary:

Objective: Inmates with a primary diagnosis of personality disorder, are generally referred for psychiatric care because of self and or other directed aggression, that is too severe to be managed in the correctional setting. An important risk factor for this aggressive behavior is affective instability. The anti aggressive effects of divalproex sodium has been reported in diverse patient populations.

Method: 21, incarcerated male patients, referred for hospitalization, primarily because of aggressive behavior, with a primary DSM 4 diagnosis of Borderline Personality Disorder, were treated with divalproex, initially in an inpatient setting. Following discharge, patients were followed within the correctional system, for 6 months. A detailed neuropsychiatric evaluation, was completed in all cases. The dose of divalproex was titrated to, and maintained at a level of 60 to 100 micrograms/ml. The response to treatment was evaluated using clinical data, and the Overt Aggression Scale (modified).

Results: 18/21 patients demonstrated a reduction in the frequency and severity of other directed violence. All patients demonstrated a reduction in subjective irritability.

Conclusions: Divalproex may be useful in the treatment of impulsive aggression in patients with borderline personality disorder.

NR519 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Childhood Trauma Relates to Adult Inpatient Assault

Martha L. Crowner, M.D., *Manhattan Psychiatric Center, Ward's Island, New York, NY 10035;* A. Jonathan Porteus, Ph.D., Konstantina Myrianthopolos, B.A.

Summary:

Recent studies have found that groups of patients with severe mental illness report rates of childhood physical or sexual abuse which are much higher than those for the general population (Greenfield SF et al.). Sequelae of trauma in unselected populations may include violent behavior. In this study we explored the relationship between childhood trauma and assaultiveness in adult psychiatric inpatients using the Childhood Trauma Questionnaire. Of 71 patients 80% were male. Mean age was 40 with range 22 to 60. Sixty-seven percent were diagnosed schizophrenic or schizoaffective. Seventy percent were African-American or Hispanic. The average length of their current admission was 3.9 years, with range 0.9 to 10. Involvement in assaults in year 1 of admission was significantly correlated with reports of childhood physical abuse (partial correlation coefficient = .3339) and sexual abuse (r = .4071). However, the relationship was stronger for assaults on staff (for physical abuse r = .4306, sexual abuse = .5319) and extended to reported emotional abuse (r = .4176), emotional neglect (r = .3452), and physical neglect (r = .2897). These relationships remained after we controlled for length of current admission. Number of assaults on staff was not related to Axis I diagnosis.

NR520 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Risk Factors for PTSD Following Severe Injury

Daniella David, M.D., *Department of Psychiatry, Miami VAMC, 1201 NW 16th Street, Miami, FL 33125;* Karin F. Esposito, M.D., Victoria Bustamante, Psy.D., Thomas A. Mellman, M.D.

Summary:

Background: Posttraumatic Stress Disorder or PTSD contributes substantially to morbidity related to life threatening injuries, yet only a minority of trauma survivors develop the disorder. In this prospective study, we assessed possible early indicators of risk based on studies of other trauma populations and evaluated their relationship to follow-up PTSD status.

Methods: 70 subjects who sustained severe injury due to accident or impersonal assault were recruited from a Level 1 Trauma Center, and evaluated a mean of 10.9 ± 12.8 days from the injury. Subjects were included if they had recall of the trauma, no loss of consciousness at the scene, a Glascow Coma Scale of 15 on admission, no evidence of alcohol and drugs, and no psychiatric disorder in the previous 6 months. Mean age was 37.3 ± 11.6. 60% were male, 20% were White, 19% were Black and 61% were Hispanic. Subjects were assessed in English or Spanish with the Structured Clinical Interview and the Clinician-Administered PTSD Scale for DSM-IV. Subjects also completed self-report measures of coping skills, social support, dissociation, initial reactions and sleep. 44 (63%) of patients were available for 6 week follow-up and were evaluated with a similar battery of instruments.

Results: Ten (23%) patients met full and 9 (20%) met subsyndromal (2 of 3 symptom clusters positive) PTSD criteria at follow-up. Of the candidate risk factors, baseline CAPS severity, and most specifically arousal cluster severity, as well as maladaptive coping mechanisms correlated positively with follow-up CAPS, while social support and use of humor correlated negatively. Peritraumatic dissociation, prior psychiatric disorders and sleep quality were not associated with follow-up PTSD severity.

Conclusion: Risk factors for PTSD following severe injury may be distinct from other settings.

NR521 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Use of Different Typologies in Sexual Homicide

Evangelia Nika, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20246, Germany;* Peer Briken, M.D., Professor Wolfgang Berner

Summary:

We conceptualized a questionnaire with 124 items, which describes the most common characteristics of sexual murderers. The relevance of these characteristics from the concerning literature about sexual homicide was examinated on the basis of psychiatric records. The hypothesis was, that persons that murdered more than once show these characteristics more evident than single murderers. We compared 20 psychiatric records about single sexual murderers with those about 10 repetitive sexual murderers. Planned offenses, chronic isolation, narcissism and tendency to perversity were found more often in persons that murdered more than once. Especially the psychosocial factors were found less often than in the angloamerican literature. More pronounced were the differences between a group of sadistic murderers compared with nonsadistic murderers.

NR522 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Impact of Risperidone on Seclusion and Restraint at a State Psychiatric Hospital

K.N. Roy Chengappa, M.D., *Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213-2593;* Joseph Levine, M.D., Richard Ulrich, M.S., Haranath Parepally, M.D., Jaspreet Brar, M.D., Rebecca Atzert, R.N.

Summary:

To evaluate the impact of risperidone on seclusion and restraint at a state psychiatric facility using a mirror image design. Patients who were hospitalized for at least 3 months, and received risperidone for at least 3 months (to a maximum of one year in either direction) formed the cohort. Those that received the older neuroleptics during the same time period were used to compute secular trends of seclusion and restraint. Seventy-four risperidone treated patients (schizophrenia mainly) experienced statistically significant reductions in the number of seclusion hours (2.2 ± 5.5 to 0.22 ± 0.06) and events (0.23 ± 0.59 to 0.05 ± 0.14) per person-month during risperidone treatment ($p \leq 0.001$). There were similar trends toward reduction in the two restraint parameters during risperidone treatment (not statistically significant). The comparison group also evidenced a trend for decreases in these parameters during the same time period, but the risperidone treated cohort achieved a proportionally greater reduction. These data support the positive impact of risperidone on violence from other studies. Violence and aggression are major factors that affect morale among psychatric patients, staff and institutions. So, any benefit in this regard as a result of risperidone treatment is salutary for patients and families.

NR523 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Psychological Correlates of Assaultive Adolescents

Dwain C. Fehon, Psy.D., *Department of Psychiatry, Yale Psychiatric Institute, 184 Liberty Street, New Haven, CT 06519;* Carlos M. Grilo, Ph.D., Deborah Lipschitz, M.D.

Summary:

Objective: To examine rates of violence exposure and current psychological and behavioral correlates in psychiatrically hospitalized adolescents with a self-reported history of violence perpetration.

Method: One hundred-seven inpatients, aged 12-18 (mean 15.5 years), were administered a battery of psychometrically well-established psychological self-report instruments. Violence exposure was assessed using the Child's Exposure to Violence Checklist (CEVC). Forty-three patients who reported perpetration of violence were compared to 64 patients who denied perpetration of violence.

Results: Perpetrators of violence were significantly more likely than non-perpetrators to report being a victim of violence and a witness of family and community violence ($p < .001$). Perpetrators and non-perpetrators did not differ in their histories of being either the victim or perpetrator of sexual abuse. Perpetrators of violence had significantly higher levels of depression, hopelessness, impulsivity, drug use, dissociation, and PTSD symptomatology ($p < .01$). Correlational analyses with the study group of violence perpetrators revealed that higher levels of PTSD, dissociation, drug use, and impulsivity were significantly associated with higher levels of violence ($p < .01$).

Conclusions: Psychiatrically hospitalized adolescents who reported histories of violence perpetration are characterized by high levels of violence exposure and present with a constellation of internalizing and externalizing psychopathology; higher levels of PTSD symptoms, dissociation, drug use, and impulsivity are associated with higher levels of violence.

NR524 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Partner and Nonpartner Violence and Victimization Among Individuals in Substance Abuse Treatment: General and Gender-Specific Markers of Violence Involvement

Stephen T. Chermack, Ph.D., *Department of Psychiatry, John D. Dingell VAMC, 4646 John R. Street, 11MH, Detroit, MI 48201;* Maureen A. Walton, Ph.D., Bret E. Fuller, Ph.D., Frederic C. Blow, Ph.D.

Summary:

Objective: This study examined past year expressed and received violence among 125 men and 125 women in substance abuse (SA) treatment, and whether markers of violence risk differ depending on gender and relationship type (e.g., partner vs. non-partner relationships).

Method: Participants recruited within 30 days of enrolling in SA treatment completed self-report measures of pretreatment violence, substance use and consequences, demographics, and family/childhood background variables.

Results: Rates of past year partner violence (PV) did not differ by gender (>55% reported PV), although men reported markedly higher rates of non-partner violence (NPV) (men: >65%; women > 40%). Compared to PV, NPV was associated with more demographic and background factors (e.g., childhood aggression and conduct problems, family history of violence). The most consistent correlates of violence across relationship types were age, minority status, drug-related problems, psychiatric distress, and childhood aggression. Only a few gender-specific correlates were identified, most notably witnessing father-to-mother violence was related to received PV only for women.

Conclusions: The results provide important information regarding violence risk markers. Further, the findings highlight that individuals in SA treatment are at high risk for violence, and that targeted screening and intervention approaches for violence should be routine in SA treatment.

NR525 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Previous Exposure to Trauma and the Psychological Effects of Air Disasters

Philippe J.R. Birmes, M.D., *Department of Psychiatry, Hopital Purpan, Place Baylac, Toulouse 31059, France;* Barbara A. Warner, M.D., Laurent J. Schmitt, M.D.

Summary:

Objective: To explore the relationship between the prospective assessment of acute stress and posttraumatic stress symptoms and depression following an air disaster.

Method: 10 plane crash survivors were assessed weekly for the month following the disaster for symptoms of traumatic stress and depression according to DSM-IV criteria. The Impact of Event Scale (IES) was administrated on day 30.

Results: 4 subjects presented with acute stress disorder (ASD), 3 of them with posttraumatic stress disorder (PTSD) at day 30 (IES scores ≥42). There was no relationship between the presence of prior ASD and the development of PTSD at one month. 2 of the victims with PTSD demonstrated comorbid depression; both had experienced previous traumatic life events. 8 subjects were not previously traumatized, only one of them had PTSD while the 2 victims previously traumatized both had PTSD and comorbid depression (Fisher's exact test: p = 0.035).

Conclusion: Traumatized victims of disasters with previous trauma may be more likely to develop PTSD plus depression than those who were not previously exposed.

NR526 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

HPA Axis Dysfunction in Depersonalization Disorder

Daphne Simeon, M.D., *Department of Psychiatry, Mount Sinai Medical Center, One Gustave Levy Pl., Box 1230, New York, NY 10029;* Orna Guralnik, Psy.D.

Summary:

Objective: While hypothalamic-pituitary-adrenal (HPA) axis dysregulation has been well-described in PTSD, it has barely been investigated in the dissociative disorders. Our aim was to investigate HPA axis functioning in depersonalization disorder (DPD).

Method: In Study I, 10 DPD and 8 normal control (NC) subjects were compared in hourly basal plasma cortisol levels from 10 a.m. to 2 p.m. In Study II, 9 DPD subjects without current major depression and 5 NC subjects were compared in 8 a.m. basal plasma cortisol, 24-hour urinary cortisol, and cortisol suppression to 0.5 mg dexamethasone challenge.

Results: In Study I, plasma cortisol levels did not differ between groups at any time point, and did not significantly correlate with dissociation or depression scores. In Study II, plasma and urinary cortisol did not differ between the two groups, but the DPD group demonstrated significantly less cortisol suppression ($t = 2.14$, $df = 12$, $p = .05$). There was a significant negative correlation between suppression and dissociation scores ($r = -.59$, $df = 12$, $p = .03$), which remained significant when controlled for depression scores ($r = -.55$, $df = 11$, $p = .05$). When controlling for depression, basal plasma cortisol was significantly correlated with depersonalization scores ($r = .75$, $df = 11$, $p = .003$).

Conclusions: These preliminary studies demonstrate HPA axis dysregulation in dissociation which distinctly differs from PTSD and merits further investigation.

NR527 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Dissociative Style and Directed Forgetting

Bernet M. Elzinga, M.S.C., *Department of Psychology, University of Amsterdam, Roetersstraat 15, Amsterdam 101 SWB, Netherlands*

Summary:

The hallmark of dissociative disorders is psychogenic amnesia. One hypothesis on amnesia is that dissociative patients may have an increased ability to selectively forget or discard information on a conscious level in order to avoid negative emotions associated with this information. This hypothesis is known as the Cognitive Avoidance hypothesis (Cloitre, 1996). Possibly, the effort to discard emotionally laden material can succeed for conscious memory, but might result in a better imprinting in nonconscious memory.

The Cognitive Avoidance hypothesis was tested in a "Directed-Forgetting" experiment employing dissociative patients (n = 14) and students high (n = 20) and low (n = 23) in dissociative style. Participants were instructed to either forget or remember neutral, sex and threat words. Conscious and nonconscious memory was assessed. Instruction to forget sex, and threat words was expected to reduce conscious but not nonconscious memory performance in dissociative patients. Results were opposite to predictions. Whereas in general the instruction to forget reduced conscious memory performance, dissociative patients were incapable of forgetting sex words when asked to do so. Dissociative patients even remembered (conscious and nonconscious) more to-be-forgotten than to-be-remembered sex words. An alternative construction-hypothesis is proposed that identifies dissociative style with enhanced skills of constructing conscious experiences.

NR528 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Dissociative Proneness and Alexithymia

Bernet M. Elzinga, M.S.C., *Department of Psychology, University of Amsterdam, Roetersstraat 15, Amsterdam 101 SWB, Netherlands;* Bob Bermono, Ph.D., Richard Van Dyck, M.D.

Summary:

Clinicians have observed that traumatized patients with a dissociative coping style tend to fail to discriminate and identify feelings. The concept of 'alexithymia' describes this difficulty that patients may have in identifying and describing feelings. Dissocia-

tion and alexithymia are both known as coping styles to alleviate painful feelings. This study investigated whether these coping styles are interrelated. It was predicted that the relation between dissociation and alexithymia would be partly mediated by current levels of stress and/or by past traumatic experiences. Furthermore, it was hypothesized that dissociation, but not alexithymia, is related to fantasy proneness.

Nine hundred and twelve participants were administered questionnaires measuring dissociation (DIS-Q), alexithymia (TAS-20 and BVAQ), trauma history, and current levels of stress. In line with predictions, dissociation was related to alexithymia, especially to a difficulty to identify feelings. This relation was partly mediated by levels of current stress, but not by a history of trauma. Interestingly, dissociation in this non-clinical group was not related to a trauma history. Furthermore, high dissociative participants were more fantasy-prone than low dissociative participants, whereas fantasy proneness was unrelated to alexithymia. Cross-validation showed that this model was reliable. Consequences of these results will be discussed.

NR529 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Use of a Screening Questionnaire to Detect Sleep Disorders

Thomas Roth, Ph.D., *Sleep Disorders Center, Henry Ford Hospital, 2799 West Grand Blvd., CFP3, Detroit, MI 48202;* Gary Zammit, Ph.D., Clete Kushida, M.D., Karl Dogharamji, M.D., Susan D. Mathias, M.P.H., Daniel J. Buysee, M.D.

Summary:

Objective: Psychiatric-associated sleep disorders remain underdiagnosed in the general population. We developed a screening instrument to assist general practitioners in recognizing sleep disorders, including those psychiatric-related.

Methods: 242 participants from 5 sleep centers and 2 primary care sites (54% male, mean age = 44 years) completed the Global Sleep Assessment Questionnaire (GSAQ), a battery-style questionnaire designed to distinguish among specific sleep disorders. Composite domain scores were computed for each disorder, including, but not limited to, Primary Insomnia (I) Insomnia associated with a Mental Disorder (IME), Apnea (A), Periodic Limb Movement (PLM), and Parasomnia (P). Sensitivity and specificity were estimated using comprehensive clinical diagnosis as the gold standard and mean domain scores as a cutpoint.

Results: Observed frequencies of disorders were 34% (I), 12% (IME), 31% (A), 7% (PLM), and 4% (P). Test-retest reliability was acceptable (ICC 0.59 – 0.89). Pearson correlation coefficients suggested that the GSAQ discriminated between diagnoses. Sensitivity and specificity were 77/57, 90/56, 85/74, 86/62, and 100/46 for I, IME, A, PLM, and P respectively, with scale-by-gender interaction trends noted for I, IME and P.

Conclusions: Preliminary findings suggest that the GSAQ can aid in recognizing sleep disorders. Future studies should be undertaken to characterize its predictive values for the primary care setting.

NR530 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Differential Diagnosis Between Primary Insomnia and Insomnia Comorbid with Mood Disorders

Tung-Ping T. Su, M.D., *Department of Psychiatry, Veterans General Hospital, 201 Shih-pai Road, Taipei 11217, Taiwan;* Wei-Chung Mao, M.D., Ian-Kai Shan, Liling Lin, Ann-Wen Lynn

Summary:

Objective: Our aim is trying to distinguish primary insomnia from insomnia related to mood disorders for better guidance in management and outcome prediction.

Methods: Three groups of our consecutive outpatients with chronic insomnia (n = 113) were categorized; primary insomnia (group 1, n = 40), insomnia with episodic mood symptoms (group 2, n = 32) and secondary insomnia to mood disorders (group 3, n = 41). Several variables, clinical course, and treatment response were compared.

Results: Age and age of onset were found 11 years older in group 1 patients than those in group 2 and 3 ($p < 0.01$). Significantly higher rate of abnormal personality trait was found in group 3 patients (85%) compared with group 1 (43%) and 2 (53%) ($p < 0.001$). Obsessive and avoidant traits were most popular. While none of group 1 and 6% of group 2 patients had previous suicide attempt, 44% of group 3 patients did before ($p < 0.001$). In contrast, 40% of the first-degree relatives in group 1 was observed to have pure insomnia (without contamination of affective disorders) as compared to 20% of those in group 2 and 3 ($p < 0.04$), indicating that pure insomnia was strongly associated with primary insomnia. While 29% of insomniacs displayed episodic pattern along the course, 63% have continuous pattern of insomnia. No differences of clinical course were found between three groups. Despite different medications were given (hypnotics for 70% of group 1 and SSRIs added on hypnotics for 80% of group 3, almost even distribution of the above two regimens for group 2), sleeping hours and quality and mood symptoms were all significantly improved in three groups after one-month treatment.

Conclusions: Age onset, suicide attempt, personality traits and family history of pure insomnia may help the guidance of differential diagnosis and treatment of primary insomnia and insomnia related to mood disorders but clinical course and treatment response did not.

NR531 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Pregabalin Improves Sleep in Neuropathic Pain Patients

Uma Sharma, Ph.D., *CNS-Neurology, Parke-Davis Pharm., 2800 Plymouth Road, Ann Arbor, MI 48105;* Don Iacobellis, Pharm.D., Coleen Glessner, B.S., MaryKay Hes, B.S., Linda Lamoreaux, M.P.H., Robert Allen, M.D., R. Michael Poole, M.D.

Summary:

Methods: Study 1008-014 compared 150 or 600 mg/day pregabalin with placebo and Study 1008-029 compared 75, 300 or 600 mg/day pregabalin with placebo. Patients recorded the extent that neuropathic pain interfered with their sleep daily on an 11-point numerical rating scale.

Results: Mean sleep interference scores at endpoint were significantly reduced for patients receiving 600 mg/day pregabalin ($p = 0.0004$ in 1008-014 and $p = 0.0002$ in 1008-029) and for patients receiving 300 mg/day pregabalin ($p = 0.0001$) compared with patients receiving placebo. These results were consistent with the primary outcome measure-endpoint mean pain- in both trials.

Conclusion: Pregabalin is effective in reducing sleep interference due to neuropathic pain at doses of 300 and 600 mg/day in addition to relieving pain in patients with diabetic peripheral neuropathy.

NR532 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Alexithymia in DSM-IV Disorder: Comparative Evaluation in Somatoform Disorders, Panic Disorder, OCD and Depression

Bettina Bankier, M.D., *Department of Psychiatry, University of Vienna, Waehringer Guertel 18–20, Vienna A-1090, Austria;* Martin Aigner, M.D., Ulrike Demal, MAG, Michael Bach, M.D.

Summary:

Objective: Only a limited number of studies has adressed a direct comparative evaluation of the alexithymia trait in different mental disorders.

Method: In a sample of 297 admittants for behavior therapy (mean age = 35.5 ± 10.8, % females = 60.3), DSM-IV diagnoses were determined using the SCID (DSM-IV), also the TAS-20 was administered.

Results: Seventy-five subjects met DSM-IV criteria for somatoform disorder (SD), 176 for panic disorder (PD), 82 for obsessive-compulsive disorder (OCD), and 53 for depressive disorder (DEP). Subjects with PD exhibited significantly lower TAS-20 total scores (50.2 ± 11.3) as compared with SD (54.2 ± 11.0), OCD (53.7 ± 9.2), and DEP (55.5 ± 12.6). DEP emerged as a significant predictor of the TAS-20 total score ($p = 0.04$), while PD was a significant negative predictor of the TAS-20 ($p = 0.02$). Subfactor 1 was significantly predicted by SD ($p = 0.03$) and a lack of PD ($p = 0.02$) and OCD ($p = 0.02$), and subfactor 3 was significantly predicted by OCD ($p = 0.001$) and DEP ($p = 0.008$), while none of the diagnoses showed a significant (positive or negative) relationship with subfactor 2.

Conclusion: Our data underline the multidimensionality of the alexithymia construct.

NR533 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Clinical Validity of ICD-10 Neurasthenia

Bettina Bankier, M.D., *Department of Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna A-1090, Austria;* Martin Aigner, M.D., Anna Spacek, M.D., Sandra Krones, Ph.D., Michael Bach, M.D.

Summary:

Background: Neurasthenia' was omitted from the DSM-III but is still present in the ICD-10. Therefore, we examined the clinical validity of ICD-10 neurasthenia in a consecutive sample of chronic pain patients.

Methods: 193 subjects were interviewed with the screening instrument for somatoform symptoms (SOMS, Rief et al., 1995): self-rating of 53 medically unexplained somatic symptoms and 11 additional screening questions concerning: illness/phobia, disease conviction, and preoccupation with pain. Operationalized psychiatric diagnoses were assessed according to ICD-10 (WHO, 1993).

Results: The mean age of subjects was 45.1 (SD ± 10.2), 121 subjects were female, 72 male. 37 subjects fulfilled ICD-10 operational criteria for somatization disorder, 78 for somatoform autonom functional disorder, 91 for neurasthenia, 64 for undifferentiated somatoform disorder, 25 for hypochondriasis, 137 for somatoform pain disorder, and 27 for sexual functional disorder. 33% of the subjects who fulfilled the criteria of ICD-10 neurasthenia fulfilled also the criteria of ICD-10 somatization disorder, 66% the criteria of ICD-10 somatoform autonom functional disorder, 69% the criteria of ICD-10 undifferentiated somatoform disorder, 14% the criteria of ICD-10 hypochondriasis, 85% the criteria of ICD-10 somatoform pain disorder, and 14% the criteria of ICD-10 sexual functional disorder.

Discussion: The clinical validity of ICD-10 neurasthenia remains questionable.

NR534 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Somatoform Disorders Symptom Checklist (SDSC): Validation of a German Version in Chronic Pain Patients

Michael Bach, M.D., *Department of Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna A-1090, Austria;* Alexandra Peternell, Ph.D., Martin Aigner, M.D., Bettina Bankier, M.D.

Summary:

Objective: The Somatoform Disorders Symptom Checklist (SDSC, Janca et al. 1994) has been developed as a screening instrument for the early detection of ICD-10 somatoform disorders. The present study aimed to validate a German version of the SDSC in chronic pain patients.

Methods: A sample of 119 chronic pain patients (56% females, mean age: 47.9 ys) was asked to complete a new German version of the SDSC, a 60-items self-rating list of ICD-10 somatoform symptoms. In addition, psychiatric diagnoses were determined using the ICD-10 Diagnostic Criteria for Research (WHO 1993).

Results: In our sample, 71% met ICD-10 criteria for a somatoform disorder (among these, 39% for persistent somatoform pain disorder, 14% for somatization disorder, and 14% for undifferentiated somatoform disorder), while 29% did not fulfill any of the ICD-10 somatoform disorders. The SDSC showed high item-total correlation (mean = 0.47), internal consistency (Cronbach's alpha = 0.94) and reliability measures (Guttmann's split half reliability = 0.88, Spearman-Brown reliability coefficient = 0.89). The sensitivity of the SDSC for screening ICD-10 somatoform disorders was 74.4%, the specificity 51.5%, and the (positive) predictive value 80.0%.

Conclusions: The German version of the SDSC appears as a reliable screening instrument for assessing ICD-10 somatoform disorders, at least in chronic pain patients.

NR535 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

The Relation Between Alexithymia, Somatic Complaint, Emotion and Vocabulary

Kuy-Haeng Lee, M.D., *Neuropsychiatry Department, Wonkwang University, Dongsan-dong 144-23, Iksan Cheonbuk 570-060, South Korea;* Hyun-Tae Jeon, M.D., Yong-Jin Yoo, M.D., Jae-Hyun Kim, M.D., Kwang So, M.D., Han-Joo Kim, M.D.

Summary:

Objectives: This study aimed to examine a correlation between the somatic complaint, emotion, vocabulary and alexithymia as a component of personality in normal persons.

Methods: 204 subjects were collected by age-based systematic sampling from the 662 persons without confirmed medical illness. We used the Korean version of 20-item Toronto Alexithymia Scale(TAS-20K) to measure alexithymia. The somatic complaints were checked by the list of somatic complaints on the diagnostic criteria of somatization disorder and major depressive episode in DSM-IV. The vocabulary was evaluated by the total number of associating-words from the spontaneous association of word and the secondary association to given words. The anxiety and depression were evaluated using 5-point self-report scale.

Results:

1) The degree of alexithymia was significantly correlated with the somatic complaints and anxiety, depression.
2) Somatic complaints were significantly correlated with the anxiety and depression.
3) The degree of alexithymia was not correlated with the number of associating-words.

Conclusions: The more degree of alexithymia increased, the more somatic complaints were experienced. There was a significant correlation between degree of alexithymia and anxiety, depression. But, it was not correlated with vocabulary. It suggest that the quality of vocabulary may be more important than the quantity of vocabulary in alexithymia.

NR536 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Gonadal and Adrenal Androgens in Women with Epilepsy

Martha J. Morrell, M.D., *The Neurological Institute, 710 West 168th Street, New York, NY 10032;* Mark V. Sauer, M.D., Linda C. Giudice, M.D., Silvia Done, B.A., Amelia J. Paulson, B.A., Cairn G. Seale, M.S.

Summary:

Objective: Hyperandrogenism is reported to arise more frequently in women with epilepsy receiving valproate (VPA) than other AEDs and in controls. Valproate mediated inhibition of androgen metabolism is the proposed mechanism.

Methods: Gonadal and adrenal androgens were examined in women with epilepsy on stable AED monotherapy for 6 months, and in controls aged 18–40 years, menstruating, and not receiving hormones. Fasting first morning sera was obtained on day 2 to 5 of the menstrual cycle.

Results: Data is presented for 19 nonepileptic controls, 11 women on lamotrigine (LTG), 9 on VPA, 16 on carbamazepine (CBZ), 9 on phenytoin (PHT) and 9 on phenobarbital (Pb). DHEA-S was higher in women receiving LTG (p .01) and lower with CBZ (p = .01), PHT (p. .01) and Pb (p .05) than controls, but was not different in women receiving VPA. However, total testosterone and free testosterone were elevated only in women receiving VPA (p = .01).

Conclusions: These results suggest that VPA preferentially affects gonadal as opposed to adrenal androgens. This argues that the association of valproate with elevated androgens is not strictly because of effects on androgen metabolism. The elevation in androgens associated with valproate use may be due to direct effects on the hypothalamic pituitary gonadal axis.

NR537 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Health Status and Pathological Gambling

Angela Ibanez, M.D., *Department of Psychiatry, Hospital Ramon Y Cajal-Alcala Universit, Crt. Colmenar, km. 9,1, Madrid 28034, Spain;* Rita Prieto, M.D., Carlos Blanco, M.D., Jeronimo Saiz-Ruiz, M.D.

Summary:

Objective: Pathological gambling is classified as an impulse-control disorder and causes significant distress to patients, their families, and society. This study was performed to assess the global health status of gamblers attending an specialized outpatient unit.

Method: We studied 40 pathological gamblers seeking treatment and 40 healthy controls matched for age and sex. Sociodemographics data were collected and all of them fulfilled the short form (SF-36) Health Survey Questionnaire to assess the health status of the subjects. A comparison between groups were performed by t-test.

Results: The respectively scores in gamblers and volunteers were: Physical functioning: 84.5 and 96.0 ($t = -3.92$; $df = 39$; $p = 0.001$); physical role limitation: 77.5 and 96.88 ($t = -3.36$; $df = 39$; $p = 0.002$); bodily pain: 68.97 and 81.05 ($t = -2.89$; $df = 39$; $p = 0.006$); general health perception: 61.15 and 80.23 ($t = -4.62$; $df = 39$; $p < 0.001$); energy/vitality: 54.63 and 70.88 ($t = -4.07$; $df = 39$; $p < 0.001$); social functioning: 59.69 and 91.25 ($t = -5.72$; $df = 39$; $p < 0.001$); emotional role limitation: 72.5 and 87.5 ($t = -2.07$; $df = 39$; $p = 0.045$); and mental health: 50.0 and 77.9 ($t = -8.49$; $df = 39$; $p < 0.001$). Significant differences were found between patients and controls in all health measures.

Conclusions: Pathological gamblers showed significant worse physical and mental health status than comparison group as measured by the SF-36.

NR538 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Psychiatric Sequelae of Amputation: Immediate Effects

Rajaram Mohan, M.D., *Department of Psychiatry, MK Medical College, 10 East Street Peramanoor, Salem 636007, India;* Rajes M. Wari, M.D.

Summary:

Thirty subjects, who had undergone amputation with in last 6 weeks, were studied for Psychiatric complications, including Phantom limb phenomena and pain. The patients were interviewed on DSM IV, HRSD and HARS. Out of a total of 30 subjects, 21 (70%) developed psychiatric disorders—acute stress disorder, post traumatic stress disorder and depressive disorder NOS. The whole sample was thus divided into 2 groups—Sick and Nonsick. Phantom limb phenomenon was seen in all subjects—21 patients in sick group and 9 patients in Non sick group. Phantom pain was seen in 7 subjects (sick group) and only in 1 subject (non sick group) Fisher's probability test was used to test the level of significance between these two groups. No significant difference was present between the two groups with regard to Age, Sex, Marital status, Religion, Site of limb, Side of limb, Type of operation, presence of Phantom limb phenomenon and Phantom pain.

NR539 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Association Between Piracetam and Nefazodone in Patients with Cognitive Disorder and Depression

Julio C. Zarra, M.D., *Department of Psychiatry, Hospital Italiano-Neurologia, Calle 51 Entre 29 Y 30, La Plata, BA 1900, Argentina*

Summary:

Objective: To evaluate the therapeutic response in patients with comorbility between Cognitive Disorder and Depression in treatment with Piracetam, Nefazodone and the two drugs associated.

Methods: a group of 150 patients with symptoms of Cognitive Disorder and Depression (DSM IV criteria) were separated in groups of 50. Each group received different treatment in a 10 months period:

Group 1: Piracetam 2400 mg./day.
Group 2: Nefazodone 400 mg./day.
Group 3: both drugs, same dose.

Results: The therapeutic response evaluated in Hamilton Scale for Depression (HAM-D), Mini Mental State Examination (M.M.S.E.) and Global Clinical Impression (G.C.I.) scores during 10 months in the third group who received the two drugs associated, had much better response than the others.

Conclusions: The group who received the association of the nootropic agent PIRACETAM with the antidepressive NEFAZODONE had a relevant satisfactory therapeutic response (the best result), so there is a possible relation between the deficit of cerebral oxygenation and depression. Cerebral oxygenation deficit could be a generator of Depressive Disorder.

NR540 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Correlates of Suicidal Behavior in an Arctic Community

John M. Haggarty, M.D., *Department of Psychiatry, London Psychiatric Hospital, 850 Highbury Avenue, Box 5532, London, ON NGA 4H1, Canada;* Zachias Cernovsky, Ph.D., Harold Merskey, M.D., Mariwan Husni, M.D.

Summary:

A random household survey in a Canadian Arctic Inuit community was conducted using a 4-item self-report questionnaire (in

English or in Inuktitut) dealing with thoughts of killing oneself in the past week, suicide attempts, plans to kill oneself, and wish to die within the last 6 months. The respondents were also administered the Hospital Anxiety and Depression Scale (HAD) and the CAGE questionnaire. 111 Inuit participated. As already reported elsewhere, 30% of those responding attempted suicide within the last 6 months, 52.9% reported a wish to die in the past six months, 30.3% reported having a plan to die in the last six months, and 43.6% have thought of committing suicide in the past week.

In the present study, we used the multiple regression analyses and calculated the odds ratio to evaluate the relationship of gender, age, and scores and HAD and CAGE scales to a combined score on the four items dealing with the suicidal attempts, suicidal thoughts, wishes, and plans. Gender was unrelated to the suicidal behaviour (Pearson r, $p > .05$). Surprisingly, HAD Depression scores was also unrelated to the suicidal score (Pearson r, $p > .05$). Significant relationships of the suicidal scores were found to the CAGE score ($r = .32$, $p = .002$), HAD Anxiety score ($r = .28$, $p = .003$), and age ($r = -.26$, $p = .10$). Persons free of alcohol abuse (OR = 2.83), those less anxious (OR = 10.2), and those younger than 35 (OR = 3.8) were less likely to contemplate, attempt, or think of suicide. When combined in the multiple regression equation, these three variables accounted for 17.3% of variance in the suicidal scores.

Anxiety, age, and alcohol abuse but not depression are important factors in managing suicidal persons in the far North.

NR541 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Analysis of Catechol-O-Methyltransferase and 5-Hydroxytryptamine Transporter Polymorphism in Patients at Risk for Suicide

Mark J. Russ, M.D., *Department of Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004;* Herbert M. Lachman, M.D., Todd Kashdan, B.A., Takuya Saito, M.D., Senada Bajmakovic-Kalila, M.D.

Summary:

Suicidal behavior appears to have a genetic component (Mann et al., 1999a; Roy et al., 1999). Functional polymorphism's in the genes encoding the serotonin transporter (5-hydroxytryptamine transporter, 5-HTT) and the enzyme catechol-O-methyltransferase (COMT) were analyzed in a group of 51 patients admitted to the hospital because of significant suicide risk, and in 51 control subjects from the same geographic area without a history of major psychiatric illness. There were no differences between these groups with respect to the genotype frequencies for either 5-HTT or COMT. Within the patient group, increased hopelessness and suicide ideation were associated with homozygosity of the 5-HTT gene). Hopelessness Scale (Beck and Steer, 1988) Score for the *ll* genotype (16.6 ± 2.3) was significantly higher than for the grouped *ss* and *ls* genotypes (11.8 ± 5.9; $t(46) = 2.9$, $p = 0.005$, 95% CI = 1.5 to 8.1). Likewise, Scale for Suicide Ideation (Beck et al., 1979) score for *ll* genotype (22.6 ± 7.1) was significantly higher than for the grouped *ss* and *ls* genotypes (16.0 ± 8.5; $t(28) = 2.7$, $p = 0.01$, 95% CI = 1.7 to 11.4). Our results are consistent with the possibility that homozygosity for the *l* allele is related to diminished postsynaptic serotonergic activity and heightened suicide risk.

NR542 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Association Study with the Tryptophan Hydroxylase Gene in Suicide Attempters

Philippe Courtet, M.D., *Department of Psychiatry, CHU Lapeyronie, Avenue Charles Flahault 39, Montpellier 34295, France;* Mocrance Abbar, M.D., Marion Leboyer, M.D., Jean-Philippe Boulenger, M.D., DiDier Castelnau, M.D., Catherine Buresi, M.D., Alain Malafosse, M.D.

Summary:

Background: The tryptophan hydroxylase (TPH) gene, coding for the serotonin synthesis enzyme, is a major candidate for association studies of suicidal behavior. In previous studies, we suggested an association between a TPH intron 7 marker and suicide attempt. Here, we analyze 5 new TPH polymorphisms.

Methods: New polymorphisms are localized in the promoter, the introns 1b, 8 and 9 and in the 3′ region. 231 suicide attempters and 250 controls, both of West European Caucasian origin, were genotyped. Alleles at the introns 7, 8 and 9 are in complete linkage disequilibrium allowing the construction of 2 haplotypes (A-T-C/C-C-T).

Results: The rarer haplotype (A-T-C) and the allele 194 at the 3′ polymorphic site are more common in suicide attempters (0.44) than in controls (0.34). Moreover, this haplotype frequency significantly increases when a history of depression and/or the violence of the gesture are taken into account. No difference was observed at the promoter and the intron 1b polymorphic sites.

Conclusion: This extend and confirms our previous results and allows to restrict the part of the gene containing the functional variant to its 3′ region. However, the precise phenotype that is associated with the TPH haplotype A-T-C-194 remains to be characterized.

NR543 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Suicide Prevention: Determining the Best Settings for Prevention Interventions

Peter L. Forster, M.D., *Department of Psychiatry, University of California-San Francisco, 211 Gough Street, Suite 211, San Francisco, CA 94102;* Patricia A. Arean, Ph.D., Carol J. Peng, B.A.

Summary:

Increased recognition and treatment of individuals with suicide potential is crucial to the reduction of suicide rates, which significantly outnumber homicide rates across the country. But where, if anywhere, are suicidal individuals most likely to be seen in the healthcare system? This study examined the public health, mental health, and substance abuse services utilization of all reported San Francisco suicide victims ($N = 298$) prior to their deaths between 1995 and 1997.

The names of these individuals were cross-referenced to San Francisco Department of Public Health administrative databases. Forty-six percent of these individuals received services through the City and County's public healthcare system at some point in their lives. From one to six months prior to the date of death, nineteen percent of these individuals visited the emergency room, twelve percent were inpatients, and fourteen percent received outpatient services. Within the same month of committing suicide, five percent visited the emergency room, seven percent were inpatients, and eleven percent received outpatient services. Twenty-three percent of all the suicide victims had received mental health services through the city system at some point in their lives. One-third of these individuals had some contact from one to six months prior to the date of death. Approximately one-quarter had received services within the same month of death. Nine percent of all suicide victims had received services from the public substance abuse program. These data point to a quite high utilization of the public healthcare system by suicide victims but indicate that non-mental health settings (particularly the emergency room) are much more likely to be the site of the latest healthcare visit before suicide.

NR544 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Medical Contacts of Suicide Attempters Prior to the Event

Francoise Chastang, M.D., *Centre Psych Esquirol, C.H.U. Cote de Nacre, Caen 14033, France;* Patrice Rioux, M.D., Laurent Leclerc, M.D., Viviane Kovess, M.D., Edouard Zarifian, M.D.

Summary:

The aim of this study, which is part of an investigation carried out in 541 suicide attempters (females: 67%, males: 33%, mean age = 34 ± 1 years; repeaters: 54%) referred to the Emergency Department of the Caen University Hospital (France) is to characterise their modality of access to medical care in the year preceding the referent suicidal act.

30% suicide attempters had visited the Emergency Unit in the year preceding the reference suicide attempt, 30% had been hospitalised; 78% had seen a general practitioner, 30% had seen a psychiatrist regularly.

Repeaters had visited Emergency Departments significantly more often than first attempters (43.6% vs 13.3%, p 0.001). Young suicide attempters had significantly less frequently consulted a general practitioner than their older counterparts (72% vs 83.4%, p 0.001), and even less in the case of repeaters (66.5% vs 85.5%, p 0.001) or those in precarious employment (67.6% vs 87.8%, p 0.001).

It also appears that those with the highest risk of suicide, namely young repeaters with poor living conditions, get less medical primary care. This situation is paradoxical in terms of primary prevention and poses a real challenge in the field of suicide prevention.

NR545 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Adolescent Suicidal Behavior in Buenos Aires and Mendoza

Guillermo J. Tortora, M.D., *Asocidcion Heuropijuistries Argentina, Ituzaingo 1250, 3A Lanus Este, Buenos Aires 1824, Argentina;* Miguel Marquez, M.D., Benigno Gutierrez, M.D., Liliana Florio, Ph.D., Edith M. Serfaty, M.D., Ignacio Brusco, M.D., Alicia Sotelo-Lago, M.D.

Summary:

Objective: The purpose of this research was to analyze the risk factors in adolescent suicidal behavior so as to determine the danger degree.

Methods: We analyzed the most prominent characteristics of the consummate suicides epidemiological profile and compared them with the suicide attempt profile. Two groups were created in order to collect material, the first one picked up data belonging to 2.097 consummate suicides occurred in Buenos Aires city during the period 1994–1998 (13.662 autopsies) and 357 suicides in Mendoza city (3.815 autopsies). The second group (suicidal attempts) took a sample of 1723 cases in Buenos Aires and 1432 case in Mendoza obtained in the same years as the psychiatric hospitalizations.

Results: The number of consummate suicides in adolescent population (age 10 to 21) was 174 (9.2%) in Buenos Aires and 58 (15.8%) in Mendoza. The following variables observed did not show greater differences between both cities: sex male: 65%; single: 79%; method: fire guns 52% (male) and 49% (female); previous attempts: 58%. In both cities a low percentage (10%–11%) of consummate suicide by overdose was observed which could be considered as a under-register. The adolescent suicide attempts (n:1134; 37%), data is coincident in the both cities: sex female: 72%; single: 67%; method overdose: 73%; previous attempts: 24%; mood disorders: 68%; personality disorders 43%; substance abuse 37%; alcohol abuse 23%; high probability of rescue only in 29% of the cases; family violence 38%; sex abuse: 23%.

Conclusions: The increase in the number of the observed suicides and the risk factors described indicate us that at this moment *the adolescent suicidal behavior should be considered as highly risky.*

NR546 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Repetitive Transcranial Magnetic Stimulation Versus ECT for Major Depressive Episode

Philip G. Janicak, M.D., *Department of Research, Psychiatric Institute, 1601 West Taylor Street, Chicago, IL 60612;* Brian Martis, M.D., Jack S. Krasuski, M.D., Dennis D. Beedle, M.D., Rajiv P. Sharma, M.D., Cherise Chase, R.N., Mauli Verma, M.D.

Summary:

Electroconvulsive therapy (ECT) is often the most effective somatic treatment for severe, major depression. Recently, repetitive transcranial magnetic stimulation (rTMS) has emerged as a possible therapeutic alternative. Studies over the past 5 years have found rTMS to be effective for depression in comparison to sham rTMS; as an augmentation to antidepressants; and in drug-resistant patients. Given this therapy's relatively benign administration and side effect profile (e.g., no anesthesia required; no seizure induced; minimal cognitive effects), we are conducting a trial of rTMS versus ECT in unipolar and bipolar depression. The goals of our study are to ascertain rTMS' relative efficacy to ECT; and whether patients who fail to adequately respond to one therapy will respond to the other. Patients appropriate for ECT are randomly assigned to a standard course of bitemporal ECT or 10–20 session of rTMS. rTMS treatments employ left DLPC stimulation at 110% of motor threshold. Each treatment consists of 20, 5 second 10 HZ stimulations given on a Monday-Friday schedule. Response is defined as at least a 50% decrease in the total baseline Hamilton Depression Rating Scale (HDRS) score and a total score no greater than 8. Nonresponders are crossed over to the other treatment arm. Thus far, 14 subjects with a DSM-IV primary diagnosis of either Bipolar Disorder or Major Depressive Disorder have completed the study. Of these 14 subjects, 9 were male and 5 were female between the ages of 18–66. Eight subjects received a treatment course of rTMS and 7 subjects had received a course of ECT. Overall, improvements based on a change from baseline HDRS scores indicate that rTMS was comparable to ECT (59% vs 50%; t = 0.4; df = 13; p = n.s.). If response criteria was defined as an endpoint Hamilton score of less then 8, then 4/8 subjects responded to rTMS and 3/7 subjects responded to ECT. Of note, one ECT nonresponder was crossed over to rTMS and showed significant improvement with rTMS; however, the patient did not meet response criteria.

NR547 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Burst-Suppression Anesthesia As Alternative to ECT

Mauro Garcia-Toro, M.D., *Department of Psychiatry, GESMA, c/ Jesus #40, Palma de Mallorca 07003, Spain;* Antonio Garcia, M.D., Lorenzo Socias, M.D., Pedro Ibanez, M.D., Catalina Rubert, M.D., Joan Salva-Coll, M.D., Gemma Rialp, M.D.

Summary:

Objective: In the limited literature concerning burst-suppression anaesthesia (BSA) in drug-resistant Major Depression, most studies have suggested a therapeutic effect comparable to electroconvulsive therapy (ECT). We carried out an open pilot study with six patients; five of them were reluctants to receive ECT, and the other one failed to improve with 13 ECT sessions.

Methods: The first four patients received 3 hours of BSA with propofol + sevoflurane, in several sessions of 30–90 minutes.

The last two patients received just one session with propofol + midazolam of twelve hours.

