AMERICAN PSYCHIATRIC ASSOCIATION

WASHINGTON, D C
MAY 10-16, 1986

PROGRAM
AND
PAPERS ON NEW RESEARCH

IN SUMMARY FORM

THE ONE HUNDRED AND THIRTY-NINTH
ANNUAL MEETING OF THE
AMERICAN PSYCHIATRIC ASSOCIATION

WASHINGTON, D.C.
MAY 10-16, 1986

Papers presented at New Research Sessions are not automatically the property of the American Journal of Psychiatry. Authors are free to submit them to the American Journal of Psychiatry, Hospital & Community Psychiatry, or another publication of their choice.

Monday, May 12, 1986, 12 noon–1:45 p.m.
New Research 1—Poster Session—Exhibit Hall B, Upper Level, Convention Center

NEW RESEARCH IN ANXIETY, EATING, PREMENSTRUAL, PERSONALITY, AND CHILDHOOD DISORDERS

Moderator: Peter S. Jensen, M.D.

NR1 A PRIMATE MODEL OF PANIC DISORDER
Gayle S. Paully, Ph.D., Steven Friedman, Ph.D., Leonard Rosenblum, Ph.D.

NR2 MRI STUDIES OF BENZODIAZEPINE RECEPTORS
Jeffrey A. Coffman, M.D., Charles Barfknecht, Ph.D., Norton Neff, Ph.D., William Hunter, M.D.

NR3 ANXIETY, PERFORMANCE, AND CEREBRAL BLOOD FLOW
Ruben C. Gur, M.D., Raquel E. Gur, M.D., Brett E. Skolnick, Susan S. Resnick, Ph.D., Walter D. Obrist, Ph.D., Martin Reivich

NR4 EPINEPHRINE INFUSION IN SOCIAL PHOBIA
Laszlo A. Papp, M.D., Jack M. Gorman, M.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D., Donald F. Klein, M.D.

NR5 PANIC DISORDER: THE SLEEP LACTATE INFUSION
Harold W. Koenigsberg, M.D., Charles Pollak, M.D., Timothy Sullivan, M.D.

NR6 LACTATE INFUSIONS: THE ROLE OF BASELINE ANXIETY
Deborah S. Cowley, M.D., Thomas S. Hyde, Ph.D., Stephen R. Dager, M.D., David L. Dunner, M.D.

NR7 NE HYPERACTIVITY ASSOCIATED WITH YOHIMBINE PANIC
Scott W. Woods, M.D., Wayne K. Goodman, M.D., Dennis S. Charney, M.D.

NR8 EFFECTS OF TWO BENZODIAZEPINES ON MEMORY AND EEG
Daniel W. Hommer, M.D., Wallace Mendelson, M.D., Herbert Weingartner, Ph.D.

NR9 3H-IMIPRAMINE BINDING IN PANIC AND ANXIETY DISORDERS
Lon S. Schneider, M.D., Dennis Munjack, M.D., James A. Severson, Ph.D., Ruby Palmer, R.N.

NR10 CLINICAL INTERACTIONS OF ALPRAZOLAM AND IMIPRAMINE
Barbara G. Wells, Pharm.D., R. Lee Evans, Pharm.D., Larry Ereshefsky, Pharm.D., Ann E. Richards, Pharm.D., Ray J. Townsend, Pharm.D., Edward J. Antal, Ph.D.

NR11 TRIAZOLAM: AMNESIA AND HYPEREXCITABLE EFFECTS
Anthony Kales, M.D., Antonio Vela-Bueno, M.D., Constantin R. Soldatos, M.D., Rocco L. Manfredi, M.D.

NR12 EFFECTS OF 5 HTP AND CLOMIPRAMINE IN ANXIETY
Rene Kahn, M.D., Herman G.M. Westenberg, Ph.D., Cristine G. Gispen-de Wied, M.D.

NR13 XANAX AND INDERAL IN PANIC AND PHOBIC OUTPATIENTS
C. Lewis Ravaris, M.D., Matthew J. Friedman, M.D., Peter J. Hauri, Ph.D.

NR14 TRAZODONE IN THE TREATMENT OF PANIC AGORAPHOBIA
Matig Mavissakalian, M.D., James Perel, Ph.D., Kathleen Bowler, R.N., Robert Dealy, M.D.

NR15 CLINICAL ANXIOSELECTIVE ACTIVITY OF GEPIRONE
Jerry M. Cott, Ph.D., Neil M. Kurtz, M.D., Donald S. Robinson, M.D., Davis L. Temple, Ph.D.

NR16 LONG-TERM EFFECTS OF EXPOSURE WITH AGORAPHOBICS
Iver Hand, M.D., Jorg Angenendt, Martina Fischer, Heidi Buttner-Westphal, Christa Maneke, Brigitte Friedrich

NR17 BEHAVIORAL THERAPY EFFICACY FOR PANIC
M. Katherine Shear, M.D., Gordon Ball, Ph.D., Bonnie Gitlin, M.S.W., Allen J. Frances, M.D.

NR18 INDICATION FOR CARBAMAZEPINE IN MENTAL DISORDERS
Dietrich Blumer, M.D., Mary Heilbronn, Ph.D., Jonathan M. Himmelhoch, M.D.

NR19 HETEROGENEITY, CO-EXISTENCE IN OBSESSIVE/COMPULSIVES
Steven A. Rasmussen, M.D., Ming T. Tsuang, M.D.

NR20 PET AND FLUORODEOXYGLUCOSE UPTAKE IN OBSESSIVE-COMPULSIVES
Lewis R. Baxter, Jr., M.D., Michael E. Phelps, Ph.D., John C. Mazziotta, M.D., Barry H. Guze, M.D., Carl E. Selin, M.S., Jeffrey M. Schwartz, M.D.

NR21 SPECIFIC ANTIOBSESSIONAL EFFECT OF CLOMIPRAMINE
Joseph Zohar, M.D., Thomas R. Insel, M.D., Ina S. Alterman, M.S., Edward A. Mueller, M.D., Dennis L. Murphy, M.D.

NR22 SEROTONIN, BULIMIA, AND MIGRAINE: RESULTS WITH MCPP
Timothy D. Brewerton, M.D., Edward A. Mueller, M.D., David T. George, M.D., Dennis L. Murphy, M.D., David C. Jimerson, M.D.

NR23 SLEEP ARCHITECTURE IN EATING DISORDER PATIENTS
Alan B. Levy, M.D., Katharine N. Dixon, M.D., Helmut S. Schmidt, M.D.

NR24 CLONIDINE CHALLENGE TEST IN BULIMIA
Allan S. Kaplan, M.D., Paul E. Garfinkel, M.D., Jerry J. Warsh, M.D., Gregory M. Brown, M.D.

NR25 NALTREXONE IN THE TREATMENT OF BULIMIA
Jeffrey M. Jonas, M.D., Mark S. Gold, M.D.

NR26 ALTERATIONS OF CSF, CRH, AND POMC IN ANOREXIA NERVOSA
Walter H. Kaye, M.D., Wade H. Berrettini, M.D., Harry E. Gwirtsman, M.D., Ted George, M.D., David C. Jimerson, M.D., Philip W. Gold, M.D.

NR27 NORADRENERGIC DISTURBANCES IN NORMAL WEIGHT BULIMIA
Walter H. Kaye, M.D., Harry E. Gwirtsman, M.D., C. Raymond Lake, M.D., David T. George, M.D., David C. Jimerson, M.D., Michael H. Ebert, M.D.

NR28 BINGE–PURGE EPISODES INCREASE AMYLASE IN BULIMIA
Harry E. Gwirtsman, M.D., Walter H. Kaye, M.D., Nicholas W. Carosella, M.D., David T. George, M.D., David C. Jimerson, M.D.

NR29 PLASMA DEXAMETHASONE LEVELS AND THE DST IN BULIMIA
B. Timothy Walsh, M.D., David C. Lindy, M.D., Ee Sing Lo, Ph.D., Thomas Cooper, M.A., Steven P. Roose, M.D., Madeline Gladis, M.D., Sondra B. Dantzic, B.A., Alexander H. Glassman, M.D.

NR30 ANOREXIA NERVOSA AND OBLIGATE RUNNING
Pauline S. Powers, M.D., Douglas D. Schocken, M.D., Peter O. Knight, M.D., Jeffrey Feld, M.D., Jeffrey T. Smith, B.S.

NR31 PREMENSTRUAL DYSPHORIA ACCORDING TO DSM-III-R
Sally K. Severino, M.D., Stephen W. Hurt, Ph.D., Margaret Anderson, M.D., Nancy A. Williams, Ph.D.

NR32 PREMENSTRUAL CHANGES IN ANXIETY PATIENTS
Diana P. Sandberg, M.D., Abby J. Fyer, M.D., Jean Endicott, Ph.D.

NR33 PREMENSTRUAL SYNDROME AND PSYCHIATRIC DISORDERS
Stephen W. Hurt, Ph.D., Nancy A. Williams, Ph.D., Sally K. Severino, M.D., Margaret Anderson, M.D.

NR34 ABNORMAL GLUCOSE TOLERANCE TEST IN PMS: A PILOT STUDY
Lee W. Vliet, M.D.

NR35 PREMENSTRUAL SYNDROME AND GALACTORRHEA: A NEW ENTITY
Bruce J. Biller, M.D., John H. Brandt, M.D.

NR36 PREMENSTRUAL DYSPHORIA: DISORDER? GONADAL IMBALANCE?
Uriel Halbreich, M.D., Jean Endicott, Ph.D., Susanna Goldstein, M.D.

NR37 MASOCHISTIC PERSONALITY: DIAGNOSIS AND SEXIST BIAS
A. Kenneth Fuller, M.D., Roger K. Blashfield, Ph.D.

NR38 BORDERLINE AND NARCISSISTIC PERSONALITY DISORDERS
Eric M. Plakun, M.D., John P. Muller, Ph.D.

NR39 COMPARISON OF DSM-III PERSONALITY DISORDER MEASURES
James H. Reich, M.D., Russell Noyes, Jr., M.D., Ed Troughton, B.S.

NR40 CHILDREN'S PSYCHIATRIC SYMPTOM CATEGORIES
Marjorie McMeniman, Ph.D., Madelyn S. Gould, Ph.D., David Shaffer, M.B., Michael Rutter, M.D., Claire Sturge, M.B.

NR41 INFANT TEMPERAMENT AND INTELLIGENCE AT FOUR YEARS
Michel Maziade, M.D., Robert Cote, Ph.D., Pierrette Boutin, M.Ps., Hugues Bernier, M.Ss., Jacques Thivierge, M.D.

NR42 DECREASED IMIPRAMINE BINDING IN CHILD AGGRESSION
David Behar, M.D., David Stoff, Ph.D., Leafy Pollock, Ph.D., Benedetto Vitiello, M.D., David Yee, M.S., Wagner Bridger, M.D.

NR43 PSYCHOLOGICAL ASPECTS OF CHILDHOOD DEPRESSION
Margaret M. Rea, M.S., John Sweeney, Ph.D., J. John Mann, M.D.

NR44 PATTERNS OF ADOLESCENT RAPE
Sophia Vinogradov, M.D., Norman I. Dishotsky, M.D., Ann Doty, M.S., Jared R. Tinklenberg, M.D.

NR45 THE COMMUNICATION DEFICIT IN ASPERGER'S SYNDROME
G. Bartolucci, M.D., Peter Szatmari, M.D., Lester Krames, Ph.D., Gordon Flett, M.A.

NR46 INTELLIGENCE IN ADOLESCENT PSYCHOSIS
Terry E. Goldberg, Ph.D., Craig N. Karson, M.D., Jimmie P. Leleszi, D.O.

NR47 TREATMENT OF HYPERACTIVITY WITH PHENYLALANINE
Alan Zametkin, M.D., Judith L. Rapoport, M.D., Farouk Karoum, Ph.D.

NR48 CLINICAL OUTCOME AND THE DST IN DEPRESSED CHILDREN
Ronald A. Weller, M.D., Elizabeth B. Weller, M.D., Mary Fristad, Ph.D., Michael Cantwell, M.D.

NR49 CORTISOL SUPPRESSION MEASURES IN CHILDREN
Ronald A. Weller, M.D., Elizabeth B. Weller, M.D., Sheldon H. Preskorn, M.D., Mary Fristad, Ph.D., Michael Cantwell, M.D.

NR50 METHYLPHENIDATE AND INFORMATION PROCESSING DEFICIT
David L. Braff, M.D., Leighton Huey, M.D.

NR51 ELECTROCARDIOGRAM ABNORMALITIES AND PIMOZIDE
George Fulop, M.D., Robert Phillips, M.D., Arthur K. Shapiro, M.D., J. Anthony Gomes, M.D., Elaine Shapiro, Ph.D., Johanna W. Nordlie, M.A.

NR52 CHILD CUSTODY AND RELITIGATION IN RURAL SETTINGS
Bruce R. Berger, M.D., Sudhakar Madakasira, M.D., Vivian Roebuck, Kevin F. O'Brien, Ph.D.

NR53 SUICIDE BY CHILDREN: AN ANALYSIS OF 31 CASES
David N. Neubauer, M.D.

Tuesday, May 13, 1986, 9:00 a.m.–10:30 a.m.

New Research 2—Oral/Slide Session—Room 27, Lobby Level, Convention Center

NEW PSYCHOSOCIAL RESEARCH

Chp.: Stuart T. Hauser, M.D.
Co-Chp.: Minna R. Fyer, M.D.

NR54	REARING CONDITION AND RESPONSE TO ANXIOGENIC DRUG Thomas R. Insel, M.D., Maribeth Champoux, James M. Scanlan, Stephen J. Suomi, Ph.D.	9:00 a.m.
NR55	INPATIENT FAMILY INTERVENTION: A CONTROLLED STUDY Ira D. Glick, M.D., Gretchen L. Haas, Ph.D., James H. Spencer, M.D., John F. Clarkin, Ph.D., Alfred B. Lewis, M.D. Veronica Lestelle, M.S.W.	9:15 a.m.
NR56	FAMILY FUNCTIONING AND THE COURSE OF DEPRESSION Gabor I. Keitner, M.D., Ivan W. Miller, Ph.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D.	9:30 a.m.
NR57	SUICIDE ATTEMPTS BY SCHOOL-AGE ADOLESCENTS R. John Kinkel, Ph.D., Norma C. Josef, M.D., Charles W. Bailey, M.S.W.	9:45 a.m.
NR58	ADOLESCENT SUICIDAL BEHAVIOR: PRELIMINARY STUDY Jill M. Harkavy, Ph.D., Gregory M. Asnis, M.D.	10:00 a.m.
NR59	BIOLOGICAL MARKERS IN COGNITIVE AND PHARMACHOTHERAPY Gary D. Tollefson, M.D., Erhard Haus, M.D., Michael Garvey, M.D., Joan M. Piasecki, B.A., Steve Hollon, Ph.D.	10:15 a.m.

Tuesday, May 13, 1986, 12 noon–1:45 p.m.

New Research 3—Poster Session—Exhibit Hall B, Upper Level, Convention Center

NEW RESEARCH ON SUBSTANCE ABUSE, ORGANIC MENTAL SYNDROMES, AND OTHER TOPICS

Moderator: Charles A. Kaufmann, M.D.

NR60 ENHANCED TSH RESPONSE TO TRH IN SONS OF ALCOHOLICS
David T. George, M.D., Howard B. Moss, M.D., Sally Guthrie, Pharm.D., Jeannette Johnson, Ph.D., Markku Linnoila, M.D.

NR61 NEUROELECTRIC CORRELATES OF RISK FOR ALCOHOLISM
Allan Tasman, M.D., Sean J. O'Connor, M.D., Victor Hesselbrock, Ph.D.

NR62 **WITHDRAWN**

NR63 IDENTIFICATION OF SUBGROUPS AT RISK FOR ALCOHOLISM
V.E. Pollock, Ph.D., Sarnoff A. Mednick, Ph.D., William Gabrielli, Ph.D., Donald W. Goodwin, M.D.

NR64 CLONIDINE VERSUS CHLORDIAZEPOXIDE IN ALCOHOL WITDRAWAL
Gregory R. Baumgartner, M.D., Randall C. Rowen, Pharm.D., Martin R. Cohen, M.D.

NR65 RESPONSE TO CRF IN ALCOHOLICS FOLLOWING WITHDRAWAL
Bryon Adinoff, M.D., Peter R. Martin, M.D., George H.A. Bone, M.D., Markku Linnoila, M.D., Philip W. Gold, M.D.

NR66 MEMBRANE ADAPTATION IN ALCOHOLISM
Alan C. Swann, M.D., Edward L. Reilly, M.D., John E. Overall, Ph.D.

NR67 ANTIDEPRESSANT PHARMACOKINETICS IN ALCOHOLICS
Domenic A. Ciraulo, M.D., Jamie G. Barnhill, B.S., Harold G. Boxenbaum, Ph.D., Jerome H. Jaffe, M.D.

NR68 NEUROPSYCHOLOGICAL AND RCBF RECOVERY IN ALCOHOLISM
Kenneth M. Adams, Ph.D., Igor Grant, M.D., Michael Boyle, D.O., Bobbe Kelly, D.O., Robert Simkins, D.O.

NR69 IMIPRAMINE BLOCKADE OF COCAINE EUPHORIA
Jeffrey S. Rosecan, M.D., Donald F. Klein, M.D.

NR70 COCAINE DETOXIFICATION USING BROMOCRIPTINE
Irl L. Extein, M.D., David A. Gross, M.D., Mark S. Gold, M.D.

NR71 BROMOCRIPTINE TREATMENT FOR COCAINE CRAVING
Charles A. Dackis, M.D., Donald R. Sweeney, M.D., John Byron, B.S., Robert Climko, M.D., Mark S. Gold, M.D., A.L.C. Pottash, M.D.

NR72 COCAINE VERSUS MARIJUANA ABUSE IN ADOLESCENTS
Richard H. Schwartz, M.D., Mark S. Gold, M.D., Michael Lehrer, Ph.D., David M. Martin

NR73 EFFECTS OF COCAINE ON HUMAN CAUDATE D2 RECEPTORS
Godfrey Pearlson, M.D., Christopher A. Ross, M.D., Dean Wong, M.D., Marian Fischman, Ph.D., Henry N. Wagner, R. Foltin, M.D.

NR74 PSYCHIATRIC EFFECTS OF FOUR HOUR INFUSIONS OF COCAINE
Michael Sherer, M.D., Karen Kumor, M.D., Jose DeBorja, B.A., Edward Cone, Ph.D., Loren Thompson, Ph.D., Jerome Jaffe, M.D.

NR75 DEPRESSED OPIATE ADDICTS: DIAGNOSIS AND TREATMENT
Steven L. Batki, M.D., Michael Rowbotham, M.D., James L. Sorensen, Ph.D., Scott M. Wheeler, M.A., Kathy Brennan, M.A., Reese T. Jones, M.D.

NR76 OPIUM ADDICTION AND DETOXIFICATION OF HMONG REFUGEES
Anthony G. Troiano, M.D., James A. Halikas, M.D., Joseph Westermeyer, M.D., Marvin Seppala, M.D., Christian Schmidt, MS3

NR77 PCP RECEPTOR CHANGES AFTER PSYCHOTROPIC MEDICATION
James C. Byrd, III, M.D., Victor Bykov, Richard B. Rothman, M.D.

NR78 INPATIENT VERSUS OUTPATIENT DETOXIFICATION
Arthur I. Alterman, Ph.D., Motoi Hayashida, M.D., Charles P. O'Brien, M.D., Edward Foulks, M.D.

NR79 EFFECT OF TRIHEXIPHENADYL ON EMOTIONAL STATE
Lawrence Plon, Pharm.D., Daniel E. Bates, Ph.D., Richard D. Danson, M.D.

NR80 ADDICTOGENESIS: A PROSPECTIVE LONGITUDINAL STUDY
Lawrence J. Hatterer, M.D., Raymond De Biase, Ph.D.

NR81 HIPDM/SPECT IMAGES IN ALZHEIMER PATIENTS OVER TIME
Hugh C. Hendrie, M.B., Henry N. Wellman, M.D., Martin R. Farlow, M.D., Kathleen S. Hall, Ph.D., Harry M. Brittain, Marian K. DeMyer, M.D.

NR82 ALZHEIMER'S DIAGNOSTIC LABORATORY TEST
Frank P. Zemlan, Ph.D., Ole Thienhaus, M.D., David Bienenfeld, M.D., H. Bruce Bosmann, Ph.D.

NR83 CIRCADIAN ACTIVITY RHYTHMS IN GERIATRIC DEPRESSION
Martin H. Teicher, M.D., Janet Lawrence, M.D., Natacha I. Barber, Seth Finklestein, M.D., Harris Lieberman, Ph.D., Ross J. Baldessarini, M.D.