Results: After the first session, BSA resulted in a 14.3 points decrease ($t = 4.66$, $p = 0.006$) in the Hamilton Depression Rating Scale (HDRS). In the third week, the decrease in HDRS was also significant ($t = 2.91$; $p = 0.032$), but two patients remain severely depressed. The greatest improvement was showed in one patient of the first group and both two patients of the second.

Conclusions: BSA might be a valuable alternative to ECT in patients with drug-resistant depression.

NR548 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Patient Expectations About ECT

Shoshana Peyser, Ph.D., *Biological Psychology, NYSP1, 1051 Riverside Drive, #126, New York, NY 10463;* Bruce Luber, Ph.D., Joan Prudic, M.D., Harold A. Sackeim, Ph.D.

Summary:

This study examined 138 people who received electroconvulsive therapy (ECT) for major depression. This is the first study to measure directly patients' expectation about the clinical outcome of ECT before receiving the treatment and examine the relationship with both objective and subjective measures of ECT efficacy. Two major findings emerged. First, expectation for treatment success was not related to either subjective or objective measures of ECT treatment outcome. This finding suggests that the mechanism of ECT is independent of expectation and largely biological in nature. Thus it is unlikely that enhancing pre-ECT expectations would augment ECT's efficacy in the treatment of major depression. Second, in the examination of what variables impacted upon expectations for treatment success, most notable was that women with prior ECT experience have the most negative expectations for ECT efficacy. These findings may have important implications for educating patients, families and health care professionals.

NR549 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Patients with SAD Report a More Complete Improvement in Summer than with Light Treatment in Winter

Teodor T. Postolache, M.D., *Biological Rhythms, National Institute Health-NIMH, 10 Center Drive, Room 3S231, Bethesda, MD 20892;* Thomas A. Wehr, M.D., Ludy Y. Yi, Norman E. Rosenthal, M.D.

Summary:

Introduction: Although light is an effective antidepressant for winter depression in patients with seasonal affective disorder (SAD), the symptoms of depression, as assessed by a rater, are lower in summer than after *two weeks* of light treatment in winter (1). In one study, the difference between light and placebo became significant only after *at least three weeks* of treatment (2). In consequence, we now compare after *at least four weeks of light treatment* the self-reported improvement in depressive symptoms with light treatment in winter vs. the improvement in depressive symptoms in summer.

Method: Subjects were 25 patients with SAD, physically healthy, with no co-morbid psychiatric conditions and unmedicated. After four weeks of to light treatment (10,000 lux cool-white fluorescent light for 45 minutes twice daily) they were invited to answer a questionnaire regarding the efficacy of light treatment. They were asked to mark the degree of improvement in depression symptoms on two 100 mm visual analogue scales (one for light treatment and one for summer) with anchor points from 0% (not at all), to 100% (completely). The scores were analyzed using a Wilcoxon test.

Results: The response rate was 92% (23 out of 25 patients responded). The degree of improvement in summer was found to be significantly ($Z = 3.929$; $p < 0.001$) more complete (median 96) than the degree of improvement with light in the winter (median 78).

Conclusion: A more complete improvement in summer than with light treatment in winter was now confirmed after a longer duration of light treatment and using a global self-report rather than rater-based depression evaluations. It is worth exploring other physical, chemical, biological, and socio-economic factors that may account for this difference. It would be clinically relevant to test if complementing light treatment with other interventions such as medication, psychotherapy or travel to the south would result in a more complete symptomatic improvement than with light treatment alone.

NR550 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Maintenance Repetitive Magnetic Stimulation in the Treatment of Resistant Major Depression

William M. McDonald, M.D., *Department of Psychiatry, Wesley Woods, 1841 Clifton Road, NE, Atlanta, GA 30329;* Eve H. Byrd, Yvonne M. Greene, M.D., Leslie E. Smith, B.A., Autumn L. Clark, B.S., Charles M. Epstein, M.D.

Summary:

Objective: In clinical trials of repetitive transcrancial magnetic stimulation (rTMS) the relapse rate on antidepressants in the month following rTMS ranges from 75–100%. We report on the efficacy and safety of maintenance rTMS.

Method: Three subjects meeting DSM-IV criteria for severe recurrent Major Depression responded to rTMS administered over the left dorsolateral prefrontal cortex at 11% of motor threshold over ten days. Subject 1 is a 53-year-old male with a history of seven failed antidepressant trials and no response to two separate trials of ECT. Subject 2 is a 62-year-old female with a history of recurrent major depression since age 31 years, ten psychiatric hospitalizations and multiple medication trials. Subject 3 is 75 years old and had ten unsuccessful medication trials plus multiple psychiatric hospitalizations and suicide attempts. All three subjects relapsed after rTMS, were administered maintenance rTMS and monitored using the Brief Psychiatric Rating Scale, Hamilton Depression Rating Scale, Clinical Global Improvement scale.

Results: All three subjects remained stable with CGI scores of 1–2 (markedly or moderately improved from baseline) over six months without significant side effects or changes in neuropschological testing.

Conclusion: Maintenance rTMS may be a safe and effective treatment in patients with severe recurrent depression.

NR551 Wednesday, May 17, 12:00 p.m.-2:00 p.m.

Is It Possible to Predict Cerebal Dysrhythmias by Measuring Pulse and Blood Pressure Before and After ECT?

Mustafa K. Saadani, M.D., *Department of Psychiatry, King Khalid N.G. Hospital, P O Box 9515, Jeddah 21423, Saudi Arabia*

Summary:

A number of patients who receive electroconvulsive therapy (ECT) have a prior abnormal Electroencephalograms (EEG). This study tries to find the relation between patients with abnormal EEG who received ECT and their pulse rate, systolic, and diastolic blood pressure. Three groups of patients (39 patients) with major depression who received ECT were studied. All patients received bilateral ECT under general anesthesia. First group of patients have abnormal EEG and clinically have seizures. In this group,

the relationship between means of pulse rate, systolic, and diastolic blood pressure before and after ECT were statistically significant where z-test results were –3.18, –3.06, and –2.93 correspondingly. Second group of patients have normal EEG but have doubtful seizures. The relationship between means of pulse rate and diastolic blood pressure were statistically significant where z-test results were –3.18 and –2.9. Third group of patients have normal EEG and clinically have no evidence of seizures. The relationship between means of pulse rate, systolic, and diaastolic blood pressure were statistically not significant where z-test results were 1.18, –0.8, and –0.82, respectively.

Conclusion: It is possible to predict the presence of abnormal EEG from marked increase in pulse rate and blood pressure one hour after ECT.

NR552 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Weight Gain in Pediatric Patients on Typical and Atypical Antipsychotics

Ann W. Mulqueen, M.S.N., *NIMH, 10 Center Drive, Room 3N202, Bethesda, MD 20892-1600;* Marianne Wudarsky, M.D., Robert J. Nicolson, M.D., Pete Gochman, M.A., Susan Hamburger, M.A., Marge Lenane, M.S.W., Judith H.L. Rapoport, M.D.

Summary:

Objective: Weight gain is a major side-effect of atypical antipsychotics. Pediatric-onset obesity carries more morbidity than adult-onset. This study examined weight gain in patients with childhood-onset schizophrenia taking typical and atypical antipsychotics.

Method: Weight was measured weekly from baseline as part of an ongoing NIMH double blind and open trials of haloperidol, olanzapine, and clozapine in patients with childhood-onset schizophrenia. Weight gain after 6 weeks of treatment was compared between the three groups.

Results: Patients on haloperidol (n = 12), olanzapine (n = 8), and clozapine (n = 15) showed significant weight gain. However, the increase was significantly greater for olanzapine (4.9kg) and clozapine (4.7kg) than for haloperidol (1.9kg). Among the 10 patients who received trials of both clozapine and haloperidol, the weight gain was significantly greater on clozapine (5.5kg) than haloperidol (2.03kg).

Conclusions: Significant weight gain is seen in pediatric patients taking olanzapine and clozapine. This may have important treatment ramifications for health and compliance among pediatric patients.

NR553 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Regional Brain Functioning During Verbal Fluency Tasks in Subjects with Asperger's Disorder

Joanna T. Szelazek, *Department of Psychiatry, Univ. of Western Ontario, P O Box 5339/339 Windermere Rd, London, ON N6A 5A5, Canada;* Peter C. Williamson, M.D., Sandra Fisman, M.D., Margaret M. Steele, M.D., Joseph Gati, M.S.C., Maria Densmore, B.S.C., Ravi Menon, Ph.D.

Summary:

Objective: Several areas of the brain have been implicated in the psychopathology of Asperger's disorder. Functional magnetic resonance imaging (*f*MRI) was used to determine possible abnormalities in regional brain activity during a verbal fluency test in subjects with Asperger's disorder.

Method: Five Asperger's children male and female between the ages of 10 to 20 years were selected. Subjects were outpatients at Children's Hospital of Western Ontario and were diagnosed according to DSM-IV criteria. Siblings of subjects were recruited as controls. Subjects and controls were medication-free at least two weeks prior to testing.

*f*MRI at 4.0 Tesla field strength was used to quantify cerebral blood flow changes during a verbal fluency task known to activate prefrontal regions in normal subjects and inappropriately activate the auditory cortex in schizophrenic patients compared to a baseline reading task.

Results: Asperger's patients demonstrated little prefrontal or temporal activation during word fluency but had marked thalamic activation in contrast to their siblings who showed predominantly prefrontal activation.

Conclusion: The lack of activation in the frontal lobes of Asperger's subjects is in keeping with executive dysfunction postulated in Asperger's disorder. However, Asperger's patients did not show inappropriate auditory cortex activation seen in schizophrenic patients suggesting intact prefrontal/auditory cortex connections. Finally, the high level of activation in the thalamic region found in Asperger's subjects supports possible basal-ganglia thalamocortical dysfunction.

NR554 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Assessing Children at Risk for Bipolar Disorder

Sarah M. Graman, B.A., *Department of Psychiatry, University of Cincinnati, 231 Bethesda Avenue, ML 0559, Cincinnati, OH 45267-0559;* Kathleen A. Lake, M.S.W., Melissa P. Del Bello, M.D., Patricia McDonough-Ryan, M.A., Cesar A. Soutullo, M.D., Susan L. McElroy, M.D., Stephen M. Strakowski, M.D.

Summary:

Objective: Children with one parent with Bipolar Disorder (BP) have a 25% chance of developing the illness. The CBCL may be useful in identifying mood symptoms in these children. We hypothesize that children at high risk for BP (HR) with mood symptoms will have greater scores on the withdrawn, somatic complaint, anxious/depressed, thought problems, delinquent behaviors, and aggressive CBCL subscales compared with HR children without mood symptoms.

Methods: (one parent meeting DSM-IV criteria for BP, N = 24) and control (parents without Axis I diagnoses, N = 22) children, group matched for age, sex and race, were evaluated using the Kiddie Schedule for Affective Disorders and Schizophrenia by raters blind to subject group. All parents received the Structured Clinical Interview for the DSM-IV to confirm their diagnosis or lack thereof, and completed the CBCL for their child.

Results: HR children have significantly greater scores on all CBCL subscales (lowest t = 3.4, df = 39, p = .01) than controls. Within the HR group, mood disorder symptoms significantly correlated with the withdrawn and aggressive subscales (lowest Spearman correlation r = .42, p = .04). HR children with syndromal BP (N = 10) had greater scores on withdrawn, anxious/depressed, delinquent, and aggressive subscales compared with HR children without BP (lowest t = –2.24, df = 22, p = .03).

Conclusions: Our data suggests that the CBCL may be useful in identifying subsyndromal and prodromal mood disorder symptoms in children at HR for BP.

NR555 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Familial Psychopathology of Children with School Refusal

Corinne Martin, M.D., *Department of Psychiatry, C.H. Ch. Perrens, 121 Rue de la Bechade, Bordeaux 33076, France;* Stephane Cabrol, M.D., Jean-Pierre Lepine, M.D., M. Christine Mouren-Simeoni, M.D., Manuel P. Bouvard, M.D.

Summary:

Objective: To examine anxiety, depressive and personality disorders in the mothers and the fathers of children with anxious school refusal, and to test for the existence of differences in familial aggregation between children suffering from school refusal related to separation anxiety disorder and those suffering from phobic disorder-based school refusal.

Method: Using a blind standardized diagnostic evaluation (SADS LA, DIGS, PAS and Kiddie SADS, we compared parental lifetime psychiatric illness for the two groups of anxious school refusers

Results: Relationships between specific anxiety disorders in children and their parents revealed increased prevalence of simple phobia, and simple and/or social phobia among the fathers and mothers of phobic disordered school refusers, and increased prevalence of panic disorder and panic disorder and/or agoraphobia among the fathers and mothers of separation anxiety disordered school refusers. Simple and/or social phobia in the father, simple phobia in the mother and age of the father were associated with the group of phobic school refusers. Lifetime diagnosis of depressive and personality disorders in parents didn't distinguish the two groups.

NR556 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Safety and Efficacy of Paroxetine in the Treatment of Children and Adolescents with OCD

David J. Carpenter, M.S., *CNSGI, Smith, Kline and Beecham, 1250 South Collegeville Road, Collegeville, PA 19426;* Graham J. Emslie, M.D., Karen Dineen-Wagner, M.D., Mark A. Riddle, M.D., Susan Lawrinson, B.S.C.

Summary:

The safety and efficacy of paroxetine (PAR) in children (8–11 yrs, n = 167) and adolescents (12–17 yrs, n = 168) with OCD was evaluated. Patients responding (≥25% decrease in CY-BOCS Total and CGI Global Improvement Score of 1 or 2) following 16 weeks of open-label (OL) PAR (10–60 mg/day) were randomized to double-blind (DB) continuation of PAR or to placebo (PBO) for 16 additional weeks.

The mean OL phase decrease in CY-BOCS Total was −13.0 (from 26.3 at entry); 68.7% of patients in the LOCF dataset and 86% of those completing Week 16 met response criteria. The proportion of DB phase patients achieving a further decrease in CY-BOCS Total from DB baseline of ≤25% was 28.9% for PAR and 14.4% for PBO ($p = 0.023$). The mean DB increase (worsening) in CY-BOCS Total was +6.9 for PBO and +3.6 for PAR ($p = 0.008$, LOCF). The proportion of patients relapsing was lower for PAR (34.7%) than for PBO (43.9%), but not statistically significantly so ($p = 0.136$).

The AE incidence was similar to that in adult OCD patients in PAR controlled trials. AEs most frequently leading to discontinuation of OL PAR were hostility (2.7%), hyperkinesia (2.1%), and agitation (1.8%). AE incidence was generally similar in the two age subgroups, however, agitation (11.4% vs 3.6%), hyperkinesia (14.4% vs 8.3%), trauma (18.6% vs 8.3%), infection (12.0% vs 7.1%), manic reaction (4.2% vs 0.6%) and myoclonus (9.6% vs 4.8%) were reported more frequently in the younger age subgroup. These findings suggest that PAR is safe and effective in pediatric OCD patients over the dosage range studied (10–60 mg/day).

NR557 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Other Half of Teen Pregnancy: Characteristics of Male Partners and Opportunities for Physician Intervention

Daniel P. Chapman, Ph.D., *Health and Aging Branch, CDC, 4770 Buford Highway NE, MS K45, Atlanta, GA 30341;* Robert F. Anda, M.D., Vicent J. Feliti, M.D., Dale Nordenberg, M.D., Janet Croft, Ph.D., John Santelli, M.D., James S. Marks, M.D.

Summary:

As teen pregnancy prevention efforts have largely focused on adolescent girls, less is known about their male partners. Because prevention of teen pregnancy has emerged as a national health priority, this represents both a serious oversight as well as an opportunity for expanded physician intervention. To better examine characteristics of men who impregnated teenage girls, we analyzed data from the Adverse Childhood Experience (ACE) Study, a retrospective cohort investigation of San Diego Kaiser Permanente patients receiving standardized medical evaluations (n = 7,399 men). Participants reported their reproductive histories, as well as their childhood exposure to eight ACEs assessing abuse and household dysfunction. 19% of men reported ever impregnating a teenage girl; of these, 63% reported at least one ACE and 33% reported >2 ACEs. Each ACE was associated with increased odds of involvement in teen pregnancy and we found a dose-response relationship between the number of ACEs and the odds of impregnating a teenage girl for each of the four birth cohorts throughout the century ($p < 0.001$). We also found a graded relationship to earlier age at first intercourse, more sexual partners, having an STD, and alcohol or drug abuse. These results suggest physician assessment of child abuse—as well as the sexual behavior and contraceptive practices of male patients who were abused—may be important components of teen pregnancy prevention.

NR558 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Personal Health and Preventive Counseling Characteristics of Women Psychiatrists: Results from the Women Physicians' Health Study

Daniel P. Chapman, Ph.D., *Health and Aging Branch, CDC, 4770 Buford Highway NE, MS K45, Atlanta, GA 30341;* Erica Frank, M.D.

Summary:

Previous research examining unique characteristics of women psychiatrists has largely been restricted to identifying clinical practices and treatment preferences. As physician characteristics are important predictors of patient outcomes and physician health, we sought to identify personal health behaviors and histories and prevention-related counseling practices including mammography, blood pressure and cholesterol screening, and other preventive care recommendations. The Women Physicians' Health Study surveyed a random sample of U.S. women physicians listed in the American Medical Association Physician Masterfile and randomly selected 2,500 women who graduated from medical school in each of the last four decades (1950 through 1989). Women psychiatrists were significantly more likely than other women physicians to report personal histories of depression or sexual abuse, poor health, and current or past smoking. Moreover, women psychiatrists were significantly less likely to report practicing preventive counseling with patients, ascribed less clinical relevance to these practices, and reported less self-confidence and less training in performing them. These results suggest considerable opportunity exists to integrate appropriate preventive counseling practices with psychiatric treatment to better optimize patient care.

NR559 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Lack of Prolactin Elevations with Quetiapine

Brian J. McConville, M.D., *Department of Psychiatry, University of Cincinnati, 231 Bethesda Avenue, #ML559, Cincinnati, OH 45267-0559*

Summary:

Objective: To examine the effect of quetiapine on prolactin in adolescents, who are particularly vulnerable to hormonal changes, compared with that reported for haloperidol and olanzapine. Wudarsky (1999) found haloperidol and olanzapine raised plasma prolactin by 38.7 ng/ml and 13.7 ng/ml, respectively, over a 6-week period.

Method: The effect of quetiapine on plasma prolactin levels in adolescents with selected psychotic disorders was evaluated in a rising-dose study. After a 2-day run-in period, 10 patients, mean age 13.1 years, received quetiapine dosages rising from 50 to 800 mg/day over 21–27 days.

Results: The efficacy of quetiapine in these patients was demonstrated by decreases in scores after 20 days on the Clinical Global Impression scale (mean –2.1), Scale for Assessment of Negative Symptoms (mean –5.3) and the Brief Psychiatric Rating Scale (mean –25.8). Quetiapine tolerability was shown by improvements in the Barnes and Simpson Akathisia scales (–1.3 and –2.1, respectively). Quetiapine did not significantly alter prolactin levels. In boys (n = 5), mean prolactin levels did not change during treatment, going from 14.6 ng/mL to 15.0 ng/mL. In girls, mean prolactin levels decreased from 25.0 ng/mL to 12.4 ng/mL 20 days later.

Conclusion: In adolescents, quetiapine was effective, well tolerated, and did not cause hyperprolactinemia, even at high dosages.

NR560 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Characteristics of Executive Dysfunctions and Change During Methylphenidate Treatment in Children with ADHD

Hyung-Bae Park, M.D., *Department of Psychiatry, Yeungnam University, 317-1 Daemyung-Dong, Namgu, Taegu 705-717, Korea;* Jong-Bum Lee, Ph.D., Hyun-Seok Sea, Hyung-Mo Sung

Summary:

Objective: To examine the characteristics of executive dysfunctions and effects of methylphenidate (MPH) on executive dysfunctions in children with attention deficit hyperactivity disorder (ADHD).

Method: The subjects were 40 children with ADHD who fulfilled DSM-IV criteria and age, IQ and sex-matched normal controls. Executive functions was measured using 5 ADHD rating scales, K-ABC. Continuous Performance Test (CPT), Stop Signal Task (SST), Wisconsin Card Sorting Test (WCST) and Trail-making B. The tests were performed at baseline (both ADHD and normal controls group) and again at 4 weeks after methylphenidate treatment (only ADHD groups). Methylphenidate was individually titrated based on therapeutic and side effects with each dose given 2 to 3 times daily (0.3 mg/kg to 0.7 mg/kg).

Results: Children with ADHD appeared to have significantly lower IQ score and poorer executive functions than compared to normal controls. After methylphenidate administration. Significant improvement were seen on the all ADHD rating scales, commission error and risk taking of the CPT, total correct of the WCST, all areas of the SST.

Conclusions: The results indicate that children with ADHD have significantly poorer executive function, compared with normal children and methylphenidate is highly effective in inhibitory dysfunction, but not all aspects of executive dysfunction.

NR561 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Comparison of the Executive Function Between Children with Tic Disorder and ADHD

Hyung-Mo Sung, *Department of Psychiatry, Yeungnam University, 317-1 Daemyung-Dong, Namgu, Taegu 705-717, Korea;* Hyung-Bae Park, M.D., Sung-Duk Jung, Jin-Sung Kim

Summary:

Objective: This study was performed to verify and compare deterioration of executive functions in the children with Tourette's disorder and attention deficit hyperactivity disorder (ADHD).

Method: We carried out Kaufman assessment battery for children (K-ABC), continuous performance test(CPT), Wisconsin card sorting test(WCST) on each 18 children outpatients diagnosed as pure Tourette's disorder and pure ADHD by DSM-IV and also 18 normal children, then compared the results. All tests are performed before medications.

Results: The ADHD group showed significantly poor performance in commission error, attentiveness and risk taking on CPT($p < 0.05$). The ADHD and the Tourette group showed poor performance in number of trials administrated, total number of errors, conceptual level response, number of categories complete, perseverative response and perseverative error on WCST from the normal children group ($p < 0.05$), but the ADHD group performed poorer than Tourette group in commission error on CPT, perseverative response and perseverative error on WCST($p < 0.05$). These differences are more apparent after adjustment for IQ.

Conclusion: Considering these results, we can infer that the abnormality of executive functions appears in both ADHD and Tourette's disorder, but ADHD may show more apparent abnormality in executive functions than Tourette's disorder.

NR562 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Comorbid ADHD and Disruptive Behavior Disorders

Boris Birmaher, M.D., *WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213;* James P. McCafferty, B.S., Kevin M. Bellew, B.S., Katherine L. Beebe, Ph.D.

Summary:

Objective: To examine the influence of ADHD and other disruptive behavior disorders on the effectiveness of antidepressant therapies, we examined the response rates to paroxetine, imipramine and placebo observed during an 8 weeks randomized blinded trial conducted in 271 adolescents with major depression (1).

Methods: Major depression and comorbidity was ascertained using the K-SADS-L interview. Disruptive disorders (DD) were defined as any one of the following: conduct disorder, antisocial personality disorder, or oppositional defiant disorder. Responders to antidepressant treatment were defined as any patient with a clinical global impression rating of moderate or marked improvement.

Results: Overall response rates to treatment were high, possibly a result of high level of supportive psychotherapy permitted in the trial. The analysis of responders shows when ADHD is comorbid with depression, the response rates are significantly lower, regardless of the treatment regimen.

Treatment	N Total	N ADHD	Responders Non ADHD	Responders ADHD	ODD Ratio (95% CI)
Paroxetine	90	8	71%	25%	0.137 (0.026, 0.732)
Imipramine	94	16	64%	31%	0.254 (0.080, 0.807)
Placebo	87	8	59%	13%	0.097 (0.011, 0.829)
All Patients	271	32	59%	24%	0.180 (0.077, 0.419)

Other disruptive behaviors, however, do not appear to significantly influence the response for the study as a whole or for any of the individual treatments (Odds Ratio (95%CI) = 0.833 (0.340,1.764)).

Conclusion: These post hoc analyses suggest that ADHD is an important consideration in the treatment of adolescents with major depression.

NR563 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Pharmacokenetics of Ziprasidone in Children and Adolescents with Tourette's Syndrome

Floyd R. Sallee, M.D., *Department of Psychiatry, Cincinnati University, 231 Bathesda Avenue, Cincinnati, OH 45267-0559;* Jeffrey J. Miceli, Ph.D., Keith D. Wilner, Ph.D., Lisa Robarge, Ph.D.

Summary:

Objective: To evaluate the pharmacokinetics and safety of ziprasidone for treating Tourette's syndrome (TS) in children and adolescents.

Method: In a single-dose, open-label study, children and adolescents (boys and girls; 7–17 years) with moderate-to-severe TS or chronic motor or vocal tic disorder received oral ziprasidone according to body weight (Group 1 – >60 kg, 20 mg, $n = 8$; Group 2 – 31–60 kg, 10 mg, $n = 7$; Group 3 – 16–30 kg, 5 mg, $n = 8$).

Results: When exposure data for all subjects is plotted as a function of dose, normalized for body weight (mg/kg), the dose-relationships for AUC(0–∞) and C_{max} appear linear. Linear regression analyses on combined data from young patients and adults support the linearity for AUC(0–∞) and, to a lesser extent, for C_{max}. Correspondingly, ziprasidone $T_{1/2}$ values were similar in children, adolescents and adults, indicating that ziprasidone's clearance is comparable between these groups.

Conclusion: Single oral doses of ziprasidone 5, 10, and 20 mg, given with food, showed linear pharmacokinetics and were well tolerated in children and adolescents with TS.

NR564 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

ADHD and Treatment of Adolescent Dysphoric Mania

Rosanne C. State, M.D., *Department of Psychiatry, Harbor-UCLA Hospital, 1000 West Carson, Box 498, Torrance, CA 90509;* Mark A. Frye, M.D., Lori L. Altshuler, M.D.

Summary:

While childhood attention deficit hyperactivity disorder (ADHD) has been reported to predict lithium resistance in adolescent mania, little comparative data on lithium and divalproex response is available. This retrospective study was conducted to assess the comparative efficacy of lithium (Li) and divalproex (DVPX) in manic adolescents with and without a history of ADHD.

Medical records were reviewed of 42 patients ages 12–19 hospitalized at the UCLA Neuropsychiatric Hospital for acute mania discharged on either lithium (N = 29) or divalproex (N = 13) monotherapy. 36 of 42 (86%) patients presented with dysphoric mania, and 14/42 (33%) subjects had a history of ADHD. A clinician blinded to diagnostic and treatment status rated improvement based upon abstracted notes in each case utilizing the clinical global impression scale modified for use in bipolar illness (CGI-BP). Subjects with a CGI-BP overall severity of illness score of 1 or 2 were considered responders.

The overall response rate was 18/42 (43%). There were no significant differences in discharge CGI overall severity of illness between DVPX vs. Li (2.57 vs. 2.65, $p = 0.78$). Subjects with ADHD histories had higher mean CGI overall severity of illness at discharge than non-ADHD subjects (3.27 vs. 2.3, $p < .0009$) No differential response to lithium or divalproex was observed.

This retrospective observation suggests overall equivalent response rates to lithium and divalproex in adolescents with dysphoric mania. Furthermore, a history of ADHD may confer resistance to both divalproex and lithium. Further controlled studies of DVPX vs. Li in adolescent mania are needed.

NR565 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Metformin Leads to Weight Loss in Adolescents Who Gained Weight on Psychotropic Drugs

Elizabeth M. Cottingham, M.D., *Department of Psychiatry, Children's Hospital, 3333 Burnett Avenue, Cincinnati, OH 45229-3039;* John A. Morrison, Ph.D., Bruce A. Barton, Ph.D.

Summary:

Psychotropic medications are effective in treating mood disorders and psychoses in adolescent patients, but their use has been associated with (1) weight-gain in as many as 50% of patients of both sexes and (2) with polycystic ovary disease (PCOD). Metformin has been shown to increase insulin sensitivity in adult patients with NIDDM and to produce weight loss in patients with PCOD. PCOD can be considered a model for insulin resistance in females. Within this context, we conducted a pilot study of metformin in adolescents of both sexes who had gained weight on psychotropics. Seven adolescent patients (4 males, 3 females) who had been stable on Zyprexa and/or Depakote for 3+ months with weight-gain >10% of baseline weight participated. Length of time on psychotropics ranged from 3 to 18 months (mean +/– sd = 9.1 +/– 7.1) and weight gain ranged from 17.6 to 114.9 lbs. (61.6 +/– 31.9). Patients were prescribed 500 mg tid and instructed not to make changes in either food intake or physical activity. Time on metformin ranged from 4 to 12 weeks. Changes in weight ranges from –18.25 to +2.75 (–6.33 +/– 7.5). Decrease in weight, graphed below, was statistically significant ($p < 0.05$), as was change in BMI ($p < 0.02$). Controlled trials of metformin to treat weight-gain in patients prescribed psychotropics are needed.

NR566 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Comparative Side Effects of Atypical Neuroleptics in Children and Adolescents

Stephen Grcevich, M.D., *Department of Psychiatry, Case Western Reserve, 8500 East Washington Street, Chagrin Falls, OH 44023;* Connie McBurney, R.N.C., Constance Ray, R.N.C., Rosemary Richards, R.N.C., Meredith Shotschar, R.N.C.

Summary:

Objective: The analysis seeks to compare weight gain and other side effects associated with use of risperidone, quetiapine and olanzapine in children and adolescents.

Methods: Medical records of 97 patients treated in an outpatient mental health clinic serving children and adolescents between January 1995 and June 1999 were reviewed. 75 patients were treated with risperidone, 25 with quetiapine, and 16 with olanzapine.

Results: Mean weight gain after three months of treatment was 8.6 lb. for risperidone, 7.3 lb. for quetiapine and 14.1 lb. with olanzapine. Weight gain was the more common side effect observed with all three agents. Patients receiving quetiapine were less likely to gain >10lb. during the first three months of treatment compared to those on olanzapine ($p < 0.05$, Kruskal-Wallace test). Weight gain was not dose-dependent for any agent at three-month follow-up (Pearson Correlation Coefficient). Extrapyramidal side effects required treatment in 7 of 75 patients receiving risperidone, 4 of 16 patients receiving olanzapine and none of 25 patients receiving quetiapine.

Conclusions: Clinicians should consider carefully the risk of weight gain and extrapyramidal side effects against potential benefits when prescribing atypical neuroleptics to children and adolescents.

NR567 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Pharmacodynamic and Pharmacokinetic Profiles of a New Modified-Release Formulation of Methylphenidate in Children with ADHD

Thomas J. Spencer, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114;* James M. Swanson, Ph.D., Sabri Markabi, M.D., Meredith Weidenman, B.A., Herbert Faleck, D.O.

Summary:

This was a randomized, double-blind, placebo-controlled, five-period crossover study of a modified-release formulation of Ritalin, in 34 children with ADHD. Time course effects and pharmacokinetics were evaluated for four variants of a new formulation of Ritalin, given once daily. Following an open-label baseline evaluation during which commercial Ritalin was given twice daily, subjects were randomized to a sequence of treatments. For each treatment, a capsule was administered in the morning and assessments were performed in a laboratory classroom setting at multiple time points across an 11.5-hour day. Subjective (teacher ratings of attention and department) and objective (scores on math tests) measures were obtained for each classroom session. These measures were used to evaluate the time-response of different variants of the new formulation. A positive treatment effect was observed for all four variants for all measures, including teacher ratings of attention and deportment as well as scores on math tests. Importantly, all measures were significantly improved relative to placebo ($p < 0.05$) in the second period of the day (hours 4–9) on once-a-day dosing. Pharmacokinetic analyses revealed that all variants produced sustained plasma concentration time profiles characterized by a bimodal release. All formulation/dose variants of modified-release Ritalin were safe and well tolerated.

NR568 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Bupropion Sustained Release Versus Methylphenidate Versus Placebo in the Treatment of Adult ADHD

Paul J. Perry, Ph.D., *Department of Psychiatry, University of Iowa, S415 Pharmacy Building, Iowa City, IA 52242;* Samuel Kuperman, M.D., Gary R. Gaffney, M.D., Kristine Bever-Stille, Pharm.D., Brian Lund, Pharm.D., Timothy Holman, M.A., Jane Paulsen, Ph.D.

Summary:

Methods: A randomized double-blind, parallel design was used in this study. Following a 7-day placebo lead-in, 29 ADHD (DSM-IV) patients (18-60 years old) were randomized to bupropion, methylphenidate, or placebo for eight weeks. Methylphenidate was titrated over 1 week to a maximum dose of 0.9 mg/kg/d divided into 3 doses while bupropion was titrated over 2 weeks to a maximum dose of 200 mg AM and 100 mg PM.

Results: The percent change scores on the ADHD patient self-rating scale demonstrated no difference between the three treatments. According to the Clinical Global Impression Ratings, much or very much improvement ratings were observed by the physicians in 7 (64%) bupropion SR patients, 4 (50%) methylphenidate patients, and 3 (30%) of the placebo treated patients (not significant, Fisher's Exact Test). Neuropsychological testing included the Hopkins Verbal Learning immediate and delayed recall tests, digit ordering, Trails A and B, and verbal fluency. The Hopkins immediate recall scores favored bupropion over methylphenidate and placebo while the 30-minutes recall task demonstrated a trend favoring bupropion SR. The other tests showed no differences.

Conclusions: Bupropion demonstrated a trend that suggest potential efficacy as a treatment for adult ADHD.

NR569 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

RCT Cognitive Group Therapy: Early Breast Cancer

David W. Kissane, M.D., *Department of Psychiatry, University of Melbourne, 104 Studley Park Road, Kew, Victoria 3101, Australia;* Sydney Bloch, M.D., David M. Clarke, M.D., Graeme C. Smith, M.D., Patricia Miach, Ph.D., Anthony Love, Ph.D.

Summary:

Objective: To test a model of group therapy whose delivery over 16 sessions corresponded with the administration of adjuvant chemotherapy and radiotherapy for early stage breast cancer. The therapy aimed to enhance coping, reduce fear and promote adjustment to improve quality of life. Survival will be studied later.

Methods: The design involved a randomised comparison of groups plus a brief relaxation program with a control arm of receiving relaxation only. Assessment was undertaken pre, post and 6 months beyond completion of therapy using the Affects Balance Scale (ABS), Hospital Anxiety and Depression Scale (HAD), Mental Adjustment to Cancer Scale (MAC), EORTC QLQ C30 and BR23, and Family Assessment Device (FAD). Analysis was based on intention-to-treat and involved variance component analysis, with coefficient estimates obtained using the restricted maximum likelihood method. Randomisation and time were treated as fixed effects while therapists and groups were modelled as random effects. One-sided p-values test the significance of interaction between randomisation and time.

Results: The group therapy reduced total negative affect (ABS) $p = 0.023$ and fear (HAD-ANX) $p = 0.026$, but did not increase positive affects compared to controls. There was a trend to reduce anxious preoccupation (MAC) $p = 0.09$, but fighting spirit (MAC) was not changed by this therapy. Family functioning (FAD) deteriorated for control compared to the group arm $p = 0.038$.

Conclusion: This model of cognitive-existential group therapy for women with primary breast cancer significantly reduced affective distress associated with the diagnosis of cancer, but did not demonstrate attitudinal change in their coping. Therapy protected against deterioration in family relationships. The model worked well as an adjuvant psychological group therapy in cancer.

NR570 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Atypical Antipsychotics, Weight Gain and Hyperlipidemia in Hospitalized Preadolescents

Michael P. Duran, M.D., *Department of Child Psychiatry, Oregon State Hospital, 2600 Center Street, NE, Salem, OR 97310;* Jonathan M. Meyer, M.D.

Summary:

Novel antipsychotics are associated with a decreased incidence of extrapyramidal side effects compared to older typical antipsychotics, but have been associated with the development of obesity and hypertriglyceridemia in adults. Prior published reports have implicated all newer antipsychotics in producing significant weight gain in children and adolescents; however, there has been no published data regarding the effects on serum lipids in this population. As untreated obesity and hyperlipidemia may cause significant long-term morbidity, metabolic outcomes data on weight gain and serum lipids were examined in 7 hospitalized preadolescents on novel antipsychotics (risperidone, olanzapine, quetiapine). A body mass index (BMI) increase of greater than 5% was seen in 4 of 7 cases, with mean fasting triglycerides of 384 mg/dl seen after an average of 11.5 months of therapy. One case reported a peak fasting triglyceride level of 1311 mg/dl. BMI increase did not correlate with change in fasting triglycerides. Underlying mechanisms for atypical antipsychotic-induced hypertriglyceridemia are unclear, but clinical monitoring of serum lipids in preadolescents must be added to the concerns about weight gain with newer antipsychotic agents in this population.

NR571 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Divalproex Effectiveness in a Pediatric Inpatient Psychiatric Unit

Gahan J. Pandina, Ph.D., *Department of Psychiatry, UMDNJ-RWJMS/UBHC, 335 George Street, #3700, New Brunswick, NJ 08901;* Karen Senese, M.D., Julie Lewerenz, M.D., Robert L. Hendren, D.O.

Summary:

Objective: To determine effectiveness of divalproex in a pediatric inpatient population via chart review.

Method: A chart review was conducted of all patients receiving divalproex during admission to an inpatient pediatric psychiatric hospital (N = 90, 32 females, mean age 12 years). Eighteen patients discontinued medication: the remaining 72 patients were divided into four groups using consensus diagnoses (mean dosage = 721.2 mg, blood level = 78.3): "Impulse Control Disorder" (n = 23), "Depressed" (n = 12), "Bipolar Disorder" (n = 27), and "Other" (n = 10).

Results: Overall, 63 of 72 patients improved in clinical global impression ratings (CGI) while on divalproex during the course of inpatient treatment. An average 1.5 CGI levels of improvement was found. "Bipolar" subjects showed significantly more improvement on the CGI than "Impulse Control Disorder" (2-tailed: p = 0.0029) and "Other" (2-tailed: 0.044) subjects. "Depressed" subjects also showed significant improvement versus "Impulse Control Disorder" subjects (2-tailed: p = 0.040). There was a positive correlation between divalproex level and CGI improvement for "Depressed" subjects (.46), and a negative correlation for Bipolar subjects (–.37).

Conclusions: Limitations include lack of formal diagnostic instrumentation, limited sample size, and additional medications. Diagnosis-dependent clinical responses to divalproex suggest that divalproex more effectively manages affective- versus impulse-related symptoms.

NR572 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Gender Differences in HIV, HBV, HCV and Associated Risks in Severely Mentally Ill Persons

Marian I. Butterfield, M.D., *Department of Psychiatry, Duke-Durham VAMC, 508 Fulton Street, Durham, NC 27705;* Hayden Bosworth, Ph.D., Keith G. Meador, M.D., Karen M. Stechuchak, M.S., Marvin S. Swartz, M.D., Jeffery W. Swanson, Ph.D., Lori A. Bastian, M.D.

Summary:

Objective: To evaluate HIV, Hepatitis B (HBV) and Hepatitis C (HCV) prevalence, risks and and to evaluate gender differences in these parameters in persons with severe mental illness (SMI).

Methods: From June 1997—December 1998, SMI persons from 5-sites (n = 969, 340 women, 629 men) were enrolled in the study. HIV, HBV, and HCV risk behaviors and serostatus were assessed. SMI diagnoses included schizophrenia, schizoaffective disorder, bipolar disorder, depression, and posttraumatic stress disorder (PTSD).

Results: Observed prevalence rates of HIV (2.7%), HBV (18.8%), and HCV (16.2%) in SMI persons. Prevalence rates among SMI men vs SMI women were similar for HIV (3.0% vs 2.1%) and HBV (19.5% vs 17.1%). However, HCV prevalence rates were higher among SMI men (19.3%) than SMI women (9.8%). Gender differences in risk behaviors were observed. SMI women were more likely to have sex for drugs than SMI men were (14.8% vs 11.4%). SMI men were more likely than SMI women to have used crack cocaine (45.0% vs 27.5%) and/or injection drugs (20.9% vs 11.2%). Adjusting for these three risk behaviors, SMI men who used needles, crack cocaine, or had sex for drugs had higher rates of HCV infection than SMI women who have had these risk behaviors. In contrast, there were not gender differences in using crack cocaine and sex for drugs, in HBV serostatus. However, SMI men who used injection drugs had higher rates of HBV infection than SMI women.

Conclusions: In this study, SMI men and SMI women have high prevalence rates of HIV, HBV, and HCV, much higher than the overall estimated population rates for these infections. SMI men were more likely than SMI women to be HCV infected. HIV and HBV prevalence rates were similar among SMI men and SMI women. Routes and risks transmission of these infections may differ in SMI men and SMI women.

NR573 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Early Cognitive Deficits in HIV-1 Patients

Paulo S. Belmonte de Abreu, M.D., *Department of Psychiatry, Hospital Clinicas, Ramiro Barcellos 2350, #4, Porto Alegre, RS 90035-003, Brazil;* Adriana C. Schoffel, M.D., Edino Parolo, M.D.

Summary:

Objective: To test if HIV-positive cognitive performance would be more impaired than executive function, compared to normal controls, in Latin-American outpatients at public health setting, using standardized neuropsychological assessment.

Method: The cross-sectional study (n = 86, age 18–50 years) compared 33 HIV-1 CDC-A-Category Asymptomatic outpatients with 53 normal controls, with a Neuropsychological battery (MMSE, Verbal Fluency, Logical Memory, Visual Recognition, Stroop Test and Wisconsin Test), Depression (MADRS) and Anxiety (HAMA) scales.

Results: 39 men and 47 women, age of 32.6 (HIV-1) and 31.6 (controls) (p = 0,61), contamination period of 33.7 months. 69.7% cases at heterosexual and 30.3% homosexual transmission. Education was 12.2 (HIV) and 11.2 years (controls). There were differences on MMSE subscores of evocation and language and on Verbal fluency, MADRS and HAMA. HIV-1 positives had similar performance on executive tests, impaired performance on cognitive tests (MMSE evocation and language, and Verbal Fluency) and higher HAMA and MADRS scores. Additionally, cognitively impaired HIV-1 subjects showed correlation with MADRS scores.

Discussion: HIV-1 Positive patients had impaired cognition on language, recall memory and constructive capacity, with no executive impairment. Additionally, depressive symptoms were associated to lower cognitive performance, although the effect on cognition remained after controlling for the effect of depressive and anxiety symptoms.

NR574 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Behavioral Benefits in Alzheimer's Disease Patients Residing in a Nursing Home Following 52 Weeks of Rivastigmine Treatment

Jeffrey L. Cummings, M.D., *Department of Neurology, UCLA/Reed Neurosciences Center, 710 Westwood Plaza, Los Angeles, CA 90095;* Ravi Anand, M.D., Barbara Koumaras, Richard Hartman, Ph.D.

Summary:

We present 1-yr results from a trial with rivastigmine in nursing home patients with AD. Results from the first 26-weeks of treatment, previously reported, indicated that rivastigmine improved behavioral symptoms, as measured by the Neuropsychiatric Inventory-Nursing Home Version (NPI-NH), as well as cognition, as measured by the Mini-Mental State Examination (MMSE).

Of the 173 patients included in this trial, 81% reported at least one behavioral symptom at baseline (mean NPI-NH 15.8) and the mean MMSE score was 9.2. Results from 52 weeks of treatment

indicate that, in contrast to the anticipated worsening in behavioral symptoms expected, the score on the NPI-NH improved by 1.03 points after 52 weeks and 49% of these patients had a clinically significant 30% improvement from their baseline score. The importance of these results is reinforced by finding that 46% of patients needing neuroleptics at baseline no longer required their use after 52-weeks of treatment with rivastigmine. Furthermore, the MMSE showed a decline of 0.17 points, compared with the expected minimum decline of 3 points over one year for this population.

These results extend earlier results demonstrating benefits of rivastigmine on cognition, activities of daily living, and global functioning, already established in mild to moderate AD patients.

NR575 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Risperidone Versus Placebo for Severe Conduct Disorder

Michael G. Aman, Ph.D., *The Nisonger Center, Ohio State University, 1581 Dodd Drive, Room 175, Columbus, OH 43210-1296;* Robert L. Findling, M.D., Albert T. Derivan, M.D., Ursula Merriman

Summary:

Objective: This randomized double-blind study compared risperidone and placebo in the outpatient treatment of severe conduct problems in children with mild (IQ 51–70) to moderate (IQ 35–50) MR or borderline IQ (71–84).

Methods: After a 1-wk placebo run-in, 118 children aged 5 to 12 years with an IQ of 35 to 84 were treated with placebo or risperidone each morning for 6 weeks. Doses could be adjusted within a range of 0.02 to 0.06 mg/kg/day. The primary efficacy variable was the Conduct Problem subscale of the Nisonger Child Behavior Rating Form (N-CBRF), from which changes from baseline were compared. Secondary efficacy variables included other subscales of the N-CBRF, the Aberrant Behavior Checklist, the Behavior Problems Inventory, and the Clinical Global Impressions scale. Safety assessments were based on reported adverse events.

Results: Statistically significant differences favoring risperidone over placebo were observed as early as week 1 and continued through the duration of the trial and at end point for the primary efficacy variable. Significant differences favoring risperidone were also observed for the secondary variables. The mean dose of risperidone was 1.23 mg/day. No serious adverse events were reported.

Conclusion: Risperidone appears to effectively and safely improve severe conduct problems in children with subaverage IQs.

NR576 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Stress, Depressive Symptomatology and Craving in Nontreatment-Seeking Individuals with Cocaine Dependence

Katherine Karlsgodt, B.A., *Department of Psychiatry, Massachusetts General Hospital, 16 Blossom Street, Boston, MA 02114;* David R. Gastfriend, M.D., Sara Krause, B.A., Igor Elman, M.D.