NR84 BRAIN ACETYLCHOLINE: A VIEW FROM THE CSF
Robert E. Becker, M.D., Ezio Giacobini, M.D., Roger Elble, M.D., J. Wesson Ashford, M.D., Kathy Sherman, Ph.D., Michael McIlhany, M.D., Jonathan Hess, Ph.D.

NR85 A DISSOCIATIVE SPECTRUM IN PSYCHIATRIC ILLNESS
Frank W. Putnam, M.D., Eva Bernstein, Ph.D.

NR86 CSF SOMATOSTATIN IN DEMENTIA AND DEPRESSION
Trey Sunderland, M.D., David R. Rubinow, M.D., Pierre N. Tariot, M.D., Paul A. Newhouse, M.D., Alan M. Mellow, M.D., Edward A. Mueller, M.D., Robert M. Cohen, M.D., Dennis L. Murphy, M.D.

NR87 ABSENCE OF CORTISOL RESPONSE TO NALTREXONE IN ALZHEIMER'S DISEASE
Nunzio Pomara, M.D., Michael Stanley, Ph.D., H. Benjamin Rhiew, M.D., Matthew P. Galloway, Ph.D., Karl Verebey, Ph.D., Carol Tamminga, M.D.

NR88 LOW AND HIGH DOSE NALOXONE IN OLDER NORMALS
Michael Gross, M.D., Pierre N. Tariot, M.D., Trey Sunderland, M.D., Julie Welkowitz, B.A., Robert M. Cohen, M.D., Dennis L. Murphy, M.D.

NR89 L-DEPRENYL IN ALZHEIMER'S DISEASE
Pierre N. Tariot, M.D., Trey Sunderland, M.D., Dennis L. Murphy, M.D., Paul A. Newhouse, M.D., Edward A. Meuller, M.D., Robert M. Cohen, M.D.

NR90 INTRAVENTRICULAR BETHANECHOL FOR ALZHEIMER'S DISEASE
Stephen L. Read, M.D., John G. Frazee, M.D., Cheryll Smith, Ph.D., Jill Shapira, R.N., Jeffrey L. Cummings, M.D., Paul Satz, Ph.D.

NR91 A GENETIC STUDY OF DEMENTIA OF THE ALZHEIMER TYPE
Ronald L. Martin, M.D., Gretchen Gerteis, M.S., William F. Gabrielli, Jr., Ph.D.

NR92 EARLY SYMPTOMS IDENTIFY SUBGROUPS OF ALZHEIMER'S DISEASE
Joe E. Thornton, M.D., Helen D. Davies, R.N., Terry Miller, M.D., Jerome A. Yesavage, M.D., Philip A. Berger, M.D., Jared R. Tinklenberg, M.D.

NR93 BEHAVIORAL CHANGES IN MILD DEMENTIA (SDAT)
Eugene H. Rubin, M.D., John C. Morris, M.D., Martha Storandt, Ph.D., Leonard Berg, M.D.

NR94 PSYCHIATRIC CARE NEEDS SURVEY OF NURSING HOMES
Michael Reinstein, M.D., Ben Gierl, M.D., Lawrence Lazarus, M.D., Lynne Jones, R.N., Lionel Dredze, A.C.S.W., Linda Gaibel, M.S.W.

NR95 MENTAL DISORDER IN ELDERLY PUBLIC HOUSING SITES
Peter V. Rabins, M.D., Pamela Fischer, Ph.D., Sam Shapiro, B.A., Morton Kramer, Sc.D.

NR96 PRL REGULATION IN GERIATRIC DEPRESSION AND DEMENTIA
George S. Alexopoulos, M.D., Robert C. Young, M.D., Jacob Kream, Ph.D., Russel Barakat, M.D., Robert Abrams, M.D., Charles Shamoian, M.D.

NR97 CLINICAL PRESENTATION OF GERIATRIC DEPRESSION
George S. Alexopoulos, M.D., Robert Abrams, M.D., Robert C. Young, M.D., Charles A. Shamoian, M.D.

NR98 TRIMIPRAMINE VERSUS IMIPRAMINE IN THE ELDERLY
Eric C. Dessain, M.D., Jonathan O. Cole, M.D., Alan F. Schatzberg, M.D., Melinda Salomon

NR99 AGING INCREASES HPA DYSREGULATION IN DEPRESSIVES
John F. Greden, M.D., Dolores Tiongco, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., Joan Kotun, M.D.

NR100 GERIATRIC BORDERLINE PERSONALITY DISORDER
Vivian Blotnick-Pender, M.D., Charles Shamoian, M.D.

NR101 OMS SCREENING DEVICES
James J. Strain, M.D., George Fulop, M.D., Barry Ginsberg, M.D., Michael Robinson, M.D., Anthony Stern, M.D., Peter Charap, M.D., Francesca Gany, M.D.

NR102 MUSCARINIC BINDING IN TEMPORAL LOBE EPILEPTIC FOCI
Ana Hitri, Ph.D., Herman Flanigin, M.D., Gavin P. Reynolds, M.D.

NR103 EFFECT OF LITHIUM ON HUMAN STRIATAL D2 RECEPTORS
Christopher Ross, M.D., Godfrey D. Pearlson, M.D., Dean Wong, M.D., Henry W. Wagner, Robert F. Dannals, Ph.D., Johathan M. Links, Ph.D.

NR104 LITHIUM, SODIUM, AND A POSSIBLE ANTIKINDLING MECHANISM
Alan G. Mallinger, M.D., Israel Hanin, Ph.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Steven Knopf, B.S.

NR105 LITHIUM WITHDRAWAL EFFECT ON 5HTP CLONIDINE TESTS
Paul J. Goodnick, M.D., Annemarie Schlegel, R.N., Ronald R. Fieve, M.D.

NR106 LITHIUM AFFECTS BALANCE OF BRAIN RECEPTOR ACTIVITY
Robert H. Lenox, M.D., John Ellis, Ph.D., Daniel D. Hendley, Ph.D., Yigal H. Ehrlich, Ph.D.

NR107 LITHIUM EXTENDS SLEEP DEPRIVATION EFFECT IN DEPRESSION
Lewis R. Baxter, Jr., M.D., Edward H. Liston, M.D., Jeffrey M. Schwartz, M.D., Lori L. Altshuler, M.D., Jeffrey N. Wilkins, M.D., Steven Richeimer, M.D., Barry H. Guze, M.D.

NR108 INSOMNIA: VALIDATION OF SLEEP LABORATORY CRITERIA
E.O. Bixler, Ph.D., Anthony Kales, M.D., Joyce D. Kales, M.D., Rocco L. Manfredi, M.D., Roger J. Cadieux, M.D.

NR109 SINGLE-DOSE KINETICS OF FLUPHENAZINE DECANOATE
George M. Simpson, M.D., Kashinath Yadalam, M.D., Douglas P. Levinson, M.D., Mary Jeanne Stephanos, R.N., Thomas B. Cooper, M.A., E-S Lo, Ph.D.

NR110 PERSISTANT FLUPHENAZINE AFTER DECANOATE WITHDRAWAL
Michael J. Gitlin, M.D., David Fogelson, M.D., Keith Nuechterlein, Ph.D., Joanne MacKenzie, R.N., Kamal Midha, Ph.D.

NR111 DO NEUROLEPTIC BLOOD LEVELS HELP?
Joseph Zohar, M.D., Zecharia Shemesh, M.D., Robert H. Belmaker, M.D.

NR112 TARDIVE DYSKINESIA: CROSS-CULTURAL PREVALENCE RATES
Daniel E. Casey, M.D.

NR113 LONGITUDINAL ASSESSMENT OF INVOLUNTARY MOVEMENTS
Spyros J. Monopolis, M.D., Douglas Heinrichs, M.D., William T. Carpenter, Jr., M.D., Jerry Levine, M.D.

NR114 AN OBJECTIVE MEASURE OF AKATHISIA
Mohamed Sabaawi, M.D., Joseph H. Friedman, M.D., Richard L. Wagner, M.D., Thomas L. Kucharski, Ph.D., Farrel Klein, M.D.

NR115 NORADRENERGIC MECHANISMS IN AKATHESIA
Lenard A. Adler, M.D., Burt Angrist, M.D., Eric Peselow, M.D., June Corwin, Ph.D., John Rotrosen, M.D.

NR116 INFUSION PUMP ADMINISTRATION OF PSYCHOTROPIC DRUGS
Walter W. Winslow, M.D., Edward Reyes, Ph.D., Wayne Meyerowitz, M.D.

NR117 SELECTION BIAS IN PSYCHIATRIC RESEARCH
Ann E. Pulver, Sc.D., Paula Wolyniec, M.S., John McGrath, M.S., William T. Carpenter, Jr., M.D., Barton Childs, M.D.

NR118 CARBAMAZEPINE IN PTSD
Steven Lipper, M.D., Jonathan R.T. Davidson, M.D. Tana A. Grady, B.S., Jack Edinger, Ph.D., Elliott B. Hammett, M.D. Steven L. Mahorney, M.D., Jesse O. Cavenar, Jr., M.D.

Wednesday, May 14, 1986, 9:00 a.m.–10:30 a.m.

New Research 4—Oral/Slide Session—Room 27, Lobby Level, Convention Center

NEW RESEARCH ON AFFECTIVE DISORDERS

Chp.: Charles R. Lake, M.D.
Co-Chp.: Abby J. Fyer, M.D.

NR119	PROLACTIN IS ELEVATED IN SAD Frederick M. Jacobsen, M.D., David A. Sack, M.D., Thomas A. Wehr, M.D., Susan Rogers, R.N., Steven A. James, M.D., Norman E. Rosenthal, M.D.	9:00 a.m.
NR120	BRIGHT LIGHT TREATMENT OF WINTER DEPRESSION Robert L. Sack, M.D., Alfred J. Lewy, M.D., L. Stephen Miller, M.S., Tana M. Hoban, Ph.D.	9:15 a.m.
NR121	LIGHT THERAPY FOR SAD: DOSING REGIMENS Michael Terman, Ph.D., Frederic M. Quitkin, M.D., Jiuan S. Terman, Ph.D.	9:30 a.m.
NR122	TRANYLCYPROMINE VERSUS IMIPRAMINE IN MANIC DEPRESSION Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Alan G. Mallinger, M.D., Carilyn Z. Fuchs, Ph.D.	9:45 a.m.
NR123	BEAM IN MELANCHOLIA: VISUAL EVOKED POTENTIALS Russel G. Vasile, M.D., David M. Bear, M.D., Frank H. Duffy, M.D., Kerry Bloomingdale M.D., Leslie K. Serchuck, M.A., Joseph J. Schildkraut, M.D.	10:00 a.m.
NR124	D-TYPE SCORES AND RESPONSES TO ANTIDEPRESSANTS Joseph J. Schildkraut, M.D., Alan F. Schatzberg, M.D., John J. Mooney, M.D., Benjamin Gerson, M.D., Jacqueline A. Samson, Ph.D., Jonathan O. Cole, M.D.	10:15 a.m.