Summary:

Objective: A growing body of data from cocaine abusers engaged in treatment implicates psychosocial stress and negative mood states in craving and subsequent relapse to drug use. Untreated individuals are another subject category that may be of clinical and scientific interest.

Methods: Thirty six non-treatment seeking subjects with cocaine dependence were split into high (N = 16) and low (N = 20) stress groups at the mean on both Tension-Anxiety subscale of the Profile of Mood States and State-Trait Anxiety Index.

Results: The high stress as compared to the low stress group had significantly more lifetime years of cocaine use (p = 0.03), higher Hamilton Rating Scale for Depression Scores (p = 0.01) and similar levels of cocaine craving. In an exploratory analysis, days of cocaine use in the last month correlated with the craving scores (p = 0.01) but not with the measures of mood or stress.

Conclusion: These finding suggest that 1) the association between stress and depression and cocaine use can be extended to the population of non-treatment seekers and 2) craving is a relatively specific construct in determining recent drug use. Further studies on the role of stress and mood states in the course of cocaine dependence may be needed.

NR577 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Effects of MAOI CA Repeat Polymorphism on Behavioral Personality Trait and Clinical Characteristic in Alcoholic Korean Male

Jung-Sik Lee, M.D., *Department of Psychiatry, Yong-In Mental Hospital, 4 Sangha-Ri Kusung-Myun, Yong-In Kyunggido 449-910, Korea;* Byung-Hwan Yang, Ph.D.

Allelic associations have been reported between MAOA CA repeat polymorphism and alcohol dependence, recently. And also, several studies have been investigated genotype-phenotype relationships between this polymorphism and clinical manifestations. The authors tried to identify differences in allelic frequency of the polymorphism between alcohol dependence and controls and in personality, behavioral trait and clinical characteristics according to length of allele. We also tried to investigate genotype-phenotype relationships between this polymorphism and behavioral trait such as aggression.

We performed semistructured interview for demographic and clinical characteristics of 49 male patients with alcohol dependence (DSM-IV). Self-report questionnaires for BDHI (Buss-Durkey Hostility Inventory) and NEO-PI-R (NEO Personality Inventory Revised) were given to all subject at least 4 weeks later after admission. Using polymerase chain reaction and polyacryamide gel electrophoresis, MAOA CA repeat polymorphism were observed in 52 male controls and 49 male alcoholics. We devided alcoholic patients into two groups according to length of allele; alcoholics with short alleles (≥119bp, N = 20) and alcoholics with long alleles (≥123bp, N = 29).

There were no significant differences in frequency of each allele and short and long allele of the polymorphism between alcoholics and controls. But In clinical symptoms, alcoholics with long alleles drank alcohol more frequently during one month before admission, had much more maximum amount of beer drinking and reported withdrawal seizure more frequently than with short alleles. In contrary, alcoholics with short alleles expressed mood and guilty feeling more frequently and wanted complete abstinence as a treatment goal more frequently than with long alleles. In personality trait, alcoholics with short alleles had much more frank and orderly trait than with long alleles. In behavioral trait, alcoholics with long alleles had higher total aggression score and showed much more self-assertive attitude than with short alleles. Length of allele was correlate with self-assertive attitude and accounted for 9% of the variance of self-assertive attitude. And also, predictable variables of allelic length were drinking frequency and self-assertive attitude.

Our findings suggest that MAOA CA repeat polymorphism may provide some behavior modifying role especially in self-assertive attitude and indirect symptom modifying role in Korean male alcoholics rather than alcohol dependence per se.

NR578 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Sociocultural Factors Associated with Binge Drinking Among College Athletes

Merry N. Miller, M.D., *Department of Psychiatry, East Tennessee State University, 325 North State of Franklin Road,*

Johnson City, TN 37604; Barney E. Miller, Ph.D., Ruth Verhegge, Holly Linville, M.D., Andres J. Pumariega, M.D., Hubert B. Vance, Ph.D.

Summary:

Objective: College athletes were assessed for associations between alcohol misuse and sociocultural factors.

Method: During an annual health screen for college athletes (10 sports), all 262 athletes were given the Alcohol Use Disorders Identification Test (AUDIT), the Beck Depression Inventory (BDI), Eating Attitudes Test 40 (EAT40), Mini-International Neuropsychiatric Inventory (MINI) and also were asked about various cultural attitudes and behaviors.

Results: Athletes who misuse alcohol (i.e. score >8 on the AUDIT) reported less contact with relatives ($p < 0.02$), feel less benefit from religion ($p < 0.08$), make less plans for the future ($p < 0.05$), and were less likely to ask for help when needed ($p < 0.08$) (t-test). Female athletes who misuse alcohol reported significantly less family support, less benefit from religion, and less trust in others. Male athletes who misuse alcohol reported significantly less patriotism and also less benefit from religion. Time spent in religious activities was inversely correlated with the amount of alcohol misuse, but did not significantly correlate with levels of depression or anxiety. Further data will be reported on the interactions between psychiatric symptoms, alcohol misuse, and cultural factors.

Conclusions: These findings suggest cultural attitudes/behaviors that may promote or protect against the development of alcohol misuse in the college athlete.

NR579 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Two-Year Follow-Up of a Group of Heroin Addicts

Eduardo Gutierez, M.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, #3, Oviedo 33006, Spain;* Pilar A. Saiz, Ph.D., Maria P. Gonzalez, Ph.D., Juan M. Fernandez, M.D., Celso Iglesias, Ph.D., Julio B. Bobes, Ph.D.

Summary:

Objective: To describe the evolution of a group of heroin addicts remaining in a methadone (MMP) or naltrexone (NMP) maintenance programme after 2 years.

Method: Out of a total of 150 patients included in a MMP or NMP (Mieres, Asturias—Northern Spain) during 1997, 93 were revaluated after 2 years. Assessment: EuropASI, IPDE.

Results: Baseline profile: mean age (SD) = 27.33 (5.93); males: 84.0%; singles: 68.7%; living with family: 85.3%; working: 65.3%; HIV+: 8.0%; HBV+: 27.3%; HCV+: 44.7%; intravenous route: 66.7%; personality disorder (PD): 67.3%; MMP: 35.3%. *Follow-up profile:* mean age (SD) = 28.99 (5.58); males: 81.7%; singles: 66.7%; living with family: 89.2%; with work: 60.2%; HIV+: 9.7%; HBV+: 25.8% HCV+: 49.5%; intravenous route: 66.7%; PD: 67.6%; MMP: 60.2%. We observed a significant decrease ($p < 0.05$) on all EuropASI areas scores but the legal status; patients with PD ($n = 63$) score lower ($p < 0.05$) on the following EuropASI areas: employment/support, alcohol, drug, and psychiatric status and worsened ($p < 0.05$) on the medical status; patients without PD ($n = 30$) score lower ($p < 0.05$) on employment/support, drug, and psychiatric status.

Conclusions: Most of the patients continue in a MMP programme after two years. The permanence on a maintenance programme is associated with a moderate improvement of the severity of the addiction.

NR580 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Dependence and Abuse in Schizophrenia Patients in Hawaii

F.M. Baker, M.D., *Department of Psychiatry, University of Hawaii, 45-710 Keaahala Road, Kaneohe, HI 96744*

Summary:

A pilot study of the prevalence of substance abuse disorders was completed on the only open unit of the only state psychiatric hospital in Hawaii to address the following questions: 1. Was the prevalence of substance abuse among our patients higher than the rates reported in the literature? 2. Was the staff perception that the majority of these patients were in denial an accurate perception? 3. Was the pattern of abuse and/or dependence different in the patients that we were treating?

Methodology: All patient admitted to the unit between June 1 to August 31, 1999 comprised the sample; N = 35. Each patient was assigned diagnoses based upon the DSM-IV criteria and level of change was assessed.

Results: The demographic characteristics of the sample were consistent with the Hawaii population; 60% were ages 20–39; 89% were male; 92% were single, 71% had an education of high school or college, and 66% had a diagnosis of schizophrenia or schizoaffective disorder. Although 20% of the sample had no substance abuse problem, 66% of the remaining patients were multiply dependent upon alcohol, cannabis, crystal methamphetamine, or cocaine with 49% of these patients in the Precontemplative Stage of Change (denial). These figures were higher than in the reported literature for in-patient populations. Further studies are needed.

NR581 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Anticonvulsant Treatment for Alcohol Dependence After Brain Injury

Thomas P. Beresford, M.D., *Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver, CO 80220;* Stephanie D. Morrison, B.A., Brandon K. Martin, B.A., David B. Arciniegas, M.D.

Summary:

Objective: Clinical studies show that alcohol dependence (AD) and traumatic brain injury (TBI) often occur together. In some cases, TBI may worsen pre-existing AD or facilitate new, uncontrolled, heavy alcohol use. In such cases, patients may use ethanol in an attempt to control labile mood and anxiety symptoms following TBI. Since anticonvulsant use offers symptom stabilization in bipolar illness and other conditions, this class of medications might offer similar stabilizing effects in AD patients with a history of TBI when symptoms of mood or anxiety dysregulation appear.

Method: We report clinical experience with a series of cases (N = 18) in which anticonvulsant medication (either valproic acid or carbamazepine) was given to ease labile mood or anxiety in the setting of AD and TBI. Clinical outcome data were gleaned from both physician impression and medical record review.

Results: We observed a remarkably high rate of ethanol abstinence in 16 (89%) of the 18 cases. All but two with improved sobriety (14/16 or 88%) also showed improvement in their mood or anxiety symptoms.

Conclusions: While anticonvulsants may be useful in treating AD complicated by TBI, double blind, placebo controlled, crossover study in a well characterized patient group must first establish a true medication effect.

NR582 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Multicenter Alcohol Use Data from Liver Transplant Candidates

Thomas P. Beresford, M.D., *Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver, CO 80220;* Brandon K. Martin, B.A., Stephen L. Snyder, M.D., Andrea F. DiMartini, M.D.

Summary:

Objective: Continuing to provide liver transplant for alcohol dependent (AD) patients depends on demonstrating long term AD survival rates similar to non-AD recipients. This necessitates longitudinal study of large samples of AD liver recipients, requiring multi-site cooperation. In developing a consortium for this purpose, our first objective is to collect ethanol use data from liver transplant candidates to identify those with high likelihood of AD diagnosis.

Method: We developed a screening questionnaire covering demographics, alcohol and substance use history, and history of psychiatric treatment. We tested it at the University of Colorado, the Mt. Sinai Medical Center, and the University of Pittsburgh. Data were collected from a total of 120 transplant candidates.

Results: 68% of the total sample reported ever having used ethanol, 52% had been instructed to stop drinking by their physician, 12% reported use in the previous six months and 6% within the last thirty days. Positive CAGE responses were, 38% Cut down, 19% Annoyed, 28% Guilty, and 12% Eye opener.

Conclusion: To our knowledge, this represents the first time alcohol data on liver transplant candidates has been acquired across several medical centers and the method appears to be useful in identifying AD candidates.

NR583 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Compliance with Court-Ordered Versus Voluntary Disulfiram Therapy

Brandon K. Martin, B.A., *Department of Psychiatry, University of Colorado, 1055 Clermont Street 116, Denver, CO 80220;* Lori Clapp, R.N., Denise C. Bridgeford, M.D., Akwasi Amponsah, M.D., Dianna Bialkowski, R.N., Levester Lyons, M.S.W., Thomas P. Beresford, M.D.

Summary:

Objective: For some patients, regular disulfiram treatment is useful in breaking a heavy drinking pattern. While large studies have shown that disulfiram compliance may be short lived, few have examined the factors that promote treatment adherence.

Method: We conducted a 12-week, prospective study of compliance with court ordered disulfiram treatment as compared to voluntary treatment. Our primary measure was the rate of completed clinic visits scheduled for dispensing disulfiram. With institutional review board approval and subject consent, we enrolled 19 court-ordered and 22 voluntary subjects who met DSM-IV criteria for either alcohol abuse or dependence. A standard dose of 500 mg of disulfiram, given orally, was administered in clinic three times weekly.

Results: The court ordered group was significantly ($p < 0.0001$) more compliant than the voluntary group, completing an average of 87% (±21%) of scheduled visits, versus 42% (±35%).

Conclusions: These results suggest that external structure, in this case provided by a court, is a useful factor for maintaining short-term compliance in patients with alcohol use disorders. This finding may apply to newly proposed medicinal treatments for alcoholism, such as naltrexone and others.

NR584 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Stable Patients Tolerate Step-Down in Targeted Assertive Outreach (TAO) Services

Richard N. Rosenthal, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Avenue at 16th St., #9F, New York, NY 10003;* David J. Hellerstein, M.D., Christian R. Miner, Ph.D.

Summary:

Objective: To assess 6-month outcomes on substance use and psychiatric rehospitalization in subjects with comorbid SCID/DSM-IV schizophrenia and substance use disorders (SUD/S) when Targeted Assertive Outreach (TAO) services are discontinued. The "programmatic" approach to assertive community treatment assumes indefinite enrollment—a model often inconsistent with clinical need and limited resources. We conducted a prospective pilot study to determine the feasibility of stepping-down TAO in SUD/S subjects who were already participating in a randomized trial comparing manualized treatment integrating psychiatric and substance abuse outpatient services plus Targeted Assertive Outreach (COPAD+TAO), to integrated treatment (COPAD) alone.

Method: Clinically stable research subjects (N = 18) who were exposed to ≥12 months of COPAD+TAO treatment were eligible for step-down of TAO services over 1 week, with follow-up at 6 months. Subjects continued to attend twice-weekly group therapy also attended by TAO assertive case managers.

Results: Following step-down, 14/18 subjects (77.8%) remained stable over 6 months, with ongoing treatment engagement, no psychiatric hospitalizations, and no substance abuse on random weekly urine screens; however, two (11%) reported single-use interruptions in their sobriety (minor slips). Only 2 subjects (11%) relapsed to substance abuse, became psychotic and were rehospitalized. Two (11%) were rehospitalized for exacerbation of schizophrenia unrelated to SUD.

Conclusions: SUD/S patients often need intensive outreach and rerecruitment early in treatment but as they attain psychiatric stability, sobriety, and stable housing, the necessity for TAO services appears to diminish. These data demonstrate the clinical plausibility of stepping-down TAO services once stability is reached, and support the feasibility of a randomized trial.

NR585 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Early Dropout of Mentally Ill Chemical Abusers in a Therapeutic Community

Serge M. Sevy, M.D., *Psychiatric Research Dept., Hillside Hospital, 75-79 263rd Street, Glen Oaks, NY 11004;* Kyra Sposato

Summary:

Objective: To examine reasons for discharge of Mentally Ill Chemical Abusers (MICA) during the first 6 months in a Therapeutic Community (TC) program.

Method: Retrospective review of MICA admitted between 5/97 and 5/99 to a TC in New York City. Exclusion criteria for admission included active suicidal, self-injury, homicidal ideation, and acute psychotic symptoms.

Results: 56 MICA were admitted during that period. 27 (48%) were discharged during the first 6 months. Reasons for discharge were violence toward others (n = 5), self-injury (n = 3), psychotic episode (n = 4), depressive episode (n = 5), manic episode (n = 1), hypomanic episode (n = 1), mixed state (n = 2), substance abuse relapse (n = 3), financial reasons (n = 1), and unknown (n = 2).

Conclusion: Our data suggest that the main reason for early discharge of MICA in a TC is a psychiatric problem, more specifically an acute risk of violence toward self or others (n = 8, 30%) and a non-remitted mood disorder (n = 9, 31%). Implications of our results for admission and treatment of MICA in a TC will be

discussed, more specifically the identification of psychiatric factors that may require particular attention in the early phase of a TC program.

NR586 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Prolactin Levels and SCH39166 in Cocaine PTS

Vasant P. Dhopesh, M.D., *Department of Psychiatry, VA Medical Center/116A, University & Woodland Avenue, Philadelphia, PA 19104;* James W. Cornish, M.D., Elmer Yu, M.D., AnnaRose Childress, Ph.D., Sabrina A. Poole, M.D.

Summary:

Objective: Acutely cocaine use is associated with increases in dopamine in various brain areas because of inhibition of dopamine reuptake. Chronic cocaine use depletes dopamine, which is believed to be responsible for the elevation of serum prolactin. Dopamine depletion is also thought to be the putative biological mechanism for recurrent craving for cocaine. SCH 39166 is a D1, D, receptor blocker that has been found to block the rewarding and addictive properties of cocaine in primates. The objective of the study was to determine if SCH39166 affects cocaine craving in humans. Prolactin levels were measured to assess the dopaminergic effects of the compound.

Methods: 20 subjects, 10 placebo and 10 drug, were enrolled in the study. The mean age was 40.7 (±5.95) Placebo and 40.0 (±6.50) Drug respectively. Of this group, 4 were females. All subjects had chronic cocaine dependency histories, a DSM-IV diagnosis of cocaine dependence and a positive benzoylecgonine urine level (>300 ng/mL) at admission. This study was a double-blind 6 day inpatient study in which cocaine cue reactivity was measured prior to and during treatment. Subjects either received SCH39166 or placebo (po) from day 2 through day 6. 12 hours following medication administration, craving scales and other assessments, including prolactin levels and other chemistries were obtained.

Results: There were no statistically significant differences by ANOVA between the drug and the placebo group for prolactin levels (Graphs will be shown).

Conclusions: Prolactin levels were not affected in the drug group. This suggests that SCH39166 does not affect the dopamine pool. Although a prior inpatient study (Romach and Glue, et al, 1999) showed SCH39166 to diminish ratings of desire for cocaine ($p = .02$), the current study did not show a significant difference in ratings of desire.

NR587 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Striatal Size and Metabolism in Elderly Schizophrenia

Lina S. Shihabuddin, M.D., *Department of Psychiatry, Mt. Sinai School of Medicine, 1 Gustave Levy Place, box 1505, New York, NY 10029;* Monte S. Buchsbaum, M.D., Erin A. Hazlett, Ph.D., Adam M. Brickman, B.A.

Summary:

Striatal size and glucose metabolic rate have been extensively studied in schizophrenia. The differences in the striatum between normal controls and schizophrenics have been linked to the pathophysiology and to the progression of the disease. The effect of aging on the striatum is more controversial. In this study we compared the striatal size and glucose metabolic rate of schizophrenics under the age of 45 with those over the age of 45 and with matched normal controls to each group. MRI scans were obtained on 28 patients with schizophrenia and 32 age-matched normal controls below the age of 45; and 14 patients with schizophrenia and 15 age matched normal controls above the age of 45. PET scans were obtained on a sub-sample of these patients: 17 patients and 20 controls below the age of 45 and 10 patients and 12 controls above the age of 45. The PET activation task was the California Verbal Learning Task. All patients were diagnosed using the structured Comprehensive Assessment of History and Symptoms (CASH) and met criteria for DSM-IV criteria for schizophrenia.

There were no differences in size between the young and the old schizophrenia patients. The glucose metabolic rate in the ventral striatum was significantly higher in the older schizophrenia group compared to young schizophrenia group as well as to age-matched normals. There was a positive correlation between the glucose metabolic rate in the ventral putamen and age in the old patient group but not in the young group. The implications of these results on the pathophysiology of schizophrenia will be discussed.

NR588 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Cingulate Gyrus Volume in Drug-Naïve Schizophrenia Patients

M. Mehmet Haznedar, M.D., *Department of Psychiatry, Mount Sinai Hospital, 1 Gustave Levy Place/Box 1505, New York, NY 10029-6574;* Erin A. Hazlett, Ph.D., Jimcy Platholi, M.A., Monte S. Buchsbaum, M.D.

Summary:

The cingulate gyrus is involved in the expression and decoding of affect, attention, memory, higher executive functions and is implicated in schizophrenia. Postmortem studies of patients with schizophrenia report cytoarchitectural changes in the anterior cingulate gyrus and functioning imaging studies show hypometabolism of the anterior cingulate, which is associated with various clinical symptoms of schizophrenia. We previously reported volume decrease in one section of the anterior cingulate gyrus in a large group of patients with schizophrenia. In the current study, we examined the volumetric changes in the cingulate gyrus of 7 never-medicated patients with schizophrenia (mean age = 23.7) and 12 controls (mean age = 29.3). MRI axial acquisitions were done with a 1.5 Tesla GE Signa 5× system (3D volume-gradient recalled acquisition in steady state [spoiled GRASS, TR24, TE5, flip angle 40 degrees, contiguous 1.2-mm slices]). Two researchers, without knowledge of diagnosis, outlined the cingulate gyrus on axial MRI slices (intertracer interclass correlation coefficient = 0.87). For the size comparison, we used Talairach coordinates and divided the cingulate gyrus into 5 Brodmann areas (25, 24, 24′, 23, 29) following Devinsky et al. A significant ANCOVA (brain volume as co-variate) Hemisphere × Brodmann Area × Group interaction was observed ($p = 0.029$). Patients with schizophrenia had a reduction in the volume of the left anterior cingulate 24′ ($t = 2.14$, $df = 17$, $p = 0.047$). Differences in gray and white matter volume, and clinical correlates of above findings will be presented.

NR589 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Follow-Up Study of Depression with Siemens-CTI Exact HR Plus PET in the Acute Stage and Clinical Remission

Vjera A. Holthoff, M.D., *Department of Psychiatry, University of Technology, Fetscherstr. 74, Dresden 01307, Germany;* Bettina Beuthien-Baumann, M.D., Antje Triemer, Ph.D., Peter Winiecki, Ph.D., Franke Wolf-Gunter, M.D., Otto Bach, M.D.

Summary:

We report the pattern of change in regional cerebral glucose metabolism as measured by PET (Siemens-CTI Exact HR Plus) in patients scanned during acute major depression (DSM-IV, mean HAM-D: 23.2) and following clinical remission. Antidepressant drugs stayed unchanged and patients were considered to be in remission when their HAM-D scores remained lower than 7 for at least 12 weeks. Additional clinical assessment was carried out 6-

months after the follow-up PET. Patients underwent neuropsychological testing in the acute and recovered state. Of 20 patients optimally matched for drug treatment 15 have fully recovered and completed the study. Data analysis revealed a significant asymmetry in areas localized to the lateral and medial prefrontal cortex (including dorsolateral cortex, pregenual region of the cingulate) with lower metabolism in the left hemisphere during acute and recovered state. The change of glucose metabolism from depressed to recovered state did not reach significance. Remission from depression was not consistently accompanied by complete neuropsychological recovery. Altered metabolism in regions of the prefrontal cortex may be related to histopathological changes in major depression as revealed by a recent morphometric study[1] and may represent trait rather than state abnormalities as previously suggested for focal abnormalities of cerebral blood flow.[2]

NR590 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Idal-Motor Symptoms Under Risperidone

Ulf Kuenstler, M.D., *Department of Psychiatry, Leipzig University, Emilienstrasse 14, Leipzig D-04107, Germany;* Ralf Regenthal, M.D., Hermann J. Gertz, M.D., Swen Hesse, M.D., Karin Hohdorf, M.D.

Summary:

Objective: Using risperidone as a neuroleptic drug the question arises whether a relationship exists between D_2 receptor occupancy, plasma level and extrapyramidal-motor symptoms. Neuroleptic pre-exposition may influence this relationship.

Method: We report on sixteen patients with a ICD-10 diagnosis of schizophrenia, who were treated with risperidone 3 to 6 mg daily. Before starting risperidone treatment, eight of them were continuously neuroleptic-medicated for at least six months, eight of them were either drug-naive or drug-free for this period. After a minimum application time of 10 days, an ^{123}I-IBZM-SPET scan for D_2 receptors was carried out and risperidone plasma levels were determined. Extrapyramidal-motor symptoms were assessed by means of the Simpson-Angus-Scale and a handwriting test before treatment and coincident with the scan.

Results: Exclusively in the drug-naive/free patients the D_2 receptor occupancy correlated positively with plasma risperidone levels (Pearson, $r = 0.81$; $p < 0.03$) as well as with the reduction of handwriting area (Pearson, $r = 0.86$; $p < 0.001$). For the other group and also for the whole group of sixteen cases no such correlations existed. Interestingly, clinical extrapyramidal-motor symptoms were only observed in the neuroleptically pre-medicated group.

Conclusions: Only in drug-naive/free patients simultaneous assessment of both plasma level and reduction of handwriting area may be a useful clinical tool for estimates of D_2 receptor occupancy under risperidone treatment.

NR591 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Morphine Is Effective in the Reduction of Phantom Limb Pain and Cortical Reorganization

Wolfgang Larbig, M.D., *Department Med Psychology, University, Gartenstrasse 29, Tuebingen 72074, Germany;* Ellena Huse, Ph.D., Herta Flor, Ph.D., Niels Birbaumer, Ph.D.

Summary:

Objective: We investigated the analgesic efficacy of morphine in phantom limb pain. We hypothesized that pain reduction should lead to a corresponding shift of reorganization in the somatosensory cortex.

Method: The study design was randomized, double-blind, placebo-controlled and cross-over. 12 amputees were assigned to one of two treatment sequences. Pain intensity was assessed using an hourly pain-diary for 12 weeks (baseline, placebo- and treatment phase, 4 weeks each). Subjects were slowly titrated to the maximum dose of morphine over 4 weeks. Medication was tapered off over 1 week. Cortical reorganization was measured by recording somatosensory evoked fields by 143 MEG-squids, during pneumatic stimulation of those body parts representing adjacent areas to the deafferentation zone.

Results: Under morphine treatment the mean pain ratings were significantly lower compared to the placebo condition. A clinically relevant response to morphine (reduction at 50%) is observed in 4 patients, a partial response (reduction at 25–50%) in 4 patients, and 4 were non-responders.

Conclusions: Morphine is an effective analgesic in phantom limb pain without intolerable side effects. Analgesic responses are associated with a shift backwards in cortical reorganization.

NR592 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Striatal Size and Metabolic Rate in Normal Aging

Adam M. Brickman, B.A., *Department of Psychiatry, Mount Sinai, 1 Gustave Levy Place, box 1505, New York, NY 10029;* Lina S. Shihabuddin, M.D., Erin A. Hazlett, Ph.D., Olga G. Berwid, B.A., Li Zhang, M.A., Monte S. Buchsbaum, M.D.

Summary:

Introduction: Several studies have demonstrated changes associated with age in the striatum. Post-mortem and functional neuroimaging studies, including Positron Emission Tomography (PET), have generally suggested age-related changes in striatal dopaminergic activity and dopamine receptor density. In this study, we used PET and high-resolution magnetic resonance imaging (MRI) to examine the effects of age on striatal relative glucose metabolic rate and size in 70 normal, healthy subjects.

Methods: Medically, neurologically, and psychiatrically healthy normal subjects ($n = 70$) were assessed with high-resolution MRI and PET utilizing ^{18}F-deoxyglucose (FDG). Subjects ranged in age from 20 to 87 (mean $\pm$ SD = 54.0 $\pm$ 20.4); there were 34 males (48.6%) and 36 females (51.4%). During the FDG tracer uptake period, subjects performed a serial verbal learning task. MR images were segmented into grey, white, and cerebrospinal fluid regions, and warped to average normal coordinates. PET images were co-registered to the MR images and similarly warped for analysis.

Results: There was a significant positive correlation between the relative size of the dorsal putamen and age (Pearson's $R = 0.268$; sig = 0.025). There was a significant positive correlation between relative glucose metabolic rate and age in the dorsal putamen (Pearson's $R = 0.267$; sig = 0.025). Size and glucose metabolic rate in the dorsal putamen did not correlate significantly. When age was grouped by decade, there was a significant main effect of age on relative size of the dorsal putamen ($F_{6,63} = 2.44$; $p = 0.035$), which was significant for linearity ($F_{1,63} = 5.55$; $p = 0.022$). The glucose metabolic rate change with age in the dorsal putamen was significant for linearity. There was a significant negative correlation between relative glucose metabolic rate and age in the dorsal caudate (Pearson's $R = -0.235$; $p = 0.050$).

Discussion: These findings suggest a role of dopamine in normal aging, which may have clinical significance in terms of motor function and cognitive changes. The implications of these findings will be discussed.

NR593 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Basal Ganglia Activation in Schizophrenia Patients Under Haloperidol and Olanzapine and in Healthy Controls Revealed by fMRI

Juergen Mueller, M.D., *University of Regensburg, Universitaetsstrasse 53, Regensburg, Germany;* Matthias Dobmeier, M.D., Helmfried E. Klein, M.D.

Summary:

Objective: Focusing on basal ganglia the results of fMRI activation studies still are discrepant (1). We studied the fingertapping induced brain activation in haloperidol and olanzapine treated schizophrenics and controls especially focusing on subcortical regions.

Methods: An unilateral self-paced fMRI fingertapping task was performed by 37 male volunteers. 24 DSM-IV-schizophrenics under different treatment with olanzapine (10OL) and haloperidol (14HA) were compared to 13 controls (CO). BrainVoyager 3.7 software package (2) was used for data-analyzing including 2d spatial and temporal Gaussian smoothing [2mm and 3 mm], removal of linear trend and nearest-neighbor cluster analysis. To evaluate subcortical regions significant results ($p < 0.01$) were obtained lowering the threshold individually.

Results: All (but 1HA) patients showed highly significant activation in the contralateral sensorimotor area, the SMA and the ipsilateral cerebellum. In all investigated persons contralateral subcortical regions were significantly activated in particular with regard to the thalamus (6/10OL; 9/14HA, 7/13CO); the pallidum (1/10OL; 1/14HA, 6/13CO); the putamen (9/10OL; 9/14HA, 12/13CO) Ipsilateral coactivation was found in putamen (3/10OL; 6/14HA, 11/13CO), pallidum (1/10OL; 0/14HA, 3/13CO) and thalamus (1/10OL; 2/14HA, 1/13CO).

Conclusions: FMRI is an important method to study the interaction between basal ganglia, thalamus and the motor cortex.

NR594 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Contradictory Findings of Brain MRI Abnormalities in Treatment-Resistant Schizophrenia

Helio Elkis, M.D., *Department of Psychiatry, Projesq Ipq HC, R. Ovidio Pires de Campos SN, #4037, Sao Paulo, SP 05403-010, Brazil;* Jose R. Oliveira, M.D., Claudio C. Campi, M.D., Paulo C. Sallet, M.D., Erley Sassi, M.D.

Summary:

Background: The only 2 neuroimaging studies which compared Treatment Resistant schizophrenics (TRS) with Non Treatment Resistant schizophrenics (NTRS) in MRI parameters showed contradictory results. In this study we compared patients with TRS with non TRS and controls in MRI brain parameters, testing the hypothesis that TRS would show more significant brain abnormalities than NTRS or controls.

Methods: 40 patients (28 TRS and 12 non TRS) with DSM IV schizophrenia (mean age 33.6 y.o, mean duration of illness 13.5 y.o) were scanned by a1.5 T Philips Gyroscan device with 1.2 T1 coronal slices. These patients were compared with 20 controls. Brain measures were: Right and Left Planum Temporale, R & L Hypoccampus, Ventricular Brain Ratio (VBR) and Total Brain Volume.

Results: Comparisons were done by ANOVA with Scheffé post-hoc test and 0.05 significance level. TR and NTR showed to have more pronounced ventricular enlargement than controls with no differences between each other. However, a smaller brain volume and a smaller left hypoccampus were found in NTRS when compared with TRS and controls which is unexpected.

Conclusions: Results comparing TRS with NTRS remain contradictory, showing that brain morfometric abnormalities are not related with response to neuroleptic treatment in schizophrenia.

NR595 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Relationship of Irritable Bowel Syndrome to OCD in India

Sumant Khanna, M.D., *Department of Psychiatry, N. I. M. H., Hosur Road, Bangalore 560 029, India;* V.M. Vidyaranya, M.D., Prakash S. Masand, M.D.

Summary:

IBS has been reported in 10–22% of normal adults. It has also been found to have a high prevalence in certain psychiatric disorders. The objective of this study was to determine 1) the prevalence of IBS in OCD in an Indian population and 2) To study the pathoplasticity of IBS in a washers subgroup of OCD. A semi-structured clinical interview for IBS (Masand 1994) was administered to patients who were seeking treatment for OCD in an outpatient setting and who had been stabilized on drugs. IBS was diagnosed on the basis of the criteria of Drossman, et al (1994); of the 62 patients interviewed with OCD, according to DSM III R criteria, 54.83% had IBS—29% had partial IBS. IBS was diarrhea predominant in seven patients (20.58%), constipation predominant in six patients (17.64%) and both in 21 patients (61.76%). There was no difference between subtypes of OCD and type of IBS. There was also no difference between OCD subtypes and the prevalence of diarrhea and constipation predominant IBS. The study needs to be replicated in other cultural settings and compared with normal populations.

NR596 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

An Open Trial of SSRIs in Patients with Dizziness and Major or Minor Psychiatric Symptoms

Jeffrey P. Staab, M.D., *Department of Psychiatry, University of Pennsylvania, 3400 Spruce Street, 11 Founders Building, Philadelphia, PA 19104;* Michael J. Ruckenstein, M.D., David A. Solomon, M.D., Neil T. Shepard, Ph.D.

Summary:

Objective: Patients with prominent dizziness have a high incidence of psychopathology, particularly anxiety disorders,[1] yet no systematic treatment studies exist for this patient population.[2] This open trial examined the efficacy of SSRIs in patients with dizziness and major or minor psychopathology.

Methods: Twenty-nine patients referred to the psychiatrist in a multi-specialty neurotology center entered the trial. All underwent a neurotology evaluation and the SCID before starting an SSRI. Outcomes were rated on the Clinical Global Improvement Scale, assessing both dizziness and psychiatric symptoms.

Results: Twenty-one patients had major anxiety or depressive disorders as the cause of their dizziness; 4 had coexisting neurotologic illnesses. Four patients had only minor avoidance of situations provoking unexplained dizziness (anxiety disorder NOS). Four had unexplained dizziness alone (undifferentiated somatoform disorder). Twenty-one of 29 patients (72%) were much or very much improved after two months on SSRIs. Three (10%) obtained no benefit. Five (17%) stopped their medication due to typical SSRI side effects. The average medication dose equaled 86 mg of sertraline daily. Six of the 8 patients (75%) with idiopathic dizziness improved.

Conclusions: SSRIs are effective for patients with dizziness accompanying major anxiety and depressive disorders. Possible SSRI benefits for patients with idiopathic dizziness and minor psychological symptoms warrants further inquiry.

NR597 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Treatment of Depression Following Acute Coronary Syndrome Reduces the Risk for Recurrent Acute Cardiac Events

Peter J. Panzarino, Jr., M.D., *Department of Psychiatry, Cedars Sinai Medical Center, E 209 Thalians, 8730 Alden Drive, Los Angeles, CA 90048;* Tasneem Z. Naqvi, M.D., Haidar Sadeghi-Razlighi, M.D., Yulius Mustafa, M.D., Russell M. Poland, M.D., Syed S. A. Naqvi, M.D.

Summary:

Background: We examined the effect of depression and its treatment on rate of recurrent acute ischemic cardiac events following unstable angina (UA) or acute myocardial infarction (MI).

Methods: Patients were mailed a Zung Self Assessment Questionnaire 2 weeks post discharge for UA or MI and followed for 3–14 months. Depressed patients were offered treatment with 4 month psychotherapy with or without Paxil.

Results: Of the 365 consecutive pts surveyed, 222 responded, 122 were non-depressed (group A, Zung Standard Depression Score (ZSDS) = 39 ± 6), 83 were depressed and refused treatment or met exclusion criteria (group B, ZSDS 57 ± 8) and 17 depressed patients participated in treatment (group C, ZSDS 57 ± 8). There was no difference in history of previous MI, diabetes mellitus, hypertension (Chi Square = NS) and in age (A = 67 ± 13, B = 70 ± 15, C = 68 ± 12, years,), and follow-up period (A = 8.4 ± 4.6, B = 8.6 ± 4 and C = 7.3 ± 4 months), (ANOVA, p = NS) among the 3 groups. Follow up data are shown in the Figure.

Conclusion: Depression is associated with a higher risk of recurrent ischemic and non-ischemic cardiac events. Preliminary results suggest that treatment of depression following UA or MI may reduce further non-ischemic and ischemic acute cardiac events.

NR598 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Adverse Reactions to Antidepressants in Consultation-Liaison Psychiatry Inpatients

Graeme C. Smith, M.D., *Psychological Medicine, Monash University Medical Ctr., 246 Clayton Road, Clayton, Victoria 3168, Australia;* David M. Clarke, M.B., Dennis Handrinos, M.B., Thomas Trauer, Ph.D.

Summary:

Standardized prospective data were collected on 5665 consecutive inpatients referred to the integrated Consultation-Liaison Psychiatry service of 2 University teaching hospitals. An adverse drug reaction, defined as a psychological or physical reaction sufficient to warrant discontinuation of the drug, was noted in 158 (10%) of the 1511 cases prescribed an antidepressant. The only demographic variable associated with a reaction was older age ($p < .05$). ICD-9 genitourinary disorder (mainly renal failure) was the only physical diagnosis significantly more likely to be associated with a reaction ($p < .01$), and DSM-IV "Delirium, Dementia, etc." the only psychiatric diagnosis ($p < .05$). Neither Global Assessment of Function nor Karnofsky ratings were associated with a reaction, nor was multiple psychotropic drug prescription. For those noted to have had a reaction, psychiatrists were more likely to have recommended laboratory tests, behavioral control and environmental manipulation. They made a greater number of visits ($p < .001$) and spent more time ($p < .05$), and the patients had longer stays ($p < .001$). Tricyclics were more likely than SSRI's to be associated with a reaction ($p < .05$).

Conclusion: Drug reactions were noted in 10% of these physically ill patients prescribed antidepressants, particularly those older or with renal failure or delirium. They stayed longer and received more psychiatric input than others prescribed antidepressants.

NR599 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Primary Care Panic: ID by Doctor Versus Screening

Peter P. Roy-Byrne, M.D., *Department of Psychiatry, Univ of WA/Harborview Med Cntr, 325 Ninth Avenue, Box 359911, Seattle, WA 98104;* Deborah S. Cowley, M.D., Joan Russo, Ph.D., Emily Cohen, B.A., Erin Michelson, B.A., Wayne J. Katon, M.D.

Summary:

Studies suggest that the recognition of depression and anxiety by primary care physicians (PCPs) is most likely in more symptomatic and impaired patients. As part of a randomized effectiveness study of expert pharmacotherapy versus usual care for primary care patients with panic disorder, we examined the baseline characteristics of study patients who were recruited by waiting room screening procedure (n = 69), versus patients who were referred to the study by their PCP (n = 41). At three Seattle clinics 110 panic disorder patients were recruited. All medical and psychiatric comorbidities except psychotic or bipolar disorder, current substance abuse and life threatening medical illness were allowed. After controlling for differences in age, gender, race, and clinic, patients referred by their physician had a significantly higher frequency of panic attacks, more intense attacks, and more anticipatory anxiety on the PDSS, and worse mental health but better physical functioning on the SF36. There were no differences in anxiety sensitivity, phobic avoidance, depression, other SF36 measures, disability, or medical service utilization. In conclusion, differences in referred versus screened patients are mostly specific for panic attack related symptoms, consistent with the notion that patients with more prominent physical symptoms (i.e., panic attacks) are more often recognized and referred in busy clinical settings. The better physical functioning of referred patients may indicate greater physician recognition of panic in patients who appear less medically ill. However, the many clinical and functional similarities between these two patient samples suggests that symptomatic primary care patients with panic may not always be identified by their PCP and argues for the value of population-based screening for panic in primary care.

NR600 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Effect of SSRI Panic Disorder Treatment on Laboratory and Emergency Department Resource Utilization and Cost

Peter P. Roy-Byrne, M.D., *Department of Psychiatry, University of WA/Harborview Medical Center, 325 Ninth Avenue, Box 359911, Seattle, WA 98104;* Cathryn M. Clary, M.D., Amy N. Grundzinski, Pharm.D.

Summary:

Objective: To examine the impact of SSRI treatment for panic disorder on laboratory and emergency department (Lab&ED) resource utilization.

Method: Patients between the ages of 18–64, with a panic disorder diagnosis and SSRI prescription claim were identified from the HCIA medical and pharmacy claims database (n = 289). Patients were excluded from the study if they had bipolar disorder, schizophrenia, substance abuse, or claims for mood stabilizers, anti-psychotics, benzodiazepines, or other antidepressant medications. All cohorts had equivalent visits and costs in the 6 month period prior to SSRI initiation. Lab&ED visits counts as well as cost were compared between the 6 month period preceding versus that following SSRI therapy initiation using a pairwise t-test.

Results: Reductions in Lab&ED visits (–0.34, p = 0.062), and significant reductions in Lab&ED cost ($–62.4, p = 0.044) were found in the 6 month period following SSRI initiation in the total patient cohort. Patients receiving sertraline (mean 78.5mg) showed significant reductions in Lab&ED visits (–0.92, p = 0.014),

and Lab&ED cost ($–156.9, p = 0.048). Patients receiving fluoxetine (mean 22.7 mg) had nonsignificant reductions in Lab&ED visits ($–0.06, p = 0.712) and Lab&ED cost ($–2.13, p = 0.523), as did patients receiving paroxetine (mean 19.6mg, visits –0.10, p = 0.735; cost $–21.4, p = 0.589).

Conclusion: Appropriate diagnosis of panic disorder and treatment with an SSRI may decrease unnecessary Lab&ED visits for the medical symptoms associated with panic disorder.

NR601 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Prime-MD Patient Health Questionnaire (PHQ) in the Specialist Medical Setting: Validation for Anxiety and Mood Disorders

Benjamin Fischler, M.D., *Department of Psychiatry, UZ Gasthuissberg, Herestraat 49, Leuven 3000, Belgium;* Phillippe M.J. Persoons, M.D., Koen Luyckx, M.A.

Summary:

Objective: To validate the first self-rating scale for axis-I disorders in a specialist medical setting.

Methods: At a university hospital, consecutive in- and outpatients attending a gastroenterology setting completed the PRIME-MD Patient Health Questionnaire (PHQ)[1]. The MINI-interview by a mental health professional was used as a golden standard to assess the concurrent validity of anxiety and affective disorders. The MOS SF-36[2] was used to test the external validity.

Results: The sensitivity and specificity (n = 95) for major depressive disorder (MDD) was respectively 94.1% and 96.7%, for any mood disorder resp. 85.2% and 86.8% and for any anxiety disorder resp. 83.3% and 88.4%. A highly significant difference between MDD and other depressive disorders (ODD) on the one hand and non-depressed medical patients was found for all dimensions of SF36 (one-way ANOVA, n = 289, F between 12.54 and 51.47; p < 0.00001). Significant differences were found between MDD and ODD for mental health, role emotional, social functioning, vitality, and bodily pain (t-tests: p < 0.005)

All SF36 dimensions were found to be significantly different between subjects with or without generalized anxiety disorder or panic disorder (data not shown).

Conclusion: The PRIME-MD PHQ appears to be a valid self-rating scale for axis-I disorders in a specialist medical setting.

NR602 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Epidemiology of Axis I Disorders in Medical Inpatients

Benjamin Fischler, M.D., *Department of Psychiatry, UZ Gasthuissberg, Herestraat 49, Leuven 3000, Belgium;* Phillippe M.J. Persoons, M.D., Koen Luyckx, M.A.

Summary:

Objectives: to assess the epidemiology of axis-I disorders in a gastroenterological inpatient-unit.

Methods: axis-I disorders were assessed with the PRIME-MD Patient Health Questionnaire (PHQ)[1]; for functioning and quality of life, SF-36 was used. Medical diagnoses were divided into three major groups: inflammatory bowel disorders (IBD), functional intestinal disorders (FID) and a heterogeneous group of other organic gastroenterological and hepatological disorders (OOD).

Results: 290 patients completed both scales. The prevalence of major depressive disorder (MDD) in FID, IBD and OOD was respectively 43.9%(+), 26.6%(Δ) and 10.1%(^{4}) (+Δ:p = 0.056; Δ^4 and $+^4$:p < 0.001); the prevalence of any mood disorder was respectively 54.7%(+), 39.1%(Δ) and 25.5%(^{4}) (+Δ:p = 0.09; Δ^4:p = 0.04) and $+^4$:p = 0.00004);. Panic disorder was found in respectively 14%, 0% and 3.6% and other anxiety disorders in respectively 24.5%, 7.8% and 5.5%. A trend towards a significant effect of gender for MDD only and no effect of age was found. A significant effect of MD and other mood disorders separately was found on all dimensions of SF-36 (p < 0.01) except for the effect of other mood disorder on physical functioning. The mood-anxiety comorbidity was not found to contribute significantly to SF-36-scores.

Conclusion: mood disorders are highly prevalent and disabling in gastroenterological inpatients, especially in functional[2] and inflammatory bowel disorders.

NR603 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

A Prospective Evaluation of Neuropsychiatric Symptoms in Patients with Hepatitis C Treated with Interferon-Alpha and Ribavirin

Eric W. Dieperink, M.D., *Department of Psychiatry, Veterans Affairs, 1 Veterans Drive, Minneapolis, MN 55417;* Mark L. Willenbring, M.D., Paul D. Thuras, Ph.D., Lori Tetrick, Samuel B. Ho, M.D.

Summary:

Background: Depression is frequent in patients receiving interferon-alpha (IFN-a) for treatment of hepatitis C, and may be severe.[1] Little is known about the course of symptoms or when treatment is indicated.[2] Aims: Prospectively evaluate the course of depression, using different depression scales, in patients with chronic hepatitis C treated with IFN-a and ribavirin.

Methods: To date, the Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HAM-D), Zung Self-Rating Scale, Profile of Mood States (POMS) and the Inventory to Diagnose Depression were administered to 10 patients at baseline, and 4,8,12 and 24 weeks of treatment. Fatigue was measured using the Multidimensional Fatigue Inventory and the POMS.