Wednesday, May 14, 1986, 12 noon–1:45 p.m.

New Research 5—Poster Session—Exhibit Hall B, Upper Level, Convention Center

NEW RESEARCH ON AFFECTIVE DISORDERS

Moderator: Susan J. Feister, M.D.

NR125 SLEEP AND CORTISOL IN ANERGIC BIPOLAR DEPRESSION
Michael E. Thase, M.D., Jonathan M. Himmelhoch, M.D., Alan G. Mallinger, M.D., David B. Jarrett, M.D., David J. Kupfer, M.D.

NR126 NUCLEAR MAGNETIC RESONANCE IN BIPOLAR DEPRESSION
Arnold Winston, M.D., Jesse Rosenthal, M.D., Larry Minkoff, Ph.D., Abbey Strauss, M.D.

NR127 A HIGH-RISK STUDY OF PRIMARY AFFECTIVE DISORDER
John I. Nurnberger, Jr., M.D., Joel Hamovit, M.S.W., Euthymia Hibbs, Ph.D., Juliet Guroff, B.A., Elliot Gershon, M.D.

NR128 BIPOLAR II FAMILY PATTERNS: A DIFFICULT CONDITION
Janice A. Egeland, Ph.D., Jean Endicott, Ph.D.

NR129 RECONCILING BIPOLAR DISORDER WITH MENDEL'S LAWS
Susan E. Folstein, M.D., J. Raymond DePaulo, Jr., M.D., Elsa Correa, M.D., Jeanne O. Gayle

NR130 DIVORCE, DEPRESSION, AND IMMUNE FUNCTION
Janice Kiecolt-Glaser, Ph.D., Laura Fisher, B.S., Paula Ogrocki, B.S., Julie Stout, B.S., Carl Speicher, M.D., Ronald Glaser, Ph.D.

NR131 SOFT NEUROLOGICAL SIGNS AT AGE 7 AND DEPRESSION AT 20
Nigel M. Bark, M.B., Mark Davies, M.P.H.

NR132 THE NATURE OF COGNITIVE CONSTRICTION IN DEPRESSION
Kenneth R. Silk, M.D., Karen Saakvitne, M.A., Naomi Lohr, Ph.D., Kevin Kerber, M.D., Drew Westen, Ph.D., Margaret C. Buttenheim, Ph.D.

NR133 RESERPINE AUGMENTATION IN REFRACTORY MELANCHOLIA
Lawrence H. Price, M.D., Dennis S. Charney, M.D., George R. Heninger, M.D.

NR134 WHITE LIGHT IN SEASONAL DEPRESSIVES AND CONTROLS
Andreas C. Schmid, M.D., Anna Wirz-Justice, Ph.D., Peter Graw, Ph.D., Kurt Kraeuchi, M.S., Hans-Ueli Fisch, M.D., Claus Buddeberg, M.D.

NR135 DEPRESSION: EEG ABNORMALITIES AND CLINICAL OUTCOME
Alan G. Mallinger, M.D., David J. Kupfer, M.D., Jonathan M. Himmelhoch, M.D., Ellen Frank, Ph.D., Victoria J. Grochocinski, Ph.D.

NR136 BRAIN WATER CONTENT IN DEPRESSION: A MRI STUDY
Thomas A. Kent, M.D., Eugenio C. Amparo, M.D., Raleigh F. Johnson, Jr., Ph.D., Adel Wassef, M.D., Robert M. Rose, M.D.

NR137 CBF IMAGING IN PSYCHIATRY WITH T1-201DDC AND SPECT
Barbara H. Byse, M.D., Thomas C. Hill, M.D., J.F. de Bruine, M.D., Russell Vasile, M.D., Eric A. van Royen, M.D.

NR138 STEROID-CATECHOLAMINE INTERACTIONS IN DEPRESSION
Owen M. Wolkowitz, M.D., Allen R. Doran, M.D., Alan Breier, M.D., David Jimerson, M.D., Rodrigo Labarca, M.D., Steven M. Paul, M.D., David Pickar, M.D.

NR139 AGE-RELATED IMMUNE CHANGES IN DEPRESSION
Steven J. Schleifer, M.D., Steven E. Keller, Ph.D., Jacob Cohen, Ph.D., Marvin Stein, M.D.

NR140 HEALTH OUTCOMES, IMMUNE STATUS, AND DEPRESSION
Marcia L. Daniels, M.D., Michael Irwin, M.D., Herbert Weiner, M.D.

NR141 OLFACTION IN DEPRESSION AND RECOVERY: A NEW MARKER
Stephen C. Suffin, M.D., Michael Gitlin, M.D.

NR142 OLFACTORY RECOGNITION AND MOOD IN MAJOR DEPRESSION
Paul J. Moberg, M.A., Godfrey D. Pearlson, M.D., Lynn J. Speedie, Ph.D., John R. Lipsey, M.D., J. Raymond DePaulo, M.D.

NR143 PSYCHOBIOLOGY OF SLEEP ONSET REM PERIODS
James E. Shipley, M.D., Anand Kumar, M.D., Alan Eiser, Ph.D., Michael Feinberg, M.D., Pamela Flegel, B.S., John F. Greden, M.D.

NR144 THE EFFECT OF DMI AND 2-OH DMI ON NK CELL ACTIVITY
Andrew H. Miller, M.D., Gregory M. Asnis, M.D., Herman van Praag, M.D., Allen J. Norin, Ph.D.

NR145 MELATONIN AND NORMAL SLEEP
Steven P. James, M.D., Wallace B. Mendelson, M.D., David A. Sack, M.D., Norman E. Rosenthal, M.D., Mary Lou Burch-Lien, R.N., Thomas A. Wehr, M.D.

NR146 MELATONIN AND MAO INHIBITORS
Gregory F. Oxenkrug, M.D., Roy B. McCauley, Ph.D., Iain M. McIntyre, Ph.D., Richard Balon, M.D., Anil K. Jain, M.D., Arthur Yuwiler, Ph.D.

NR147 GH RESPONSE TO LEVODOPA AND PROPANOLOL IN PSYCHIATRIC PATIENTS
Patrick Rogue, M.D., Fabrice Duval, M.D., Marc-Antoine Crocq, Jean-Paul Macher, Madame Francois Fleck, Madame J. Gindein

NR148 PITUITARY RESPONSIVITY TO TRH: CLINICAL STUDIES
James C. Garbutt, M.D., James P. Mayo, Jr., M.D., Arthur J. Prange, Jr., M.D., George A. Mason, Ph.D., Gregory M. Gillette, M.D.

NR149 IN VITRO GLUCOCORTICOID SENSITIVITY IN DEPRESSION
Anthony T. Reder, M.D., Martin T. Lowy, Ph.D., Jack P. Antel, M.D., Herbert Y. Meltzer, M.D.

NR150 ANTIBODIES TO EPSTEIN-BARR VIRUS IN DEPRESSION
Jay D. Amsterdam, M.D., Werner Henle, M.D., Owen Walkowitz, M.D., Andrew Winokur, M.D., Steven M. Paul, M.D.

NR151 ACTH TEST IN DEPRESSION BEFORE AND AFTER TREATMENT
Jay D. Amsterdam, M.D., Gregory Maislin, M.S., Ellen Abelman, B.A., Marian Droba, M.D., Andrew Winokur, M.D.

NR152 ACTH AND CORTISOL DISSOCIATION IN DEPRESSION
K. Ranga Rama Krishnan, M.B., James C. Ritchie, MPH, Ananth N. Manepalli, M.D., Randal D. France, M.D., Charles B. Nemeroff, M.D., Bernard J. Carroll, M.D.

NR153 GRH STIMULATION TEST IN DEPRESSION
K. Ranga Rama Krishnan, M.B., Ananth N. Manepalli, M.D., James C. Ritchie, MPH, Krishnaiah Rayasam, M.D., Jean Rivier, Wiley Vale, M.D., Michael Thorner, M.D., Charles B. Nemeroff, M.D.

NR154 CLINICAL UTILITY OF URINARY MHPG
Arnold L. Lieber, M.D.

NR155 SEVERITY OF DEPRESSION AND MULTIPLE HPA MEASURES
James H. Meador-Woodruff, M.D., Roger F. Haskett, M.D. Huda Akil, Ph.D., Stanley J. Watson, M.D., Leon Grunhaus, M.D., John F. Greden, M.D.

NR156 THE DST AND PHASES OF DIAGNOSTIC MARKER RESEARCH
Andrew A. Nierenberg, M.D.

NR157 SEROTONERGIC ACTIVITY AND DRUG-INDUCED MYOCLONUS
James R. Merikangas, M.D., Kathleen R. Merikangas, Ph.D., Jonathan M. Himmelhoch, M.D.

NR158 MHPG, MAO, AND CONTROL BELIEFS IN DEPRESSIONS
Jacqueline Samson, Ph.D., Stuart Hauser, M.D., Steven Mirin M.D., David Borelli, M.D., Benjamin Gerson, M.D., Joseph J. Schildkraut, M.D.

NR159 NEUROBIOLOGY OF HUMAN LEARNED HELPLESSNESS
Alan Breier, M.D., Margot Albus, M.D., Theodore P. Zahn, Ph.D., David Pickar, M.D., Owen M. Wolkowitz, M.D., Steven M. Paul, M.D.

NR160 NORADRENERGIC INDICES IN REMITTED DEPRESSIVES
Larry J. Siever, M.D., Emil Coccaro, M.D., Oren Kalus, M.D., Karen Rubinstein, M.Ed., Kenneth L. Davis, M.D.

NR161 AUTOIMMUNE THYROIDITIS IN FEMALE DEPRESSIVES
Victor I. Reus, M.D., Jeffrey L. Berlant, M.D., Maurice Galante, M.D., Nathan Becker, M.D.

NR162 5HT UPTAKE EFFECT OF ANTIDEPRESSANT WITHDRAWAL
Jeffrey L. Rausch, M.D., S.C. Risch, M.D., David S. Janowsky, M.D., Lewis L. Judd, M.D.

NR163 CSF, CRH, AND PLASMA ACTH LEVELS IN DEPRESSION
Alec Roy, M.B., David Pickar, M.D., Steven M. Paul, M.D., Markku Linnoila, M.D., Allen Doran, M.D., Philip Gold, M.D.

NR164 ADRENERGIC RESPONSIVENESS IN ENDOGENOUS DEPRESSION
J. John Mann, M.D., Richard P. Brown, M.D., James P. Halper, M.D., John A. Sweeney, Ph.D., James H. Kocsis, M.D.

NR165 POSTRECEPTOR REGULATION OF ADENYLATE CYCLASE BY NE
John J. Mooney, M.D., Joseph J. Schildkraut, M.D., Alan F. Schatzberg, M.D., Benjamin Gerson, M.D., Kathleen Pappalardo, B.S., Jonathan O. Cole, M.D.

NR166 DIMINISHED SEROTONERGIC FUNCTION IN DEPRESSION
Robert N. Golden, M.D., John Hsiao, M.D., Susan Rogers, R.N., Matthew V. Rudorfer, M.D., William Z. Potter, M.D.

NR167 5-HT IN AFFECTIVE AND PERSONALITY DISORDERS
Emil F. Coccaro, M.D., Larry J. Siever, M.D., Howard Klar, M.D., Karen Rubinstein, M.Ed., Andrea Moskovitz, R.N., Kenneth L. Davis, M.D.

NR168 FLUOXETINE ALTERS BETA-ADRENERGIC, 5HT1, AND 5HT2 RECEPTORS
William F. Byerley, M.D., James K. Wamsley, Ph.D., Tyler McCabe, B.A., Elizabeth McConnell, B.S., Fred W. Reimherr, M.D., Bernard I. Grosser, M.D.

NR169 EFFECT OF AGE ON MEASURES OF SEROTONERGIC FUNCTION
P. Anne McBride, M.D., J. John Mann, M.D., Michael DeMeo, M.D., Jacob Kream, Ph.D., George Anderson, Ph.D., Amy Wiley, B.S.

NR170 URINARY FREE CORTISOL IN PSYCHOTIC DEPRESSION
Raymond F. Anton, M.D.

NR171 MILITARY INDUCTION CAN CAUSE DST NON-SUPPRESSION
Mihaly Arato, M.D., Istvan Magyar, M.D., Hedi Lukacs, M.D., Laszlo Mod, M.D., Antal Alfoldi, M.D.

NR172 EFFECTS OF DEPRESSIVE SYMPTOMS ON HPA FUNCTION
Richard P. Brown, M.D., Peter M. Stoll, Peter E. Stokes, M.D., Allen J. Frances, M.D., John A. Sweeney, Ph.D., James H. Kocsis, M.D., J. John Mann, M.D.

NR173 MELATONIN RELATED TO DEPRESSED MOOD AND PSYCHOSIS
Richard P. Brown, M.D., James H. Kocsis, M.D. Stanley Caroff, M.D., Jay D. Amsterdam, M.D., Andrew Winokur, M.D., Peter E. Stokes, M.D., Alan Frazer, Ph.D.

NR174 DOES SEVERITY EXPLAIN MELANCHOLIA? A DST VALIDATION
John F. Greden, M.D., Roger Haskett, M.D., Leon Grunhaus, M.D., Hans Bendz, M.D., Pamela Flegel

NR175 THE DST IN THE LEARNED HELPLESSNESS PARADIGM
John L. Haracz, M.D., Thomas Minor, Ph.D., Jeffery N. Wilkins, M.D., Emery G. Zimmermann, M.D.

NR176 PLASMA DEXAMETHASONE LEVEL AND CORTISOL RESPONSE
Peter E. Stokes, M.D., Betty J. Lasley, Ph.D., Carolyn R. Sikes, M.A., Peter M. Stoll, B.A.

NR177 SERUM DEXAMETHASONE LEVELS AND THE DST
Martin T. Lowy, Ph.D., Anthony T. Reder, M.D., Jack P. Antel, M.D., Herbert Y. Meltzer, M.D.

NR178 DESIPRAMINE DOES NOT CAUSE WEIGHT GAIN
Stephen L. Stern, M.D., Thomas B. Cooper, M.A., Mark Johnson, Ph.D., Bruce Jones, M.D., Linda Nelson, Ph.D.

NR179 ANTIDEPRESSANT PLASMA LEVELS AND DOSE PREDICTION
Sudhakar Madakasira, M.D., David A. Ames, M.D., Prabhaker G. Khazanie, Ph.D.

NR180 TRICYCLICS AND CARDIAC CONDUCTION DISEASE
Steven P. Roose, M.D., Alexander H. Glassman, M.D., Elsa G.V. Giardina, M.D., B. Timothy Walsh, M.D., Sally Woodring, R.N., J. Thomas Bigger, Jr., M.D.

NR181 NORTRIPTYLINE IN PATIENTS WITH HEART FAILURE
Steven P. Roose, M.D., Alexander H. Glassman, M.D., Elsa G.V. Giardina, M.D., B. Timothy Walsh, M.D., Sally Woodring, R.N., Lynne L. Johnson, M.D.

NR182 TCA ALONE CAN BE EFFECTIVE IN PSYCHOTIC DEPRESSION
Henry A. Nasrallah, M.D., William H. Coryell, M.D., Mona McCalley-Whitters, M.A., Mark Zimmerman, M.D.

NR183 FAILURE OF T3 TO POTENTIATE TRICYCLIC RESPONSE
Michael J. Gitlin, M.D., Herbert Weiner, M.D., Lynn Fairbanks, Ph.D.

NR184 THE EFFECT OF ECT ON ENDORPHINS IN DEPRESSION
A. Missagh Ghadirian, M.D., Christina Gianoulakis, Ph.D., N.P. Vasavan Nair, M.D.

NR185 WITHDRAWN

NR186 NEUROENDOCRINE RESPONSES TO ECT
Richard D. Weiner, M.D., C. Edward Coffey, M.D., James C. Ritchie, M.P.H., Jonathan R.T. Davidson, M.B., K. Ranga Rama Krishnan, M.B.

NR187 UNILATERAL VERSUS BILATERAL ECT IN MELANCHOLIA
Rajiv Tandon, M.D., Leon Grunhaus, M.D., Tina Krugler, John F. Greden, M.D.

NR188 CARROLL AND HAMILTON RATING SCALES FOR DEPRESSION
Rajiv Tandon, M.D., Pamela Flegel, B.S., John F. Greden, M.D.

NR189 BIOCHEMICAL EFFECTS OF ECT VERSUS ANTIDEPRESSANT DRUGS
Matthew V. Rudorfer, M.D., John K. Hsiao, M.D., Emile D. Risby, M.D., Markku Linnoila, M.D., William Z. Potter, M.D.

NR190 ECT IN SUBCORTICAL ARTERIOSCLEROTIC ENCEPHALOPATHY
C. Edward Coffey, M.D., Phillip Hinkle, M.D., Richard D. Weiner, M.D., Charles B. Nemeroff, M.D., K. Ranga Rama Krishnan, M.B., Indu Varia, M.D., Burton P. Drayer, M.D.

NR191 AUGMENTATION OF ECT SEIZURES WITH CAFFEINE
C. Edward Coffey, M.D., Phillip Hinkle, M.D., Richard D. Weiner, M.D., Martha Cress, R.N.

NR192 EEG IMAGING IN PSYCHIATRY: ARTIFACT CONSIDERATIONS
Michael W. Torello, Ph.D., Henry A. Nasrallah, M.D.

Thursday, May 15, 1986, 9:00 a.m.–10:30 a.m.

New Research 6—Oral/Slide Session—Room 27, Lobby Level, Convention Center

NEW RESEARCH ON SCHIZOPHRENIA

Chp.: Llewellyn B. Bigelow, M.D.
Co-Chp.: Charles A. Kaufmann, M.D.

NR193	ANIMAL MODELS OF SENSORY GATING AND SCHIZOPHRENIA David L. Braff, M.D., Neal Swerdlow, M.D., Mark A. Geyer, Ph.D., George Koob, Ph.D.	9:00 a.m.
NR194	EVOKED POTENTIAL AND BRAIN METABOLISM CORRELATIONS Henry H. Holcomb, M.D., William E. Semple, Ph.D., Monte S. Buchsbaum, M.D., Robert M. Cohen, M.D., Lynn E. DeLisi, M.D., Anna C. King	9:15 a.m.
NR195	UNDERRECOGNITION OF NEUROLEPTIC MOVEMENT DISORDER Peter J. Weiden, M.D., Gretchen Haas, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Marlin Mattson, M.D.	9:30 a.m.
NR196	TD PREVALENCE: RESEARCH AND CLINICAL DIFFERENCES Thomas E. Hansen, M.D., Daniel E. Casey, M.D., Ronald M. Weigel, Ph.D.	9:45 a.m.
NR197	RUBIDIUM AND NEUROLEPTIC DOSAGE REDUCTION Guy Chouinard, M.D., Lawrence Annable, B.Sc., Pierre Mercier, Ph.D., Luc Turnier, M.D.	10:00 a.m.
NR198	ANDROGYNY IN SCHIZOPHRENIA: MRI EVIDENCE Henry A. Nasrallah, M.D., Nancy C. Andreasen, M.D., Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D., Val D. Dunn, M.D., James C. Ehrhardt, Ph.D.	10:15 a.m.

Thursday, May 15, 1986, 12 noon–1:45 p.m.

New Research 7—Poster Session—Exhibit Hall B, Upper Level, Convention Center

NEW RESEARCH ON SCHIZOPHRENIA AND OTHER TOPICS

*Moderator:*Wendy J. Bernstein, M.D.

NR199 PET OF ACUTE AND CHRONIC SCHIZOPHRENICS (SCZ)
John M. Cleghorn, M.D., Edmund Stephen Garnett, M.B., Ronald D. Kaplan Ph.D., Janice Mitton, R.N., Peter Cook, M.D., Stanley W. Dermer, M.D.

NR200 SCHIZOPHRENIA AND INCREASED BASAL GANGLIA ACTIVITY
Susan M. Resnick, Ph.D., Raquel E. Gur M.D., Abass Alavi, M.D., Ruben C. Gur, Ph.D., Martin Reivich, M.D.

NR201 CEREBELLAR ATROPHY IN SCHIZOPHRENIA BY MRI METHODS
Jeffrey A. Coffman, M.D., Henry A. Nasrallah, M.D., Nancy C. Andreasen, M.D., Stephen C. Olson, M.D., Val D. Dunn, M.D., James Ehrhardt, Ph.D.