Results: Depression scores were highly correlated at all time points. Fatigue scales showed little change. Baseline scores did not predict future scores or the need for treatment. A BDI of ≥12 at 12 weeks predicted for increasing depression and the need for antidepressant therapy, even when diagnostic criteria were not met.

Conclusions: Prophylactic treatment with antidepressants would result in unnecessary treatment for many patients. At a minimum, the BDI should be given at baseline and 12 weeks, and if ≥12 at any time, antidepressant treatment should be initiated.

NR604 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Risperidone Oral Solution Versus Intramuscular Haloperidol

Glenn W. Currier, M.D., *Department of Psychiatry, Univ. of Rochester Medical Ctr, 300 Crittenden Boulevard, Rochester, NY 14542-8409;* George M. Simpson, M.D.

Summary:

This study compared treatment with 2 mg oral risperidone solution plus 2 mg oral lorazepam with 5 mg intramuscular haloperidol plus 2 mg intramuscular lorazepam in 60 agitated patients. Agitation was rated on five subscales of the PANSS (excitement, hostility, hallucinations, uncooperativeness, and impulsivity) at baseline and 30 and 60 minutes after treatment. Both groups had similar mean (±SD) agitation scores at baseline (22.7 ± 5.5). Scores in both treatment groups declined significantly at 30 (mean 10.0 ± 9.3) and 60 (mean 3.5 ± 6.7) minutes (p < .0001) with no significant between-group differences. Of the patients receiving haloperidol, 15 (50%) refused oral medications, 8 (27%) were unable to follow verbal instructions, 6 (20%) specifically requested intramuscular medications, and 1 (3%) described an allergy to risperidone. The majority of patients were sedated to the point of sleep: at 2 hours, 2/30 (7%) of the haloperidol group and 5/31 (16%) of the risperidone

group remained awake. The mean time to sleep was 43.0 ± 25.1 minutes for patients receiving risperidone and 44.3 ± 25.7 minutes for those receiving haloperidol. The only adverse event was an episode of acute dystonia in a patient receiving haloperidol. In conclusion, risperidone oral solution plus lorazepam may be an effective and safe alternative to intramuscular haloperidol plus lorazepam in many patients with acute psychotic agitation.

NR605 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Parental Sedation in 385 Psychiatric Emergency Room Patients

Murat Pakurek, M.D., *Department of Psychiatry, Suny Stony Brook, Health Science Center T-10, Stony Brook, NY 11794;* Fahim Kazi, M.D., Horacio Preval, M.D., Laura J. Fochtmann, M.D., Andrew J. Francis, Jr., M.D.

Summary:

Objective: To compare efficacy of parenteral sedatives in agitated patients at a tertiary psychiatric emergency center using duration of physical restraint and need for re-medication as outcomes.

Method: Charts were reviewed for 385 agitated patients receiving parenteral sedation at the initiation of physical restraints. Efficacy was determined both by time in restraints and need for re-medication, and sorted by demographic, clinical, and toxicological variables.

Results: In the sample, 211 received droperidol, 67 lorazepam, 9 haloperidol, and 98 a combination. Median and mean restraint times were 2.0 hr and 2.8 ± 0.1 [SEM] hr, respectively. 16% required re-medication. In the total sample, gender and age did not affect these outcomes. Longer restraint times were recorded for mania ($p < .01$). Compared to single agents, a combination of neuroleptic and lorazepam reduced the need for re-medication (20% vs. 8.2%, $p < .01$), but did not reduce restraint time. For intoxicated patients, droperidol showed shorter restraint time than lorazepam.

Conclusion: Duration of restraint was generally brief. Analyses to date suggest that combining neuroleptic and benzodiazepine decreased the need for re-medication relative to single agents but did not alter restraint time. In intoxicated patients, droperidol may be superior to lorazepam for treating agitation.

NR606 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

An Open-Label Trial of Citalopram for Major Depression in Hepatitis C

Ondria C. Gleason, M.D., *Department of Psychiatry, University of Oklahoma, 2808 South Sheridan, Tulsa, OK 74129;* William R. Yates, M.D.

Summary:

Hepatitis C affects neariy 4 million Americans. Depression is a common comorbid condition found among patients with hepatitis C and may be induced by interferon alpha, an approved treatment for hepatitis C. Depression is a major indicator for discontinuation of interferon therapy.

Objectives: To estimate the response rate of major depression in an 8-week trial of citalopram, to evaluate the effect of citalopram on markers of hepatitis activity in hepatitis and to examine the effect of citalopram on quality of life measures.

Methods: A community sample of adults with both hepatitis C and major depressive disorder were treated with citalopram for 8-weeks. Hamilton Depression scores, SF-36 and Clinical Global Impression (CGI) scores, and liver function tests were obtained at baseline, 4 weeks and 8 weeks.

Results: Subjects demonstrated significant improvement in HAMD-17 scores (−11.8 (3.5), $t = 0.00016$, $p = 0.002$, $df = 4$). Statistically significant improvement was also demonstrated on four subscales of the SF-36, including: emotional well- being (+28.8 (13.4), $t = 0.03$, $p = 0.004$, $df = 4$), role limitations due to emotional health (+33.32 (36.5), $t = 0.0004$, $p = 0.03$, $df = 4$), social functioning (+27.5 (31.1), $t = 0.03$, $p = 0.03$, $df = 4$), and pain (+16 (17.0), $t = 0.04$, $p = 0.04$, $df = 4$). All subjects demonstrated improvement on CGI ratings. Tests of liver function showed no worsening of AST, ALT or GGT levels, rather there was a trend toward improvement of all three measures, though not statistically significant.

Conclusions: These results suggest that depression in the setting of hepatitis C may be effectively and safely treated with citalopram. Controlled trials are indicated and necessary.

NR607 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Ethnic Variations in Psychiatric Treatment

Wendy L. Colquitt, Ph.D., *Office of Research, American Psychiatric Assoc., 1400 K Street, NW, Washington, DC 20005;* Diane Herbeck, M.A., Harold Alan Pincus, M.D.

Summary:

Purpose: Members of racial-ethnic minorities experience more limited access to health care in the U.S. in a variety of ways. This research examines variation in psychiatric conditions observed in racial-ethnic minority and nonminority patients, comparing patients' sociodemographic characteristics, health plan characteristics, diagnoses, severity and complexity of conditions, and treatments received.

Methods: Bivariate and multivariate analyses were conducted on detailed patient-level data collected from a nationally representative sample of 1,843 psychiatric patients included in the *1999 PRN Study of Psychiatric Patients and Treatments.* Differences in the diagnostic and clinical characteristics of patients, treatments, treatment settings and health plan characteristics by patients' minority-nonminority status (defined as black/African-American, Hispanic, American Indian/Eskimo/Aleut, Asian/Pacific Islander-white/other) were assessed.

Results: Statistically significant differences were observed with respect to diagnosis, symptom severity, level of impairment, treatment, and health plan coverage. Among the most prominent differences were the presence of psychotic symptoms ($\chi^2 = 42.06$, $p < .0001$), inpatient status ($\chi^2 = 45.98$, $p < .0001$), use of public treatment settings ($\chi^2 = 129.56$, $p < .0001$) and Medicaid/uncompensated care ($\chi^2 = 138.43$, $p < .0001$).

Conclusions: These findings document differential psychiatric conditions and type of care received by minority patients. Additional research is needed to assess whether there are also observed differences in the quality and outcomes of care associated with race-ethnicity.

NR608 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Interpersonal Support Evaluation List in American Indians

Brett Koplin, M.D., *Department of Psychiatry, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905;* Gary Leonardson, Ph.D., Thomas Welty, M.D.

Summary:

The Strong Heart Study (SHS) is the first study of cardiovascular disease in American Indians using a standardized protocol and involves tribal members who were 45 to 75 years old at the time of the first examination, representing thirteen different tribes from the United States. The second examination of the SHS included pilot psychosocial measures from participants enrolled in tribes from North Dakota, South Dakota and Oklahoma. The measures included: the Center for Epidemiological Studies Depression Scale

(CES-D), Spielberger Anger Expression Scale, cultural questions and the Interpersonal Support Evaluation List (ISEL). The current study focuses on social support as measured by the ISEL.

We examined the twenty-one item scale version of the ISEL used in the SHS. Scales from 422 participants were examined. Chronbach's alpha ranged from .76 to .83. There was a negative correlation ($p < .05$) between levels of social support on the ISEL and the CES-D score. Univariate analysis revealed no significant correlations related to age, gender, alcohol or smoking on the ISEL. High levels of identification with American Indian culture correlated ($p < .05$) with higher ISEL scores. The results suggest further evaluation of the ISEL in American Indians and its relationship to cardiovascular risk factors.

NR609 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Anxiety in Individuals with Self-Reported Coronary Heart Disease

Nils H. Dahl, M.D., *Department of Psychiatry, Innherred Hospital, Levanger N-7600, Norway;* Alv A. Dahl, M.D., Oystein Kruger, M.D.

Summary:

Emotional factors influence the outcome of coronary heart disease (CHD). Depression has been mostly studyed, and less is known about the influence of anxiety.

Objective: To examine the relationship between the presence of CHD and the self-reported level of anxiety.

Method: The Nord-Trøndelag Health Study was a population based study (1995 to 1997). Among those aged 40–79 years, 52,432 persons were invited and (80.4%) participated. Angina pectoris (AP) and myocardial infarction (MI) were registered by self-report. Participants rated their level of anxiety by HADS-A. (Hospital Anxiety and Depression Scale). Cut off level for "clinical anxiety" ≥11. Age adjusted odds ratios were estimated in a logistic regression model.

Results: Having AP was associated with clinical anxiety with an odds ratio (OR) of 2.1 (95% CI 1.5–2.9) among men and 1.8 (1.3–2.5) among women. Having had MI showed correspondingly an OR of 1.0 (0.7–1.4) and 1.2 (0.8–1.8). With both AP and MI in the same regression model the age-and sex adjusted OR was 1.9(1.5–2.6) for AP and 1.1(0.7–1.7) for MI.

Conclusions: Having AP seemed to double the risk of having an anxiety disorder. Having had MI did not alone seem to have significant influence on caseness of anxiety in this study.

NR610 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Stress Among Kenyans Exposed to the 1998 Bombing of the U.S.Embassy in Nairobi

Victoria E. Wells, M.D., *IHPHSR, University of Cincinnati, 202 Goodman Drive, p o box 670840, Cincinnati, OH 45267-0840;* Margaret Ma'Kanyengo, M.D., Pius A. Kigamwa, M.D., Josephine Omondi, M.D., Lawson R. Wulsin, M.D.

Summary:

Objective: To assess the psychological stress, risk factors, and benefits of counseling, in a sample of Kenyans six months following exposure to the bombing of the US Embassy.

Methods: A convenience sample of survivors of the bombing, seeking care at Kenyatta Hospital, was evaluated with the Impact of Event Scale (IES). The Nairobi authors collected and transferred the data electronically to Cincinnati for analysis. Reports were iteratively exchanged.

Results: The sample (N = 104) was 53% female with a mean age of 36.5. 99% were injured by the blast and as many as 97% received some form of counseling; 87% of those found it beneficial. The mean IES score was 38.8, with a range of 70–0. The intrusion sub-scale had a mean of 19.8, and the avoidance sub-scale had a mean of 19. These mean scores approximate those reported for a **clinical** US sample (IES = 39.5 (range 69-0); intrusion = 21.4; avoidance = 18.2) while differing markedly from those reported for a **non-traumatized** US sample.

Conclusions: Psychological questionnaires created in the US may require additional interpretation to be relevant to an African population. The reported rates of psychological stress in this injured clinical sample should be further studied to differentiate cultural from event-specific factors.

NR611 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Depression Among Kenyans Exposed to the 1998 Bombing of the U.S. Embassy

Victoria E. Wells, M.D., *IHPHSR, University of Cincinnati, 202 Goodman Drive, p o box 670840, Cincinnati, OH 45267-0840;* Josephine Omondi, M.D., Pius A. Kigamwa, M.D., Margaret Ma'Kanyengo, M.D., Lawson R. Wulsin, M.D.

Summary:

Objective: To assess the severity and risk factors of depressive symptoms, risk factors among Kenyan citizens 6 months following exposure to the bombing of the US Embassy.

Methods: A convenience sample of survivors of the bombing, seeking care at Kenyatta Hospital, was evaluated with the Zung Depression Scale. The Nairobi authors collected and transferred the data electronically to Cincinnati for analysis. Reports were iteratively exchanged.

Results: The sample (N = 89) was 54% male; 94% Christian; 69% married, 29% single; and had a mean age of 35 years. Ninety-eight percent were injured by the blast and 48% received some form of counseling. Six (7%) met criteria for severe/extreme depression; 33 (37%) met criteria for moderate/marked depression; and 21 (24%) met criteria for minimal/mild depression. This injured clinical sample reported rates of depression warranting treatment in 67% of the subjects. The mean score for men was 39.0, for women, 47.2.

Conclusions: The point prevalence of depression was much higher among the Kenyans than that reported for survivors of the Oklahoma City bombing (major depression = 22.5%). Female gender appears to be a risk factor for depression among the Kenyan sample as was demonstrated in Oklahoma City (female:male = 2:1).

NR612 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Mother Tongue and Psychopathology: A Representative Study Among Migrants with Schizophrenia

Oktay Yagdiran, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20246, Germany*

Summary:

Introduction: The higher rate of schizophrenia among migrants has in part been explained with misdiagnoses due to cultural factors. Problems with the exploration of psychopathology not in the mother tongue have been described in several studies, although not with consistent results.

Methods: The present study represents an analysis of all admissions of migrants during 1993 and 1995 to the Psychiatric Clinic of the University Hospital in Hamburg, Germany and for 1995 at the Psychiatric Clinic of the Allgemeinen Krankenhaus Ochsenzoll.

Results: 905 migrants were assessed. 37.6% had documented language problems, significantly more among those receiving a diagnosis of a schizophrenic disorder ($\chi^2 = 5.03$; $p < 0.05$)

Discussion: The study shows a relationship between language proficiency and diagnosis, which seems to lie in a different assess-

ment of psychopathology. These results call for a greater emphasis in transultural training in psychiatry as well as employing professionals who speak foreign languages. Since an evaluation of psychotic symptoms as specific for schizophrenia is limited when communication is insufficient, this represents a possible cause for errors. As this also seems to correlate with a higher rate of compulsory admission, this shows the need for an improvement of treatment of migrants in psychiatry.

NR613 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Navajo Religious Healing: Patient-Healer Profiles

Michael G. Storck, M.D., *Department of Psychiatry, University of Washington, 5756 29th Avenue, NE, Seattle, WA 98105-5522;* Thomas Csordas, Ph.D.

Summary:

Background: Although the Navajo routinely receive their medical care in Western medical clinics and hospitals, they nonetheless widely utilize traditional and religious healing systems.

Objective: As part of an ethnographic study of non-medical healing among the Navajo, we examined the relationship between patients and their healers involved in Traditional Navajo, Native American Church, and Christian healing.

Methods: Healers (n = 95) and patients (n = 79) were interviewed via ethnographic methods. Patients were also administered the Structured Clinical Interview for DSM within three to six months of their religious healing ceremony.

Results: Healers were more likely than patients to be primary Navajo language speakers, male, older, and had less formal education. Healers were often related to patients by family or other Navajo kinship ties. The most common patient lifetime SCID diagnoses were depression (37%), post-traumatic stress disorder (34%), and alcohol use related (45%). One in 5 patients were depressed at the time of the intervention.

Conclusion: Navajos use multiple healing systems. Those who seek out religious healers have high lifetime rates of psychiatric distress. Further efforts to assess the complementarity of Western medical and Navajo healing systems are indicated.

NR614 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Race Differences in Diagnosis of Comorbid Disorders in Schizophrenia

Lisa D. Green-Paden, M.D., *Department of Psychiatry, University of Maryland, 630 West Fayette Street, Unit 7W, Baltimore, MD 21201;* Alicia Lucksted, Ph.D., Janine C. Delahanty, M.A., Leticia T. Postrado, Ph.D., Lisa B. Dixon, M.D.

Summary:

Objectives: To compare African American and Caucasian cohorts in a large sample of patients diagnosed with schizophrenia on affective and anxiety disorder diagnoses and treatment as well as symptoms.

Methods: A total of 685 patients with schizophrenia receiving treatment were interviewed as part of the Schizophrenia Patient Outcomes Research Team study. The sample was randomly selected from a variety of treatment settings in two states. The impact of race on past and current diagnoses as well as on treatment for depression, mania, and anxiety disorders was assessed with logistic regression analyses.

Results: African Americans were significantly less likely to have a past diagnosis, current diagnosis, and to be receiving current treatment for depression, anxiety disorders and manic-depression. Specifically, Caucasians were 2.2 times more likely to have a lifetime depression diagnosis ($P < .001$), 1.9 times more likely to have a lifetime manic-depression diagnosis ($P < .001$), and 2.6 times more likely than African-Americans to report a lifetime diagnosis of an anxiety disorder ($P < .001$). African Americans also had more psychotic symptoms ($p < .01$).

Conclusions: The study confirms and extends previous work on possibility of racial bias in the diagnosis and treatment of patients diagnosed with schizophrenia and co-morbid affective and anxiety disorders.

NR615 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Evaluating Changes in Sexual Dysfunction in Depressed Patients: Sensitivity to Change of the Changes in Sexual Functioning Questionnaire (CFSQ)

Maria P. Gonzalez, Ph.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, Oviedo 33006, Spain;* Julio B. Bobes, Ph.D., Maria T. Bascaran, M.D., Fernando Rico-Villademoros, M.D., Sebastian Banus, M.D., Margarita Garcia, M.D.

Summary:

Objective: To assess sensitivity to change in the Changes in Sexual Functioning Questionnaire (CSFQ).

Methods: 107/127 evaluable depressed patients starting antidepressant treatment with nefazodone (n = 39), fluoxetine (n = 20), paroxetine (n = 30), venlafaxine (n = 12) and clomipramine (n = 6) completed the CSFQ at baseline and after 2, 4 and 6 months of treatment. Sensitivity to change was assessed using the change from baseline scores by treatment, sex and remission/non-remission. Mean Standardized Effect Sizes (SES) of changes were calculated.

Results: Non substantial ceiling and floor effects were found. Statistically significant pre-postreatment improvement was found for 1/5 of dimensions on men and 4/5 and total score on women in nefazodone group, and for 4/5 and total score on remitters in nefazodone and venlafaxine groups. Statistically significant worsening was found for 2/5 of dimensions on men and 1/5 on women in paroxetine group, and on non-remitters for 1/5 of dimensions in fluoxetine group and 3/5 and total score in paroxetine group. No improvement changes were found on Sexual Desire/Interest. Highest effect sizes were found on Sexual Desire/Frequency when improving and on Arousal/Erection when worsening.

Conclusion: CSFQ is sensitive to bidirectional changes, resulting appropriate for measuring Sexual Dysfunction.

NR616 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Changes in Peripheral Thyroid Function with Antidepressant Treatment

Michael J. Gitlin, M.D., *Department of Psychiatry, UCLA, 300 UCLA Medical Plaza, #2200, Los Angeles, CA 90095;* Lori L. Altshuler, M.D., Mark A. Frye, M.D., Rita A. Suri, M.D., Lynn Fairbanks, Ph.D., Emily K. Lee, M.D.

Summary:

Method: Before treatment with one of three SSRIs, (fluoxetine (n = 8), sertraline (n = 19) and paroxetine (n = 2)), thyroid indices-T4, free T4, T3, and TSH were measured in 29 depressed subjects (15 women, 14 men; mean age = 41 years). No individual was taking thyroid hormones during the study. A subset (n = 20) had thyroid measures repeated after ten weeks of antidepressant treatment.

Results: Baseline TSH correlated highly with change in Hamilton depression scores ($r = .602$, $p < .005$) in that lower TSH predicted a greater improvement in depressive symptoms. No other thyroid indices correlated significantly with Hamilton change scores. Antidepressant treatment resulted in a decrease of T3 and T4 values, although not to a significant degree. Change in thyroid indices

during treatment did not correlate with change in Hamilton depression scores.

Conclusions: Lower baseline TSH predicted a positive response to SSRI treatment. In contrast to some previous studies, treatment response was not associated with a significant decrease in T4 values.

NR617 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Bupropion As a Treatment for SSRI-Induced Sexual Side Effects

Michael J. Gitlin, M.D., *Department of Psychiatry, UCLA, 300 UCLA Medical Plaza, #2200, Los Angeles, CA 90095;* Rita A. Suri, M.D., Lori L. Altshuler, M.D., Joni Zuckerbrow-Miller, B.A., Lynn Fairbanks, Ph.D.

Summary:

Method: 24 subjects treated with SSRIs for a depressive disorder who had new onset sexual side effects coincident with antidepressant treatment were treated in an open label fashion with escalating doses of bupropion-SR up to 300 mg daily for seven weeks. All patients were euthymic for at least two weeks at the time of study entry.

Results: Response rates were 46% for women and 75% for men. At baseline, women had significantly higher rates of orgasmic dysfunction compared to men (p. < 04) with similar rates of decreased libido and arousal dysfunction. All sexual side effects improved in response to bupropion with no differential effect on any one side effect. Men and women showed equal rates of improvement for each side effect. Most of the improvement (>50%) occurred relatively early (within the first two weeks) and at low dose. Increasing improvement, however, was seen over the entire time of the study. No significant difference in the speed of improvement was seen across the different sexual side effects.

Conclusions: When prescribed in an open fashion, bupropion-SR is effective in treating all the major side effects with positive effects seen relatively early and at low dose.

NR618 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Antidepressant Treatment Received by Depressed Subjects in the Finnish General Population

Tanja I. Laukkala, Ph.D., *Department of Mental Health and Alcohol, National Public Health Institute, Mannerheimintie 166, Helsinki, FI 00300, Finland;* Erkki T. Isometsa, Ph.D., Juha Hamalainen, M.D., Martti E. Heikkinen, Ph.D., Hillevi Aro, Ph.D.

Summary:

Studies that have investigated the treatment of depression in general population indicate that depressive disorders are often neither recognized nor treated effectively (1,2). However, the use of antidepressant medications has markedly increased during the last few years in most western countries. In the present study, a representative sample (N = 5993) of adult Finnish population was interviewed in 1996 using the Short Form of UM-CIDI, a standardized interview including the DSM-IIIR criteria for a major depressive episode (MDE). Altogether 9.3% (N = 557) were found to have suffered from MDE within the preceding 12-months. Their perceived need and use of general health and psychiatric services, as well as use of psychotropic medication were examined.

Less than half (41%) of the persons with MDE reported that they had either subjectively needed or would have expected to benefit from the use of mental health services. Only a quarter (27%) of the persons with MDE had actually used health services because of their depressive episode. At the time of the interview, only 13% used an antidepressant, and 14% benzodiazepine and 4% neuroleptic medication. Of the persons with MDE within the preceding 6-months (N = 464), 13% reportedly received antidepressant medication. The use of antidepressants was found to be associated with higher severity and longer duration of the MDEs. No significant gender differences in the treatment received were found.

Overall, our findings suggest that only a fraction of people who suffers from MDE receive antidepressant treatment. Many subjects are prescribed pharmacotherapy that is unlikely to alleviate depression. An unmet need seems to still exist in the recognition and treatment of depression.

NR619 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Marital Dissatisfaction and Psychiatric Disorder

Tess Sheldon, M.S.C., *Health Systems Research, CAMH-Clarke Div., 250 College Street, Toronto, ON M5T 1R8, Canada;* Mark A. Whisman, Ph.D., Paula N. Goering, Ph.D.

Summary:

Objective: The specificity of the association between psychiatric disorders and dissatisfaction in relationships with spouse, relatives, and friends was evaluated among married respondents who completed the Mental Health Supplement to the Ontario Health Survey (N = 4,933).

Method: Dissatisfaction in relationships with spouse, relatives and friends (derived from survey items) was compared for spouses with and without the assessed CIDI psychiatric disorders using log linear regression analyses. Sociodemographic factors and comorbid psychiatric disorders were controlled for.

Results: Marital dissatisfaction was uniquely related to 7 of 9 psychiatric disorders, with the strongest associations observed for generalized anxiety disorder, major depression, and alcohol abuse or dependence. In comparison, dissatisfaction with relationships with relatives and friends were generally unrelated to psychiatric disorders. Most of the univariate associations remained significant when controlling for comorbid psychiatric disorders.

Conclusion: Results suggest that the association between psychiatric disorders and social relationships appears to be restricted primarily to the marital relationship, and that this association is significant for a variety of psychiatric disorders.

NR620 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Chronic Therapy of Schizophrenic Relapse

Thomas R. Ten Have, Ph.D., *Department of Biostatistics, University of Pennsylvania, 423 Guardian Dr., 607 Blockley, Philadelphia, PA 19104-6021;* Alfredo Morabia, Philippe Huguelet, Francois P. Ferrero, M.D.

Summary:

In assessing the efficacy of anti-psychotic therapy on relapses from schizophrenia, the effect of medication on outcome needs to be distinguished from the influence of relapse on medication. Typically, medication is expected to prevent relapse and relapse generally induces medication. Conventional modeling uses either treatment or disease as outcome. We propose an alternate approach that uses both treatment and schizophrenic relapse as random variables. Data from 58 schizophrenic patients, with up to 60 consecutive monthly determinations of anti-psychotic medication and schizophrenic events were analyzed using a bivariate transition model with random effects. Previous medication did not have an effect on current risk of relapse overall (Model OR = 1.0, 95 percent CI: (0.7–1.6). In contrast, the cross-sectional association of current relapse and current medication was negative when the patients had been previously medicated (OR = 0.5, 95 percent CI: 0.2–1.1) but positive otherwise (OR = 4.5, 95 percent CI: 1.6–12.9). Thus, mixed effect, time series models can be used to study the complex time-dependence of medication for the treatment of chronic diseases, using the cross-sectional association between

medication and relapse as outcome. This analysis revealed that the risk of schizophrenic relapse is reduced by continuous medication (previous month and current month) but not necessarily by current medication.

NR621 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Longitudinal Study of the Association Between Alcohol Dependents and Major Depression in the General Population

Stephen E. Gilman, S.M., *Dept of Health & Social Behavior., Harvard University, 677 Huntington Avenue, Boston, MA 02115;* Henry D. Abraham, M.D.

Summary:

Objective: To investigate the risk that 1) alcohol dependence confers on the one-year incidence of depression and 2) that depression confers on the one-year incidence of alcohol dependence.

Method: Data come from the first two waves of the Epidemiologic Catchment Area Study, a general population survey with structured diagnostic interviews (n = 14,480). Multivariate logistic regression was used to identify risk factors for new cases of alcohol dependence and major depression occurring during the one-year follow-up period.

Results: The one-year risk of depression increased with the number of symptoms of alcohol dependence as recorded at baseline (odds ratios for depression associated with low, medium, and high levels of alcohol dependence: 1.23, 3.19, and 2.63 for men, P = .0001; 1.80, 4.70, and 5.42 for women, P = .0001). Conversely, the odds of incident alcohol dependence associated with baseline depressive symptoms were 1.59, 2.34, and 3.74 (P = .001) for genders combined.

Conclusions: Symptoms of alcohol dependence and major depression pose a significant risk for the development of the other disorder at one year; moreover, the risk increases with the number of symptoms. The severity of alcoholic and depressive symptoms may be a more salient predictor of psychiatric disorders than the presence of a primary psychiatric diagnosis.

NR622 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Illicit Drug Consumption and Personality in Teenagers

Pilar A. Saiz, Ph.D., *Department of Psychiatry, University of Oviedo, Julian Claveria No 6-30, Oviedo 33006, Spain;* Juan L. Lopez, M.D., Jesus M. Delgado, M.D., Maria P. Gonzalez, Ph.D., Sara Martinez, M.D., Luis Jimenez, M.D., Julio B. Bobes, Ph.D.

Summary:

Objective: To determine the prevalence of illicit drug use and its relationship to personality traits in secondary students.

Method: The World Health Organization Drug Consumption Questionnaire, the Eysenck Personality Questionnaire (EPQ-A), and the Zuckerman Sensation Seeking Scale Form V (SSS) were administered to 2,862 secondary students from public centers of Oviedo (Northern Spain), during the academic year 1998–99.

Results: Mean age (SD): 15.87 (1.48). Males: 50.59%. Lifetime prevalence of consumption: cannabis (35.6%), hallucinogens (11.0%), tranquilizers (10.8%), amphetamines (8.5%), volatiles (8.2%), other drugs (lower than 8.0%). Males showed higher lifetime prevalence for cocaine, amphetamines, hallucinogens, volatiles, opiates, and MDMA, and females showed higher lifetime prevalence for tranquilizers ($p < .05$). First drugs used: volatiles [13.75 (2.93) years], tranquilizers [14.47 (2.14)], and cannabis [14,67 (4.23)] (no gender differences). Males showed a high mean number of illicit drugs consumed than females [0.98 (1.76) in males vs 0.76 (1.35) in females; $p = .000$]. Both males and females who consumed illicit drugs score higher than non-consumers on all EPQ-A and SSS subscales ($p < .05$).

Conclusions: Moderate prevalence of illicit drug consumption. Illicit drug use is associated with higher levels of emotional instability, extroversion and psychoticism, as well as a marked sensation seeking profile.

NR623 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Risk Factors for Completed and Attempted Suicides

Halise Ozgeven, M.D., *Department of Psychiatry, University of Ankara, Dicle Sokak 19/1 Yenimahalle, Ankara, Turkey;* Isik Sayil, M.D., Oguz Berksun, M.D.

Summary:

Background: This study investigated the rate and associated demographic features of attempted and completed suicides in a catchment area representative of a metropolitan area in Turkey, as a part of the WHO/Euro Multicentre Study, on Parasuicide.

Method: All hospitals in the catchment area were screened to detect attempted suicides. Statistics for completed suicides were obtained from state official statistics department (1).

Results: The rate of attempted and completed suicides were 21.4 for males and 57.5 for females, 6.6 for males and 3.5 for females per 100000, respectively. The female/male ratio was 2.5 and 0.49 for attempted and completed suicides, respectively. The sex difference was significant (chi-square = 39.1, DF = 1, $p \leq 0.001$). Cases were loaded at "15–24" age group for both attempted and completed suicides. In all other European countries, although attempted suicides were loaded at the same age group, completed suicides were loaded at the age of "above 40". Overdose for attempted and hanging for completed suicides were the most frequent means. The rates of both attempted and completed suicides were lower than the other participating centers in Europe (2).

Conclusion: Male sex is a risk factor for completed and female sex is a risk factor for attempted suicides, but 15–24 age group may be a risk factor for both groups.

NR624 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Disability and Mental Disorders Among Primary Care Patients: A French Perspective

Patrick Martin, M.D., *Department of Psychiatry, AMC, 70 BD de Courcelles, Paris 75017, France;* Catherine Richard-Berthe, M.D., Jean-Pierre Lepine, M.D.

Summary:

Introduction: Mental disorders are associated with significant social and health consequences. The present study assessed the disability of patients with mental disorders, with or without comorbidity.

Method: This cross-sectional survey included 2 414 primary care subjects with mental disorders, particularly depressive symptoms. Subjects were screened for mental disorders using the structured clinical interview for Mini International Neuropsychiatric Interview for the DSM-III-R (MINI). Data on each patient's sociodemographic characteristics, functional disability, (Sheehan Disability Scale), assessment of quality of life (RFS/FSQ), CGI and treatments, were collected at the time a of medical visit.

Results: The most prevalent disorders were MDD (81.2%), GAD (65.7%), SP (22.6%) and PD (14.8%). A total of 75.1% of the patients met the criteria for the more than one mental disorder. Assessment of the quality of life indicate that subscales emotional, social function, sexual function and well being were dramatically altered. Patients with mental disorders have significally increased disability as measured by the Sheehan Disability Scale. Compared

with patients who had a single mental disorder, patients with co-occuring disorders reported more disability in emotional, well-being, sexual function and social functioning.

Conclusion: Primary care patients with mental disorders are common and highly disabled. Furthermore, some mental disorders (e.g. MDD, TAG) rarely occur in isolation.

NR625 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Prediction of Treatment Response in OCD Via Functional Brain Imaging

Yehuda Sasson, M.D., *Department of Psychiatry, Chaim Sheba Medical Center, Tel Hashomer 52621, Israel;* Talma Hendler, M.D., Elinor Goshen, M.D., Zila Zwas, M.D., Joseph Zohar, M.D.

Summary:

Objective: To evaluate the correlation between brain activity and specific behavioral exposure in obsessive-compulsive disorder (OCD) patients, focusing on differences between responders and non-responders to treatment, and to determine whether these differences can be used to predict treatment response.

Method: Thirty-one patients with OCD underwent four brain imaging trials with SPECT before and following six months of sertraline treatment. The first pair of trials was attained at relaxed (R) condition and the second pair was attained while patients underwent an individually tailored behavioral challenge (BC) condition. Changes in blood flow between R and BC conditions before and at the end of treatment were compared for patients who responded to treatment (n = 16) and for those who did not (n = 15). Response was defined as a decrease of 25% or more on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).

Results: Significant differences in brain activity in the caudate, thalamus and temporal regions emerged between responders and non-responders. Further analysis suggested that only responders demonstrated changes in the inferofrontal regions.

Conclusions: It is suggested that functional brain imaging during symptom provocation may be used to investigate the dynamic changes of responders versus non-responders to pharmacological treatment and may also serve as a possible tool for predicting treatment response.

NR626 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Exaggeration of Post-Concussive Symptoms in Mild Head Injury Litigants

Jim Andrikopoulos, Ph.D., *Ruan Neurology, Mercy Hospital, 1750 48th Street, Suite 2, Des Moines, IA 50310-1993*

Summary:

Objective: The present study hypothesized that the overendorsing of post-concussive symptoms in mild head injured litigants is reflected in significantly greater elevations on selected MMPI-2 scales and feigned cognitive impairment.

Method: One hundred consecutive patients seeking compensation for a mild head injury were separated into a Low Motivation Group (LMG, $N = 46$) and High Motivation Group (HMG, $N = 54$) based on level of test performances. Patients with three borderline scores on at least three neuropsychological tests were assigned to the LMG. Lack of statistical differences on a test of verbal memory and attention between the LMG and a severely head injured group ($N = 38$) not in litigation was used to operationally define possible malingering. All litigants received a structured interview consisting of 36 post-concussive symptoms and the MMPI-2.

Results: The LMG endorsed a greater number of post-concussive symptoms ($t = (98) = 4.01$, $p < 001$) compared to the HMG. The overendorsement of post-concussive symptoms in the LMG was reflected in statistically and clinically greater elevations on the Hysteria, Depression, Psychasthenia, and Schizophrenia scales.

Conclusions: Excessive endorsement of post-concussive symptoms is related to possible malingered cognitive impairment and a somatoform type MMPI-2 profile recently termed "somatic malingering."

NR627 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The 5HT Transporter Protein Gene and OCD: Application of the Transmission Disequilibrium Test for Quantitative Traits

Margaret A. Richter, M.D., *Anxiety Clinic, CAMH-Clarke Division, 250 College Street, Room 1148, Toronto, ON M5T 1R8, Canada;* Emanuela Mundo, M.D., Sam Fariba, B.S.C., James L. Kennedy, M.D.

Summary:

Objective: It is widely accepted that Obsessive-Compulsive Disorder (OCD) is genetically mediated, likely via involvement of the serotonergic system. Recent studies have shown the presence of linkage and association between OCD and the serotonin transporter protein gene, which has a functional polymorphism in the promoter region (SCL6A4). The aim of the present study was to investigate the presence of linkage disequilibrium between SCL6A4 and OCD symptom severity.

Methods: 46 OCD probands (31 women and 15 men) meeting DSM-IV criteria, evaluated for severity by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (mean 23.8 $\pm$ 6.9 sd), were selected together with their living parents. From all subjects written informed consent to participate in the study was obtained. Genomic DNA was extracted from whole blood and genotyping of the SCL6A4 was performed using standard procedures. Data were analyzed employing the Transmission Disequilibrium Test for Quantitative Traits (QTDT) as described by Rabinowitz (1997).

Results: The QTDT analysis showed a preferential transmission of the long allele to the probands with higher Y-BOCS scores (chi-square = 5.5667, df = 1, $p < .02$).

Conclusions: These results are preliminary and need replication on larger samples. Further investigations considering the antiobsessional response to serotonergic agents as an alternative phenotype are also suggested.

NR628 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

A Novel Nonsense Mutation of MECP2 in a Patient with Rett Syndrome

Soo-Jeong Kim, M.D., *Department of Psychiatry, University of Chicago, 924E 57th Street, KNAPP RO22, Chicago, IL 60637;* Edwin H. Cook, Jr., M.D.

Summary:

Objective: Rett syndrome (RTT) is a pervasive developmental disorder that almost exclusively affects females. Because of the recent identification of several mutations of *MECP2* in patients with RTT, 10 female patients from an autism clinic were screened for mutations of *MECP2.*

Method: PCR was conducted using genomic DNA under the conditions described elsewhere (Amir et al. 1999). Bidirectional cycle sequencing of PCR products was performed. The androgen-receptor polymorphism was studied to assay X inactivation pattern.

Results: The patient with profound mental retardation and loss of purposeful hand use was found to have a novel *de novo* heterozygous nonsense mutation (Q19X) in *MECP2* and had a moderately skewed X inactivation pattern. Although two patients without *MECP2* mutation had hyperventilation, all of the nine patients without *MECP2* mutation did not have loss of hand use.

Conclusion: Given the atypical features of this patient with RTT, screening of *MECP2* and other MBD genes may reveal mutations in patients with similar features.

NR629 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Gender Differences in the 5HT Transporter Link Polymorphic Region in Geriatric Depression

David C. Steffens, M.D., *Department of Psychiatry, Duke University, Trent Drive-Duke S/Box 3903, Durham, NC 27710;* Ingrid Svenson, B.S., Douglas A. Marchuk, Ph.D., Bobby Levy, B.S., Judith C. Hays, Ph.D., Elizabeth P. Flint, Ph.D., K. Ranga R. Krishnan, M.D.

Summary:

There have been inconsistent reports of an association between mood disorders and the serotonin transporter gene linked polymorphic region (5HTTLPR). We studied 157 depressed subjects and 89 non-depressed controls who agreed to participate in a genetic study of affective disorders. Diagnosis of major depression was established using Diagnostic Interview Schedule and a clinical interview with a geriatic psychiatrist. PCR amplification was used to generate short and long 5HTTLPR alleles from genomic DNA. While none of the comparisons for the whole sample were statistically significant, among men, 26% of depressed patients (5% of controls) had two short alleles ($p = 0.012$). Among women, the frequency of short alleles was similar among depressives and controls; however, 70% of women with more than one episode had one or two short alleles, compared with 36% of patients with one episode ($p = 0.01$). Among female patients with a positive family history of psychiatric disorder, 76% had one or two short alleles, compared with 54% with at least one short allele among patients without a family psychiatric history ($p = 0.01$). In this sample, the 5HTTLPR gene exerted differential gender effects, contributing to the occurrence of depression in older men, and to the course of depression in older women.

NR630 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Quantitative TDT on the 5HT-1D Beta-Receptor in OCD

Emanuela Mundo, M.D., *Neurogenetics Department, CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada;* Margaret A. Richter, M.D., Sam Fariba, B.S.C., James L. Kennedy, M.D.

Summary:

Objective: Obsessive-Compulsive Disorder (OCD) is a psychiatric condition that has strong evidence for a genetic component and for the involvement of serotonergic system. Recent studies have shown that the selective ligand of the 5HT1Dβ autoreceptor, sumatriptan, modifies OCD symptoms. Preliminary results have also suggested the presence of association and linkage between 5HT1Dβ receptor gene and OCD. The aim of this study was to investigate the presence of linkage disequilibrium between the 5HT1Dβ receptor gene and OCD symptom severity.

Methods: Thirty-eight OCD probands (28 women and 10 men), diagnosed according to DSM-IV criteria and evaluated by the administration of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) (mean 25.2 ± 5.9 sd), were selected together with their living parents. From all subjects written informed consent to participate in the study was obtained. Genomic DNA was extracted from whole blood and genotyping of the G861 variant of the 5HT1Dβ receptor gene was performed using standard procedures. Data were analyzed employing the Transmission Disequilibrium Test for Quantitative Traits (QTDT) as described by Rabinowitz (1997).

Results: The QTDT analysis showed a preferential transmission of the G allele to the probands with higher Y-BOCS scores (chi-square = 4.000, df = 1, $p < .05$).

Conclusions: These results are preliminary and need replication on larger samples. If they are confirmed, there may be important implications for the 5HT1Dβ receptor gene in the pathogenesis and treatment of OCD.

NR631 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Childhood-Onset Neuropsychiatric Disorders in Adult Forensic Psychiatric Patients

Henrik Soderstrom, M.D., *Department of Forensic Psychiatry, Goteborg University, Box 2440, Hisings Backa 42204, Sweden;* Anders Forsman, M.D., Agneta Nilsson, M.D.

Summary:

Population-based studies in children have shown prevalences of 0.5% for pervasive developmental disorders (PDD), 0.5% for Tourette syndrome, and 5% for severe AD/HD with motor dyscoordination. These disorders often continue to cause problems and are associated with a considerable risk for comorbid psychiatric disorders in adult life. We have diagnosed these disorders by using operational DSM-IV, Gillberg & Gillberg, and Szatmari criteria in two groups of forensic psychiatric patients. Among 100 patients in a special hospital, 4 had a PDD, 3 Tourette syndrome and 9 severe forms of AD/HD. Among 37 subjects of pretrial forensic psychiatric investigation. 14 fulfilled DSM-IV criteria for AD/HD and 9 for one of the PDDs often combined with tics. A good multisource case history and a thorough clinical knowledge of these disorders are sufficient for reliable criterion-based diagnostics. Somatic investigations and psychological tests are important for etiology, treatment planning, and prognostics. Deficits in social reciprocity, identity, consistency, and impulse control combined with dissociative stress reactions may meet operational criteria for personality disorders, but when a neuropsychiatric disorder is diagnosed, interpretation and treatment should focus on underlying dysfunctions in empathy, central coherence and executive abilities.

NR632 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

The Goteborg Forensic Neuropsychiatry Project: Results from Two Pilot Groups

Henrik Soderstrom, M.D., *Department of Forensic Psychiatry, Goteborg University, Box 2440, Hisings Backa 42204, Sweden;* Anders Forsman, M.D.

Summary:

In two pilot studies, 1995–1996 ($n = 21$) and 1997 ($n = 49$), we used a broad range of clinical and biological diagnostic tools to study possible neuropsychiatric vulnerability to impulsive violence in subjects of forensic psychiatric investigation. No evidence of structural cerebral pathology was detected by MRI or CSF-tau-protein and GAP-43, but violent offenders showed signs of CNS and blood-brain barrier dysfunction: significantly reduced rCBF in the right temporal lobes, hippocampi, and left white frontal matter, and increased CSF/S albumin ratios even in the absence of Axis I DSM-IV psychiatric diagnoses, including a history of substance abuse, or other factors known to influence the CNS. Violent offenders did not differ from normal references in CSF HVA, MHPG and 5-HIAA, platelet MAO-B, and S-TSH, free and total T3, T4, and testosterone, but the CSF HVA/5-HIAA and the T3/T4 ratios predicted interpersonal, aggressive, and impulsive traits of psychopathy. MAO-B was negatively correlated to novelty seeking, CSF-5-HIAA to borderline traits, and testosterone to harm avoidance and cluster C personality disorders. Neurobiological substrates

to psychological dysfunction related to impulsive violence might constitute a basis for treatment studies.

NR633 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

A Follow-Up Study of Neuropsychiatric Sequelae in Patients with Varying Degrees of Mild Traumatic Brain Injury

Scott R. McCullagh, M.D., *Department of Psychiatry, Sunnybrook Hospital, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada;* Donna Ouchterlony, M.D., Alison Jardine, O.T., Andrea Protzner, M.A., Nancy Blair, M.A., Anthony Feinstein, M.D.

Summary:

Background: Earlier research has shown that in the acute phase of recovery following mild TBI, patients with GCS 15 do not differ from those with GCS 13/14 on a spectrum of neuropsychiatric symptoms [1]. Whether this holds at 6 months is unknown [2].

Objective: To assess neuropsychiatric differences at 5–6 months follow-up between patients with GCS 15 verses GCS 13/14.

Methods: 57 consecutive subjects with mild TBI (GCS 13–15, post-traumatic amnesia (PTA) ≤ 24 hours) attending an outpatient TBI clinic were examined with regard to demographic, injury-related, and neuropsychiatric variables. The latter comprised the 28-item General Health Questionnaire (GHQ) and the Neurobehavioral Rating Scale (NRS). Somatic complaints, functional (Glasgow Outcome Scale (GOS)) and psychosocial (Rivermead Outcome Questionnaire (ROQ)) outcome, plus return to work status were noted. Comparisons between patients with GCS 15 (n = 37) verses GCS 13/14 (n = 20) were undertaken.

Results: Subjects were assessed at ± 160 (SD = 62.8) days post-injury. Demographic features were similar. Patients with GCS 13/14 had significantly longer PTA (p = .001) and more frequent CT abnormalities (p = .005). However, no significant group differences emerged for measures of psychological distress (GHQ), additional neurobehavioral variables (NRS), frequency of somatic complaints, rate of return to work, and overall outcome (GOS, ROQ).

Conclusions: Despite clear neurosurgical differences, this study demonstrates that neuropsychiatric homogeneity exists among varying degrees of mild TBI. Whether cognitive data proves a more sensitive discriminator is the subject of ongoing investigation.