NR202 III VENTRICULAR ENLARGEMENT IN CHRONIC SCHIZOPHRENICS
Shigenobu Kanba, M.D., Satoru Shima, M.D., Yutaka Masuda, M.D., Taizo Tukumo, M.D., Toshinori Kitamura, M.D., Masahiro Asai, M.D.

NR203 VBR IN LATE ONSET SCHIZOPHRENIA (PARAPHRENIA)
Peter Rabins, M.D., Godfrey Pearlson, M.D., Jayaram Geetha, M.D., Cynthia Steel, R.N., Larry Tune, M.D.

NR204 EEG SPECTRA IN SCHIZOPHRENICS-TOPOGRAPHIC ANALYSIS
E. Michael Kahn, M.D., Richard D. Weiner, M.D., Richard Ulrich, M.S., Harold S. Kudler, M.D.

NR205 USING CEREBRAL LATERALITY TO SUBTYPE PSYCHOSIS
Bruce E. Wexler, M.D., Earl L. Giller, Jr., M.D.

NR206 ANOMALOUS MOTORIC DOMINANCE AND SCHIZOPHRENIA: CLINICAL IMPLICATIONS
Peter Hauser, M.D., Jane Hood, M.A., Craig Hudson, B.S., Mary Seeman, M.D.

NR207 NEGATIVE SCHIZOPHRENIC SYMPTOMS AND BRAIN DAMAGE
John A. Sweeney, Ph.D., John G. Keilp, M.A., Paul Jacobsen, Ph.D., Carla M. Solomon, Ph.D., Michael Deck, M.D., J. John Mann, M.D.

NR208 TRAIT AND STATE ATTENTION DEFICITS IN SCHIZOPHRENIA
David L. Braff, M.D.

NR209 EYE MOVEMENTS IN CHRONIC SCHIZOPHRENIC PATIENTS
Takuya Kojima, M.D., Steven G. Potkin, M.D., Mohammad Kharazmi, Eisuke Matsushima, M.D.

NR210 EYE TRACKING AND NUCLEAR SCHIZOPHRENIA
Carla M. Solomon, Ph.D., John A. Sweeney, Ph.D., J. John Mann, M.D.

NR211 TRAINING SCHIZOPHRENICS IN MEDICATION MANAGEMENT
Robert P. Liberman, M.D., Thad Eckman, Ph.D., Catherine C. Phipps, M.S.

NR212 TIASPIRONE IN TREATMENT OF SCHIZOPHRENIA
Anil Kumar Jain, M.D., Norman C. Moore, M.D., Elaine Meyendorff, M.D., Samuel Gershon, M.D.

NR213 STRESSFUL LIFE EVENTS AND SCHIZOPHRENIC RELAPSE
Joseph Ventura, M.A., Keith H. Nuechterlein, Ph.D., David Lukoff, Ph.D.

NR214 A PREVENTION PROGRAM FOR YOUNG SCHIZOPHRENICS
James J. Gange, Ph.D., Randall C. Jordan, M.D., Paul A. Schneider, Ph.D.

NR215 CHILDHOOD HEAD TRAUMA AND SCHIZOPHRENIA
James Wilcox, D.O., Henry A. Nasrallah, M.D.

NR216 GENDER DIFFERENCES IN SCHIZOPHRENIA
Karen K. Bardenstein, Ph.D., Thomas H. McGlashan, M.D.

NR217 WITHDRAWN

NR218 CHARACTERISTICS OF VERY POOR OUTCOME SCHIZOPHRENIA
Richard S.E. Keefe, B.A., Richard C. Mohs, Ph.D., Michael Davidson, M.D., Jeremy M. Silverman, M.A., Kenneth S. Kendler, M.D.

NR219 PROGNOSTIC SCALE FOR CHRONIC SCHIZOPHRENIA
Wayne S. Fenton, M.D., Thomas H. McGlashan, M.D.

NR220 SUSTAINED REMISSION IN DRUG-FREE SCHIZOPHRENICS
Wayne S. Fenton, M.D., Thomas H. McGlashan, M.D.

NR221 SINEMET CHALLENGE AND RELAPSE IN SCHIZOPHRENIA
Michael Davidson, M.D., Richard S.E. Keefe, B.A., Richard C. Mohs, Ph.D., Thomas B. Horvath, M.D., Kenneth L. Davis, M.D.

NR222 LYMPHOCYTE FUNCTION IN MANIA
Ziad Kronfol, M.D., J. Daniel House, Ph.D.

NR223 ECT IN MANIA: EFFICACY AND TREATMENT FREQUENCY
Steven D. Roth, M.D., D.P. Devanand, M.D., Sukdeb Mukherjee, M.D., Harold A. Sackeim, Ph.D., Carl Lee, M.D., Sidney Malitz, M.D.

NR224 THIOTHIXENE VERSUS CHLORPROMAZINE FOR ACUTE MANIA
Philip G. Janicak, M.D., David B. Bresnahan, M.D., John M. Davis, M.D., Charles Malinick, M.D., Rajiv Sharma, M.D., Joseph E. Comaty, M.S.

NR225 SCHIZOPHRENIA VERSUS MANIA: NEUROENDOCRINE DIFFERENCES
John Mason, M.D., Earl Giller, M.D., Thomas Kosten, M.D.

NR226 THE SCHIZOPHRENI FORM DIAGNOSIS: CONSTRUCT VALIDITY
J.A.E. Fleming, M.D., Tsung-yi Lin, M.D., Morton Beiser, M.D., William T. Iacono, Ph.D.

NR227 PREDICTING OUTCOME IN SCHIZOAFFECTIVE PSYCHOSIS
Paul V. Williams, M.D., Thomas H. McGlashan, M.D.

NR228 BIOLOGICAL STUDIES OF PARANOIA
Kenneth L. Davis, M.D., Bonnie M. Davis, M.D., Gordon Campbell, Ph.D., Richard C. Mohs, Ph.D., Michael Davidson, M.D., Thomas B. Horvath, M.D.

NR229 BIOGENETIC ASPECT OF BORDERLINES AND SCHIZOTYPALS
Howard Klar, M.D., Larry J. Siever, M.D., Emil F. Coccaro, M.D., Miklos Loconszy, M.D., Jeremy Silverman, M.A., Kenneth L. Davis, M.D.

NR230 SIGNIFICANCE OF BORDERLINE AND SCHIZOTYPAL OVERLAP
Eric M. Plakun, M.D., John P. Muller, Ph.D.

NR231 CLASSIFICATION OF PSYCHOSIS IN MARYLAND STATE HOSPITALS
Lawrence W. Adler, M.D., Ann E. Pulver, Sc.D., William T. Carpenter, Jr., M.D.

NR232 PET AND CLINICAL STATUS IN SCHIZOPHRENIA
Raquel E. Gur, M.D., Susan Resnick, Ph.D., Ruben C. Gur, Ph.D., Abass Alavi, M.D., Martin Reivich, M.D.

NR233 NEUROPSYCHOLOGIC DYSFUNCTION IN HTLV SEROPOSITIVES
Charles Silberstein, B.A., F. Patrick McKegney, M.D., Mary Alice O'Dowd, M.D., Peter A. Selwyn, M.D., Ernest Drucker, Ph.D., Gerry H. Friedland, M.D.

NR234 CORONARY BYPASS: DENIAL IMPROVES ADAPTATION
Arthur M. Freeman, III M.D., David G. Folks, M.D., Roberta S. Sokol, M.A.

NR235 THE CONSULTATION PSYCHOPATHOLOGY RATING SCALE
Penelope Krener, M.D., Mary Kay Simmons, M.S., Rebecca True, R.N.

NR236 DEVELOPMENT OF A NEW ALEXITHYMIA SCALE
R. Michael Bagby, Ph.D., Graeme Taylor, M.D., David Ryan, Ph.D.

NR237 WORK ON CORE THEME AS MEASURE OF CHANGE IN THERAPY
Dinko Podrug, M.D.

NR238 MASSACHUSETTS LAWS AND SECLUSION RATE CHANGES
Steven J. Spitz, M.D.

NR239 PATIENT PERCEPTIONS OF CIVIL COMMITMENT
Gail A. Edelsohn, M.D., Virginia Aldige Hiday, Ph.D., Jo Anne Earp, Sc.D., Gary A. Chase, Ph.D.

NR240 FACTORS INVOLVED IN A SUCCESSFUL INSANITY PLEA
Caryl E. Boehnert, Ph.D.

NR241 SUICIDE AND UNEMPLOYMENT IN CANADA
Isaac Sakinofsky, M.D., Professor Robin Roberts

NR242 SUICIDE AND VIOLENCE RISK IN PSYCHIATRIC PATIENTS
Robert Plutchik, Ph.D., Herman van Praag, M.D., Hope R. Conte, Ph.D.

NR243 OPERATIONAL CRITERIA FOR SUICIDE CLASSIFICATION
Lucy Davidson, M.D., Mark L. Rosenberg, M.D., Jack C. Smith, M.S.

NR244 UNTREATED SUICIDAL BEHAVIOR: SUBSTANCE ABUSERS
Deborah Hasin, M.S., Bridget Grant, Ph.D., Jody Weinflash, M.P.H.

NR245 SUICIDE IN BORDERLINE PERSONALITY DISORDER
Minna R. Fyer, M.D., Allen J. Frances, M.D., Timothy Sullivan, M.D., Steven Hurt, Ph.D., John F. Clarkin, Ph.D.

NR246 NEUROLEPTIC DOSE ADJUSTMENT BY DOPAMINE BLOCKADE
R.J. Hitzemann, Ph.D., J. Hirschowitz, M.D., D.C. Garver, M.D.

NR247 PSYCHOPATHOLOGY IN VIETNAM VERSUS VIETNAM ERA VETERANS
Glenn C. Davis, M.D., Naomi Breslau, Ph.D.

NR248 SAAB: A SCALE FOR ASSESSING AGGRESSIVE BEHAVIOR
David A. Brizer, M.D., Antonio Convit, M.D., Menahem Krakowski, M.D., Jan Volavka, M.D.

NR249 PHYSOSTIGMINE: MEMORY VERSUS PLASMA CHOLINESTERASE
J. Wesson Ashford, M.D., Rodger Elble, M.D., Kathleen Sherman, Ph.D., Jonathan Hess, Ph.D., Sandy Best, M.A., Connie Higgins

NR250 MEASURING TREATMENT RESPONSE BY COMPUTER INTERVIEW
D. Robert Fowler, M.D., Allan S. Finkelstein, Ph.D., Walter Penk, Ph.D., William Bell, M.S.

NR251 A COMPARISON OF DSM-II AND DSM-III IN 10,000 CASES
Armand W. Loranger, Ph.D.

NR252 DIAGNOSIS BY CONTENT ANALYSIS: SYSTEMS COMPARISON
Thomas E. Oxman, M.D., Paula P. Schnurr, Ph.D., Stanley D. Rosenberg, Ph.D., Marc Clemente, M.D.

NR253 PRELIMINARY VALIDATION OF A FAMILY ATTITUDE SCALE
Gretchen L. Haas, Ph.D., Anthony T. DiVittis, M.A., Marylin Levitt, D.S.W., James H. Spencer, M.D., John F. Clarkin, Ph.D., Ira D. Glick, M.D.

NR254 THE EVANS-BROWN RATING SCALE
Susan Evans, R.N., Richard P. Brown, M.D.

NR255 INCREASED SPECIFICITY IN MEASURING SATISFACTION
Barbara Urquhart, R.N., John A. Sweeney, Ph.D., Barbara Bulow, M.S.W., M. Katherine Shear, M.D., Allen J. Frances, M.D.

NR256 ESTIMATES OF SERVICE NEED FROM COMMUNITY SURVEYS
Philip J. Leaf, Ph.D., Gary L. Tischler, M.D.

NR257 EVALUATION OF A SEXUAL ABUSE PREVENTION PROGRAM
Renee L. Binder, M.D., Dale E. McNiel, Ph.D.

NR258 SHORT REM LATENCY IN IMPOTENCE WITHOUT DEPRESSION
Helmut S. Schmidt, M.D., Kathy Shy, M.D.

NR259 MENTAL HEALTH TRAINING FOR PHYSICIANS
James J. Strain, M.D., Linda K. George, M.D., Harold A. Pincus, M.D., Leslie H. Gise, M.D., Jeffrey Houpt, M.D.

NR260 THE PSYCHIATRIC IMPACT OF AIDS ON PHYSICIANS
James W. Dilley, M.D., Leon McKusick, Ph.D., William Horstman, Ph.D., Donald Abrams, M.D., Thomas J. Coates, Ph.D.

NR261 COMPLIANCE WITH CHEMOTHERAPY PROTOCOLS
Sushil Bhardwaj, M.D., Madelyn R. Messe, Ph.D., Allen H. Lebovits, Ph.D., Steven J. Schleifer, M.D., James J. Strain, M.D.

NEW RESEARCH PAPERS

in Summary Form

NR1 **Monday, May 12, 12:00 noon - 1:45 p.m.**

A PRIMATE MODEL OF PANIC DISORDER

Gayle S. Paully, Ph.D., Department of Psychiatry, Downstate Medical Center, 450 Clarkson Avenue, Box 120, Brooklyn, NY 11203; Steven Friedman, Ph.D., Leonard Rosenblum, Ph.D.

Summary:

Efforts to investigate the pathogenesis, underlying mechanisms, and treatment of panic disorders suffer from the ethical and practical problems with which the systematic study of human psychiatric problems is often confronted. As with other areas of clinical medicine, the creation of a relevant animal model provides a means for overcoming many of these difficulties. Recent research from our laboratory indicates that a number of the features of panic attacks produced in susceptible human subjects when given i.v. sodium lactate can be induced in unrestrained nonhuman primates using an alternative method of lactate administration. Freely behaving monkeys were evaluated by an observer who was blind to the subjects' treatment with either sodium lactate of a dextrose control solution. These studies demonstrated temporally circumscribed episodes characterized by agitation, wariness, and motor responses, normally elicited under stressful conditions, following the administration of sodium lactate. The development of this model offers promise for the systematic examination of etiological factors in susceptibility to lactate induction of panic attacks, the physiological bases of the response, and as a means of investigating modes of treatment of panic disorder. In particular, the model may offer an ideal opportunity for testing new drugs in the treatment of panic states, both for efficacy and safety. Use of the lactate induction model in conjunction with conditioning paradigms and examination of the effects of early environment will provide the means for studying the developmental course and the potential role of learning and association in panic disorders.

NR2 **Monday, May 12, 12:00 noon - 1:45 p.m.**

MRI STUDIES OF BENZODIAZEPINE RECEPTORS

Jeffrey A. Coffman, M.D., OSU Department of Psychiatry, 473 West 12th Avenue, Columbus, OH 43210; Charles Barfknecht, Ph.D., Norton Neff, Ph.D., William Hunter, M.D.

Summary:

Important extensions of autoradiographic findings regarding benzodiazepine and dopamine and serotonin receptors in animals to *in vivo* human studies have been made through positron emission tomography (PET) techniques, for example, the dopamine and serotonin receptor studies of Wong et al. We report here our initial steps toward development of a useful benzodiazepine receptor ligand labelled in a fashion which makes the localization of the compound apparent by magnetic resonance imaging (MRI) techniques. We have synthesized in our laboratory clonazepam labelled with the nitroxide stable free radical (NSFR), TEMPO, and administered it to rabbits in comparison to vehicle and unlabelled clonazepam. Subsequent to administration, we have studied the animals with 0.5 tesla and 1.5 tesla MRI systems using spin-echo and inversion-recovery sequences expecting that NSFR-induced relaxation enhancement would cause measurable changes in image intensity in neurocortical regions where one would expect selective binding. Methodologic issues and potential implications of the results will be discussed.

NR3 **Monday, May 12, 12:00 noon - 1:45 p.m.**

ANXIETY, PERFORMANCE, AND CEREBRAL BLOOD FLOW

Ruben C. Gur, Ph.D., University of Pennsylvania, Brain and Behavior Laboratory, 205 Piersol, Philadelphia, PA 19104; Raquel E. Gur, M.D., Brett E. Skolnick, Susan S. Resnick, Ph.D., Walter D. Obrist, Ph.D., Martin Reivich

Summary:

A fundamental "Law" of behavior stipulates a curvilinear inverted-U relationship between anxiety and performance. Cortical physiologic underpinnings for this law have not yet been demonstrated. We report human data on cortical cerebral blood flow (CBF) measured during rest and while performing an easy and a difficult reasoning tasks. The performance data for males upheld the Law, and the inverted-U relations between state anxiety and performance measures were paralleled by inverted-U relations between anxiety and CBF. Positive linear relations between CBF and performance in males also permitted the conclusion that the effects of anxiety state on performance are mediated by CBF changes. Deterioration of cognitive performance in high anxiety states appears caused by reduced cortical activity, perhaps reflecting increased demands on subcortical brain regions in "fight-or-flight" situation. Performance of females did not adhere to the Law. Both performance and CBF were either maintained at a steady level or even showed increase with increased anxiety states.

NR4 **Monday, May 12, 12:00 noon - 1:45 p.m.**

EPINEPHRINE INFUSION IN SOCIAL PHOBIA

Laszlo A. Papp, M.D., Anxiety Clinic, P.I., 722 West 168th Street, New York, NY 10032; Jack M. Gorman, M.D., Michael R. Liebowitz, M.D., Abby J. Fyer, M.D., Donald F. Klein, M.D.

Summary:

Purpose: The fact that patients with social phobia (SP) appear to manifest signs of beta adrenergic hyperactivity and benefit from beta blockers, coupled with findings that epinephrine (E) levels increase during social stress, make E infusion of interest as a possible specific provocative agent in SP. We hypothesized that patients with SP are more sensitive than normals to performance mediated surges of E. Therefore E infusion, in a dose sufficient to raise plasma E level to that developed during social stress experiments should reproduce typical anxiety feelings.

Method: 11 outpatients with social phobia were infused with i.v. E at a rate of 2.5 ug/min (N=8) and 4 ug/kg/hr (N=3) for 60 min. HR, BP and avg.min.vent. were recorded. A symptom checklist (API) was administered and 5 consecutive blood samples were collected to measure plasma E, norepinephrine, lactate and pyruvate levels.

Results: The infusion raised the mean plasma E level from 113 pg/ml to 928 pg.ml. Although 3 patients had some sort of anxiety, none of them experienced the full symptomatology of the naturally occurring phenomenon.

Significance: E failed to provoke anxiety in our patients with SP. Hence, unless it requires even higher surges of E, it is unlikely that SP anxiety begins with an increase in plasma E level that in turn stimulates beta receptors and provokes peripheral autonomic arousal. CNS factors must clearly be at work, as Cannon originally suggested in his dispute of the James-Lange hypothesis.

NR5 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PANIC DISORDER: THE SLEEP LACTATE INFUSION

Harold W. Koenigsberg, M.D., NYH/CMC Westchester, 21 Bloomingdale Road, White Plains, NY 10605; Charles Pollak, M.D., Timothy Sullivan, M.D.

Summary:

Panic attacks are sudden, episodic experiences of terror, associated wtih physiological changes, that are believed to occur spontaneously. The underlying mechanism of these attacks is not understood; various models propose sudden discharge involving the locus ceruleus or other brain centers, special sensitivity to fluctuations in the body's chemical environment (e.g. pH, pCO_2, calcium, lactate), and a psychophysiological over-reactivity to frightening situations. Noting the existence of another sudden, spontaneous terror phenomenon associated with dramatic physiological changes — Night Terrors, — we wondered whether these two disorders were related. If so, the study of terror experiences in sleep could aid in understanding panic disorder. In order to investigate this, the authors have extended the use of the sodium lactate infusion methodology to the sleep state. They have administered 0.5 M sodium lactate solution and normal saline intravenously during sleep to panic disorder patients demonstrated to have a lactate response during wakefulness. Infusions were given to 5 patients during stage 3-4 sleep, the sleep stages from which night terrors arise. Arousals immediately followed 5 out of 6 lactate infusions, while an immediate arousal followed only 1 out of 7 saline infusions. Plots of the sleep architecture of these subjects will be presented along with split-screen video recordings of the subjects' behavior and EEG tracings at the time of sleep lactate infusion.

NR6 **Monday, May 12, 12:00 noon - 1:45 p.m.**

LACTATE INFUSIONS: THE ROLE OF BASELINE ANXIETY

Deborah S. Cowley, M.D., Department of Psychiatry, Harborview Medical Center ZA-99, 325-9th Avenue, Seattle, WA 98104; Thomas S. Hyde, Ph. D., Stephen R. Dager, M.D., David L. Dunner, M.D.