NR634 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Tourette's Syndrome and Psychiatric Comorbidity

Miguel Marquez, M.D., *Association Neuropsiguistrica Argentina, Ituzaingo 1250 3A Lanus Este, Buenos Aires 1824, Argentina;* Guillermo J. Tortora, M.D., Beatriz Moyano, M.D., Silvia Figiacone, M.D., Ignacio Brusco, M.D.

Summary:

Objective: Conceptions about the neuropsychiatric aspects of the Tourette syndrome (TS) have evolved. The original construction was about a new neurological disease. Others neurologist considered the *maladie des tics* as a some kind of chorea or hysteria. In the 1920's the psychoanalytical theories had conected the tics with masturbation and repressed familial psychosexual conflicts (psychoanalytical etage). In the 1960's started the next critical period of TS, (neuroleptical era), when was established that haloperidol was an effective agent for the management of motor tics and coprolalia. In the modern time of the history of TS (comorbidity era) the comorbid psychiatric disorders became the target of the diagnostic and treatment concerns. The objective of this research is to investigate the psychiatric comorbidity in patients with Tourette syndrome.

Method: We studied thirty two patients, referred by neurologist, who meet the DSM IV criteria of TS. We administred psychiatric and psychopedagogic semistructured interview Ham-A BDI, Yale BOCS, MADRS and Millon Clinical Multiphasic Inventory-3 (MCMI-3).

Results: TS has high psychiatric comorbidity in clinical populations. The most prevalents comorbid disorders was attention deficit disorder and learning disorders (69%), anxiety disorders, excluded OCD, (56%); obsesive-compulsive disorder (50%), personality disorder (50%) and mood disorder (43%). Most patients has more than two disorders at the time of the examination.

Conclusions: TS have high psychiatric comorbidity and must be conceptualized as a neurobehavioral disorder.

NR635 5/16/00, 3:00 p.m.-5:00 p.m.

Metalloproteinases and Neurological Disorders

Marion E. Wolf, M.D., *Department of Psychiatry, VA Medical Center, 3001 Green Bay Road, North Chicago, IL 60064;* Maria A. Valenzuela, Ph.D., Luis Cartier, M.D., Lucia Collados, Ph.D., Ana M. Kettlun, Ph.D., Aron D. Mosnaim, Ph.D.

Summary:

Several neurological disorders appear to be accompanied by significant changes in the patterns of CSF's metalloproteinases (MMPs), a family of neutral proteolytic enzymes involved in extracellular matrix modeling. In this study we characterized biochemically the various MMPs present in the CSF of 37 patients with neurological disorders that included vascular lesions (n = 14), inflammatory infectious diseases (n = 17), demyelinating or other degenerative disease (n = 6), and 21 controls (non-neurological patients who received spinal anesthesia). Biochemical characterization of MMPs included determination of substrate specificity and Ca^{2} dependency, as well as the effects of protease inactivators, carboxylic and His residue modifiers, and antibiotics. The results obtained indicate that CSF samples from both controls and neurological disorder patients expressed MMP-2 (gelatinase A) activity, mostly in its latent form (proenzyme). While the majority (13 of 17) patients with inflammatory neurological disorders showed the presence of a second enzyme, MMP-9 or gelatinase B, this enzyme was seen infrequently in patients with vascular lesions (3 out of 14 cases). Patients with demyelinating or degenerative diseases showed MMP-9 activity in 3 out of 6 cases. Myelin proteolysis is central to the demyelination process, which in association with perivascular inflammation, is a major pathological feature of multiple sclerosis. These preliminary findings that must be viewed within the limitations imposed by the small number of subjects studied, provide additional evidence for the role of MMPs in various physiological and pathological conditions involving remodeling of diverse tissues' extracellular matrix. Further studies in this field are needed to elucidate the possible role of MMP-9 in the pathophysiology of inflammatory and demeylinating neurological disorders.

NR636 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Training General Practitioners in the Management of Depression

Clare Dixon, B.S.C., *Department of Psychiatry, Manchester University, Withington Hospital, Nell Lane, Manchester M2O 8LR, England;* Linda Gask, M.D., Christopher F. Dowrick, M.D., Rachel Perry, M.A., Tim Usherwood, M.D., David Torgerson, Ph.D., Christopher Sutton, Ph.D.

Summary:

Objective: To measure the health gain for depressed patients from providing general practitioners with training in the assessment and management of depression.

Methods: In this randomised-controlled trial 38 Primary Care Physicians (PCPs) were recruited and randomised into either intervention or control groups following completion of baseline measurements (2). PCPs in the intervention group received 10 hours of training. Patients with recognised depression were recruited by their PCP. 194 patients were successfully recruited. Outcome measures included Hamilton Depression Rating Scale (HDRS), GHQ12, SF36 and economic and patient satisfaction scales.

Results: Analyses of HDRS and GHQ data showed no significant difference overall between the intervention and control groups at 3, 6 or 12 months. However, there were significant differences between the groups in Manchester and Liverpool, which appear to relate to major differences in mental health training before attending the course.

Conclusions: Our intervention was ineffective overall but differential effects were found between the two study sites. Isolated training for PCPs may be most effective for those with little mental health experience or training, but must form part of a wider strategy which may involve application of other evidence-based strategies designed to improve patient outcome.

NR637 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Assessing Psychiatry Residents' Cultural and Religious Beliefs Before and After a Related Course

Roubini Kambolis, M.D., *Department of Psychiatry, Bergen Regional Medical Center, 230 East Ridgewood Avenue, Paramus, NJ 07652;* Essam-Eldin Ellabbad, M.D., William M. Greenberg, M.D., Farah Farooq, M.D.

Summary:

Cultural and religious beliefs can importantly affect diagnostic and clinical practices, but have received limited study in the relevant area of psychiatry residency training. A pilot study was undertaken to: 1) develop a questionnaire and related scale assessing psychiatry residents' awareness and sensitivity to cultural and religious issues, and 2) test this questionnaire on residents both before and after they attended an interactive course on cross-cultural and religious issues. The questionnaire's 58 items covered one's personal religious beliefs, how these might influence clinical work, and awareness of how cultural beliefs could influence psychiatric classifications. 15 residents (from all four years), representing diverse cultures and religions themselves, completed the questionnaire anonymously, as did 14 residents after they attended the course. Both before and after the course, 80% professed religious beliefs, and strongly believed that religion affected human psychological growth.

Most believed that psychiatric classification had cross-cultural validity, but contrary to expectation, after taking the course they believed that cultural background had *less* effect on diagnosis. Although only a pilot study on a small sample (anonymous, but not exactly the same group on both occasions), we did not find an expected effect of a course influencing resident attitudes. Possible explanations are discussed. The questionnaire, however did appear useful and reliable.

NR638 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Effectiveness of Olanzapine Upon Psychiatric and Vocational Rehabilitation Outcomes

Ralph Aquila, M.D., *Department of Psychiatry, St. Luke's Roosevelt Hospital, New York, NY 10025;* Peter J. Weiden, M.D., Bruce J. Kinon, M.D., Denai R. Milton, M.S., Annette Zygmunt, Ph.D., Ralph W. Swindle, M.D., Virginia L. Stauffer, Pharm.D.

Summary:

Objective: An objective of this analysis was to determine whether patients treated with olanzapine (OLZ) as compared with conventional antipsychotics or risperidone performed better in their psychiatric rehabilitation programs as measured by total number of days worked.

Methods: In this single-site study, 100 clinically stable patients with a diagnosis of schizophrenia or schizoaffective disorder and attending a rehabilitation program were randomized to receive open-label treatment with either OLZ (N = 49) 5 mg to 20 mg per day or a comparator [conventional antipsychotic (N = 15) or risperidone (N = 36)] dosed within the package labeling for a total of 58 weeks. Rehabilitation outcome was evaluated by the total number of days worked and patient's attitudes towards medication compliance were captured by the Rating of Medication Influences Scale (ROMI).

Results: Stable patients in both OLZ and Comparator groups involved in psychiatric rehabilitation programs demonstrated substantial within-group improvement in the BPRS Total, as well as, Negative Symptom scores. The majority of all study patients were able to work at least 25% of the Ideal Total Number of Working Days. OLZ patients demonstrated a differential of working more days, although this comparison did not reach statistical significance.

Conclusion: Clinically stable patients who were able to participate in a program of psychiatric rehabilitation demonstrated continued clinical improvement up to one year of continued treatment. OLZ patients versus Comparator demonstrated a numerical advantage in number of days worked.

NR639 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Low Levels of Antibodies to Cardiolipin in First-Episode and Chronic Schizophrenia

Pinkhas Sirota, M.D., *Abarbanel Mental Health Center, 15 Keren Kayemet, #6A, Bat-Yam 59100, Israel;* Irene Bogdanov, M.D., Aviva Katzav, M.D., Ruth Hershko, M.D., Joab Chapman, M.D.

Summary:

Objective: To measure anticardiolipin antibodies (aCL) in major psychiatric diseases. Samples: Experiment 1.96 subjects were evaluated: 20 first episode schizophrenia patients, [SCZ1] 20 chronic schizophrenia patients in acute exacerbation [SCZ2]. 19 bipolar patients, 20 schizoaffective patients and 17 healthy age matched controls. Experiment 2: 97 subjects: 20 first episode schizophrenia patients [SCZ1]. 60 chronic schizophrenia patients in acute exacerbation [SCZ2] and 17 healthy age matched controls.

Methods: Diagnosis was according to DSM-IV guidelines. Serum samples were tested for aCL in parallel by enzyme linked immunosorbant assay in the presence of bovine serum. 6 positive control samples with high levels of aCL were run in parallel. Background binding to wells uncoated with cardiolipin (CL) was also measured.

Results: Experiment 1: aCL levels were similar in the control, bipolar and schizoaffective groups. In contrast, aCL levels in the SCZ1 and SCZ2 groups were significantly lower than controls ($p = 0.000002$ and 0.00002 respectively).

Experiment 2 supported these results ($p = 0.0002$ for all schizophrenic patients versus controls). Interestingly, background levels in both experiments were higher in the schizophrenic groups than controls.

Conclusions: Serum aCL levels are lower in schizophrenic patients, and especially in first episode cases, compared to controls. One possible explanation for the lower levels of aCL in schizophrenic patients is the consumption of these antibodies in an active phase of the disease. The higher background levels in

these groups may indicate a high level of antibodies to some serum component in schizophrenic patients.

NR640 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Neuroleptic Effects on Cytokines in Schizophrenia

Pinkhas Sirota, M.D., *Abarbanel Mental Health Centr, 15 Keren Kayemet, #6A, Bat-Yam 59100, Israel;* Meital Meiman, Bella Epstein, M.D., Irene Bogdanov, M.D., Ruth Hershko, M.D., Ruben Benatov, Ph.D.

Summary:

Background: Patients with schizophrenia possess different immunological aberrations but their significance is not clear.

Objective: In the present study the authors analyzed the production of cytokines in serum of 33 schizophrenic patients, before and after neuroleptic treatment, and 21 age and sex matched healthy controls.

Methods: IL-1 receptor antagonist (IL-1ra), and IL-2 soluble receptor antagonist (IL-2sR) levels were evaluated by a sandwich enzyme immunoassay.

Results: No significant differences were found in serum levels of IL-1ra between schizophrenic patients and controls, but it was highly increased in schizophrenic patients after neuroleptic treatment ($p < 0.017$). Significant increased levels of IL-2sR was found in schizophrenic patients before and after treatment as compared to healthy controls ($p < 0.02$, $p < 0.004$, respectively).

Conclusions: The present study supports evidence for immune activation in some schizophrenic patients and neuroleptic medications differently affect the production of various cytokines.

NR641 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Monocyte Activation in Depressed Patients

Javier Schlatter, M.D., *Department of Psychiatry, University Clinic, APDO 4209, Pamplona, NA 31080, Spain;* Felipe Ortuno, M.D., Maria L. Subira, M.D., Salvador Cervera-Enguix, M.D.

Summary:

Method: We studied monocyte activation parameters (monocyte counts; interleukin(IL)-1β, IL-6, TNFα, and IFN-γ production; phagocytic index; oxidative burst; and surface molecules CD14, CD16, and HLA-class II expression) in 24 depressed patients and 15 healthy controls. We performed a correlation analysis between these parameters and HAM-D and HAM-A scores.

Results: In the group of depressed patient we found increased monocyte oxidative burst ($p = 0.04$), IL-1β ($p = 0.02$) and IL-6 ($p = 0.001$) production; and decreased HLA-class II expression and phagocytic index ($p = 0.001$) compared to healthy controls. In the depressed group we found a negative correlation ($r: -.4$; $p = 0.05$) between monocyte phagocytosis and HAM-D and HAM-A scores, and a positive correlation ($r: .7$; $p = 0.001$) between CD16 expression and HAM-A scores.

Discussion: These results suggest that in patients with depression there may be a monocytic activation, however, there is also a reduction of monocyte phagocytic function. CD16 expression may be a useful parameter of the severity of anxiety in depressed patients.

At the conclussion of this presentation the participant will be familiar with patherns of dysfunction of monocyte activation in patients with depression.

NR642 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Psychometric Analyses of the Modified Rush Sexual Inventory

John M. Zajecka, M.D., *Department of Psychiatry, Rush-Presbyterian Medical Ctr, 1725 West Harrison St., #955, Chicago, IL 60612;* Deepa Rao, M.A., Taisa Skubiak, B.A.

Summary:

Objective: The impact of sexual dysfunction as a result of antidepressant therapy is often underestimated by clinicians, and it can impede a patient's optimal recovery and quality of life. Thus, the Modified Rush Sexual Inventory (MRSI) was created to assess sexual functioning and satisfaction changes due to medication effects and mood variations. This research presents the reliability and validity findings of the MRSI.

Method: Psychiatric clinical trial subjects, medical students, hospital employees, and other volunteers completed the MRSI ($N = 99$ males, $N = 122$ females) at Rush Medical Center. Cronbach's alpha was calculated to establish internal consistency. Concurrent validity was established for males with the Brief Sexual Function Questionnaire for men (BSFQ, $N = 79$) and the Brief Index of Sexual Functioning for women (BISF, $N = 73$).

Results: The MRSI appears to have good internal consistency ($\alpha = 0.77$ for females, 0.75 for males). A significant correlation was achieved between the MRSI and the BISF ($r = 0.57$, $p < 0.01$) as well as the MRSI and the BSFQ ($r = 0.55$, $p < 0.01$).

Conclusions: Analyses of the MRSI items demonstrated that the MRSI is a reliable and valid measure of sexual functioning and satisfaction. The measure's strong psychometric properties suggest its benefit in use as a clinical and research tool.

NR643 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Depression and Family Functioning in the Caregivers of Patients with Chronic Mental Illness

Alison M. Heru, M.D., *Department of Psychiatry, Brown Univ./ Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906-9980;* Kim Vlastos, M.H.A., Maria Bassi, M.H.A., Dorota Gawlas, M.D., Christine E. Ryan, Ph.D.

Summary:

Objective: Increasingly, family members provide care and support for relatives with chronic psychiatric illness. This study focuses on family functioning and how it mediates in the health and burdens of the caregivers of chronically mentally ill patients.

Method: 43 caregivers of patients admitted to a psychiatric hospital with chronic mental illness completed assessments measuring their perceptions of family functioning (FAD), perceived burdens and rewards and depressive symptomatology. Patient diagnoses included major depression, bipolar illness, schizophrenia, and schizoaffective disorders. Patients age ranged from 19 to 76 years with a mean of 48 years.

Results: Caregivers are more likely to be male (58%) and spouses (63%) with an average age of 54 years. Family functioning was unhealthy in communication, roles, affective involvement, and overall functioning. 24% of caregivers met criteria for depression; those with poor family functioning were significantly more likely to report depressive symptoms compared to caregivers who reported good family functioning (26.0 vs. 12.5, $t = -2.17$, $p < .05$). 30% of caregivers reported help from other relatives; less than 5% reported help from organizations such as NAMI, MDDA.

Conclusion: A substantial percent of caregivers of patients with chronic mental illness are at risk for depression, particularly those with poor family functioning.

NR644 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Race and Age Differences in Illness Knowledge and Empowerment in Schizophrenia

LeaAnn Moricle, M.D., *Department of Psychiatry, University of Maryland, 630 West Fayette Street, WPCC, Baltimore, MD 21201;* Janine C. Delahanty, M.A., Leticia E. Nostrado, Ph.D., Lisa D. Green-Paden, M.D., Alicia Lucksted, Ph.D., Lisa B. Dixon, M.D.

Summary:

Objectives: To describe the extent to which persons with schizophrenia who are receiving treatment report: 1) knowledge about their illness and services, and 2) the extent to which specific services are helpful, and 3) their degree of empowerment they feel from services. Demographic correlates of these outcomes were also examined.

Methods: The Schizophrenia Patient Outcomes Research Team survey conducted face-to-face interviews with random sample of 715 persons with a clinical diagnosis of schizophrenia who received care in two states. Multivariate analyses were conducted regarding patient knowledge, helpfulness of services and empowerment.

Results: Most patients subjects reported knowing only "a little" about the services that were available Caucasians knew *significantly* more about most services that were offered and felt *significantly* more empowered. Younger patients reported *significantly* more knowledge about schizophrenia and other sources of assistance with housing, employment and SSI/SSDI.

Conclusions: Level of knowledge about one's illness and the sense of empowerment one has concerning it can effect the quality of life and illness course. Psychoeducational models of care that rely on teaching patients and families about the illness have been shown to improve patient outcomes. The observed racial differences are compatible with what previous knowledge about the impact of race in other disorders. Usual systems of care should perhaps pay more attention to patients' education and empowerment needs, especially of African-Americans and older patients.

NR645 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Stress and Emotional Response in Patients with Mood Disorder

Min-Cheol Park, M.D., *Neuropsychiatry, Wonkwang Univ Psych Hospital, 144-23 Dongsan-Dong, Iksan Cheonbuk 570-060, Korea;* Jung-In Koh, M.D., Sang-Woo Oh, Ph.D., Sang-Yeol Lee, M.D.

Summary:

Objective: This study was investigated to demonstrate the relationship between stress and emotional responses of depression, anxiety, and anger in patients with mood disorder.

Method: Fifty patients with major depressive disorder were compared to those with bipolar manic disorder. All subjects were evaluated for perceived stress, Beck depression inventory, dysfunctional attitude, state-trait anxiety, state-trait anger and anger expression. The data were analyzed by t-test, correlation, and multiple regression analysis.

Results: The results were as follows.

1. Depressive group had significantly higher score of perceived stress, depression, state anxiety and trait anxiety than manic group.

2. Perceived stress in depressive group was positively correlated with depression, anxiety, state and trait anger, anger expression and sex, however that in manic group was positively correlated with state anger and anger expression.

3. In depressive group, trait anxiety, trait anger, age, and dysfunctional attitude predicted 70.6% of variance on depression, perceived stress predicted only 1.2%. Trait anxiety predicted 67.6% for state anxiety.

4. In manic group, education and trait anger predicted 28.7% of variance of depression, trait anger predicted 38.3% for state anxiety, and trait anger and education predicted 29.4% for state anger.

Conclusion: The results suggest that emotional responses to perceived stress in depressive group are related to depression, anxiety, and anger but those in manic group are related to anger.

NR646 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Cognitive Therapy Versus Intensive Behavior Therapy

Jean A. Cottraux, M.D., *Department of Neurology, Anxiety Disorder Unit, 59 Boulevard Pinel/HOP Neurol, Lyon Cedex 03 69394, France;* Ivan Note, M.D., Sainan Yao, M.D., Alain Sauteraud, M.D., Brigitte Note, M.A., Sylviane Lafont, M.A., Jean-Francois Dartigues, M.D.

Summary:

Objective: To compare the effectiveness of Cognitive Therapy (CT) and Behavior Therapy (BT) in OCD

Design: Sixty five ambulatory patients with DSM-4 obsessive-compulsive disorder and without major depression were randomized into two groups for a 16 week psychological treatment in three centers. Group 1 received CT. Group 2 received BT (exposure with response prevention) along a 4 week intensive treatment period followed by a maintenance phase of 12 weeks. No medication was prescribed. Both groups had 20 hours of therapist contact time.

Outcomes: Baseline variables were balanced in the two groups, except for outcome expectations which were higher in CT ($p = 0.05$). Sixty two patients were evaluated at week 16, and 48 were present week 52. At week 16 the rates of responders were similar in the two groups. Depression (BDI) was significantly more improve in the group which received CT ($p = 0.005$). Improvement in depression was correlated with expectations in BT but not in CT. At week 26 and 52, improvement was retained without between-group difference.

Conclusions: CT and BT were equally effective on OCD. CT had specific effects on depression which were stronger than those of BT at post test.

NR647 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Donepezil Improves Neuropsychiatric Symptoms in Moderate to Severe Alzheimer's Disease

Serge Gauthier, M.D., *McGill Centre for Studies, Douglas Hospital, 6825 Boul Lasalle, Verdun, PQ H4H IRS, Canada;* Howard Feldman, M.D., Jane Hecker, M.D., Bruno Vellas, M.D., Ponni Subbiah, M.D., Ed Whalen, Ph.D.

Summary:

Objective: Controlled clinical trials of donepezil have demonstrated short- and long-term benefits on cognition, activities of daily living and global function in mild to moderate Alzheimer's disease (AD). The current study investigated the benefit of donepezil on neuropsychiatric symptoms in moderate to severe AD.

Method: Patients with baseline sMMSE scores of 5–17 received either donepezil (5 mg/day for 28 days, and 10 mg/day thereafter; $n = 144$) or placebo ($n = 147$) in this 24-week, randomized, double-blind, multicenter trial. Outcome was measured using the Neuropsychiatric Inventory (NPI) 12-item total. Safety was assessed by recording adverse events (AEs), vital signs and laboratory tests.

Results: Mean age of study patients was 73.6 years and mean sMMSE scores at baseline were 11.8 and 12.2 (NS) for the donepezil and placebo groups, respectively. Improvements on the NPI 12-item total were observed at all visits for donepezil- compared

with placebo-treated patients, reaching statistical significance at Weeks 4 and 24 ($p < 0.05$) and Endpoint (Week 24 ITT LOCF; $p < 0.001$). Selected individual NPI items also showed significantly favorable benefits with donepezil compared with placebo. AEs were similar between treatment groups; the majority were rated mild in severity and were most commonly gastrointestinal in nature.

Conclusions: These data suggest that donepezil improves behavior in moderate to severe AD patients, demonstrating a continued benefit of donepezil at more advanced stages of AD than previously investigated.

NR648 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Paroxetine Versus Behavior Therapy in Tricotillomania: Interim Results of a Pilot Study

Annett Neudecker, *Department of Psychiatry, University Hospital, Martinistrasse 52, Hamburg 20246, Germany;* Iver E. Hand, M.D.

Summary:

Objective: We hypothesize that trichotillomania is appropriately treated with either behavior therapy or SSRIs. In contrast to most studies, but inkeeping with common practice, these pilot study patients were allowed to choose either multimodal behavior therapy (MBT) or treatment with the SSRI Paroxetine (non-randomized) to consider separately treatment effects and patients' motivation.

Method: To date, 36 patients have been included, 17 of them completed. In baseline and endpoint assessment, intensity of hairpulling and comorbid symptomatology was measured. MBT patients had 45 weekly outpatient individual sessions, SSRI patients have been augmented with 20 to 60 mg Paroxetine for 12 weeks and got bi-weekly supportive contacts. The baseline assessment showed increased rates in comorbid depression (BDI > 11 in X%) and high social insecurity in both groups.

Results: Hairpulling as well as comorbid depression decreased significantly from pre- to posttreatment in both groups; there were no significant group differences in outcome. MBT patients showed an additional clear improvement in social skills.

Conclusions: Both MBT and Paroxetine treatment lead to a significant reduction of trichotillomania. It is assumed that the improvement in social skills in the MBT group will contribute to a better outcome in the follow-up period. All patients welcomed the free choice. However, the differences between the treatment groups were fewer than expected.

NR649 Wednesday, May 17, 3:00 p.m.-5:00 p.m.

Computer-Assisted Cognitive Therapy for Depression

Jesse H. Wright, M.D., *Norton Psychiatric Center, University of Louisville, 200 East Chestnut, Louisville, KY 40202;* Andrew S. Wright, M.D., Aaron T. Beck, M.D., Paul Salmon, Ph.D., L. Jane Goldsmith, Ph.D., Jeffrey Kuykendall

Summary:

Efficacy of computer-assisted cognitive therapy for depression was studied in a randomized controlled trial of 45 subjects with major depression. Drug-free subjects who met DSM-IV criteria for major depression were randomly assigned to computer-assisted cognitive therapy (CCT, N = 15), standard cognitive therapy (CT, N = 15), or a waiting list (N = 15). Depressive symptoms were measured with the Beck Depression Inventory and the Hamilton Rating Scale for Depression. Subjects also completed the Automatic Thoughts Questionnaire and the Cognitive Therapy Awareness Scale, a measure of knowledge of cognitive therapy.

Treatment with CCT or CT consisted of nine sessions over a period of eight weeks. Therapist contact in CCT was reduced, as compared to CT, by having sessions 2–9 consist of twenty-five minutes of therapist time and approximately twenty-five minutes working with the multimedia computer program. All CT sessions lasted fifty minutes. Therapy sessions were audiotaped for measurement of treatment adherence. Results of the study indicated that CCT and CT were equally efficacious treatments for depression, and both were superior to delayed treatment. Data from this preliminary trial indicate that CCT may be a potential method of improving treatment efficiency and reducing costs of delivering cognitive therapy for depression.

NR650 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Point Prevalence of Hepatitis-C and Comorbid Psychiatric Diagnosis in the Baltimore VA Medical Center

Peter Hauser, M.D., *Department of Psychiatry, Baltimore, VAMC, 10 North Greene Street, Baltimore, MD 21201;* Jaswinder S. Khosia, M.D., Richard Calabria, M.A., Susan Reed, R.N., Naomi Tomoyasd, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that patients with hepatitis C commonly have a comorbid psychiatric diagnosis, which suggests an important role for mental health professionals in the management of Hepatitis C patients.

Summary:

Hepatitis C virus infection (HCV) is now the most common bloodborne infection in the United States and the leading cause of liver transplantation in this country. Recent studies have shown that the prevalence of HCV infection among veterans is higher than in the general U.S. population. The Department of Veterans Affairs (VA) conducted a nationwide screening in March 1999 in which 26,000 veterans were screened for HCV. Eight percent were positive; four times the national average. As it is well known that the most common cause of HCV transmission is intravenous drug use, we undertook a study in the Baltimore VA to determine the frequency of HCV and the relationship between HCV and psychiatric illness.

Methods: A total of 294 veterans were randomly screened for hepatitis C antibody in the Baltimore VA Medical Center as part of the nationwide VA HCV screening initiative. Subsequent to the screening a detailed chart review was conducted to determine psychiatric diagnoses; human immunodeficiency virus (HIV) status was also determined.

Results: Of the 294 patients tested, 53/294 (18%) tested positive for HCV antibody. Amongst those who tested positive for HCV, 25/53 (47.17%) also had a substance abuse diagnosis, whereas of those who tested negative for HCV only 22/241 (9.13%) had a substance abuse diagnosis. Amongst those who were HCV positive, 21/53(39.6%) were also HIV positive as compared with 6/241(2.5%) in the HCV negative group. Other psychiatric diagnoses in the HCV positive group were as follows: major depression 10/53(18.87%), bipolar disorder2/53(3.77%), posttraumatic stress disorder 3/53(5.66%).

Conclusion: This study shows that the prevalence of HCV infection in the Baltimore VA Medical Center, which serves an inner-city population, is significantly higher than in the general population. Furthermore, we found that 47% of veterans who tested positive for HCV had a substance abuse diagnosis and over 20% had a mood disorder. An odds ratio calculation showed that veterans with a substance abuse diagnosis were 8.8 times more likely to have HCV and veterans with HCV were 27.8 times more likely to be HIV positive. Our data suggest that addressing mental health issues should be a significant component of the management of patients with hepatitis C.

References:

1. Matt Pueschel: VHA Hepatitis C costs placed at $250 Million. U.S. Medicine, 1999:35(7)
2. McHutchison J G, Gordon S C, Schiff E R, et al: Interferon Alpha-2b alone or in combination with ribavirin as initial treatment for chronic Hepatitis C. New England Journal of Medicine 1998;339:1485–92

NR651 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Outcomes of Experimental Cocaine Administration

Igor Elman, M.D., *Department of Psychiatry, Massachusetts General Hospital, 16 Blossom Street, Boston, MA 02114;* Sara Krause, B.A., Katherine Karlsgodt, B.A., David R. Gastfriend, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate a familiarity with clinical assessment tools and biological markers used to evaluate drug exposure. The participants should also appreciate the value of these tools in the diagnosis and follow up of individuals with drug dependence.

Summary:

Objective: Although cocaine administration in humans is a commonly used research paradigm, its clinical outcomes have not yet been investigated.

Methods: Twenty-one non-treatment-seeking individuals with cocaine dependence were reevaluated five and ten months following cocaine infusion in a functional MRI scanner, using computerized clinical assessments and hair radioimmunoassay (RIAH). For comparison, data were collected from a group of 19 matched subjects who did not participate in the cocaine infusion study.

Results: The infused and non-infused groups did not differ on days of cocaine use (corroborated by RIAH), Addiction Severity Index drug composite score, Hamilton Rating Scale for Depression, and craving scores at both follow ups. Time-related trends analysis revealed significant reduction in days of cocaine use ($p = 0.05$) and in craving ($p = 0.03$).

Conclusions: Our results suggest that laboratory-based cocaine administration is a safe paradigm and that participation in clinical research studies may be beneficial for the individuals who are not engaged in any type of treatment for their addiction.

References:

1. Woodward B: Challenges to human subject protections in US medical research. *JAMA* 282(20):1947–52
2. Baumgartner WA, Hill VA: Hair analysis for organic analytes: Methodology, Reliability Issues, and Field Studies in Drug Testing in Hair. Edited by Kintz P. Boca Raton, CRC Press, 1996

NR652 Thursday, May 18, 9:00 a.m.-10:30 a.m.

The Influence of Prior Major Depressive Episode on Sertraline Treatment Response in Premenstrual Dysphoric Disorder

Kimberly A. Yonkers, M.D., *Department of Psychiatry, Yale Univ. School of Medicine, 200 College Street, Ste 206. New Haven, CT 06519;* Anna Stout, Ph.D., Grady Tanna, M.D., Teri B. Pearlstein, M.D., Andrea B. Stone, M.D., Jean Endicott, Ph.D., Ellen W. Freeman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the symptoms of PMDD and comorbid diagnoses and have a greater understanding of treatment strategies for PMDD.

Summary:

A prior history of major depressive episode (MDE) occurs in about 30% of women with premenstrual dysphoric disorder (PMDD)[1]. Although MDE and PMDD share a number of characteristics including similar symptoms and abnormalities in markers of serotonergic functioning, there are also important differences, including treatment response. For example, women with PMDD preferentially respond to serotonergic antidepressants while women with MDD respond similarly to serotonergic and non-serotonergic antidepressants[2].

Objective: This analysis explored whether a prior history of MDE influenced PMDD treatment response.

Method: 237 women with PMDD were randomly assigned to sertraline (50–150 mgs daily) or placebo for 3 menstrual cycles. A SCID was administered at baseline to identify lifetime psychiatric illness. Response was defined as a CGI ≤ 2.

Results: Prior MDE occurred in 78 women and 159 had no prior MDE. In women *with* prior MDE, placebo and sertraline response was 37% and 53% respectively. In women *without* prior MDE, 28% responded to placebo and 65% responded to sertraline ($p < 0.001$).

Conclusion: PMDD women, with or without prior MDE had a better response to sertraline compared with placebo. Those without prior MDE showed a higher response rate to sertraline. These data provide further demonstration that PMDD is a diagnostic entity discreet from MDE.

References:

1. Yonkers K. MD et al: The Association between PMDD and other Mood Disorders. *J Clin Psych.* 1997; 58:S(15)19–25.
2. Freeman E, PhD et al: Differential Response to Antidepressants in Women with Premenstrual Syndrome/Premenstrual Dysphoric Disorder: A Randomized Controlled Trial. *Arch Gen Psych* 1999; 56(10):932–939.

NR653 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Dually Diagnosed Schizophrenia Patients Display More Craving than Individuals with Cocaine Dependence

Genata Carol, Ph.D., *VA New Jersey, 151 Knollcroft Road, Building 143, Lyons, NJ 07939;* David A. Smelson, Psy.D., Claudia Gerigk, B.S., Miklos F. Losonczy, M.D., Douglas M. Ziedonis, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the need to assess and treat cocaine craving among individuals previously diagnosed with schizophrenia.

Summary:

Introduction: Cocaine abuse remains a chronic problem among the non-psychiatric and psychiatric population. Among the psychiatric population, individuals with schizophrenia and cocaine dependence are frequently burdened by substance abuse relapses and acute symptom exacerbation. Because the same neurobiological system is involved in the etiology of schizophrenia and the rewarding effects of cocaine, we were interested in examining whether individuals with schizophrenia and cocaine dependence have a heightened craving state compared with cocaine addicts without schizophrenia.

Methods: Nonhospitalized veterans were asked to rate their craving at baseline and again 72 hours after the initial assessment. This design was used to examine group differences in addition to ensuring the reliability of the ratings among these subjects.

Results: Preliminary results suggest that individuals with cocaine dependence and schizophrenia ($N = 20$) had significantly higher scores in craving intensity (.02), mood (.008), energy (.007),

and health (.02) compared with cocaine addicts without schizophrenia (N = 20). Test retest reliability over the 72-hour period was high for depression (73), energy (.64), and feeling (.68), with craving intensity being slightly lower (.53).

Discussion: Future research could include a longitudinal design to examine how long the craving state persists as well as developing interventions designed specifically to target the craving state.

References:

1. Smelson DA, Roy M, Roy A, Santana S: Electroretinogram in withdrawn cocaine-dependent subjects. Relationship to cue-elicited craving. *British Journal of Psychiatry* 1998; 172:537–9
2. Ziedonis DM, Fisher W: Assessment and treatment of comorbid substance abuse in individuals with schizophrenia. *Psychiatric Annals* 1994; 24:477–483.

NR654 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Association of OPRMI +118A Allele with Alcoholism

Patricia I. Ordorica, M.D., *Department of Psychiatry, USF, 3515 East Fletcher Avenue, Tampa, FL 33612;* Terrance Town, M.S., Laila Abullah, B.S., John A. Schinka, Ph.D., James A. Mortimer, Ph.D., Amy B. Graves, Ph.D., Michael Mullan, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the fact that the genetic foundation of addictive disorders includes genes common to multiple disorders and genes specific to individual disorders. This study provides evidence that the μ-opioid receptor +118A allele may be specific to alcohol dependence.

Summary:

The human μ-opioid receptor (OPRMI) has been implicated in the reward, tolerance, and withdrawal-associated effects of alcohol and other drugs. OPRMI contains a functional coding polymorphism (+118A/G), which has been shown to modify the binding affinity of the receptor for endogenous β-endorphin. We previously investigated this polymorphism in samples of controls and individuals in treatment for alcohol dependence and reported a novel association between alcohol dependency and the +118A variant. That study did not allow, however, an examination of whether the +118A allele was specific to alcohol dependency or associated more generally to addiction status per se, as is the case for the dopamine D2 receptor. We have now extended our study by the addition of 209 individuals from a population that has been well characterized in terms of alcohol and nicotine use. Our results indicate that the +118A variant is associated with alcohol dependency ($p = .04$), but not with nicotine dependency ($p = .45$) or with alcohol consumption within the normal ranges of social use (less than average of 27 drinks per month, $p = .29$). These data lend support to the hypothesis that the +118A variant is specifically associated with alcohol dependency as opposed to other addictive behaviors.

References:

1. Swan GE, Carmelli D, Cardon LR, Heavy consumption of cigarettes, alcohol and coffee in male twins. *Journal of Studies in Alcohol* 1997; 58:182–190.
2. Town T, Abdullah L, Crawford F, Schinka J, et al: Association of a functional in opioid receptor allele (+118A) with alcohol dependency. American Journal of Medical Genetics: *Neuropsychiatric Genetics* 1999; 88:458–461

NR655 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Risk Factors for Substance Abuse in First-Episode Schizophrenia Patients

Serge M. Sevy, M.D., *Psychiatric Research Dept., Hillside Hospital, 75-79 263rd Street, Glen Oaks, NY 11004;* Jose Alvir, D.Phil., Delbert G. Robinson, M.D., Margaret Woerner, Ph.D., Robert Goldman, Ph.D., Jeffrey A. Lieberman, M.D., John M. Kane, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify first-episode schizophrenic patients at risk for substance abuse.

Summary:

Objective: to identify risk factors associated with substance abuse in first episode schizophrenic patients.

Method: analysis of data from the prospective study of psychobiology in first-episode schizophrenia at Hillside hospital. A total of 118 first-episode schizophrenic patients were included in the study. Ninety-one patients had no history of substance abuse, and 27 patients had a past or current history of substance abuse. They were compared on demographic and psychopathological measures before being treated for their first episode of psychosis and on cognitive measures after six months of treatment.

Results: There were no statistically significant differences between groups for sex, schizophrenia subtype, marital status, education, family history of schizophrenia, course of illness, obstetric complications at birth, age of onset, baseline symptoms, time to treatment response, attention span, memory, and executive functioning. However, dual-diagnosis patients were found to have higher familial socioeconomic status ($\chi^2 = 9.3$; $df = 4$; $p = 0.06$), better pre-morbid functioning ($t = -2.9$; $df = 76$; $p < 0.01$), higher IQ ($t = -2.8$; $df = 87$; $p < 0.01$), and better language skills ($t = -2.5$; $df = 76$; $p < 0.05$).

Conclusion: First-episode schizophrenic patients with substance abuse have higher intellectual functioning, which may be associated with higher pre-morbid socioeconomic status and functioning. Our results contradict stereotypes about low functioning schizophrenic patients being at higher risk for substance abuse. Clinicians should be particularly vigilant about substance abuse in high functioning schizophrenic patients.

References:

1. Sevy S, Kay SR, Opler LA, et al: Significance of cocaine history in schizophrenia. *J Nerv Ment Dis* 1990; 178:642–648
2. Lieberman JA, Alvir JM, Woerner M, et al: Prospective study of psychobiology in first-episode schizophrenia at Hillside Hospital. *Schizophrenia Bull* 1992; 18:351–371

NR656 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Maintained Efficacy of Paroxetine in the Treatment of Social Anxiety Disorder

Tanya Hair, M.S.C., *CNSGI, Smith-Kline and Beecham, 1250 South Collegeville Road, Collegeville, PA 19426;* Rajinder Kumar, M.B., Timothy E. Rolfe

Summary:

Social anxiety disorder is a disabling, distressing condition characterized by excessive fear of social or performance situations. It is a chronic disorder, and recovery is rare without treatment. To date, only the results of shorter-term pharmacologic treatment have been published. We assessed the effectiveness of paroxetine in maintaining the benefit of treatment over 48 weeks. In the first 12 weeks all patients were administered single-blind paroxetine; in the second phase, responders were randomized to paroxetine or placebo double-blind for an additional 36 weeks. The pri-

mary outcome variable was the proportion of patients relapsing during the second phase. In the paroxetine group 14% of patients relapsed compared with 39% in the placebo group (OR 95% CI = 0.24 [0.138, 0.431] P < 0.001). The mean change from baseline in LSAS in the paroxetine group was –6.8 compared with +9.1 (P < 0.001). Significant heterogeneity was observed across centers. Paroxetine was well tolerated; the most frequently reported adverse events were abnormal ejaculation (26%), nausea (24%), headache (20%), and somnolence (17%). These data indicate that long-term treatment with paroxetine produces continued efficacy and prevents relapse.

References:

1. Stein MB, Liebowitz MR, Lydlard RB, Pitts CD, Bushnell W, Gergel I: Paroxetine treatment of generalized social phobia (social anxiety disorder). J of Amer Med Assoc 1998;280:708–713
2. Scholing A, Emmelkamp PMG: Treatment of generalized social phobia: results at long-term follow-up. Behav Res Ther 1996;34:447–452

NR657 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Comparing Modafinil to Dextroamphetamine in the Treatment of Adult ADHD

Fletcher B. Taylor III, M.D., *Rainier Associates, 5909 Orchard Street, West, Tacoma, WA 98467-3824*

Educational Objectives:

Participants should know of the DSMIV criterion for diagnosing ADHD, Distinguish between the subtypes of ADHD, know the standard drug treatments of ADHD and their potential side effects. They should be aware of the atypical stimulant modafinil, its use, side effects, and its potential as a treatment alternative for ADHD.

Summary:

Objective: To compare the efficacy of the new wake-promoting drug modafinil, to dextroamphetamine for adult ADHD treatment.

Method: 22 adult ADHD outpatients meeting the DSMIV criterion for ADHD participated in a randomized double-blind placebo-controlled crossover study comparing the effects of modafinil with dextroampheramine for ADHD symptoms: Measures included the DSMIV Adult ADHD Rating Scale and the Copeland Symptom Checklist for ADD. Objective measures of attention included the Stroop, Digit Span sub test of the WAIS, and the Controlled Oral Word Association Test (COWAT, CFL version). Drugs and placebo were titered up to optimum doses (maximum efficacy and minimum side effects), then data collected.

Results: For the 21 completers, the DSMIV ADHD symptom scales were improved over placebo for both drug conditions (p < .001), and Copeland measures for modafinil only (p < 004). COWAT performances were improved over placebo for modafinil (p < .039), and dextroamphetamine (p < .023) conditions. The average optimal daily dose of modafinil was 206.8 (SD = 84.9), and was associated with fewer side effects than dextroamphetamine. Ten subjects chose to continue modafinil after the study, and seven of these subjects were of the inattentive ADHD subtype.

Conclusions: Modafinil is a viable treatment alternative for adult ADHD with minimal side effects and low addition potential.

References:

1. Wilens TE, Biederman J, Spencer TJ, Price J. Pharmachotherapy for adult attention deficit/hyperactivity disorder: A review. J Clin Psychopharm 1995;15:270–279
2. Ferraro L, Antonelli T, O'Connor WT, et al. Modafinil: An anti-narcoleptic drug with a different neurochemical profile to d-amphetamine and dopamine reuptake blockers. Soc Biol Psychiatry 1997;42:1181–1183

NR658 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Comparing Guanfacine and Dextroamphetamine for Adult ADHD: Efficacy and Implications

Fletcher B. Taylor III, M.D., *Rainer Associates, 5909 Orchard Street, West, Tacoma, WA 98467-3824;* Joan Russo, Ph.D.

Educational Objectives:

At the conclusion of this presentation, participants should know the standard drug treatments of ADHD and their potential side effects. They should be aware of the pharmacologic properties of guanfacine and its potential as a treatment alternative for ADHD.

Summary:

Objective: To compare the efficacy of the alpha2a agonist guanfacine with dextroamphetamine in the treatment of ADHD in adults.

Method: Seventeen adult outpatients meeting DSM-IV criterion for ADHD, participated in a double-blind, placebo-controlled crossover study comparing drug effects on ADHD symptoms. Measures of change included the DSM-IV ADHD Behavior Checklist for Adults and the Copeland Symptom Checklist for Adult Attention Deficit Disorders. Cognitive measures of attention included the Stroop and Controlled Oral Word Association Test (COWAT, CFL version). The three successive drug trials were separated by washout periods. During trial, the drug or placebo was titered up to an optimum dose, and then data were collected.

Results: Both drugs significantly reduced ADHD symptoms on the DSM-IV Behavior Checklist for Adults over placebo (p < 0.05). The Stroop color (p < .005), and color-word measures (p < .05) showed a significant drug effect for guanfacine only. The average dose of guanfacine was 1.10 (SD = 0.60), and the most common side effect on guanfacine was fatigue. No subjects discontinued drug trials.

Conclusions: This preliminary study indicates that guanfacine is a well-tolerated treatment alternative for adult ADHD with no addiction potential.

References:

1. Wilens TE, Beiderman J, Spencer TJ, Price J: Pharmachotherapy for adult attention deficit/hyperactivity disorder: a review. J Clin Psychopharm 1995;15:270–279
2. Arnsten AF, Steere JG, Hunt RD: The contribution of alpha-2 noradrenergic mechanisms to prefrontal cortical cognitive function: potential significance for attention-deficit hyperactivity disorder. Arch Gen Psy 1996;53:448–455

NR659 Thursday, May 18, 9:00 a.m.-10:30 a.m.

SSRI and Benzodiazepine Treatment for Panic

Andrew W. Goddard, M.D., *Department of Psychiatry, Yale University, 100 York Street, #2J, New Haven, CT 06511;* Ahmad M. Almai, M.D., Praveen Jetty, M.D., Kathleen A. Morrissey, B.A., Katherine K. Shobe, Ph.D., Cathryn M. Clary, M.D., Dennis S. Charney, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the benefits and the risks of combination SSRI/benzodiazepine treatment of panic disorder and recent data supporting the use of this strategy.

Summary:

There is debate about combining benzodiazepines with SSRIs in the acute treatment of panic disorder (PD). Therefore, we tested the efficacy of early coadministration of clonazepam with sertraline in a double-blind trial.

Methods: Forty-seven, unmedicated, DSM-IV PD patients (27 F; 20 M; mean age = 38 ± 9 yrs; baseline PDSS mean score ± SD = 15 ± 4; CGI-severity = 4.8 ± 0.6) gave consent. They

received open-label sertraline for 12 weeks (target dose = 100 mg/d), and, in addition, were randomized to either active clonazepam 0.5 mg one capsule tid (ACT)(n = 22) or placebo clonazepam (PLAC) (n = 25), for the first four weeks. Clonazepam was then tapered over three weeks and discontinued.

Results: 68% (32/47) of the patients completed the trial. Drop-out rates were similar in the PLAC group compared with ACT (36% vs 27%, p = 0.5). An intent-to-treat analysis (on LOCF data) revealed a much greater proportion of responders (50% decrease in the PDSS total score from baseline) in the ACT group compared with PLAC at the end of week 1 (43% vs 4% chi square = 9.7, p < 0.002). This difference was not observed at the end of weeks 2 (p = 0.4), 4 (p = 0.4) or 12 (p = 0.2).

Discussion: These data show that rapid stabilization of PD can be safely achieved with a sertraline/clonazepam combination, supporting the use of this type of regimen as a first-choice treatment for moderate to severe PD.

References:

1. Woods SW, et al: A controlled trial of alprazolam supplementation during impramine treatment of panic disorder. J Clin Psychopharmacology 1992;12:32–38
2. Pollack MH, et al: Sertraline in the treatment of panic disorder: a flexible-dose multi-center trial. Arch Gen Psychiatry 1998;55:1010–1016

NR660 Thursday, May 18, 9:00 a.m.-10:30 a.m.

Antipsychotic-Related Change in Glucose Regulation

John W. Newcomer, M.D., *Department of Psychiatry, Washington University, 4940 Children's Place Box 8134, St. Louis, MO 63110-1002;* Angela K. Melson, M.A., Gregg Selke, B.A., Robert Fucetola, Ph.D., Julie A. Schweiger

Educational Objectives:

At the conclusion of this presentation, the participant should understand the potential adverse effects of antipsychotic medications on glucose regulation.

Summary:

Abnormalities in glucose regulation, and type 2 diabetes may be more common in schizophrenia than in the general population. Abnormal glucose regulation and new-onset type 2 diabetes are also associated with antipsychotic treatments, particularly clozapine and olanzapine. Increased adiposity can decrease insulin sensitivity, and antipsychotics can increase adiposity (e.g., body mass index; BMI). However, abnormal glucose regulation and type 2 diabetes have also been reported during antipsychotic treatment in the absence of weight gain. We examined the effect of an oral 50 gram dextrose challenge on plasma glucose and insulin levels in patients with schizophrenia and healthy controls, comparing glucoregulatory effects of different antipsychotics with the effect of no medication in healthy controls, matching for age and BMI. Clozapine and olanzapine treatment were associated with elevated fasting plasma glucose levels, in comparison with treatment with risperidone and untreated healthy controls. Clozapine and olanzapine treatment were also associated with elevated plasma glucose and insulin levels following oral glucose loading, in comparison with healthy. These effects were not explained by differences in adiposity. Treatment-associated changes in glucose regulation may occur independent of changes in adiposity, and may be an independent risk factor for the development of diabetes.

References:

1. Newcomer JW, Craft S, Fucetola R, Moldin SO, et al: Glucose-induced increase in memory performance in patients with schizophrenia. Schizophr Bull 1999;25(2):321–335
2. Wirshing DA, Spellberg BJ, Erhart SM, Marder SR, Wirshing WC: Novel antipsychotics and new onset diabetes. Biol Psychiatry 1998;44:778–783

NR661 Thursday, May 18, 9:00 a.m.-10:30 a.m.

A Double-Blind, Placebo-Controlled Study of Naltrexone in the Treatment of Pathological Gambling Disorder

Suck Won Kim, M.D., *Department of Psychiatry, University of Minnesota MC, F256/2A West 2450 Riverside Dr, Minneapolis, MN 55454;* Jon E. Grant, M.D., David E. Adson, M.D., Young Chul Shin, M.D., Julie A. Toth, B.A.

Educational Objectives:

At the conclusion of this presentation, participants should be able to diagnose and treat patients suffering from pathological gambling disorder.

Summary:

Objective: To test the efficacy and safety of naltrexone in the treatment of Pathological Gambling Disorder (PGD).

Method: Eighty-nine patients who met DSM-IV PGD criteria and were free from concurrent Axis I diagnosis by SCID were enrolled in a one week, single-blind placebo lead-in followed by an 11-week double-blind naltrexone or placebo treatment. The naltrexone dose was titrated to 250mg/day as needed. Gambling symptom change was assessed with patient- and clinician-rated. Clinical Global Impression (CGI-PT, CGI-MD), and the Gambling Symptom Rating Scale (G-SAS). Side effects were monitored weekly and liver function biweekly. The MIXREG program was used for the data analyses.

Results: Data from 45 patients (F = 25, M = 20, average age 49, naltrexone N = 20, placebo N = 25) who completed six or more visits were used. Their average South Oaks Gambling Scale score was 15; average G-SAS score was 47 (maximum 80). Their average HDRS score (17-item) was 6.2; HARS was 6.5. Significant improvement was noted in all three gambling symptom measures (CGI-PT, $p < 0.001$; CGI-MD, $p < 0.001$; G-SAS, $p < 0.019$; G-SAS test-retest reliability N = 58, r = 0.70, Cronbach's $\alpha = 0.89$; convergent validity $p < 0.01$). Average naltrexone and placebo doses at the end of the study were 188 and 243 mg/day.

Conclusion: Naltrexone seems to be effective in reducing gambling symptoms especially for those who have excessive urges.

References:

1. Hedeker D: MIXREG: a fortran program for mixed-effects linear regression models. Prevention Research Center: School of Public Health, University of Illinois at Chicago, 1993
2. Lesieur HR, Blume SB: The South Oaks Gambling Screen (SOGS): a new instrument for the identification of pathological gamblers. *Am J Psychiatry* 1987;144:1184–1188

NR662 Thursday, May 18, 12:00 p.m.-2:00 p.m.

BP-II With and Without Cyclothymic Temperament

Hagop S. Akiskal, M.D., *Department of Psychiatry, University of CA at San Diego, 9500 Gilman Drive (La Jolla), San Diego, CA 92093-0603;* Elie G. Hantouche, M.D., Jean-Francois Allilaire, M.D., Sylvie Lancrenon, Ph.D., Jean-Michel Azorin, M.D., Marc L. Bourgeois, M.D., Daniel Sechter, Liliane Chatenet-Duchene, M.D.

Summary:

This paper presents data from a French multi-center study (EPIDEP). The aim of EPIDEP is to show the feasibility of validating the spectrum of soft bipolar disorders by practicing clinicians. In this report we focus on data concerning the relationships between

cyclothymic temperament and recurrent hypomanic episodes within "BP-II spectrum".

Method: EPIDEP involves 1) training 48 French psychiatrists in 15 sites; 2) construction of a protocol based on criteria of DSM-IV (Semi-Structured Interview for Hypomania), Akiskal (Soft Bipolarity), as well as criteria modified from the work of Angst (Hypomania Checklist), the Ahearn-Carroll Bipolarity Scale, HAM-D and Rosenthal Scale; Semi-Structured Interview for Affective Temperaments (based on Akiskal-Maliya). Cyclothymia (CT) was both clinician- and self-rated.

Results: Are presented on the total of 537 patients included at "visit 1" and 493 assessed for soft bipolarity at "visit 2". The global rate of BP-II disorder was estimated to 39.7% by systematic search for hypomania. Mean score on CT was significantly higher in BP-II than in Unipolars (UP). Moreover, 88% of cases categorically assigned to CT were recognized as BP-II. In total population, scores of self-rated CT correlated at a high significant level with hypomania checklist score ($r = .,49$, $p < .,0001$), but less in BP-II group ($r = .,22$), which suggests that not all patients in BP-II group were cyclothymic. Within the BP-II group (n = 194 patients), systematic comparison of cases categorically assigned to CT (n = 74) *versus* those without CT (n = 120) was undertaken. From these analyses, we found in BP-II with CT : 1) younger ages of disorder onset ($p = .,005$) and seeking help ($p = .,05$); 2) higher scores on Ham-D ($p = .03$) and Rosenthal ($p = .,007$) scales; 3) longer delay between onset and recognition of bipolarity ($p = .,0002$); 4) higher rate of psychiatric comorbidity ($p = .,04$); 5) different profits on axis II (more histrionic, passive-aggressive personality disorders in BP-II with CT and more OCPD in BP-II Without CT); 6) higher rate of family history with psychiatric disorder (63% vs 53%, p not significant), especially chronic syndroms (34% vs 21%) and suicidal attempts (22% vs 13%).

Conclusion: Cyclothymic temperament (CT) emerged as a robust clinical marker of BP-II disorder. However, BP-II with CT seemed to represent a more recurrent and severe disorder by comparison to BP-II without CT

NR663 Thursday, May 18, 12:00 p.m.-2:00 p.m.

EPS Variations in the Elderly

Jacobo E. Mintzer, M.D., *DSIR/AGTPIRB, NIMH, 6001 Executive Blvd. R7160 MSC, Bethesda, MD 20892-9635;* Paul P. Yeung, M.D., Jamie A. Mullen, M.D., Dennis Sweitzer, Ph.D.

Summary:

Objective: To provide preliminary data regarding incidence of EPS in elderly psychotic patients treated with either quetiapine or risperidone.

Methods: A subanalysis of the elderly subgroup (age 65 or older) of a multicenter, 4-month, open-label trial comparing the tolerability and efficacy of quetiapine and risperidone in elderly psychotic patients was conducted. From a total of 92 patients (mean age 67), 65 received quetiapine (200 mg median daily dose), and 27 were treated with risperidone (3 mg median daily dose); patients were flexibly dosed. Assessments included the EPS Checklist, Positive and Negative Syndrome Scale (PANSS) and Clinical Global Impression (CGI).

Results: After 4 months, 3.4% of quetiapine patients and 16.0% of risperidone patients had substantial EPS ($p = 0.003$), defined as requiring a dosage adjustment or the addition of an anti-EPS medication. Quetiapine was less likely than risperidone to cause akathisia ($p = 0.02$) or hypertonia ($p = 0.01$). In addition, no statistically significant differences between groups were evident in the PANSS positive scale, negative scale, total score, or the CGI.

Conclusion: Quetiapine is less likely to produce EPS than risperidone, and is equally effective in treating the positive and negative symptoms of psychosis in elderly patients. Funded by a grant from AstraZeneca.

NR664 Thursday, May 18, 12:00 p.m.-2:00 p.m.

The Influence of Personality Variables on Psychophysiological Responsivity Within a Startle Reflex Paradigm

Paul M. Ramirez, Ph.D., *Department of Psychology, Long Island University, I University Plaza. H-Building 8th Floor. Brooklyn, NY 11201;* Vivian M. Mougios, M.A.

Summary:

It has been widely demonstrated that the intensity of the startle reflex systematically varies with a person's emotional state. This study investigated the relationship between psychophysiological reactivity within the startle reflex paradigm and personality variables as measured by the Symptom Checklist List-90R (SCL-90R) (Derogatis, 1977). Specifically, it was hypothesized that, when viewing negative stimuli, the intensity of one's startle response or lack there of, would be related to one's reported symptomatology using the SCL-90R. A nonclinical sample of forty-five subjects, ages 18 to 30, viewed sixteen slides depicting classical artwork representing positive or negative emotional themes. The positivity or negativity of the emotional themes depicted in the artwork had been determined in a previous study. When viewing artwork with subtle negative emotional themes, significant startle response differences were noted for subjects who endorsed items related to the depression, hostility, phobic, and psychotic subscales (p-value range: .047-.0021). In contrast, when positive stimuli were shown these individuals did not respond with an exaggerated startle response. While reactions to startle are typically described as a reflex reaction, this study demonstrates that personality factors can augment this reflex. In addition, while psychophysiological responses to startle has been examined in psychopathological populations, this is the first study which utilized a nonclinical sample in examining the modifying role of personality variables in psychophysiological reactivity within a startle reflex paradigm.

NR665 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release for the Treatment of Hypoactive Sexual Desire Disorder in Nondepressed Women

R. Taylor Segraves, M.D., *Department of Psychiatry, Case Western Reserve Univ., 2500 Metro Health Drive, Cleveland, OH 44109-1998;* Harry A. Croft, M.D., Richard J. Kavoussi, M.D., John A. Ascher, M.D., Sharyn R. Batey, Pharm.D., Vicki J. Foster, M.S., Carolyn Bolden-Watson, Ph.D.

Summary:

Objective: This pilot study evaluated the safety and efficacy of bupropion sustained release (SR) for the treatment of hypoactive sexual desire disorder (HSDD) in non-depressed women.

Methods: Eligible subjects entered a 4-week single-blind placebo phase. Non-responders (CGI-I < 2) during the placebo phase entered an 8-week, single-blind treatment phase in which they received bupropion SR. Improvement in HSDD was assessed bi-weekly using investigator-rated scales evaluating desire and sexual functioning and global evaluation scales (CGI-I and CGI-S). HSDD response was defined as a CGI-I of 1 or 2.

Results: Sixty-six subjects entered the placebo phase. There were no responders during this phase. Fifty-one subjects continued into the treatment phase and received bupropion SR (average daily dose 290mg/day). The majority of subjects were white and premenopausal, with an average age of 41 years (range 23–65). In contrast to the placebo phase, fifteen (29%) of subjects during the treatment phase were considered to be responders, with response seen as early as two weeks after treatment with bupropion SR. Bupropion SR was generally well tolerated.

Conclusion: The results of this pilot study suggest that bupropion SR may be an effective treatment of HSDD and that further study is warranted.

NR666 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Reduced Cue-Elicited Cocaine Craving and Relapses

David A. Smelson, Psy.D., *Department of Psychiatry, VA New Jersey, 151 Knollcroft Road, Bldg 143, Lyons, NJ 07939;* Jill Williams, M.D., Maureen Kaune, M.D., Jacqueline Constantino, M.D., Miklos F. Losonczy, M.D., Mathew Menzza, M.D., Douglas M. Ziedonis, M.D.

Summary:

Introduction: There is a high prevalence of cocaine abuse among individuals diagnosed with schizophrenia. These dually diagnosed patients have a more severe psychiatric course, increased hospitalizations, and poor long-term outcome (Serper et al. 1995). Because the same neurobiological systems are involved in the etiology of schizophrenia and the rewarding effects of cocaine, individuals with the combined disorders may have a heightened craving state, which predisposes them to relapse. This suggests a need to develop effective pharmacological anti-craving interventions to prevent frequent deterioration.

Methods: We conducted a preliminary open-label trial comparing risperidone to typical neuroleptics for decreasing cue-elicited craving and relapses among withdrawn cocaine-dependent schizophrenics (N=17). Symptom severity was rated weekly and patients completed a craving questionnaire before and after the cue-exposure procedure.

Results: Patients receiving risperidone (N=7) were less likely to drop out of the study (P=.05) or relapse with drugs (P=.02) and had lower pre/post cue-exposure change scores on the energy/arousal (P=0.01), and feeling (P=.07) dimensions of craving compared to individuals receiving a typical neuroleptic (N=10).

Discussion: Risperidone may prove to be an effective treatment for decreasing craving and relapses. Future research could include a double-blind trial comparing risperidone to another typical neuroleptic in this population.

NR667 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Once-Daily Methylpheniadate HCL, Standard Methylphenidate and Placebo in Children with ADHD

Laurence L. Greenhill, M.D., *Department of Psychiatry, NY St Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032*

Summary:

Objective: To compare efficacy and safety of investigational once-daily OROS® methylphenidate hydrochloride extended-release tablets (OROS® MPH qd) with standard methylphenidate three times daily (MPH tid) dosed at 4 hour intervals, and placebo in children with attention deficit/hyperactivity disorder (ADHD).

Methods: ADHD patients, aged 5–13 years, at 14 centers, were randomized in a double-blind, double-dummy fashion to one of the three treatments for 28 days. Efficacy was measured in multiple settings by multiple raters using standardized tests for behavior and attention, including IOWA Conners, global assessments, among others.

Results: 206 patients completed the study. Using the primary efficacy measure (IOWA Conners scale for inattention/overactivity as rated by community schoolteachers) OROS® MPH qd (n = 79) was similar to MPH tid (dosed every 4 hours) (n = 81) (p = 0.54) and both were statistically superior to placebo (n = 46) (p < 0.001). Most side effects were mild; all were consistent with known effects for MPH in children.

Conclusions: Efficacy measures were similar between investigational OROS® MPH qd and the MPH tid comparator. Both were superior to placebo. OROS® MPH qd was well liked by patients, teachers, and clinicians. Findings were consistent across multiple settings, measures, and raters.

NR668 Thursday, May 18, 12:00 p.m.-2:00 p.m.

A Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Paroxetine in the Treatment of Pathological Gambling Disorder

Suck Won Kim, M.D., *Department of Psychiatry, University of Minnesota MC, F256/2A West 2450 Riverside Dr, Minneapolis, MN 55454;* Jon E. Grant, M.D., Young Chul Shin, M.D., Julie A. Toth, B.A., David E. Adson, M.D., Rocco M. Zaninelli, M.D.

Summary:

Objective: To investigate the efficacy and safety of paroxetine in the treatment of Pathological Gambling.

Method: Patients fulfilling DSM-IV criteria for Pathological Gambling Disorder[1] and scoring ≥5 on the South Oaks Gambling Screen[2] were enrolled if no other Axis-I disorder was present. A 1-week placebo run-in phase was followed by 8 weeks treatment with paroxetine or placebo. The initial paroxetine dose of 20 mg could be increased gradually to a maximum of 60 mg/day. Changes in clinical status were assessed using the clinician-and patient-rated CGI and a prototype of the Gambling Symptom Assessment Scale (G-SAS). Treatment emergent symptoms (TES) were assessed weekly.

Results: Data were obtained from 41 patients (20 paroxetine, 21 placebo). Improvement in clinical condition was greater in the paroxetine than in the placebo group, but the group difference was statistically significant only for the clinician-rated CGI (random regression analysis: $z = 1.99$, $p < 0.05$). The improvement in CGI score in the paroxetine group was significantly greater than in the placebo group at weeks 6 through 8 (MANOVA: $F = 4.29$, $p = 0.05$; $F = 5.50$, $p = 0.02$; $F = 5.95$, $p = 0.02$). For the G-SAS, test-retest reliability was .70, internal consistency (α-coefficient) .89, and convergent validity with the CGI .82 ($p < .01$). There were 2.3 TES per patient in the paroxetine and 1.2 in the placebo group, the most frequent being headache, fatigue and dry mouth.

Conclusions: The results of this trial indicate that paroxetine may be effective in the treatment of Pathological Gambling. There were no unexpected side effects from this treatment. However, additional studies with larger patient samples and a longer treatment phase are required to establish conclusively the efficacy and safety of paroxetine for this indication. This study also shows that the G-SAS is reliable and valid, although its structure may have to be refined for use in future investigations.

NR669 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Kinetics and Safety of a Novel Risperidone Depot

Marielle Eerdekens, M.D., *Janssen Research Foundation, Turnhoutseweg 30, Beerse B-2340, Belgium;* Merete Rasmussen, M.S.C., An Vermeuzen, Ph.D., Richard Lowenthal, M.S.C., Achiel Vanpeer, Ph.D.

Summary:

Objective: The bioavailability of a new intramuscular depot formulation and of oral doses of risperidone was assessed in patients with schizophrenia.

Methods: Three groups of stable patients with schizophrenia received oral doses of risperidone (2, 4, or 6 mg/day) during weeks 1–3 and oral risperidone at half those doses during weeks 4–5. During weeks 2–10, the three groups received depot doses of risperidone (25, 50, or 75 mg, respectively) every 2 weeks (5 injections). Plasma concentrations of unchanged risperidone and

of the active moiety (risperidone + 9-hydroxyrisperidone) were determined. Efficacy, and tolerability measures, were assessed regularly.

Results: Total daily exposure to the active moiety was equivalent after oral and depot dosing, i.e., the 90% confidence intervals for the mean steady state AUC and Cav ratio (depot vs. oral) were all within the bioequivalence range of 80% to 120%. Peak plasma concentrations were significantly lower (25% to 32%) after depot than oral dosing. The most frequent adverse events were either influenza-like symptoms or of a psychiatric nature. No consistent, clinically relevant changes in vital signs, ECG, or laboratory test results were observed. Patients remained symptomatically stable when treatment was changed from an oral to a depot regimen.

Conclusions: Bioequivalence of oral and IM depot dosing of risperidone was demonstrated. Moreover, IM depot dosing was as well tolerated and efficacious as oral dosing.

NR670 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Adherence to Atypical Versus Typical Antipsychotic

Esperanza Diaz, M.D., *Department of Psychiatry, Yale University, 34 Park Street, Room 510, New Haven, CT 06519-2103;* Michelle C. Sullivan, B.S.N., Elizabeth Neuse, M.A., H. Rowland Pearsall, M.D., Keith A. Hawkins, Psy.D., Scott W. Woods, M.D.

Summary:

Medication adherence is a major influence in the treatment of schizophrenia and crucial in the prevention of relapse [1]. Efficacy trials have demonstrated that atypical antipsychotics have a better side effect profile [2] but little is known about adherence rates. The purpose of this study was to determine whether the better side effect profile translated into superior medication adherence.

Methods: Patients with schizophrenia and schizoaffective disorder were followed weekly for three months after hospital discharge. Discharge medications were dispensed in a bottle with a cap capable of measuring the amount of openings. On weekly visits the electronic monitors were downloaded to show the number of openings. Medication adherence was defined as the average ratio of recorded bottle openings across available data.

Results: We followed 36 subjects. In 26 subjects the principal antipsychotic was an atypical and in 10 subjects only oral typical antipsychotic was used. Preliminary analysis indicate that medication adherence rate was 82.3 in patients receiving atypical antipsychotics and 53.0 in patients receiving typical antipsychotics, $p = .001$.

Conclusion: These data suggest that the medication adherence might be higher over the short term in patients receiving atypical antipsychotic than in patients receiving typical antipsychotics.

NR671 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Quetiapine Regulates Neuroprotective Genes

Ou Bai, *Department of Psychiatry, University of Saskatchewan, 103 University Drive, Saskatoon, SK S7N 0W8, Canada;* Augusto Juorio, Rudy Bowen, M.D., David L. Keegan, M.D., Vern Bennett, M.D., Satish Shrinkhande, Xin-Min Li, M.D.

Summary:

Objectives: Recent clinical and anatomical investigations on schizophrenia have suggested that progressive neuropathological changes occur over the life time course of the disease. Early intervention with atypical neuroleptics could prevent the progression of some symptoms. We have recently shown that clozapine and olanzapine may have some neuroprotective properties. In this study the effects of quetiapine on the gene expression of p75 (low affinity nerve growth factor receptor), whose downregulation is associated with reduced cell death, and superoxide dismutase (SOD1), an enzyme which reduces oxidative damage to neurons, were investigated.

Methods: Quetiapine was administered to PC12 (rat pheochromocytoma) cells in culture and its effects analyzed by northern blot after 48 hours of incubation.

Results: Quetiapine downregulates p75 and upregulates SOD1 mRNA in a dose dependent manner, with the greatest upregulation observed at longer time points and higher doses.

Conclusion: The effects of quetiapine to regulate the gene expression of p75 and SOD may indicate its neuroprotective potential.

NR672 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Modafinil Augmentation of Antidepressant Treatment in Depression

Matthew A. Menza, M.D., *Department of Psychiatry, RWJ Medical School, 675 Hoes Lane, Piscataway, NJ 08854;* Kenneth R. Kaufman, M.D.

Summary:

Objective: Despite the advances in antidepressant therapy over the past decades, patients with non-response and partial response remain common and there is now a renewed interest in the psychostimulants as augmenters for these patients. Modafinil is a novel psychostimulant drug that was recently marketed for treating excessive daytime sleepiness associated with narcolepsy. The mechanism of action of modafinil is unknown, but, unlike other stimulants, it is highly selective for the CNS, has little effect on dopaminergic activity and appears to have low abuse potential.

Methods: In this retrospective case series we describe seven patients with depression (4 with major depression and 3 with bipolar depression) who responded to modafinil augmentation of an antidepressant. The Hamilton Rating Scale for Depression (24 item) was done prior to treatment and at each subsequent visit.

Results: At doses of 100–200 mg/day, all seven patients achieved full or partial remission, generally within one to two weeks. The mean HDSD score went from 19.7 to 7.6 with augmentation. All patients had some residual tiredness or fatigue prior to starting modafinil and this symptom was particularly responsive to augmentation. Side effects were minimal and did not lead to discontinuation of the drug in any of the patients.

Conclusions: Modafinil appears have promise as an augmenter, especially in patients with residual tiredness or fatigue. It is a particularly attractive alternative to other stimulants because of its low abuse potential and Schedule IV status.

NR673 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Cognitive Impairment Associated with Antidepressant Treatment

Stefano Pini, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy;* Isa Corradi, Ph.D., Concettina Mastrocinque, M.D., Ciro Conversano, Ph.D., Patrizia Panicucci, M.D., Liliana Dell'Osso, M.D., Giovanni B. Cassano, M.D.

Summary:

Background: There is increasing evidence that antidepressant medications may determine cognitive dysfunctions. It is not clear whether tricycle antidepressants (TCA) have a different impact on cognitive functioning compared to serotonin selective reuptake inhibitors (SSRIs). This preliminary study aimed to investigate neurocognitive functioning in older patients with depression treated with a TCA or with a SSRI.

Method: Subjects were 18 consecutive outpatients aged 50 and over with mild DSM-III-R major depressive episode. Neuropsychological assessments included the Wechsler Adult Intelligence

Scale-Revised (WAIS-R), Mini Mental State Exam (MMSE) and Wechsler Memory Scale. Patients with dementia were excluded from this study.

Results: Overall, the mean age of the sample was 64.4 ± 9.3 years and 12 patients were females. Seven patients were taking a SSRI and 11 patients were taking a TCA from at least one month and no longer than three years. The two groups did not differ significantly in MMSE total score (respectively, 24.9 ± 2.2 vs 25.0 ± 2.3, $p < .90$) nor in educational level. Compared to the TCA group, the SSRI group showed a higher Verbal IQ score (100.9 ± 9.1 vs 88.0 ± 9.7, $p < .02$) and a higher Full Scale IQ score (99.4 ± 7.3 vs 89.6 ± 10.6, $p < .05$). The Memory Quotient did not differ significantly in the two groups.

Conclusions: Depressed patients taking a SSRI performed significantly better on intellectual functioning tests than those taking a TCA. Implications of these findings for treatment of depression will be discussed.

NR674 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Intranasal Sumatriptan for Post-ECT Headache

John S. Markowitz, Ph.D., *Department of Psychiatry, Medical University of SC, 67 President St/PO Box 250861, Charleston, SC 29425;* Charles H. Kellner, M.D., C. Lindsay DeVane, Ph.D., Mark D. Beale, M.D., Jeffery W. Folk, M.D., Carol Burns, M.S.N.

Summary:

Introduction: Headache (HA) following electroconvulsive therapy (ECT) is a frequent side effect and may be unresponsive to conventional analgesics. Reports suggest that sumatriptan (Imitrex®) may have utility in treating post-ECT HA. We assessed intranasal sumatriptan for post-ECT HA in an open-label study.

Methods: Following evaluation by the ECT team, informed consent was obtained. After ECT, subjects experiencing HAs rated pain as mild, moderate, or severe. HAs rated moderate or severe were treated with 20 mg intranasal sumatriptan. Ratings were repeated at 0.25, 0.5, 1.0, 1.5 and 2 hrs post-dose. Treatment response was defined as a reduction in HA pain from moderate or severe to mild or none after 2 hrs.

Results: Six females, 34–45 yrs old experienced 10 post-ECT HAs (3 [30%] "moderate" and 7 [70%] "severe"). Eight (80%) HAs responded at 2 hrs and 7 (70%) had responded by 1 hr. Of the 8 responders at 2 hrs, 6 (75%) reported no pain while 2 (25%) reported mild pain. No significant side effects were reported.

Conclusion: Intranasal sumatriptan nasal spray may be an effective and well-tolerated treatment for post-ECT headache. Further controlled trials are required.

NR675 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Paroxetine: Preliminary Data on Breast Cancer Survivors

Vered Stearns, M.D., *Georgetown University, 3970 Reservoir Road NW, Washington, DC 20007;* Claudine Isaacs, M.D., Julia Rowland, Ph.D., Jeanette Crawford, R.N., Matthew Ellis, Ph.D., Daniel P. Hayes, M.D., Katherine L. Beebe, Ph.D.

Summary:

Many breast cancer survivors suffer debilitating hot flashes associated with chemotherapy-induced or natural menopause. Estrogen replacement therapy, the drug of choice for hot flashes and other perimenopausal symptoms, is generally avoided in women with prior breast cancer or at high risk for developing the disease.

Anecdotal clinical reports suggest that the SSRI, paroxetine, might be effective in relieving hot flashes and psychological symptoms in perimenopausal women with a history of breast cancer. The present study was initiated as a pilot trial to explore the effectiveness of paroxetine in reducing hot flashes and related symptoms.

Thirty women with prior breast cancer who suffered at least two hot flashes/day completed daily diaries of hot flash severity and intensity for one week on no therapy and during subsequent open-label paroxetine for five weeks. All women received 10 mg daily for the first week of active treatment and 20 mg daily for the remaining 4 weeks. Psychological functioning was assessed at baseline and week 6 with the Center for Epidemiologic Studies Depression Scale (CES-D), the Medical Outcomes Study Sleep Scale, and the Hospital Anxiety and Depression Scale.

Among the 27 completers, there was a 67% mean reduction in hot flash frequency (95% C.I. 56–79%), and a 75% reduction in hot flash severity (95% C.I. 66–85%). Significant improvement was observed on patient-rated measures of depression, anxiety, sleep, and quality of life. Therapy was well tolerated and 25 participants chose to continue treatment following completion of the study.

Paroxetine is a potential treatment for vasomotor and psychological symptoms in breast cancer survivors. A double blind, randomized placebo-controlled trial testing the effectiveness of paroxetine in the treatment of hot flashes is underway to confirm these findings.

NR676 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Effects of Nefazodone and Psychotherapy on Sleep Disturbance in Chronic Depression

Michael E. Thase, M.D., *Department of Psychiatry, Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh, PA 15213;* A. John Rush, M.D., Rachel E. Manber, Ph.D.

Summary:

Introduction: Insomnia is a key feature of depression and may be differentially affected by various forms of antidepressant treatments.

Methods: During the initial 12-week phase of this study, patients were randomized to receive nefazodone alone (n = 226), Cognitive Behavioral Analysis System of Psychotherapy (CBASP) (n = 228), or combination nefazodone/CBASP (COMB) (n = 227). All patients met DSM-IV criteria for chronic Major Depressive Disorder (≥2 years' duration). Mean age was 43 ± 11 years; 65% were female. Patients received nefazodone, titrated up to 300 mg bid and/or CBASP up to 20 sessions. No concomitant therapies for sleep were permitted. Efficacy measures included the HAM-D-24, administered by raters "blinded" to patient treatment, and the self rated IDS-SR. The HAM-D sleep factor consisting of 3 insomnia items was analyzed at baseline, weeks 1, 2, 3, 4, 6, 8, 10, and 12 using an ITT analysis (Bonferroni-corrected alpha level of 0.0167).

Results: Patients treated with nefazodone (alone or COMB) experienced statistically significant improvement in sleep beginning at week 2 and continuing through week 12, compared with CBASP alone ($p < 0.01$). The differential improvement in sleep in the nefazodone treated groups was independent of overall treatment response, suggesting a drug-mediated effect.

Conclusion: These findings suggest that depressive sleep disturbances are not readily responsive to psychotherapy. Rather, insomnia may warrant pharmacotherapy with an antidepressant agent that improves sleep, such as nefazodone, or necessitates modifying psychotherapy to include an empirically supported insomnia module.

NR677 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Mirtazapine in Relapse Prevention

Michael E. Thase, M.D., *Department of Psychiatry, Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh, PA 15213;*

Andrew A. Nierenberg, M.D., Martin B. Keller, M.D., John Panagides, Ph.D.

Summary:

Objective: We evaluated the efficacy of mirtazapine (Remeron®) in preventing relapse in depressed outpatients, using a randomized, placebo-controlled discontinuation study.

Method: The 40 week controlled trial followed up to 8–12 weeks of open-label mirtazapine (15–45 mg/day). Patients were enrolled in the continuation phase if they achieved a HAMD-17 <8 and CGI-Improvement of 1 or 2. Relapse was defined by investigator (primary analysis), or as HAMD-17 ≥18 in a single visit or 15–17 at two consecutive weekly visits, suicide, or a suicide attempt (secondary analysis).

Results: In the open-label phase of the study (N = 410), 8-week LOCF response was 57%; 46% of patients were in remission. During the double-blind phase (N = 156), mirtazapine reduced the risk of depressive relapse by more than half, with only 19.7% of treated patients relapsing across 40 weeks, compared with 43.8% of patients on placebo. Mirtazapine was well tolerated in both study phases, with discontinuation rates for adverse events 16.6% (open-label) and 11.8% (double-blind). Of note, mirtazapine was associated with no more weight gain than placebo during double-blind therapy.

Conclusion: The results of this study confirm the efficacy of mirtazapine for preventing depressive relapse.

NR678 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Citalopram Treatment of Depressed Patients Discontinued from Fluoxetine Because of Adverse Events

Michael E. Thase, M.D., *Department of Psychiatry, Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh, PA 15213;* Peter D. Londborg, M.D., Joseph R. Calabrese, M.D.

Summary:

Introduction: Patients who fail therapy with one selective serotonin reuptake inhibitor (SSRI) may be treated with a number of different strategies, including a switch to a different class of antidepressant agent. However, there are significant pharmacological and pharmacokinetic differences among the SSRIs. Consequently, patients who cannot tolerate one SSRI may benefit from a different SSRI. The purpose of this study was to examine the response to citalopram in patients who were unable to tolerate fluoxetine.

Methods: Fluoxetine-treated patients with Major Depressive Disorder and intolerable adverse events were discontinued from fluoxetine and entered a 2–4 week single-blind placebo washout period. The most common reasons patients had discontinued fluoxetine were reduced libido (43%), anorgasmia (33% of females), and insomnia (22%). When the adverse events resolved, patients were switched to citalopram 20 mg/day, with titration permitted to 10 or 40 mg/day over a 6 week open label treatment period.

Results: A total of 55 patients enrolled in this trial. No patients discontinued citalopram because of adverse events. Side effects associated with fluoxetine did not usually appear during citalopram treatment. The mean citalopram dose was 24.6 mg/day. Citalopram produced a significant reduction in the HAMD after one week of treatment. After 6 weeks of treatment the response rate on the CGI-Improvement scale ("much" or "very much" improved) was 67%.

Conclusion: Depressed patients who are unable to tolerate fluoxetine can be successfully treated with citalopram.

NR679 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Sidenafil for SRI-Associated Sexual Dysfunction: A Three-Center, Six-Week, Double-Blind, Placebo-Controlled Study in 90 Men

H. George Nurnberg, M.D., *Department of Psychiatry, University of New Mexico, 2600 Marble Avenue, NE, Albuquerque, NM 87131;* Alan J. Gelenberg, M.D., Maurizio Fava, M.D., Paula L. Hensley, M.D., John Lauriello, M.D., Wilma M. Harrison, M.D., Richard Siegel, M.D.

Summary:

Objective: This study reports preliminary results of a three-center six weeks double blind placebo controlled study of sildenafil (Viagra®) for SRI antidepressant associated sexual dysfunction [SD]. This describes the six weeks double blind phase.

Method: Ninety men with clinically recovered major depression and SRI associated SD are randomly assigned to placebo or sildenafil for six weeks double blind treatment and 23 weeks open label continuation. Subjects had to be without preexisting sexual dysfunction, on minimum 8 weeks stable antidepressant dose continued for study duration, HAM-D&A < 10, and significant SD by IIEF and ASEX inventories. The dose of sildenafil was 50 or 100 mg. CGI-SF (primary) and ASEX/MGH (self-rated/clinician-rated) at baseline, 2, 4, 6 weeks evaluated SD.

Results: Sildenafil demonstrated significant improvement in sexual function on primary CGI-SF measures (2.2 v. 4.3; p < 004) and secondary ASEX/MGH measures (18.8/20.3 to 13.6/14.6 for sildenafil; 19.7/21.4 to 21.2/22.6 for placebo; p < .006) from baseline to week six. HAM-D remained <10 without sildenafil/placebo differences.

Conclusion: Sildenafil was effective for reversing SRI associated sexual dysfunction in men, allowing subjects to continue the antidepressant and dose that effectively treated their depression. This confirms earlier reports of efficacy of sildenafil for treatment of SRI associated SD.

NR680 Thursday, May 18, 12:00 p.m.-2:00 p.m.

The Schizo-Obsessive Subtype of Schizophrenia

Roberto A. Dominguez, M.D., *Department of Psychiatry, University of Miami, 1695 NW 9th Avenue, #3208J, Miami, FL 33136;* Karl E. Backman, M.D., Susana C. Lugo, M.D.

Summary:

The schizo-obsessive subtype of schizophrenia has been proposed to describe the condition of patients with chronic psychotic disorders and prominent obsessive-compulsive (OC) symptoms. These patients differ from others with schizophrenia not only in their psychopathology, but perhaps also in their prognosis and pharmacotherapeutic response. Potent serotonin uptake blockers, in conjunction with antipsychotics, can prove helpful in improving their OC symptoms. This study assessed the demographics, prevalence, and clinical features of the schizo-obsessive subtype in established outpatients with a principal diagnosis of schizophrenia or schizoaffective disorder treated at a large urban public hospital. More than 50% of the hospital's psychiatric population is Hispanic. The Modified Maudsley Obsessive Compulsive Inventory (MMOCI) was used to identify prominent compulsive symptoms. Of the 52 patients who fulfilled the specific screening criteria, 17 (33%) also had prominent OC symptoms. Surprisingly, there was a statistical trend (*P = 0.06*) for Hispanic patients to meet our threshold for the schizo-obsessive subtype. The MMOCI proved to be an adequate and efficient self-rated screening tool. The prevalence of the schizo-obsessive subtype, especially among Hispanic patients, highlights the importance for mental health professionals working with this population to identify and appropriately treat this group of patients.

NR681 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Novel Antipsychotics and Severe Hyperlipidemia

Jonathan M. Meyer, M.D., *Mental Health and Development, Oregon State Hospital, 2600 Center Street NE, Salem, OR 97310*

Summary:

Novel antipsychotics are associated with a decreased incidence of extrapyramidal side effects compared to older typical antipsychotics, but some of these novel antipsychotics have been associated with the development of obesity and new-onset diabetes. Prior published reports have implicated clozapine in producing modest elevations of serum triglycerides, but not severe hypertriglyceridemia (>600 mg/dl). Presented here are 13 cases of severe hypertriglyceridemia (>600 mg/dl) associated with olanzapine and quetiapine treatment, including 5 patients with serum triglyceride levels exceeding 1000 mg/dl. Three of these patients also developed new-onset diabetes. Eight of the 13 cases occurred during the first 8 months of treatment, with 2 cases identified within 2 months of commencing olanzapine or quetiapine therapy. Underlying mechanisms for atypical antipsychotic-induced hypertriglyceridemia are unclear, but clinical monitoring of serum lipids must be added to the concerns about the metabolic consequences of therapy with some of the newer antipsychotic agents.

NR682 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Fluvoxamine for Obsessive-Compulsive Symptoms in Schizophrenia Patients

Michael Poyurovsky, M.D., *Research Unit, Tirat Carmel Mental Health Center, PO Box 9, Tirat Carmel 30200, Israel;* Victoria Isakov, M.D., Sofia Hromnikov, M.D., Ilan I. Modai, M.D., Boris Rauchverger, M.D., Michael Schneidman, M.D., Abraham Weizman, M.D.

Summary:

Obsessive-compulsive (OC) symptoms are observed in a substantial proportion of schizophrenic patients[1,2]. In the present study we sought to determine the therapeutic effect of adding the serotonin-selective reuptake inhibitor fluvoxamine (up to 150 mg/day for 12 weeks) to the ongoing antipsychotic regimen of 10 schizo-obsessive patients. The patients were evaluated before and at weeks 1, 2, 4, 6, 8 and 12 with the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the Schedule for Assessment of Positive Symptoms and the Schedule for Assessment of Negative Symptoms. A significant improvement in obsessions ($p < 0.02$), but not compulsions, and both positive ($p < 0.01$) and negative ($p < 0.05$) schizophrenic symptoms was observed. Three patients showed a more than 50% reduction in the Y-BOCS score, with complete amelioration of the OC symptoms in one of them. Three patients were dropped from the study during the first 4 weeks, two because of aggressiveness and one because of psychotic exacerbation. Fluvoxamine addition was well tolerated and no exacerbation or new onset of extrapyramidal side-effects was noted. We conclude that fluvoxamine may be an effective adjunctive agent in some schizo-obsessive patients.

NR683 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Fluvoxamine Treatment of Hypochondriasis

Altamash I. Qureshi, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, #69, New York, NY 10032;* Brian A. Fallon, M.D., Michael R. Liebowitz, M.D., J. Arturo Sanchez-Lacay, M.D.

Summary:

Background. Because SSRIs may be a particularly effective treatment for hypochondriasis, we explored the efficacy of fluvoxamine.

Methods. 18 patients with DSM-IV hypochondriasis entered. All received placebo for 2 weeks and fluvoxamine for 10 weeks starting at 50 mg/day and increasing to 300 mg/day. Ratings included SCID-I and -II, patient-rated measures (Analog scale, Whiteley Index [IAS], MOS Short-Form 36), and physician-rated measures (CGI, HIC Severity Scale, and a modified Y-BOCS). Responder status was defined by physician-rated CGI improvement of at least "much improved". Minimum treatment required at least 6 weeks of fluvoxamine.

Results. Among the 18 patients, 4 were dropped during the 2-week placebo run-in. Among the 14 patients given active medication, 3 discontinued before week 6. Of the remaining 11 patients, 8 (72.7%) were responders. One non-responder was later identified as having Lyme disease. Detailed results from the various ratings will be presented.

Discussion. The CGI responder rate from this fluvoxamine trial (72.7% for the minimum treatment analysis and 57.1% for the intent-to-treat analysis) was comparable to the results reported previously for fluoxetine. Fluvoxamine therefore appears to be an effective treatment for hypochondriasis. A controlled trial is needed.

NR684 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release for SSRI-Induced Sexual Dysfunction: A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study

Adam K. Ashton, M.D., *Department of Psychiatry, Buffalo Medical Group, 295 Essjam Road, Williamsville, NY 14221;* Prakash S. Masand, M.D., Sanjay Gupta, M.D., Bradford L. Frank, M.D.

Summary:

Introduction: Sexual dysfunction is a side effect of serotonin reuptake inhibitors (SSRIs) affecting up to 60% of patients.

Methods: In this study, 30 adults who had been receiving SSRIs for at least six weeks who were euthymic and who had sexual dysfunction as determined by the Arizona Sexual Experience Scale (ASEX) (total scores > 19 out of a possible 30) were randomized to bupropion sustained release (SR) 150 mg once daily at 6 p.m. or placebo for three weeks.

Results: There were no significant differences between the bupropion SR and placebo groups as measured by change in ASEX or HAM-D scores or side effects.

Conclusion: In this first randomized double-blind placebo controlled study bupropion SR 150 mg at 6 p.m. was equal to placebo in treating sexual dysfunction secondary to SSRI therapy.

NR685 Thursday, May 18, 12:00 p.m.-2:00 p.m.

SSRIs and Ejaculation: A Double-Blind, Randomized, Comparative Fixed-Dose Study with Paroxetine and Citalopram

Marcel D. Waldinger, M.D., *Department of Psychiatry, Leyenburg Hospital, Leyweg 275, The hague, CH 2545, Netherlands;* Aeilko Zwinderman, Ph.D., B. Olivier, Ph.D.

Summary:

Introduction: SSRIs are known to delay male orgasm. However, there is evidence that SSRIs differ in the extent to which they delay ejaculation, with paroxetine having the strongest delaying effect. The cause of this difference is unknown. As yet no data are available about the ejaculation delaying effect of citalopram.

Objective: To evaluate the effects of citalopram on ejaculation.

Methods: This was a 6-week double-blind study. Healthy men with lifelong rapid ejaculation were recruited. These men and their female partners measured the man's Intravaginal Ejaculation Latency Time (IELT) at home using a stopwatch for 4 weeks. Those men (n = 30) with an IELT of less than 1 minute were randomized into two groups. Men in group 1 (n = 15; mean age 37.5 + 10.9 years) received paroxetine 20 mg/day and those in group 2 (n = 15; mean age 38.8 + 7.9 years) received citalopram 20 mg/day, and ILET was measured.

Results: The trial was completed by 23 men. At baseline the mean geometric IELT was 22 seconds. Analysis of variance revealed a significant between-groups difference in the evolution of IELT delay (p = 0.0004); in the paroxetine group there was a gradual increase to about 170 seconds, whereas in the citalopram group, IELT was increased to only approximately 44 seconds. Paroxetine exerted the strongest delay in ejaculation. The ejaculation delay with citalopram was only mild and in this group of men not clinically relevant.

Conclusions: Citalopram, in contrast to paroxetine, has only very mild ejaculation delaying effects.

NR686 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Duration of Side Effects and Changes in Brain Levels with Fluoxetine Discontinuation

Michael E. Henry, M.D., *Medical Clinic, McLean Hospital, 115 Mill Street, Belmont, MA 02478;* Constance M. Moore, M.D., Christina M. Demopulos, M.D., Janis Breeze, Gary S. Sachs, M.D., Eve P. Stoddard, B.A., Perry F. Renshaw, M.D.

Summary:

Objective: Side effects associated with antidepressant medications have been shown to play an important role in noncompliance with therapy (1). Few studies have assessed whether drugs with longer elimination half-lives are associated with less rapid resolution of side effects that occur during therapy. To test this hypothesis, patients experiencing side effects on fluoxetine were taken off drug and fluorine (19-F) magnetic resonance spectroscopy (MRS) (2) was used to measure the change in brain drug levels.

Methods: 15 (13 females), patients, aged 19–52 years, meeting DSM-IV criteria for major depression, treated with fluoxetine for > 1 month, and experiencing at least 1 common side effect, were taken off fluoxetine. Side effects and mood were monitored via daily self-report. Patients underwent MRS at baseline and upon resolution of symptoms.

Results: Patients reported an average of 1.8 (median = 2) side effects, which resolved after an average 18 + 10 days (median = 14). The average decrease in brain fluoxetine concentration was 43% + 15% (median = 44%).

Conclusion: Among this group of patients experiencing side effects to fluoxetine, multiple side effects were more common than not, and time to resolution of side effects was consistent with the elimination kinetics of fluoxetine and norfluoxetine.

NR687 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Quetiapine in Psychotic Patients with Parkinson's Disease

Jorge L. Juncos, M.D., *Neurology Department, Emory Univ. School of Medicine, 1841 Clifton Road, NE, Atlanta, GA 30329;* Matian L. Evatt, M.D., Rita D. Jewart, Ph.D., Vivki J. Roberts, Ph.D., Larry S. Potter, M.S., Hann-Chang Jou, Ph.D., Paul P. Yeung, M.D.

Summary:

Objective: The atypical agent quetiapine was studied to determine its effectiveness and tolerability in patients with Parkinson's disease (PD) and psychosis who are particularly susceptible to the extrapyramidal symptoms (EPS), anticholinergic side effects associated with other atypical antipsychotic agents.

Methods: In a 24-week, open-label trial, the safety, tolerability, and efficacy of quetiapine were evaluated in patients with parkinsonism who failed treatment with risperidone, olanzapine, or clozapine due to lack of efficacy, intolerable side effects, or noncompliance with blood-monitoring. 29 patients (mean age 73 years) received quetiapine up to 400 mg/day. Assessments included the Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI) Severity of Illness, Neuropsychiatric Inventory (NPI), and Unified Parkinson's Disease Rating Scale (UPDRS).

Results: Mean BPRS scores improved by >30% (p = 0.0054). The CGI score also improved significantly (p < 0.05) The mean NPI psychosis subscale (delusions, hallucinations, agitation/aggression) score improved 50% (p = 0.03). Mean UPDRS total and motor subscale scores remained stable. No important effects were observed on mean vital signs, weight gain, laboratory tests, or electrocardiograms.

Conclusion: These results provide evidence that quetiapine is effective and well tolerated in patients with PD and demonstrate that patients failing treatment with other atypical antipsychotics could benefit from quetiapine therapy. Funded by a grant from AstraZeneca.

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5HT Response to Quetiapine

Hugh M. Jones, M.R.C., *Dept of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, United Kingdom;* Michael J. Travis, M.R.C., Rachel Mulligan, M.S.C., Ridrigo Bressan, M.D., Peter J. Ell, Ph.D., Robert W. Kerwin, D.Sc., Lyn S. Pilowsky, Ph.D.

Summary:

Objective: To investigate whether the antagonist activity at serotonergic ($5\text{-}HT_{2a}$) receptors may contribute to the novel therapeutic actions of atypical antipsychotic drugs.

Method: 6 patients with schizophrenia had a single photon emission tomography (SPET) study using a selective $5\text{-}HT_{2a}$ ligand, after at least 6 weeks quetiapine treatment (mean daily dose 350 mg). 5 patients were switched to quetiapine from typical neuroleptic treatment. A SPET scanner acquired a whole brain multi-slice sequence. Region-of-interest templates were fitted to cortical and cerebellar regions. Reduced frontal cortex:cerebellum ratio implies greater specific drug binding to $5HT_{2a}$ receptors within the frontal cortex.

Results: Mean BPRS declined from 46.3 to 32.3 and mean AIMS declined from 7.3 to 1.8. Mean frontal cortex:cerebellum ratio for quetiapine-treated patients was 0.98 (SD = 0.09) compared with 1.4 in healthy subjects and 0.88 in patients treated with risperidone and clozapine. Mean frontal cortex:cerebellum ratio after quetiapine treatment was negatively correlated with reduction in AIMS score (r = 0.94 p = 0.05), but not with the BPRS score (p = 0.4).

Conclusion: The significant in vivo occupancy of cortical $5\text{-}HT_{2a}$ receptors by quetiapine may be relevant to its low propensity to induce extrapyramidal symptoms compared with typical antipsychotic drugs.

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The Effects of Reboxetine or Nefazodone on the Pharmacokinetics and Pharmacodynamics of Alprazolam

Y.W. Francis Lam, Pharm.D., *Clinical Pharmacology Dept., Univ. of Texas H. S. C., 7703 Floyd Curl Drive, San Antonio, TX 78229-3900;* Larry Ereshefsky, Pharm.D., Gregory B.

Toney, Pharm.D., John P. Houston, M.D., Joseph C. Fleishaker, Ph.D., L. Haley Burgess, Pharm.D.

Summary:

Objectives: A three part randomized crossover study to determine the potential for a significant drug interaction between nefazodone or reboxetine with alprazolam, a cytochrome P450 (CYP) 3A4 substrate.

Methods: 12 healthy medication free subjects received 1 mg doses of alprazolam at baseline and at the conclusion of 12 days of treatment for each antidepressant (reboxetine 4 mg BID and nefazodone 200 mg BID). Timed interval blood sampling for alprazolam concentrations (Cp) and for tests of recent and delayed memory were obtained to determine pharmacokinetic parameters and pharmacodynamic effects, respectively.

Results: 14 enrolled, with 12 completing the study (dropouts for abnormal baseline laboratory exclusions). Nefazodone significantly decreased correct responses ($p > 0.0025$) and response accuracy ($p > 0.0025$) for recent memory compared to both baseline and reboxetine conditions (ANOVA with post hoc analysis).

Conclusion: Reboxetine showed no significant change in alprazolam pharmacokinetic or pharmacodynamic parameters. In comparison to nefazodone, it is unlikely that reboxetine will demonstrate significant interactions with CYP3A4 substrates.

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Incidence and Treatment of Side Effects with Clozapine Treatment: A Retrospective Study of 1,000 Patients After One Year of Clozapine Therapy

Michael J. Reinstein, M.D., *Dept of Psychiatric Research, Forest Foundation, 4755 North Kenmore Avenue, Chicago, IL 60640;* Larissa A. Sirotovskaya, M.D., Maxim A. Chasanov, M.D., Lynne E. Jones, R.N., Shephali A. Patel, M.D., Sangarapillai C. Mohan, M.D., John Sonnenberg, Ph.D.

Summary:

Objective: This is the first psychiatric study on the relationship of formally determined incidence and treatment of side effects with clozapine treatment of one thousand patients after one year of clozapine therapy.

Method: This is a retrospective, open, nonrandomized, uncontrolled chart review of a one thousand patients diagnosed with schizophrenia who was treated with clozapine therapy for a period of one year.

Results: One thousand patients were studied. Of the 1000 patients enrolled, 0.6% developed agranulocytosis, 8% showed significant weight gain and 2.8% developed diabetes, 31.2% had hypersalivation, 14.2% complained of constipation, 4.7% suffered from enuresis and in 0.8% were observed myoclonic jerks, in 0.6% seizures, 6.3% had tachycardia, 3.6% had fever, 1.2% dizziness and 3.6% drowsiness. However, each side effect was successfully managed.

Conclusion: The results suggest that the great majority of patients can be safely maintained on clozapine with appropriate identification and management of side effects.

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The Impact of Dosing Regimen on Medication Compliance

Ami J. Claxton, Ph.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center DC 2033, Indianapolis, IN 46285;* Joyce Cramer, B.S., Courtney Pierce, B.A.

Summary:

Objective: Previous research has shown that compliance to medications for physical and psychiatric conditions is similar[1]. A review of the literature was undertaken to describe and compare compliance to alternative medication dosing regimens.

Methods: Data on compliance were compiled via a literature review limited to studies reporting compliance as measured by the most accurate compliance assessment method, electronic monitoring (EM) devices. Two major categories of compliance rates were defined; dose-taking (taking right number of pills per day) and dose-timing (taking pills within an correct window of time). Within each category, compliance to alternative dosing regimens was compared by pairwise t-tests.

Results: A total of 74 studies were identified (n = 4 in psychiatry). The predominant form of compliance assessment was dose-taking, and primary results are reported in the table below:

Dosing Regimen	Compliance
Overall	70 ± 17%
QD (1/day)	78 ± 14%
BID (2/day)	69 ± 14%*
TID (3/day)	65 ± 16%*
QID (4/day)	51 ± 20%[4]

*p-value < 0.05 vs. QD

Results using dose-timing definitions of compliance were similar.

Conclusion: The number of doses per day is inversely related to compliance.

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Risperidone Dosing Pattern Effectiveness: Indian Survey

Amresh K. Shrivastava, M.D., *Silver Mind Hospital, Gokhale Road Thane West, Mumbai 400602, India;* Sanjay Gupta, M.D., M. Srinivasa, M.D., Rajesh C. Maniar, M.D., Gpd Rao, M.D., Nilesh Shah, M.D.

Summary:

Objective: Considerable differences have been reported in prescribing pattern of risperidone & its efficacy. Eastern countries in particular have recorded low dose usage of conventional antipsychotics. Present study was planned to see dose related efficacy in a Nation wide sample.

Method: Data was compiled from a prospective, open level, variable dose design of risperidone in acute symptoms of chronic schizophrenia. Efficacy was assessed using CGIS & PANSS over three months.

Result: 484(80%) of 606 patients completed study. At the endpoint 35.5% patients were significantly improved on 2 mg/day, $4.5% on 2 to 4 mg/day & 10% on 4 to 6 mg/day (Stat.sig.in PS,NS scores at 3 months). Patients maintained on 2 mg/day had significantly shorter duration of illness (12.9 months mean 12.9, SD 13.4, $p < 0.0005$, 4–6 mg – >28 months). Dosing did not differ on other clinical & demographic parameters. 48.5% (N = 294) patients concomitantly received another antipsychotic & 10.2% antiparkinsons, 14.5% (N = 82) showed EPS, akathesia being commonest (9.1%, N = 55).

Conclusion: Ninety percent patients in Indian survey required less than four mg/day dose & 35% needed only 2 mg 15% only had WFS.

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A Naturalistic Study of Mirtazapine in the Chilean Psychiatric Practice

Sandra Kroeze, *Hormoquimica de Chile, 16357 Casille Correo 9 Prov, Loreley/La Reina 1582, Chile;* C. Fuenzalida, L. Plaza, J. Hernandez

Summary:

Aim: To assess clinical efficacy and tolerability of mirtazapine in everyday clinical practice in Chile.

Method: Depressed outpatients (n = 175) of both sexes older than 15 years were treated with mirtazapine (15–60 mg/day) for 8 weeks in an open-label study. The efficacy was assessed after 1, 3 and 8 weeks of treatment by an adapted version of the CGI scale. Tolerability was assessed by registering treatment-emergent adverse events.

Results: Group characteristics at baseline: The majority of patients were females (73%). At baseline 98% of the patients had a major depressive episode (single or recurrent) according to DSM IV criteria. The severity was coded as moderate (45%) and severe (52%). The majority of patients had at baseline a disturbed sleeping pattern (97%), feelings of anxiety (86%) and ideas of suicide (51%). Fifty-one per cent of the patients were treated with antidepressants prior to inclusion in the study. The most common reasons for switching to mirtazapine were lack of efficacy (29%), lack of tolerability (10%) or a combination of both (13%).

Efficacy and dosing: The majority of the patients received a starting dosage of 30 mg/day (70%). Already after one week of treatment with mirtazapine a marked improvement (clinical efficacy was classified as better/much better) of mood (52%), sleeping pattern (75%) and anxiety (51%) was seen. After 8 weeks of treatment these ratios increased to 95% (mood), 91% (sleeping pattern) and 82% (anxiety). With regard to the patients with ideas of suicide, 45% declared to feel better/much better after one week of treatment. This ratio increased to 61% after 8 weeks of treatment.

Tolerability: Mirtazapine was very well tolerated during the treatment period. 15% of the patients prematurely terminated the study. Only 4.5% of the total number of patients prematurely terminated the study because of adverse events. The most frequently reported adverse events were weight gain and somnolence.

Conclusion: Mirtazapine is a highly effective and well-tolerated antidepressant treatment in everyday clinical practice in Chile. Despite methodological limitations of naturalistic studies, the results are in line with previously reported randomised double-blind studies of mirtazapine.

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Antipsychotic Treatment and Menstrual Irregularity

Ruta M. Nonacs, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 812, Boston, MA 02114;* Mary H. Collins, M.D., Suzanne M. Bouffard, B.A., Lee S. Cohen, M.D.

Summary:

Introduction: Previous studies describe treatment-emergent hyperprolactinemia associated with the use of most typical and some atypical neuroleptic medications. Elevated prolactin levels may be associated with amenorrhea, galactorrhea, and sexual dysfunction. The prevalence of these symptoms in women treated chronically with antipsychotic drugs is unknown. This study describes the impact of treatment with typical or atypical neuroleptic medications on menstrual and sexual functioning.

Methods: 30 women treated with risperidone (dose range 0.25–3 mg), olanzapine (5–25 mg qd), or a typical neuroleptic were followed prospectively for 4 months. Data regarding menstrual cycle and sexual functioning and hormone levels (prolactin, TSH, FSH, estradiol, progesterone, testosterone) were collected.

Results: Menstrual irregularities were observed in 33.3% of women on risperidone. Only 16.7% of women on traditional antipsychotic medication and no women on olanzapine exhibited menstrual irregularities. Disruptions in menstrual cycle were associated with elevated prolactin levels, although absolute prolactin levels did not predict degree of menstrual irregularity.

Conclusions: Chronic neuroleptic treatment may be associated with elevated prolactin levels. Although hyperprolactinemia may be asymptommatic, menstrual irregularities are commonly associated with high prolactin levels and frequently occur in women treated with risperidone. Further research is necessary to clarify the clinical significance of menstrual irregularities observed in women treated with various antipsychotic medications.

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Risperidone Treatment of Tourette's Syndrome: A Double-Blind, Placebo-Controlled Trial

Yves Dion, M.D., *Department of Psychiatry, Allan Memorial Institute, 1025 Pine Avenue West, Montreal, QC H3A 1A1, Canada;* Lawrence Annable, Paul Sandor, M.D., Guy Chouinard, M.D.

Summary:

Objective: A double-blind, placebo-controlled trial was carried out to determine the efficacy and tolerability of 8 weeks of treatment with risperidone in the management of adolescents and adult patients with TS.

Methods: 48 patients with TS were selected to enter an 8-week dose-ranging, parallel-group, double-blind, placebo-controlled trial at two Canadian centres. At the time of selection, all other psychotropic drugs were discontinued. 24 patients were randomly assigned to treatment with risperidone in doses of 0.5 to 6.0 mg/day, and 24 to placebo. The dosage of study medication was increased in fixed increments during the first week of double-blind treatment and thereafter in a flexible dose regimen according to clinical response. Patients were assessed at baseline and during treatment on the Tourette's Syndrome (TS) Severity Scale, Clinical Global Impression (CGI), Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), Extrapyramidal Symptom Rating Scale (ESRS), and Global Assessment of Functioning (GAF) Scale

Results: Risperidone was found to be significantly ($p < 0.05$) superior to placebo on the Global Severity Rating of the TS Severity Scale. The proportion of patients who improved by at least one point on this scale was 60.8% in the risperidone group and 26.1% in the placebo group. Treatment with risperidone was accompanied by an improvement in global functioning in patients with average-to-above-average impairment at baseline as measured by the GAF. With respect to ESRS scores, hypokinesia and tremor increased significantly in the risperidone group, although the effect on tremor was largely confined to subjects with higher baseline scores. There were no significant differences in dystonic reactions, dyskinetic movements, or subjective dystonia. Risperidone did not increase obsessive-compulsive symptoms. Fatigue and somnolence were the most common adverse events associated with risperidone.

Conclusions: Risperidone at a median dose of 2.5 mg/day (range 1 to 6 mg/day) was found to be an effective and well-tolerated treatment for tics in patients with TS.

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Switching to Olanzapine in Patients with Antipsychotic-Induced Sexual Dysfunction: A Prospective and Naturalistic Study

Angel L. Montejo, M.D., *Department of Psychiatry, Hospital Clinico, P. San Vincente S/N, Salamonca 37007, Spain;* Gines Llorca, M.D., Juan A. Izquierdo, M.D.

Summary:

Objective: To assess the efficacy and tolerability of switching to olanzapine in out-patients with neuroleptic-induced sexual dysfunction (SD).

Methods: 18 patients (4 females and 14 males mean age ± SD = 41,3 ± 3,57 and 38,6 ± 10,1) diagnosed of schizophrenia experiencing poor tolerance to orgasmic or erectile dysfunction under stable treatment with risperidone (n = 12; 4,85 mg/day), pimozide (n = 2; 2mg/day), sertindol (n = 1; 16mf/day) and zuclopentixol (n = 3; 20mg/day in one patient and 200 mg depot in two patients) were included in this prospective, open-label and naturalistic study. Paitints were evaluated at baseline and at least for 2 months on olanzapine treatment using a Sexual Dysfunction Questionnaire measuring libido, orgasm and erectile functioning (Montejo et al, 1997), as well as Physician and Patient Global Assessment. The intensity of sexual dysfunction prior to switching was measured with a scale from 0 = absence of SD to 3 = severe SD (libido: 1,84; delay of orgasm: 2,33; anorgasmia: 2,16 and erectile dysfunction: 1,39).

Results: Dosage of olanzapine was titrated until mean dosage 7,5 ± 2.5 mg/day. Significant improvement in all 5 dimensions of the SDQ was seen in patients switched from risperdone to olanzapine in one week and continued until the end of the follow-up. At endpoint sexual dysfunction was rated as much or very improved in 14/18 (77.8%), mildly improved in 2/18 (11.1%) no improved in one patient. One patient did not tolerate the switch due to adverse events (anxiety and insomnia). Only one patient under risperidone relapsed suffering from psychotic symptoms 20 days after switching to olanzapine.

Conclusion: Switching to olanzapine could be an efficacious and well-tolerated therapeutic alternative for treating neuroleptic-induced sexual dysfunction. Further studies to confirm these results are needed.

NR697 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Switching to Nefazodone in Patients with Antidepressant-Induced Sexual Dysfunction: A Six-Month Prospective and Naturalistic Study

Angel L. Montejo, M.D., *Department of Psychiatry, Hospital Clinico, P. San Vincente S/N, Salamonca 37007, Spain;* Gines Llorca, M.D., Juan A. Izquierdo, M.D., Fernando Rico-Villademoros, M.D., Margarita Garcia, M.D.

Summary:

Objective: To assess the efficacy and tolerability of switching to nefazodone in patients with antidepressant-induced sexual dysfunction (SD).

Methods: LOCF data set comprised 41 out of the 44 patients recruited: 26 females and 15 males who had at least one postbaseline evaluation, diagnosed of major depression (n = 20,48; 8%) or dysthymic disorder (n = 21,51; 2%) experiencing SD under stabilized treatment (HDRS-17 ≤ 10) with paroxetine (n = 18), sertraline (n = 11), fluoxetine (n = 7), citalopram (n = 3) and other antidepressants (n = 4) (Note: two patients were receiving two antidepressants). Patients were evaluated at baseline and after 1,2,3, and 6 months using HDRS-17, a Sexual Dysfunction Questionnaire (Montejo et al, 1997), CGI of severity and improvement, and a Physician and Patient Global Assessment.

Results: All patients underwent a wash-out (1.15 ± 0.46 wks) and/or tapering (1.29 ± 0.66 wks). Mean initial and final dose of nefazodone was 145 ± 58 and 362 ± 75 mg/day respectively. Significant improvement in all 5 dimensions of the SDQ was seen as early as 1-month ($p < 0.05$, Friedman Test) and continued until the end of the follow-up. At the endpoint sexual dysfunction was rated as much or very much improved in 75.6% of the patients and 80.5% of them were satisfied or very satisfied with their treatment. Twelve out of the 44 (27.3%) discontinued (lost to follow-up: 9.1%; adverse events: 9.1%). Tolerability was rated as good or very good in 81.8% of the patients. Only 2 (4.4%) patients relapsed (HDRS-17 ≥ 18 in two consecutive visits).

Conclusion: Switching to nefazodone is an efficacious and well-tolerated therapeutic alternative for treating antidepressant-induced sexual dysfunction.

NR698 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Early Reduction of Anxiety and Insomnia Symptoms in the Therapy of Depression

Thomas E. Schlaepfer, M.D., *Department of Psychiatry, University Hospital, Murtenstrasse 21, Bern 3010, Switzerland;* Lorenzo Hess, Ph.D., Hans U. Fisch, M.D.

Summary:

Insomnia and anxiety frequently coexist with depression. Some new antidepressants (such as nefazodone or mirtazapine) have intrinsic receptor-blocking properties (in particular, serotonin-2 [5-HT2] receptor blockade) that can be linked to an early relief of these symptoms in treatment. This effect has been established in registration studies but implications in for everyday outpatient treatment remain unclear.

We serially assessed Visual Analog Scales (VAS) for depression, anxiety and insomnia in 232 clinically depressed outpatients (mean age 45.9 +/– SD 13.39 years) which were treated with nefazodone. The onset of symptom reduction over time was compared by calculating percentages of anxiety in relation to depression at each respective day. Each time point (day 7, 14, 21, 28, 35, 42) was compared to the baseline (day 1) by the Wilcoxon Signed Rank Test. Subgroups (e.g. gender) were compared at each time point by the Mann-Withney Test. Significantly less anxiety than depression symptoms were observed at day 7 (90,8%, $p < 0.05$), day 14 (82,0%, $p < 0.01$) and day 21 (88,1%, $p < 0.05$). Significantly less insomnia than depression symptoms were observed at day 14 (73,3%, $p < 0.01$), day 28 (67,1%, $p < 0.001$), day 35 (53,8%, $p < 0.001$) and day 42 (40,0% $p < 0.001$).

We demonstrated that an antidepressant with preferential 5-HT2 blocking properties provides early and effective relief of both depressive and anxiety symptoms in a large outpatient population, thus reducing the need for polypharmacy.

NR699 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Patterns of Antidepressant and Anxiolytic Usage

George Fulop, M.D., *DMA, Merck-Medco, 100 Parsons Pond Drive, F2-2, Franklin Lakes, NJ 07417;* Joseph R. Bona, M.D., Richard Brookler, M.B.A., Charles B. Nemeroff, M.D.

Summary:

Objective: To observe patterns of antidepressant use and concomitant anxiolytics, sedative/hypnotics, and buspirone as an index of clinical prescribing practice.

Method: Among 1.6 million members of Merck-Medco Managed Care, L.L.C. followed continuously between 1/1/96 and 12/31/98, we identified all patients (N = 42,510) who received a new antidepressant prescription (defined as none within the prior 12 months) in 1997 (Index AD). We observed the time between the use of other concomitant psychotherapeutics (e.g. benzodiazepine anxiolytics (ANX)/buspirone(ANX-B), sedative/hypnotics (SH) and zolipidem (SH-Z)) in the year prior to or after the index AD prescription.

Results: (n = 14,792, 34.8%) of AD patients were prescribed a concomitant psychotherapeutic agent. These patients displayed a parallel pattern in use of all classes of concomitants: 1.6–12.3% using at least one additional class in the year prior to, 0.4–2.0% same day, and 1.8–7.0% in the year after the index AD. However, a greater proportion of patients were more likely to receive an anxiolytic or sedative/hypnotic prior to the index AD, and buspirone after the index AD. On the same day as the index AD, a greater

proportion of patients received an anxiolytic, followed by zolipidem and sedative/hypnotics.

Concomitant	% of AD patients	Pre-Index AD (cumulative -1 yr)	Same Day	Post-Index AD (cumulative -1 yr)
ANX	21.30	12.30	1.99	7.00
ANX-B	3.73	1.58	.36	1.79
SH	5.73	2.98	.37	2.37
SH-Z	8.96	4.25	.75	3.97

Conclusion: Although we hypothesized excessive benzodiazepine and hypnotic usage pre- and post-index AD, we noted lower than expected usage, particularly after AD prescription. All classes of concomitant psychotherapeutics revealed a similar general pattern: a steady increase in daily use in the year prior to an index AD, a peak on the index AD date, and a tapering over the next year, except buspirone. We speculate that continuing medical education of physicians may be contributing to a decrease in the putative misuse of benzodiazepines.

NR700 Thursday, May 18, 12:00 p.m.-2:00 p.m.

The Effect of Risperidone on Serum Prolactin Concentrations

Jin-Sook Cheon, M.D., *Neuropsychiatry, Kosin Univ. Gospel Hospital, 34 Am Nam Dong SEO GU, Pusan 602 702, South Korea;* Byoung-Hoon Oh, M.D., Woong Cho, M.D.

Summary:

Objectives: The aims of this study were to identify sex differences of risperidone-induced hyperprolactinenmia, to find out affecting factors on the RL levels, and to evaluate association with cognition and PRL levels.

Methods: The PRL and TSH levels of 25 male and 25 female schizophrenics were measured by enzyme immunoassay for baseline as well as the 2nd and the 4th wks of risperidone administration. Severity of psychotic symptoms using CGI, BPRS and PANSS, and the cognitive dysfunction using PANSS-CF were assessed. The PRL and TSH levels of 29 healthy males and 25 females were also evaluated.

Results: 1) The baseline PRL levels of female schizophrenics were higher than males and controls ($p < 0.005$). The PRL levels measured on the 2nd wks and the 4th wks after risperidone administration were higher in females ($p < 0.001$). The mean dosages of risperidone on the 2nd wks were 3.8 ± 1.7 mg for females and 4.0 ± 1.6 mg for males, and on the 4th wks were 4.5 ± 2.1 mg and 5.4 ± 2.2 mg. 2). The higher serum prolactin levels of schizophrenics were seemed to be related with dosage in males and with primary pathological process in females. 3) Risperidone-induced cognitive improvement seemed to be correlated with improved psychopathology in both, and with increased PRL levels only in females.

Conclusions: The fact that effect of risperidone on PRL levels and cognitive function were more in females suggested a different mechanism could be exerted on.

NR701 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Long-Term Treatment Outcomes of Depression/ Anxiety

Mark E. Schmidt, M.D., *Neuroscience, Eli Lilly and Company, Lilly Corporate Center DC 1730, Indianapolis, IN 46285;* David Michelson, M.D., Rajinder A. Judge, M.D., James Robinson, B.S., Roy Tamura, Ph.D., Robert Johnston, Ph.D.

Summary:

Objective: To assess the efficacy of a new convenient weekly formulation of fluoxetine in maintaining an antidepressant response in patients treated for depression who reported high baseline levels of anxiety.

Methods: Patients whose major depression remitted after 13 weeks of treatment with fluoxetine 20 mg/day were randomized to continuation treatment with a new weekly formulation of fluoxetine, fluoxetine 20 mg/day, or placebo for up to 25 weeks. Using baseline HAMD Anxiety/Somatization factor score, the patient sample was stratified using a median split. Patients were categorized into high anxiety (>7) or low anxiety (≤7) subgroups, and the efficacy of weekly and daily fluoxetine compared with placebo in maintaining response was assessed during continuation treatment.

Results: Relapse rates for patients treated with either daily or weekly fluoxetine were significantly lower than those of placebo-treated patients. Remission rates of highly anxious patients were very similar for the two active drug treatments over 25 weeks of treatment.

Conclusion: The new convenient weekly formulation of fluoxetine appears to be effective in maintaining remission in patients with high baseline levels of anxiety.

NR702 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release in the Treatment of Dysthymic Disorder

David J. Hellerstein, M.D., *Department of Psychiatry, Beth Israel Medical Center, 1st Ave & 16th Street, #2B34, New York, NY 10003-2992;* Sarai Batchelder, Ph.D., David Kreditor, M.D., Michael Fedak, M.D.

Summary:

Background: Many studies of antidepressants in the treatment of dysthymic disorder (DD) have been conducted, but none with the sustained release preparation of bupropion (bupropion-SR). Our aim was to provide preliminary data on the tolerability and effectiveness of bupropion-SR for patients with DD.

Method: Twenty-one adult subjects meeting DSM-IV criteria for DD were enrolled in this 8-week open-label study. Bupropion-SR was initiated at 150 mg/day, and increased to a maximum of 200 mg BID. Response was defined as ≥50% drop in score on the Hamilton Depression Rating Scale (HDRS).

Results: Of these 21 subjects, 15 (71.4%) were treatment responders. All paired sample t-tests were highly significant, demonstrating significant average improvement on all measures of symptomatology and functioning. Scores on the HDRS decreased from 22 ± 6 at baseline to 6 ± 4 at Week 8. The average final dose was 364 mg/day. Patients with diagnoses of past alcohol or chemical abuse were significantly less likely to respond to bupropion. None of the subjects dropped out during the trial. Side effects were reported by 8 subjects (38.1%). The most frequent were headache, decreased appetite, insomnia, gastrointestinal problems, restlessness, and tremulousness. None resulted in discontinuation of treatment. Sexual dysfunction or weight gain were not reported.

Conclusion: These findings suggest the effectiveness and high tolerability of bupropion-SR in treating Dysthymic Disorder. Double-blind prospective studies are needed comparing bupropion-SR both to placebo and to other medications, assessing both initial and sustained response to treatment.

NR703 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Onset of Action of Mirtazapine on Anxiety Symptoms Related to Depression

Ilse Van Hensbeek, M.D., *Medical Services Department, NV Organon, Molenstraat 110, Oss 5340 BH, Netherlands;* Albert J. Schutte, M.D., Paul D. Reimitz, Ph.D.

Summary:

Background: A pooled-analysis was performed to assess the efficacy of mirtazapine in comparison with fluoxetine, paroxetine and citalopram in the relief of anxiety symptoms related to depression.

Method: Data from three double-blind controlled studies of mirtazapine (MIR) vs fluoxetine (FLU), paroxetine (PAR) and citalopram (CIT) in depressed patients were analysed. The studies had similar in/exclusion criteria. Statistical analyses were performed on the basis of the Intention-To-Treat group(s). To evaluate the onset of efficacy on anxiety symptoms related to depression, the absolute change from baseline on anxiety/somatization factor of the HAMD-17 scale, which was used in the FLU and PAR trials, and of the scores on the HAM-A scale, which was used in the CIT and PAR trials, were analysed. In addition, responder rates on HAM-A factors 1 ("Somatic anxiety") and 2 ("Psychic anxiety"), defined by a reduction of at least 50% and remitter rates on HAM-A, defined as a HAM-A total score ≤8, were analysed.

Results: In the pooled analysis on the absolute change from baseline on HAMD-17 anxiety/somatization factor, mirtazapine showed a statistically significantly greater reduction from week 1 onwards. On HAM-A, a statistically significant difference at week 1 was seen. Responder rates on HAM-A factors 1 and 2 were detected in favor of mirtazapine with a statistically significant difference at week 1 for both factors. More mirtazapine-treated patients were classified as remitters from week one onwards, reaching statistically significant levels at week two, three and four.

Conclusion: Mirtazapine proved to have a better efficacy on anxiety symptoms related to depression with a faster onset of anxiolytic effect compared to the SSRIs.

NR704 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Onset of Action of Mirtazapine on Depression-Related Symptoms: Factor Analysis of Pooled Data Mirtazapine Versus SSRIs

Albert J. Schutte, M.D., *Medical Services Department, NV Organon, Molenstraat 110, Oss 5340 BH, Netherlands;* Ilse Van Hensbeek, M.D., Paul D. Reimitz, Ph.D.

Summary:

Background: A pooled analysis was performed to compare the efficacy of mirtazapine with fluoxetine and paroxetine on the HAMD factors I (Anxiety/somatization), V (Retardation) and VI (Sleep disturbance).

Method: Data from two double-blind controlled studies of mirtazapine vs fluoxetine and paroxetine in depressed patients were pooled with regard to the HAMD factors I, IV and VI and analyzed. The studies were comparable in design. Statistical analyses were performed on the basis of the Intention-To-Treat group(s). To evaluate the onset of therapeutic efficacy on depression related anxiety/somatization, retardation and sleep disturbance, the absolute change from baseline on HAMD-17 and responder rates, defined by a reduction of at least 50%, were analyzed.

Results: In the pooled analyses, on all analysed HAMD-factors, treatment with mirtazapine results in a larger magnitude of change from baseline on HAMD-17 than fluoxetine and paroxetine. Statistical differences were detected on all assessments, from week one onwards for the factors I and VI. Statistically significant results regarding responder rates in favor of mirtazapine could be detected at week 1, two and four for factor I; week 1 for factor V and at week 2 for factor VI.

Conclusion: Mirtazapine proved to have a faster onset of the relief of depression related symptoms, such as anxiety and sleep disturbances, assessed by the HAMD-factor analysis.

NR705 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release and Sleep in Depression

Eric A. Nofzinger, M.D., *Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Room E1118, Pittsburgh, PA 15213;* Amy L. Fasiczka, Susan R. Berman, Carolyn C. Meltzer, M.D., Michael E. Thase, M.D.

Summary:

Objective: Depression is characterized by motivational and emotional symptoms that are thought to be mediated by the anterior paralimbic system. In contrast to healthy subjects, depressed patients fail to activate anterior paralimbic structures from waking to REM sleep. Bupropion is one of the few antidepressants that enhances REM sleep in depression, thus, it is hypothesized that the effects of bupropion SR on EEG sleep may be accompanied by a reversal of anterior paralimbic functional deficits in depressed patients.

Method: Ten unipolar depressed subjects underwent 3-nights EEG sleep, brain MR, and [^{18}F]FDG PET studies during waking and REM sleep. Identical evaluations were repeated on-drug following 10 weeks open-label treatment with bupropion SR (final total daily dose = 400 mg). Five subjects successfully completed all studies. State (waking vs REM sleep) by treatment (pre- vs. post) interactions were analyzed in the anterior paralimbic system.

Results: Depressed patients showed significantly greater activation in anterior paralimbic structures from waking to REM sleep following treatment with bupropion SR. This effect was maximally significant in the anterior cingulate cortex ($Z = 4.19$, $p < .001$ at Talalrach x, y, z coordinates = –4, 30, 32).

Conclusions: Bupropion SR reverses anterior paralimbic functional deficits in depressed patients in this waking to REM sleep brain imaging probe. Further studies are needed to determine if this effect is specific to bupropion SR or if it applies to other effective antidepressants.

NR706 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Methylphenidate-Ethanol Interaction to Form Ethylphenidate

C. Lindsay DeVane, Ph.D., *Department of Psychiatry, Medical University of SC, 67 President Street, #502N, Charleston, SC 29425-0742;* Kennerly Patrick, Ph.D., John S. Markowitz, Ph.D., David Boulton, Ph.D., Samuel C. Risch, M.D., Juliet Goldman, M.D.

Summary:

Little is known of the pharmacology of ethylphenidate (EPH) whose carboxylesterase-dependent formation appears to proceed in an analogous fashion to that of cocaethylene following concomitant cocaine and ethanol use. We sought to characterize EPH formation and its pharmacokinetics in six healthy volunteers (3M, 3F). Subjects received a single oral dose of methylphenidate (MPH), 20 mg, followed 30 minutes later by orally administered ethanol 0.6 g/kg consumed over 15 minutes. Blood and urine samples were analyzed for MPH, ritalinic acid and EPH using LC/MS. Following ethanol consumption, EPH appeared in plasma of all 6 volunteers in low concentration. The area under the plasma concentration v. time curve (AUC) for EPH was 2.3 ± 1.3% of MPH AUC. No significant correlation was found between EPH and ethanol AUCs ($r^2 = 0.11$, $P = 0.14$) while the concentration of plasma MPH and EPH appeared related ($r^2 = 0.48$, $P < 0.001$). The amount of MPH, EPH and ritalinic acid excreted in the urine over 6 hours was 1.4 ± 0.8%, 0.02 ± 0.1%, and 19.9 ± 10.8% of the MPH dose, respectively. The formation of EPH appeared more dependent upon MPH concentration rather than ethanol concentration. Increasing ethanol intake would be unlikely to increase EPH formation from the same dose of MPH. Overall, EPH

was not formed extensively in subjects who received MPH/ethanol.

NR707 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release for SSRI-Resistant Major Depression

Patrick J. McGrath, M.D., *Therapeutics, NY State Psychiatric Hospital, 1051 Riverside Drive, Unit 51, New York, NY 10032-2695;* Maurizio Fava, M.D., Jonathan W. Stewart, M.D., Frederic M. Quitkin, M.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D.

Summary:

Many patients with Major Depression fail to respond to an initial SSRI trial. For these patients, treatment with a medication like bupropion, having predominantly noradrenergic actions, may be a more rational strategy than switching to another SSRI. We report preliminary results for the first 28 such subjects from a clinical trial who failed to respond to fluoxetine (≥40 mg for ≥8 weeks) and were switched to bupropion SR 150 mg. BID without washout. No evidence of significant adverse interaction with remaining fluoxetine and norfluoxetine was seen.

Of 28 subjects, 6 (21%) dropped out due to adverse events. Responders were considered those with a ≥50% decrease in baseline HAM-D score, partial responders those with ≤50% but ≥25% decrease, and nonresponders those with a ≤25% decrease. Of 28 patients, 10 (35%) were considered responders, 6 (21%) partial responders, and 6 (21%) nonresponders. Ten of 22 (45%) of those who completed 8 weeks of therapy were responders and 6 (27%) partial responders. These data suggest that bupropion SR treatment is well tolerated in fluoxetine nonresponders without a washout and may be effective for some SSRI nonresponders.

NR708 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Pharmacokinetics of Risperidone/Donepezil Combination

Luana Pesco-Koplowitz, M.D., *Janssen Research Foundation, 1125 Trenton-Harbourton Road, Titusville, NJ 08560;* Jean-Loup Barier, Qinying Zhao, M.D., Charles Xie, M.D., Jerry Heron, M.D.

Summary:

Purpose: Dementia is accompanied by psychotic symptoms and behavioral disturbances in many patients and thus an atypical antipsychotic such as risperidone is often combined with a cholinesterase inhibitor such as donepezil in these patients. No interactions of risperidone and donepezil have been reported in the literature or noted on the pharmacovigilance database of the risperidone manufacturer (Janssen Pharmaceutica). However, since CYP 2D6 is involved in the metabolism of both compounds, the pharmacokinetics of the drug combination were examined.

Methods: In a randomized, three-way, crossover study, 24 healthy male volunteers received 0.5 mg of risperidone twice daily or 5 mg of donepezil once daily, or both, for 14 consecutive days per trial, with a 21-day washout period between each trial.

Results: No significant differences were noted in the pharmacokinetics (AUC and Cmax) of either the risperidone active moiety (risperidone plus 9-hydroxyrisperidone) or donepezil when given alone or in combination. Adverse events seen with risperidone alone, donepezil alone, or the donepezil/risperidone combination were similar (predominantly headache, nervousness, and somnolence).

Conclusion: Consistent with the published literature and the pharmacovigilance profile, there appears to be no pharmacokinetic interaction between risperidone and donepezil in healthy subjects receiving these agents at therapeutic doses.

NR709 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Topiramate As an Anti-obesity Agent

Mohammad Z. Hussain, M.D., *2727 2nd Avenue West, Prince Albert, SK S6V 5E5, Canada;* Seema Hussain, M.D., Zubaida A. Chaudhry, M.B.

Summary:

Obesity is an increasing problem, associated with health concerns, including cardiovascular disease, osteoarthritis, type II diabetes, psychological morbidity of mood and anxiety disturbance and low self-esteem. Topiramate, an anticonvulsant with demonstrated therapeutic potential as a mood stabilizer has been associated with weight loss. We investigated topiramate's potential as an antiobesity agent. Topiramate was given at a maximum dose of 100 mg/d to 3 groups, each consisting of 25 patients with weight concern: those with no formal psychiatric disorder, stable treatment responsive bipolar patients; and partial treatment responsive bipolar patients. Patients were rated on the BPRS and interviewed at baseline and monthly intervals following topiramate initiation. Mean weight loss in the three groups after 12 weeks was: 16.4 lbs., 16.7 lbs., and 13.5 lbs. respectively. Responders also noted improved mood and alertness, and relief from premenstrual symptoms. Discontinuation secondary to intolerance in the three groups was 3, 9 and 14 patients respectively. Most common adverse effects were numbness/tingling, dizziness, and sleep disturbance. These findings are consistent with those weight changes observed with topiramate used as a mood stabilizer and given the best response of the nonpsychiatric population, topiramate appears to show promise as an antiobesity agent.

NR710 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Clozapine Bioequivalence in Patients

Larry Erehefsky, Pharm.D., *Clinical Pharmacology Dept. Univ. of Texas H.S.C.-S.A., 7703 Floyd Curl Drive, San Antonio, TX 78229-3990;* Y.W. Francis Lam, Pharm.D., Gregory B. Toney, Pharm.D., Cheryl L. Gonzales, M.D., Daniel J. Dugan, Pharm.D., Monica Leftwich, Pharm.D.

Summary:

Objective: A prospective randomized (blinded rater and laboratory) 2 x 2 crossover evaluation of Clozaril® (Novartis) vs. clozapine (Zenith-Goldline) 100 mg tablets in stabilized patients (≥3 months of treatment).

Methods: 2 week run-in period on current Clozaril® then randomized assignment: 2 weeks each on clozapine or Clozaril®. Blood samples were obtained at specified times over one dosing interval of 12 hours. Published FDA guidance and *a priori* criteria for analyses included determination of proportion of patients within 80–120% of the reference drug's AUC and Cmax; parameters transformed as appropriate; and confidence interval (CI) testing.

Results: 6 of 33 patients screened were not randomized, 21 subjects are evaluable.

PK Parameter Dose normalized*	Least squares mean (SE)		Mixed-effects ANOVA p value	90% CI Ratio
	Clozapine	Clozaril®		
ln (AUC 0–12 h)[4]	2.63 (0.13)	2.72 (0.13)	0.066	0.85, 0.99
ln (Cmax) ng/mL[4]	0.45 (0.12)	0.61 (0.12)	0.002	0.78, 0.92
ln (Cmin) ng/mL[4]	−0.23 (0.15)	−0.17 (0.15)	0.354	0.85, 1.05
Tmax (hr)	2.40 (0.90)	2.19 (1.71)	0.074	
T 1/2 hr	14.01 (2.08)	11.51 (2.08)	0.342	0.83, 1.60

PK Parameter	Proportion of patients within range	95% Lower-limit CI
AUC (0–12 h)-within 80–120%	76.2% (16/21)	52.5%
Cmax-within 80–120%	62% (13/21)	34.4%
Cmax-within 70–130%	90.5% (19/21)	68.2%

Conclusion: Clozapine AUC and Cmax in 5 and 8 patients,

respectively, were outside of the usually accepted 80–120% range of the reference drug (Clozaril®) when on clozapine. The CI testing for AUC and Cmax demonstrate a distribution bias towards higher values for Clozaril® than clozapine. Additional studies are necessary.

NR711 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Interchangeability of Clozapine Formulations in Stabilized Patients

Gregory B. Toney, Pharm.D., *Clinical Pharmacology Dept., Univ. of Texas H.S.C.-S.A., 7703 Floyd Curl Drive, San Antonio, TX 78229-3900;* Larry Ereshefsky, Pharm.D., Y.W. Francis Lam, Pharm.D., Daniel J. Dugan, Pharm.D., Albana M. Dassori, M.D., Jerry G. Olsen, M.D., Cheryl L. Gonzales, M.D.

Summary:

Objective: Evaluate the interchangeability of Clozaril® (Novartis) and clozapine (Zenith-Goldline) 100mg tablets in patients at steady-state.

Methods: Post-hoc analysis of a prospective, randomized (blinded rater and laboratory) 2 x 2 crossover bioequivalence study divided the 21 patients into two groups: Grp1 being outside and Grp2 being inside of the 80–120% AUC ratio (generic compared to reference drug). Pharmacokinetic (PK) parameters were dose normalized and $\log_e$ transformed as appropriate; confidence interval (CI) testing was performed.

Results: 5 of 21 (23.8%) patients are in Grp1, 16 are in Grp2. No differences between groups were observed for demographics, daily dose, or change from baseline total PANSS score. One subject in Grp1 clinically deteriorated when switched from long-term Clozaril® to clozapine (29% increase in PANSS) and continued to worsen despite cross-over to branded drug (further 47% increase); there were concomitant psychosocial stressors. This subject demonstrated the largest difference in AUC amongst all patients.

PK Parameter Dose normalized*	Least squares mean (SE)		Mixed-effects p value	90% CI Ratio
	Clozapine	Clozaril®		
Grp1 ln (AUC 0–12 hr)	2.02 (0.26)	2.41 (0.26)	0.089	0.47, 0.98
Grp2 ln (AUC 0–12 hr)	2.80 (0.12)	2.83 (0.12)	0.297	0.92, 1.02
Grp1 ln (Cmax) ng/ml	–0.15 (0.21)	0.30 (0.21)	0.021	0.50, 0.81
Grp2 ln (Cmax) ng/ml	0.62 (0.12)	0.71 (0.12)	0.046	0.85, 0.98

The proportion of Grp1 patients with Cmax within 80–120% and 70–130% of the reference drug are 20% (95% CI lower-limit 6.8%) and 60% (95% CI lower-limit 36.9%), respectively. The proportion of Grp2 patients with Cmax within 80–120% and 70–130% of the reference drug are 68.8% (95% CI lower-limit 45.1%) and 100% (95% CI lower-limit 80.7%), respectively.

Conclusion: Despite the small sample size there appear to be substantial differences in pharmacokinetic parameters for a subgroup of patients.

NR712 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Weight Changes in Patients Treated with Quetiapine

A. Martin Jones, M.S.C., *Medical Research, AstraZeneca, Mereside Alderley Park, Macclesfield SK10 4TG, England;* Ihor W. Rak, M.D., Joher Raniwalla, B.W., De Phung, B.S., Karen Melvin, B.S.

Summary:

Objective: Weight gain is a side effect often associated with antipsychotic treatment that can affect compliance, quality of life, and long-term health. We report data on weight changes observed in a large cohort of patients treated with quetiapine.

Method: Patients (n = 2216) from controlled, uncontrolled, and open-label extension trials were studied. Weights were grouped using an LOCF approach, within specified time intervals.

Results: There was a small mean weight increase of 2.08 kg (±0.15; n = 778) over the first 5–6 weeks. Similar mean weight increases of 2.16 kg (±0.46; n = 171) at 9–10 weeks, 1.85 kg (±0.48; n = 556) at 6–9 months, and 2.77 kg (±0.56; n = 360) at 9–12 months were observed. The average mean daily dose of quetiapine for the patients at 9–12 months was 428 mg/day. Only 1 patient from the 2216 cohort (0.05%) withdrew due to an adverse event of weight gain.

Conclusion: Based on available weight gain data, the weight gain during quetiapine treatment is approximately equal to the weight gain associated with risperidone and approximately 50% of the weight gain reported with olanzapine and clozapine.

NR713 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Open Study of Lamotrigine in Mood Disorder with Substance Use Comorbidity

Simon S. Chiu, M.D., *Addiction Rehabilitation Unit, St Thomas Psychiatric Hospital, PO Box 2004, St. Thomas, ON N5P 3V9, Canada*

Summary:

Introduction: Recent studies of lamotrigine have reported highly positive therapeutic responses in rapid cycling bipolar affective disorder; however, it is not known whether co-occurring substance use disorders affect lamotrigine response.

Objective: To evaluate the efficacy and tolerability of lamotrigine in mood disorders with substance use co-morbidity and examine whether lamotrigine reduces relapse of substance use.

Method: The study was naturalistic, open-label and prospective. Flexible dosage of lamotrigine was used. Patients diagnosed with DSM IV mood disorder were recruited from psychiatric and addiction services and were detoxified for at least 3 weeks prior to entry to the 12-week study. Efficacy measures consisted of CGI (Clinical Global Impression scale: Improvement scale), GAF (Global Assessment Functional scale), BPRS (Brief Psychiatric Rating Scale), Self-report substance use and craving. Tolerability was monitored with treatment-emergent adverse events.

Results: 15 patients (male: 12, female: 3) were dually diagnosed with mood disorders and substance use disorders (bipolar affective disorder type II: 75%; schizoaffective disorder: bipolar type: 25%; cocaine dependence: 20% and alcohol dependence: 80%). 1 patient developed generalised dermatitis and was terminated from the study. The average daily dosage of lamotrigine was 125 mg. As compared to baseline values, BPRS, CGI and GAF were statistically significant (paired t-test, $p < 0.05$). 75% % of the patients maintained abstinence from substances of abuse during the 12-week of study. Medication compliance was coupled with attendance at self-help and addiction treatment groups. Side effects included mild restlessness.

Conclusion: The initial promising results of lamotrigine in dual disorder mood disorder patients warrant large controlled clinical trials to establish the possible role of lamotrigine in relapse prevention among mood disorder patients.

NR714 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Comparison of Costs and Effects of Risperidone Treatment Versus Olanzapine Treatment in Daily Practice

Anton J.M. Loonen, M.D., *Delta Psychiatric Hospital, PO Box 800, Poortugaal, NL 317 0DZ, Netherlands;* Jacques C.M. Loos, M.D., Theodora H. Van Zonneveld, M.D.

Summary:

Introduction: Because of the obvious absence of adverse drug reactions, novel antipsychotics are increasingly popular with psychiatrists in the Netherlands. However, the hospital management and insurance companies are primarily interested in the costs of this development. Delta Psychiatric Hospital participated in the RODOS Program, an international series of single-center studies involving several countries and organized by the Janssen Research Foundation, to compare drug usage patterns and the costs and outcomes associated with treatment with risperidone and olanzapine in naturalistic clinical settings. An analysis of our single-center study is presented.

Design: This study existed of a retrospective chart review of 2 x 32 psychotic patients who received either risperidone or olanzapine shortly after admission to the hospital. Patient characteristics, diagnosis, length of stay, concomitant medications, treatment efficacy and adverse events were registered.

Results: Both medications were rated as effective (72% vs. 68%) and there was no difference between length of stay (38.5 vs. 42.5 days) or reported adverse events. Treatment with risperidone turned out to be twice as cheap as that with olanzapine (Dfl. 4.58 vs. Dfl. 8.60 a day; $p < 0, 001$).

NR715 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Nefazodone Improves Subjective Sleep Measures and Decreases the Use of Sleep Aids in Depressed Patients

Jose L. Ayuso, Ph.D., *Department of Psychiatry, Hospital San Carlos, Martin Lago, sn, Madrid 28040, Spain;* Julio B. Bobes, Ph.D., Juan Gibert, Ph.D., Maria P. Gonzalez, Ph.D., Jeronimo Saiz-Ruiz, M.D., Julio Vallejo, M.D., Fernando Rico-Villademoros, M.D.

Summary:

Objective: To evaluate the quality of sleep in a large sample of depressed patients treated with nefazodone.

Methods: 1483 patients (those who met the entrance criteria and had at least one post baseline evaluation) older than 18 years who met DSM-IV criteria for nonpsychotic major depression were enrolled in a 12-week open-label and naturalistic study of nefazodone. Study assessments consisted of HAM-D-17, CGI, and the Oviedo Sleep Questionnaire-COS (a validated semistructured interview for sleep disorders). Data are presented as completers analysis.

Results: Overall response (CGI-improvement ≤ 2) and discontinuation rates were 75% and 23.3% respectively. COS total score (insomnia severity) diminished from 30 to 15 at week 12 ($p = .000$). Rate of patients who were satisfied to very much satisfied with their sleep increased from 6.5% to 70% ($p = .000$). Patients with a subjective sleep efficiency greater than 80% accounted 16% at baseline and 78% at week 12 ($p = .000$). Frequent somnolence (≥ 3 days/week) decreased from 28% of the patients to 5% ($p = .000$). Proportion of patients who did not required sleep aids increased from 36% to 51% ($p = .000$).

Conclusions: Nefazodone shows a beneficial effect over the sleep of depressed patients in everyday clinical practice.

NR716 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Sexual Functioning in Depressed Patients Under Treatment with Nefazodone, Fluoxetine, Paroxetine and Venlafaxine: A Prospective Naturalistic Study Using the Changes in Sexual Functioning Questionnaire (CSFQ)

Julio B. Bobes, Ph.D., *Department of Psychiatry, University Oviedo, Julian Claveria 6, Oviedo 33006, Spain;* Maria P. Gonzalez, Ph.D., Maria T. Bascaran, M.D., Fernando Rico-Villademoros, M.D., Sebastian Banus, M.D., Margarita Garcia, M.D.

Summary:

Objective: To assess sexual functioning in depressed patients receiving antidepressants.

Method: 107/127 evaluable patients older than 18 years who met DSM-IV criteria for non-psychotic major depression were included in the intent-to-treat analysis. Assessments: HAM-D-17, CSFQ (validated Spanish version) at baseline, 2, 4, and 6 months. Patients were classified as remitters (HAM-D ≤ 8) or non-remitters. Data on clomipramine ($n = 6$) were not included in this analysis.

Results: All treatments were equally effective and tolerated as evaluated by % of responders (HAM-D $\leq$ 50%), % of remitters and discontinuation rates. Nefazodone ($n = 39$) significantly ($p < 0.05$, T-Wilcoxon Test) improves CFSQ total score as well as pleasure, sexual desire/frequency, sexual desire/interest, arousal/erection in remitters. Nefazodone did not impair sexual functioning in non-remitters. Paroxetine ($n = 30$) did not improve sexual functioning in remitters while significantly worsened it in non-remitters except pleasure. Fluoxetine ($n = 20$) did not improve sexual functioning in remitters and trended to impair it in non-remitters reaching statistical significance for orgasm/ejaculation. Venlafaxine ($n = 12$) appears to improve sexual functioning in remitters while trends to impair it in non-remitters especially arousal/erection and orgasm/ejaculation ($0.05 < p < 0.1$, T-Wilcoxon Test).

Conclusions: Nefazodone preserves sexual functioning. Paroxetine, Fluoxetine and to a lesser extent Venlafaxine adversely affects sexual functioning.

NR717 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Risperidone and Olanzapine: Patterns of use in a Veterans Administration System

John C. Voris, Pharm.D., *Clinical Pharmacology, University of South Carolina, 1312 Country Squire Drive, Columbia, SC 29212-2202*

Summary:

This retrospective study compared risperidone and olanzapine use in 7 VA systems during August 1996 and August 1999. The increases from year 1 to year 3 in total prescriptions were 8913 to 19,980 for risperidone and 3824 to to 20,682 for olanzapine. The average dose and cost were similar in year 1 and year 3: 3.33 mg/day and $3.31/day for risperidone and 10.65 mg/day and $5.53/day for olanzapine. A random sampling was taken of 25% of patients at the Dorn (South Carolina) VA system (risperidone, $n = 43$; olanzapine, $n = 48$). In year 1 the median age of risperidone patients (64 years) was significantly higher than that of olanzapine patients (48 years), but by year 3 the median ages had declined to 57 years in risperidone patients and increased to 50 years in olanzapine patients. Significant between-group differences were seen by diagnostic groups. For example, the proportion of patients with psychosis treated with risperidone increased from 37% in year 1 to 44% in year 3 and those treated with olanzapine declined from 68% to 46%. The average doses (all diagnoses) declined from 3.01 mg/day of risperidone in year 1 to 2.06 mg/day in year 3 and increased from 8.36 to 9.29 mg/day of olanzapine. In patients with schizophrenia, concomitant use of a second neuroleptic was significantly greater with olanzapine (20%) than risperidone (6%). The results indicate that risperidone and olanzapine use differed in this VA system with respect to patient age, diagnosis, and concomitant medications.

NR718 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Six-Week, Double-Blind, Placebo-Controlled Trial of Bupropion Sustained Release in the Treatment of Adults with ADHD

Frederick W. Reimherr, M.D., *Department of Psychiatry, University Hospital, 50 North Medical Drive, Salt Lake City, UT 84132;* Robert E. Strong, D.O., Barrie Marchant, M.S., Dawson W. Hedges, M.D., Erika Williams, M.S.W., Paul H. Wender, M.D.

Summary:

ADHD has become increasingly diagnosed and treated in adults. Treatment modalities have grown to include several antidepressants as well as stimulant medications. This study was designed to evaluate the effectiveness of bupropion SR in an acute study followed by an open six-month extension. Sixty subjects were selected using the Utah Criteria and DSM-IV for ADHD. Sixty percent were assigned to bupropion SR and 40% to placebo in a double-blind manner. A greater percent were assigned to bupropion SR to produce a larger exposure to bupropion in the longterm portion of the study. Outcome measures included: Wender Reimherr Attentional Deficit Disorder Scale (WRADDS), and the physician-rated Clinical Global Improvement Scale (CGI). Twelve patients equally divided between medication and placebo dropped out prior to obtaining any outcome measures. On the WRADDS, using a 40% decline in symptoms to define responders, 41% responded to bupropion SR while 16% responded to placebo ($X = 3.50$, $df = 1$, $p < .065$). There were similar charges on the CGI using a categorical analysis. All measures favored bupropion SR, but due to the unequal assignment of patients, did not reach a $p < .05$ level of statistical significance.

NR719 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Use of Atypical Neuroleptics in Younger Adults

Stephen Curran, Ph.D., *Fieldhead Hospital, Ouchthorpe Lane, Wakefield WF1 3SP, England*

Summary:

This was a cross-sectional survey of the use of atypical neuroleptics in patients aged 18-65 with mental health problems in the city of Wakefield, England. The mental health service caters for a total population of 300,000. All patients included in the study were being cared for by six community mental health teams. In total 469 patients had been prescribed neuroleptic drugs. Of these, 7% were in-patients and 93% were community-based. ICD-10 diagnoses included schizophrenia and related illnesses (49%), BAD (11%), anxiety disorders (9%), depressive disorders (26%) and "other" (5%). 64% of patients received their medication by prescription from their consultant, 34% from their general practitioner (primary care) and in 2% the source was unknown. 89% of patients were taking "older" neuroleptics. The two most commonly prescribed atypicals were risperidone (7.1%) and olanzapine (8.2%) followed by clozapine (2.8%) and amisulpride (1.5%). Some patients were taking both an atypical and an "older" neuroleptic. The cost of prescribing atypicals has gradually increased in Wakefield since 1996 and the approximate figures are: 1996/97 ($164,000), 1997/98 ($230,000) and 1998/99 ($326,000).

NR720 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Efficacy of Mirtazapine in Stimulant-Associated Insomnia in Patients with ADHD

Lenard A. Adler, M.D., *Department of Psychiatry, New York Veterans Administration Center, 423 East 23rd Street, New York, NY 10010;* Lauren M. Braverman, B.A., David L. Ginsberg, M.D.

Summary:

Introduction: Stimulants are the most commonly prescribed medications for Attention Deficit Hyperactivity Disorder (ADHD). One major side effect of these medications can be an exacerbation of induction of insomnia. Approved hypnotics have not been well studied in stimulant-associated insomnia (SAI). The antidepressant, mirtazapine can be mildly sedating in the lower ranges of therapeutic doses.

Methods: Sixteen patients with early insomnia and ADHD, who were receiving stimulants, were offered four to six weeks of open treatment with mirtazapine (starting dose: 3.75–7.5 mg qHS, final daily dose: 3.75–45 mg/day, mean: 9.41 ± 10.8 SD mg/day). Two patients developed significant daytime sedation on the first day and therefore their results are not included. Patients ranged in age from 12 to 47 years. All patients were receiving stable doses of stimulants and met DSM-IV and childhood K-SADS criteria for ADHD. Sleep patterns were assessed by self-report of average number of hours slept nightly over the past week, at baseline and then during treatment.

Results: Mirtazapine was well tolerated by the remaining fourteen patients. Sleep was improved in all patients (mean hours of sleep: baseline 5.3 + 1.2; after mirtazapine; 7.9 ± 0.6; $t(13) = 11.7$, $p < 0.0001$). All patients elected to continue treatment at the end of the trial.

Conclusions: Mirtazapine significantly improved SAI in this open, pilot trial.

NR721 Thursday, May 18, 12:00 p.m.-2:00 p.m.

New Neuroleptics: An Eight-Year Naturalistic Study

Cheryl K. Cantrell, M.D., *Delaware Psychiatric Center, 1901 North Dupont Highway, New Castle, DE 19720;* Eric S. Cole, Ph.D.

Summary:

Objective: This investigation reports utilization patterns of new and atypical neuroleptics and cummulative response rates in chronic inpatients to naturalistic trials of these agents in a state facility over an eight year period.

Method: Between 1991 and 1999, 491 psychiatric inpatients were given 724 clinical trials of clozapine (130 trials averaging 12.5 months at 470 mg/day), risperidone (358 trials averaging 7.3 months at 5.1 mg/day), olanzapine (207 trials averaging 8.3 months at 15.2 mg/day), quetiapine (15 trials averaging 2.9 months 314 mg/day) or combinations of two of these medications (14 trials averaging 8.3 months). Response rates were assessed longitudinally by physician report on a 6 point Likert scale.)

Results: Patient response rates of good to excellent were 55% for clozapine, 46% for risperidone, 42% for olanzapine, 40% for quetiapine and 64% for combination therapies. The rates of discharge were 32%, 32%, 26%, 7% and 43%, respectively. Analysis using the Chi Test showed clozapine to be superior to both risperidone ($p = 0.016$) and olanzapine ($p = 0.012$) and the latter two drugs to be indistinguishable ($p = 0.087$).

Conclusions: All of these agents have demonstrated good effectiveness in our refractory patient population. The use of two novel agents together appears promising and requires further study.

NR722 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Double-Blind, Randomized, 28-Week Continuation Study of Sertraline and Placebo in PTSD

Jonathan R.T. Davidson, M.D., *Department of Psychiatry, Duke University Medical Center, Box 3812, Durham, NC 27710;* Peter D. Londborg, M.D., Teri B. Pearlstein, M.D., Barbara O. Rothbaum, Ph.D., Kathleen T. Brady, M.D., Gail M. Farfel, Ph.D.

Summary:

Objective: Since no data are published examining the duration of pharmacotherapy required for the treatment of PTSD, the objective was to compare the safety and efficacy of sertraline and placebo in the prevention of PTSD relapse in patients who had responded to 24 weeks of open-label sertraline treatment.

Method: Outpatients with PTSD who completed and responded to 24 wks of open-label sertraline were eligible to be randomized to sertraline (n = 46) or placebo (n = 50), flexibly titrated between 50–200 mg/day, in this 28 week study. Primary efficacy measures were time to and rate of relapse, or discontinuation due to insufficient clinical response (ICR). Secondary efficacy measures were the Clinician-Administered PTSD Scale, Clinical Global Impression ratings of Severity and Improvement, and the Impact of Event scale.

Results: Patients receiving placebo relapsed or discontinued due to ICR significantly earlier than patients receiving sertraline ($p < .01$). The proportion of patients who relapsed on sertraline, 5.3% (2/38), was significantly lower ($p = .02$) than patients who relapsed on placebo, 26.1% (12/46). The mean changes in secondary efficacy measures at endpoint were also significantly different between the groups ($p < .05$), indicating sertraline-treated patients maintained greater symptom improvement than placebo-treated patients. Sertraline was generally well-tolerated. The most common adverse events (≥10% in the sertraline group) were: headache, malaise, insomnia and infection. Treatment discontinuations due to adverse events or lab abnormalities occurred in 9% of sertraline and 6% of placebo patients. There were no differences in the incidences of lab or vital sign abnormalities, or ECGs, between the groups.

Conclusion: Sertraline (50–200 mg/day) is effective and well-tolerated in the prevention of PTSD relapse in patients who have completed 6 months of open-label sertraline treatment.

NR723 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Citalopram Pharmacokinetic Profile Is Unaffected by the CY3A4 Inhibitor Ketoconazole

Marcelo Gutierrez, Ph.D., *Forest Laboratories, 909 Third Avenue, New York, NY 10022;* Wattanaporn Abramowitz, Ph.D.

Summary:

Introduction: Citalopram, the most selective serotonin reuptake inhibitor (SSRI), is used in over 60 countries for the treatment of depression, panic, and obsessive compulsive disorder. Citalopram is metabolized by the specific cytochrome P450 (CYP) isozymes 3A4, 2C19, and 2D6. Unlike other SSRIs, citalopram produces no significant inhibition of any of the major drug metabolizing CYP isozymes. The objective of the present study was to investigate the converse question of whether citalopram plasma levels are affected by the potent inhibition of CYP3A4 activity produced by the antifungal agent ketoconazole.

Method: This was a double-blind, randomized, crossover study in 18 young healthy male and female subjects. Each subject received: 1) citalopram [40 mg] plus placebo and 2) citalopram [40 mg] plus ketoconazole [200 mg]. The washout period between treatments was at least 14 days. Blood samples were taken after each treatment and analyzed for citalopram and its metabolite, demethylcitalopram. Pharmacokinetic parameters were determined following each treatment.

Results: The pharmacokinetic profile of citalopram administered alone was identical to that obtained when citalopram was administered with ketoconazole. Likewise, the pharmacokinetic parameters for demethylcitalopram were unaltered by ketoconazole.

Conclusion: These results demonstrate that the pharmacokinetic profile of citalopram is unaltered when this agent is co-administered with the potent CYP3A4 inhibitor ketoconazole. Thus, agents that produce significant inhibition of the CYP3A4 system are unlikely to affect citalopram plasma levels. No adjustment of citalopram dosage is necessary when CYP3A4 inhibitors are coadministered with citalopram.

NR724 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Validation of Antidepressant Utilization Rates in the Pacific Northwest

Annette M. Fehr, M.B.A., *Research Department, PCS Health Systems, 9501 East Shea Blvd, MC034, Scottsdale, AZ 85260;* David S. Hutchins, M.B.A., Bentson H. McFarland, M.D., Chistopher Young, Ph.D., William F. Signa, B.S.

Summary:

Objectives: This study used methodology reported by Johnson et al (1997) to analyze a pharmacy benefits manager's (PBM) prescription claims for the same region and timeframe to validate a health maintenance organization's 70% increase in antidepressant utilization driven by SSRI use.

Methods: Prescription claims from 1991 through 1994 were extracted for 10 Pacific Northwest counties. Counts were totaled by client. Clients filling the majority of prescriptions in those counties were selected, and their members used to calculate *annual member years.* Members filling antidepressant prescriptions comprised *utilizer members.*

Results: Overall crude antidepressant utilization rates increased from 17.5/1000 to 48.0/1000 (+174%) with a 525% increase in SSRI utilization (4.8/1000 to 30/1000). Johnson et al reported crude antidepressant utilization rates increased from 49/1000 to 83/1000 (+69%) driven by a 240% SSRI increase (10/1000 to 34/1000). Final analyses are forthcoming, but preliminary age and sex adjustments brought PBM rates within 10% of HMO rates.

Conclusions: This study found that overall antidepressant and SSRI utilization increased, supporting the hypothesis that the HMO's increased antidepressant utilization was not unique to its members, but reflected the Pacific Northwest managed care population. Final age and sex adjustments are expected to find negligible utilization rate differences between PBM and HMO.

NR725 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Effectiveness of Using Templates to Comply with Medicare Regulations and Impact on Revenue

Niamh M. Holohan, M.D., *Department of Psychiatry, University of Maryland, 22 South Greene Street, Box 351, Baltimore, MD 21201;* Jill A. RachBeisel, M.D.

Summary:

Objective: Increased federal scrutiny of documentation and billing for services to Medicare recipients and recent severe penalties paid by institutions due to billing errors has caused heightened concerns among clinicians often resulting in under-coding to avoid accusations of over-billing for services rendered. This study examines the effectiveness of using templates to comply with Medicare regulations and impact on revenue.

Methods: Attending psychiatrists were trained in the use of documentation templates for admission and follow-up visits for hospitalized patients and included the identification of the appropriate billing codes for services rendered according to Medicare evaluation and management criteria. The billing records of two attending psychiatrists working on the same unit were reviewed over a four day period prior to and again following implementation of template use. Variance in coding and revenue were evaluated.

Results: Pre-template billing in 80 cases showed that the lowest billing (99231) was submitted in 52% (N = 42) of cases, median billing (99232) in 40% (N = 32) and the highest (99233) in 8% (N = 6). Review of the 84 cases post template implementation showed that in 12% (N = 10) of the cases the lowest level of billing

was done, 36% (N = 30) for median level and 50% (N = 42) for the highest level of billing.

Conclusions: The study suggests that there was a significant tendency for physicians to under-code for services rendered when specific templates were not used, thus seriously impacting the revenue potential for programs and institutions. These results have serious implications for programs when establishing billing procedures. Further analysis on the impact on revenue will be presented.

NR726 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Depot Antipsychotic Versus Oral Olanzapine Treatment

Linda S. Godleski, M.D., *Mental Health Department, VA Medical Center, 800 Zorn Avenue, # 116, Louisville, KY 40206;* L. Jane Goldsmith, Ph.D., Nancy C. Zettwoch, R.N., Dejzi C. Stikovac, M.D., Susan J. Lewis, Ph.D.

Summary:

Objective: To evaluate whether patients taking decanoate antipsychotic medication can be successfully transitioned to oral olanzapine.

Method: Open-label trial of 26 patients randomly assigned to continue current decanoate dose or to switch to oral olanzapine (10–20 mg every day clinically titrated). MMSE, PANSS, HAM-D, AMDP, AIMS, GAF, and CGI scores were obtained monthly.

Results: Patients randomly assigned to maintain their decanoate antipsychotic medication were compared to those switched to oral olanzapine over a three-month period. Baseline to the average of three treatment month measures demonstrated significant improvement (ANOVA with Helmert contrasts) in the olanzapine group compared to the decanoate group in: PANSS total ($p = .052$), PANSS negative ($p = .047$), GAF ($p = .048$), CGI severity ($p = .034$). Baseline to the final third month measure demonstrated significant improvement (ANOVA) in the olanzapine group compared to decanoate in: CGI improvement ($p = .007$), CGI severity ($p = .026$), PANSS total ($p = .012$), PANSS general ($p = .068$), PANSS negative ($p = .098$). The decanoate group did not demonstrate any statistically significant superiority in any rating measured. The olanzapine group continued on the medication for a total of 6 months and demonstrated additional improvement (ANOVA first to final sixth month measure) in MMSE ($p = .022$) and AIMS scores ($p = .038$).

Conclusion: Decanoate patients can be successfully transitioned to oral olanzapine with significant improvement in PANSS, GAF, and CGI ratings as compared to those maintained on decanoate with longer-term improvement in MMSE and AIMS scores.

NR727 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Emotion-Focused Psychotherapy for Panic Disorder: A Randomized Controlled Trial

M. Katherine Shear, M.D., *Department of Psychiatry, University Pittsburgh Medical Center/WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593;* Ellen Frank, Ph.D., Kim Weiner, Ph.D., Patricia Houck, M.S., Sphia Masters, B.S., Catherine Greeno, Ph.D.

Although medication and panic focused cognitive behavioral therapy are now considered standard treatments for Panic Disorder, there is reason to continue to explore the possibility that other types of psychotherapy may also be helpful. We devised an emotion-focused treatment (EFT) focusing on identification and management of negative emotions, especially as they related to common psychological themes of fear of separation, fear of constriction and the need for high levels of interpersonal control. The purpose of this paper is to report results of a randomized controlled trial comparing EFT to CBT, imipramine (IMI) and placebo medication (PLA). Subjects were 122 individuals who met structured interview DSM III-R criteria for Panic Disorder with no more than mild Agoraphobia. Subjects received either EFT (n = 30), CBT (n = 36), IMI (n = 22) or Placebo (n = 24) for approximately 11 weekly acute and 6 monthly maintenance sessions. Primary outcome measures were the Panic Disorder Severity Scale and the Anxiety Sensitivity Index. Results indicated higher rate of treatment completion of EFT subjects. However, change on both PDSS and Anxiety Sensitivity scales was significantly less than for either CBT or IMI and not different from placebo medication. We conclude that EFT is a highly credible treatment for Panic Disorder, that does not provide efficacious treatment for panic symptoms.

NR728 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Relationships Between Creativity and Temperament in Bipolar Disorder Patients and Healthy Controls

Connie M. Strong, M.S., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723;* Claudia M. Santosa, M.A., Nadia Sachs, M.Eng., Courtney M. Rennicke, B.A., Po W. Wang, M.D., Anne-Marie Hier, M.S.W., Terence A. Ketter, M.D.

Summary:

Objective: To explore relationships between creativity and temperament.

Method: Euthymic bipolar disorder patients (mean age: 35.3 ± 10.6, 12M/20F) and healthy controls (mean age: 35.5 ± 14.8, 12M/20F) were administered Creative Personality Scale of the Adjective Check List (CPS-ACL), Barron-Welsh Art Scale (BWAS), and Torrance Test of Creative Thinking, Verbal (TTCT-V) and Figural (TTCT-F) creativity ratings; and NEO Personality Inventory (NEO PI-R), Cloninger's Temperament and Character Inventory (TCI), and Akiskal's Affective Temperament Scale (ATS).

Results: Controlling for age, gender, and diagnosis effects, CPS-ACL correlated with Openness (NEO-O) ($r = .604$); Novelty Seeking (TCI-NS) ($r = .480$), and Hyperthymia (ATS-H) ($r = 0.293$); and BWAS correlated with Neuroticism (NEO-N) ($r = 0.230$). Controlling for age and gender effects, TTCT-V correlated negatively with Agreeableness (NEO-A) ($r = -.518$), and positively with irritability (ATS-I) ($r = 0.475$) for controls but not patients.

Conclusion: Independent of bipolar disorder, CPS-ACL was most closely related to NEO-O, consistent with prior studies; and BWAS was modestly related to NEO-N. In controls only, TTCT-V was related to the negative traits of disagreeableness (negative of NEO-A) and irritability (ATS-I).

NR729 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Aging and Creativity in Bipolar Disorder

Claudia M. Santosa, M.A., *Department of Psychiatry, Stanford University, 401 Quarry Road, Rm 2116B, Stanford, CA 94305-5723;* Nadia Sachs, M.Eng., Connie M. Strong, M.S., Courtney M. Rennicke, B.A., Anne-Marie Hier, M.S.W., Po W. Wang, M.D., Terence A. Ketter, M.D.

Summary:

Objective: We recently found bipolar disorder patients compared to healthy controls had enhanced creativity on the Barron-Welsh Art Scale (BWAS), but not the Creative Personality Scale of the Adjective Check List (CPS-ACL), or the Torrance Test of Creative Thinking, Figural (TTCT-F) and Verbal (TTCT-V) versions. BWAS scores decline with age in the general population. We explored creativity and aging-creativity interactions in an expanded sample.

Method: Euthymic bipolar disorder patients (mean age: 35.3 ± 10.6, 12M/20F) and healthy controls (mean age: 35.5 ± 14.8, 12M/20F) were administered creativity ratings.

Results: Bipolar disorder patients had higher BWAS (28.4 ± 12.2 versus 18.9 ± 10.1, $p = 0.001$), but similar CPS-ACL, TTCT-F and TTCT-V scores. Age correlated negatively with BWAS in controls ($r = -0.56$, $p < 0.002$) but not patients, and positively with TTCT-F in patients ($r = 0.46$, $p = 0.01$) but not controls.

Conclusion: BWAS scores were 50% higher in patients than controls, and decreased with age in controls but not patients. TTCT-F scores improved with age in patients but not controls. Hence, a more benign aging effect may contribute to enhanced creativity in patients.

NR730 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Prevalence of Depressive Disorders Among Women with Disability

Vincent A. Campbell, Ph.D. *Environmental Health Dept., CDC, 4770 Buford Highway, NE, MSF29, Atlanta, GA 30341;* Daniel P. Chapman, Ph.D.

Summary:

Previous research assessing the relationship between disability and depression among women has largely been confined to examination of specific conditions in clinical populations. In this study, we analyzed population data from the National Health Interview Survey Disability Supplement Phase 1, a probability sample household survey of health status in the U.S. civilian noninstitutionalized population (n = 56,222 women). Respondents were categorized as either unable to perform the major activity for their age group (i.e., attend school, work, keep house), limited in their major activity, limited in other activities (i.e., attend school, work, keep house), or as having no limitation. Respondents were asked if they frequently felt depressed or anxious; those who reported they had experienced depressed mood and loss of interest in almost all activities for at least two weeks in the previous year were categorized as having experienced major depression. A positive dose-response relationship emerged between degree of disability and both frequent depressive or anxiety symptoms and major depression. While only 3.0% of respondents with no limitations reported they were frequently depressed, 24.0% of those who were unable to perform a major activity reported frequent depression. These findings suggest the presence and severity of activity limitation may be important indicators of depressive disorders in women.

NR731 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Benzodiazepine Discontinuation Program: Two-Year Follow-Up

Jaap E. Couvee, M.S.C., *Medical Department, SB Farma BV, Jaagpad 1, 2280 GC Rijswijk, Netherlands;* Manuela A. Timmermans, M.A., Frans G. Zitman, Ph.D.

Summary:

Objective: To assess (re)use and reasons for (re)use of psychoactive medication after taking part in a benzodiazepine discontinuation program.

Method: Between August 1994 and September 1995 230 depressed patients with chronic benzodiazepine use in Dutch General practice took part in a discontinuation program. From March till June 1998 all medical records were reviewed, and GP's were interviewed. Follow-up was achieved for 207 pts (90%). Mean follow-up was 2.3 years (range: 29 days till 3 yrs).

Results: 13% of patients remained benzodiazepines free throughout the follow-up period. 45% were tapered off successfully but restarted after 220 days (range: 1–1111) on 6 mg (range 0.3–15 mg) of diazepam equivalents, 42% continued using benzodiazepines after the program. Of the total group 33% kept using benzodiazepines chronically. Main reasons of prescribing benzodiazepine were sleep disorder (30%), nervousness/anxiety (26%) or a combination of these two (21%). At the time of follow-up 32% of patients use a benzodiazepine. Important reasons for stopping benzodiazepine during follow-up was improvement (55%) or switch to other medication (23%).

112 (57%) patients used an antidepressant in 187 episodes. Main diagnosis for prescription was depression in 80% of cases. Average duration of antidepressant use was 353 days (1-1326 days). Mostly prescribed antidepressants were paroxetine (57%) and fluoxetine (19%). At the time of follow-up 29% used an antidepressant. Main reasons for stopping antidepressants were improvement (43%), deterioration of symptoms (30%) or adverse events (13%).

Ninety three (48%) of patients used a combination of a benzodiazepine and the antidepressant at some point in time. There was no difference in benzodiazepine use (dosage, duration) between patients who were or who weren't prescribed an antidepressant.

Conclusion: Two-third of depressed patients (n = 207) stopped using benzodiazepines chronically after taking part in a discontinuation program. Use of antidepressants seems to be independent of benzodiazepine use.

NR732 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Minority Patient Response to Physician Race and Nonverbal Behavior in Analogue Medical

Mara S. Arguette, Ph.D., *Department of Psychology, Lincoln University, 820 Chestnut Street, #310FH, Jefferson City, MO 65102-0029;* Kimberly M. Collins, Carlos A. Roberts

Summary:

Objective: This research experimentally investigates minority patient response to Black and White physicians. Specifically, are there obstacles to interracial communication and can the nonverbal styles of physicians facilitate communication?

Method: Seventy-nine minority patients, recruited from a university health center, each viewed one of four videotapes that varied in the race of the physician (Black or White) and the degree of nonverbal immediacy (high or low levels of eye contact, smiling, etc.). Patients then completed a questionnaire evaluating the videotape.

Results: Nonverbal immediacy of physicians increased patient recall, motivation to comply, and self-disclosure. Patient satisfaction with physicians showed an interaction between race and nonverbal behavior. When physicians displayed high nonverbal immediacy, patients were satisfied with both Black and White physicians. When physicians displayed low nonverbal immediacy, patients became less satisfied with White physicians, although evaluations of Black physicians were relatively unaffected.

Conclusions: Nonverbal immediacy had a strong positive effect on minority patient outcome regardless of the race of the physician, suggesting that physicians should strive to display nonverbal concern with patients. The satisfaction data suggest that minority patients are satisfied with Black physicians regardless of nonverbal behavior. However, White physicians may increase minority patient satisfaction by displaying nonverbal immediacy.

NR733 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Encounters
Psychological Barriers As Predictors of Antidepressant Adherence

JoAnne Sirey, Ph.D., *Geriatric Psychiatry Dept., NY Hospital/ Cornell University, 21 Bloomingdale Road, White Plains, NY*

10605-1504; Martha L. Bruce, Ph.D., Barnett S. Meyers, M.D., George S. Alexopoulos, M.D.

Summary:

Aim: Psychological barriers to treatment are obstacles that can disrupt the doctor-patient relationship and the course of care if not addressed. We examine the impact of barriers present at treatment initiation on medication adherence among a mixed age sample of outpatients with major depression.

Methods: A two-stage sampling design was used to identify outpatients with SCID diagnosed Major Depression seeking outpatient mental health treatment. New admissions (N = 134) who took a prescribed antidepressant medication for at least one week were administered instruments to assess perceived stigma, self-rated illness severity and patients' views of treatment. Three months later, patients were reinterviewed. Patients were classified as adherent or nonadherent based on patient self-report estimates of the number and frequency of missed doses.

Results: Among the mixed age group, medication adherence was predicted by lower perceived stigma (OR = .92, p = .05), higher self-rated illness severity (OR = 1.22, p = .05) being older than 60 years old (OR = 2.91, p = .04) and screening negative for personality pathology (OR = 0.32, p = .02).

Conclusions: Perceived stigma associated with mental illness and patients' views of the illness play important roles in undermining adherence to treatment for depression. Clinician attention to psychological barriers early in outpatient treatment may improve medication adherence, and ultimately, affect the course of illness.

NR734 Thursday, May 18, 12:00 p.m.-2:00 p.m.

The Doctor-Patient Relationship and the Willingness to Use Psychiatric Medications

Molly E. Tomlin, M.S., *Health Outcomes Department, Eli Lilly and Company, Lilly Corporate Center/DC 1850, Indianapolis, IN 46285;* Jack K. Martin, Ph.D., Bernice A. Pescosolido, Ph.D., Thomas W. Croghan, M.D., Keri Lubell, M.S., Ralph W. Swindle, M.D.

Summary:

Objective: Despite surveys on public trust in physicians and the Surgeon General's concern with mental health care barriers, we know relatively little about how Americans' attitudes toward doctors affect their willingness to use psychiatric medications. We analyze how four aspects of the doctor-patient relationship affect willingness—trust in personal physicians; concerns about the denial of necessary treatment; concerns about physician quality; and overall trust in physicians.

Method: Data come from the "Pressing Issues in Health and Medical Care Module" of the 1998 General Social Survey (GSS). The GSS is a nationally representative, face-to-face interview survey, conducted by the National Opinion Research Center, University of Chicago. The sampling design is based on randomly selected clusters (N = 1,387; response rate of 76.4%).

Results: Trust in the doctor-patient relationship and in the efficacy of psychiatric medications are high. However, the willingness to use them is much lower and trust in the doctor-patient relationship has little direct effect on likely use. Rather, trust in the doctor-patient relationship affects attitudes toward medication efficacy, which, in turn, strongly influences the willingness to use them.

Conclusions: Physicians have an important educational role regarding psychiatric medications, but the trust in the doctor-patient relationship appears to have little influence on willingness to use psychiatric medications.

NR735 Thursday, May 18, 12:00 p.m.-2:00 p.m.

DSM-IV Diagnoses and Data Deficiencies

Paul R. Miller, M.D., *2406 Astral Drive, Los Angeles, CA 90046*

Summary:

Objective: This study tests the hypothesis that *psychiatrists collect data that are deficient to meet DSM-IV requirements for the diagnoses that they make.*

Method: Diagnostic write-ups on 50 inpatient-subjects done by 35 experienced psychiatrists were scrutinized to find all references to the 72 criteria in DSM-IV algorithms necessary to assess six diagnostic groups (disorders of cognitive impairment, drug misuse, alcohol misuse, schizophrenia/psychoses, depression, mania).

Results: Analysis of the 50 write-ups found that they made on average 1.5 (75/50) diagnoses per subject, which were based on evaluating on average 23% (16.9/72) of necessary criteria. Only 43% (32/75) of the write-ups included enough *symptom criteria* (hallucinations, depression), and only 9% (7/75) included enough *general criteria* (duration and severity of illness, level of dysfunction) to meet DSM-IV requirements.

Conclusions: The results confirm the hypothesis. Limitations and implications regarding these findings are discussed.

NR736 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Data Deficiencies and Diagnostic Inaccuracies

Paul R. Miller, M.D., *2406 Astral Drive, Los Angeles, CA 90046*

Summary:

Objective: Psychiatrists use Initial Diagnostic Assessments (IDA, my acronym) as the traditional and standard method of first evaluation. This study tests the hypothesis that *psychiatrists who use IDAs frequently collect deficient data and consequently make inaccurate diagnoses.*

Method: 50 patient-subjects were first assessed by 35 experienced psychiatrists using IDAs, then re-assessed by myself using CADI (Computer Assisted Diagnostic Interview). CADI directs the collection of complete data—72 DSM-IV criteria are always evaluated to assess for six groups of disorders (cognitive impairment, drug misuse, alcohol misuse, schizophrenia/psychosis, depression, mania). A prior study found CADI's accuracy comparable to two "gold standards" (SCID-CV, Consensus Diagnosis).

Results: For the 50 IDA write-ups, only 64% (32/50) included enough *symptom criteria* and only 14% (7/50) included enough *general criteria* (duration of illness, intensity) to meet requirements of DSM-IV diagnostic algorithms. CADI evaluated 100% of both *symptom criteria* and *general criteria.* As a consequence of examining more criteria and finding many of them positive, CADI formulated a different diagnosis in 54% (27/50). CADI's different diagnoses were always more complex than IDAs' diagnoses.

Conclusions: These findings sustain the hypothesis.

NR737 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release in the Treatment of Stimulant-Responsive Adolescents

James J. Hudziak, M.D., *Department of Psychiatry, University of Vermont, Given Room B229, Burlington, VT 05405-0001;* Thor C. Bergersen, M.D., Larry Rudiger, Ph.D., Ben Marte, M.D., G. Scott Waterman, M.D., Joan Kemsley, B.S.

Summary:

Objective: To assess the efficacy, tolerability, and safety of bupropion sustained release in an open label trial for adolescents with ADHD who have been successfully treated with methylphenidate.

Methods: 16 subjects (14 male) aged 13 to 17, referred from outpatient pediatric and psychiatric settings, were screened with a semistructured DSM-IV interview. Methylphenidate was discontinued one day prior to the start of treatment with bupropion SR. After one week, dosage was increased from 150mg once to twice daily (a.m. and p.m.). Treatment continued for eight weeks except for two patients who discontinued at five and six weeks respectively. Patients were assessed using the Child Behavior Checklist, Teacher Report Form, Youth Self-Report, and Conners Self, Parent, and Teacher Rating Scales.

Results: Repeated measures t-tests revealed statistically significant improvements between first and final visits in the CBCL Attention Problems, $t(15) = 19.84$, $p < .001$, Aggression, $t(15) = 10.25$, $p = .006$, and Anxious/Depressed scales, $t(15) = 13.19$, $p = .002$. Total ADHD scores on the Conners Parent, $t(15) = 51$, $p < .001$, and Self Rating Scales, $t(15) = 5.29$, $p < .05$, were also significantly improved. Reported adverse effects were minimal, and did not result in study termination for any patients.

Conclusions: Bupropion SR is an effective and well-tolerated treatment for adolescents with ADHD. These data suggest that bupropion SR may more effectively treat some symptoms than methylphenidate.

NR738 Thursday, May 18, 12:00 p.m.-2:00 p.m.

Gaps in the Maintenance Antipsychotic Treatment of First-Admission Schizophrenia

Ramin Mojtabai, Ph.D., *Department of Psychiatry, Columbia University, 200 Haven Avenue, #6P, New York, NY 10033;* Evelyn Bromet, Ph.D., P. Joseph Gibson, Ph.D., Janet Lavelle, M.S., Nancy Sohler, M.P.H.

Summary:

Objective: To study the gaps in antipsychotic medication use in schizophrenia in the 1-year period following discharge from the first-admission.

Method: Data are from the Suffolk County Mental Health Project (SCMHP), an epidemiological follow-up study of consecutive first-admissions with psychosis from 12 psychiatric facilities in Suffolk County, NY. Of the 674 individuals recruited, 189 with DSM-IV schizophrenia completed the follow-up. Medication use was assessed by a review of medical records and interviews using a standardized protocol. Research team had no involvement in treatment decisions.

Results: Seven of the 189 had received no antipsychotic medication prior to discharge. This report focused on the 182 who had received such medication prior to discharge. Of these 63% experienced one or more gaps and 51% experienced gaps lasting 1 month or longer with an average duration of 204 days. Most gaps were patient-initiated and the most common single reason for stopping the medication was the feeling that it was not needed.

Conclusions: There is considerable discontinuity in antipsychotic treatments of schizophrenia in its early course with potential long-term effects. There is a need for interventions aiming to improve compliance with treatment in early stages of illness.

NR739 Thursday, May 18, 12:00 p.m.-2:00 p.m.

The S-Enatiomer of Citalopram (Lu 26-054): Cytochromes P450 Mediating Metabolism and Cytochrome Inhibitory Effects

David J. Greenblatt, M.D., *Department of Pharmacology, Tufts University, 136 Harrison Avenue, Boston, MA 2111;* Lisa L.G. Von Moltke, Richard I. Shader, M.D.

Summary:

Objective: To determine the metabolic profile and Cytochrome P450 (CYP) inhibitory capacity of S-citalopram (S-CT), the active enantiomer of racemic citalopram.

Methods: The sequential conversion of S-CT to S-monodesmethylcitalopram (S-DCT) and S-didesmethylcitalopram (S-DDCT), were studied *in vitro* using human liver microsomes (HLM) and heterologously expressed individual human CYPs.

Results: Biotransformation of S-CT to S-DCT was mediated by three human CYPs, with relative contributions as follows: CYP2C19, 37%; CYP3A4, 35%; CYP2D6, 28%. Biotransformation of S-DCT to S-DDCT, however, was mediated entirely by CYP2D6. S-CT, S-DCT, and S-DDCT were separately tested as potential inhibitors of CYPs in HLM. All were weak or negligible inhibitors of CYP2D6, CYP3A, CYP1A2, and CYP2E1. S-CT and S-DCT likewise weakly or negligibly inhibited CYP2C9 and CYP2C19. S-DDCT produced moderate inhibition of CYP2C9 (IC_{50} vs. tolbutamide: 26 μM) and CYP2C19 (IC_{50} vs. S-mephenytoin: 12 μM). However, these are probably clinically unimportant due to the low plasma levels of S-DDCT relative to the IC_{50} values.

Conclusions: Metabolism of S-CT is mediated by three CYPs, similar to the racemate. S-CT and its metabolites are unlikely to produce significant inhibition of human CYPs and therefore the probability of drug interactions by this mechanism is small.

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