Summary:

Intravenous infusion of sodium lactate has been shown to provoke panic attacks in patients with panic disorder and agoraphobia with panic attacks but not in normal controls. The lactate infusion has been used as a model to study the biochemistry of spontaneous panic. It has been suggested, however, that panic disorder patients and controls respond similarly to lactate, with the apparent difference in response accounted for by greater anxiety at the onset of the infusion in panic disorder patients. We studied baseline anxiety before lactate infusion and its relationship to response to lactate in 18 panic disorder patients, 23 agoraphobics with panic attacks, and 8 normal controls, using patient ratings of anxiety or panic and the Acute Panic Inventory (API). There was no significant difference between panic disorder patients and agoraphobics in baseline anxiety or response to lactate infusion. Baseline API scores, but not subjective ratings of anxiety, were strongly correlated with a typical panic response to lactate and a shorter duration of lactate before onset of panic in the patient groups. Patients showed significantly higher baseline scores on both measures than controls; however, this difference was accounted for by 7 patients with very high baseline scores, all of whom went on to panic with lactate. 14 other patients with typical panic responses to lactate had baseline scores indistinguishable from those of controls. Thus, although some patients are very anxious at baseline and therefore may have a more severe response to lactate, there is another group who panic with lactate despite low baseline anxiety, arguing against the lactate infusion's being merely a nonspecific stressor causing panic in vulnerable patients as a result of high baseline anxiety. Demographic, clinical, biochemical, and autonomic variables in these patients, and their relationship to baseline anxiety and response to lactate, will be discussed.

NR7 **Monday, May 12, 12:00 noon - 1:45 p.m.**

NE HYPERACTIVITY ASSOCIATED WITH YOHIMBINE PANIC

Scott W. Woods, M.D., Connecticut Mental Health Center, Yale University Medical School, 34 Park Street, New Haven, CT 06508; Wayne K. Goodman, M.D., Dennis S. Charney, M.D.

Summary:

Recent evidence suggests that regulation of norepinephrine (NE) neuronal activity may be abnormal in panic disorders (PD). The effects of the a_2 adrenergic receptor antagonist yohimbine (YOH), 20 mg PO and placebo, on heart rate (HR), blood pressure (BP), and plasma free 3-methoxy-4-hydroxyphenylglycol (MHPG), cortisol (CORT), growth hormone (GH), and prolactin (PRL), were determined in 68 PD patients and 20 controls. YOH-induced panic attacks meeting DSM-III criteria and similar to naturally-occurring attacks occurred in 37/68 PD patients and 1/20 controls ($p<.001$, chi square). YOH significantly increased plasma MHPG in all groups; MHPG increases were significantly greater in panicking patients in comparison to controls and to non-panicking patients. The peak YOH-induced increases in plasma MHPG and anxiety were significantly correlated in the patients ($r=.37$, $p<.003$) but not in controls. YOH significantly increased HR in the panicking patients but not in the other groups. The YOH-induced increase in systolic BP was greater in patients than controls but was similar in panicking and non-panicking patients. YOH prevented the diurnal decline of CORT in the total patient group but not in controls. Although YOH significantly increased CORT in the panickers and not in the non-panickers, differences between the two patient groups were not significant. YOH had no significant effect upon GH or PRL in panicking patients. *CONCLUSIONS:* The MHPG results suggest that abnormal regulation of presynaptic NE function may exist in PD patients who experience YOH-induced panic attacks. The CORT results suggest that regulation of the hypothalamic-pituitary-adrenal (HPA) axis or NE-HPA interactions may be abnormal in PD patients.

NR8 **Monday, May 12, 12:00 noon - 1:45 p.m.**

EFFECTS OF TWO BENZODIAZEPINES ON MEMORY AND EEG

Daniel W. Hommer, M.D., National Institute of Mental Health, Building 10, Room 4N214, 9000 Rockville Pike, Bethesda, MD 20892; Wallace Mendelson, M.D., Herbert Weingartner, Ph.D.

Summary:

It has been clearly demonstrated that benzodiazepines (BZ) produce an antegrade amnesia. To characterize the precise nature of this amnesia we examined the effects of two BZ hypnotics on memory, attention and scalp recorded EEG beta frequencies (a marker for BZ action in the brain). Triazolam 0.25 mg, 0.5 mg, placebo, flurazepam 15 mg or 30 mg were administered orally at weekly intervals in a double-blind, randomized, crossover design to 12 normal subjects. Memory, attention and EEG power spectra were measured before drug and 1, 3 and 8 hours afterwards. Both triazolam and flurazepam produced significant, dose-dependent impairments in free recall of verbal material 1 and 3 hours after administration. On a mg per mg basis triazolam was over 150 times more potent than flurazepam (i.e., triazolam 0.5 mg produced 250% greater impairment of free recall than flurazepam 30 mg); however, at 8 hours the triazolam-induced amnesia was completely gone while flurazepam still produced significant impairment. Despite large changes in episodic memory neither drug affected semantic memory (knowledge) or procedural memory (i.e., skill in solving anagrams continued to improve irrespective of BZ administration). Only the high dose of triazolam had a significant effect on attention. The high doses of both BZs produced significant increases in frontal EEG beta frequencies which significantly correlated with impairment in free recall. Thus BZs can impair the ability to learn new verbal information while not affecting attention, access to previously acquired knowledge or the ability to learn new procedures. BZs may provide a valuable probe into the biological basis of different types of human memory.

NR9 **Monday, May 12, 12:00 noon - 1:45 p.m.**

^{3}H-IMIPRAMINE BINDING IN PANIC AND ANXIETY DISORDERS

Lon S. Schneider, M.D., University of Southern California School of Medicine, 1934 Hospital Place, Los Angeles, CA 90033; Dennis Munjack, M.D., James A. Severson, Ph.D., Ruby Palmer, R.N.

Summary:

The density of platelet ^{3}H-imipramine binding sites is reported decreased in unipolar depression, and hence is a putative biological marker. There is considerable evidence for a phenomenological and genetic relationship of panic disorders with affective disorder. We studied platelet ^{3}H-imipramine binding in unmedicated subjects with generalized anxiety disorder (GAD; $n = 55$), panic disorder with and without agoraphobia ($n = 52$), and normal controls ($n = 26$) in order to determine whether patients with panic disorder differed from controls in this biological assay. We found no difference in binding site density (Bmax) or affinity (Kd) among the panic, agoraphobic, GAD patients and controls. Nor did we find a relationship between Bmax and Kd and the severity of depressive symptoms. In view of two conflicting prior studies, the use of ^{3}H-imipramine binding in panic disorder remains problematic.

NR10 **Monday, May 12, 12:00 noon - 1:45 p.m.**

CLINICAL INTERACTIONS OF ALPRAZOLAM AND IMIPRAMINE

Barbara G. Wells, Pharm.D., University of Tennessee Pharmacy School, Mental Health Pharmacy, 26 South Dunlap Street, Room 202, Memphis, TN 38163; R. Lee Evans, Pharm.D., Larry Ereshefsky, Pharm.D., Ann E. Richards, Pharm.D., Ray J. Townsend, Pharm.D., Edward J. Antal, Ph.D.

Summary:

Clinical outcome and adverse effects associated with concurrent alprazolam and imipramine administration were studied using patients as their own controls. Twenty–nine adult patients diagnosed major depressive disorder who were stabilized on imipramine 100–300 mg/day had alprazolam added to their regimen while imipramine doses remained unchanged. Alprazolam dosage was initiated on day 8 and increased from 1 to 4 mg/day over 10 days, maintained for 7 days, then tapered over 15 days. The Hamilton Depression and Anxiety Rating Scales and Side Effects Evaluation were completed on days 1 and 8 (while on imipramine alone) and days 15, 22 and 33 (while on imipramine and alprazolam). Total scores on all three scales were corrected for baseline of days 1 and 8 and evaluated accepting statistical significance as $p<0.05$. Significant decreases in all three total scores were observed at all later study days utilizing day 1 as baseline and at all later study days except for side effect severity on day 15 utilizing day 8 as baseline. For most side effects total number of reports remained constant or decreased from day 1 to later evaluation days. Increased reports of moderate or severe intensities between study initiation and day 22 (corresponding to the highest alprazolam dose) were observed for sedation, weight gain, diplopia, increased appetite, sleep disturbances and amnesia. The only response to any side effect was increased surveillance. Alprazolam can be co–administered with imipramine without adverse pharmacodynamic effects.

NR11 **Monday, May 12, 12:00 noon - 1:45 p.m.**

TRIAZOLAM: AMNESIA AND HYPEREXCITABLE EFFECTS

Anthony Kales, M.D., Pennsylvania State University Sleep, Research and Tx Center, P.O. Box 850, Hershey, PA 17033; Antonio Vela–Bueno, M.D., Constantin R. Soldatos, M.D., Rocco L. Manfredi, M.D.

Summary:

Triazolam, a triazolobenzodiazepine with an ultra short elimination half–life, in a 0.5 mg dose has been studied extensively. Findings have included: a high degree of initial efficacy with rapid development of tolerance, reports of serious behavioral side effects and the occurrence of rebound insomnia following withdrawal. Accordingly, in a double blind sleep laboratory study of 12 insomniacs for 22 consecutive nights, we evaluated and compared the effectiveness and side effects of two benzodiazepine hypnotics, triazolam, 0.25 mg, and quazepam, a benzodiazepine with a long elimination half–life, in a 15 mg dose.

Quazepam significantly improved sleep during both short– and intermediate–term use. Daytime sleepiness, which decreased with continued use, was the side effect most often associated with quazepam administration. In contrast, triazolam administration did not significantly improve any of the major sleep efficiency parameters and there was a rapid development of tolerance for the drug's slight initial effectiveness. In addition, there were a number of behavioral side effects during triazolam administration including: amnesia, confusion, hyperexcitability and disinhibition. For example, one subject reported having memory difficulties during the day that required her to keep daily notes, while another subject was observed to have undergone a striking change in behavior. Withdrawal of triazolam was associated with sleep and mood disturbances (rebound insomnia and rebound anxiety). The seriousness and frequency of spontaneously reported side effects was surprising considering the relative ineffectiveness of this dosage level of triazolam. We propose that the chemical structure of triazolam, its high potency and its rapid elimination all contribute to the drug's adverse effects.

NR12 **Monday, May 12, 12:00 noon - 1:45 p.m.**

EFFECTS OF 5 HTP AND CLOMIPRAMINE IN ANXIETY

Rene Kahn, M.D., Department of Psychiatry, Montefiore Hospital, KLAU 1, 111 East 210 Street, Bronx, NY 10467; Herman G. M. Westenberg, Ph.D., Cristine G. Gispen-de Wied, M.D.

Summary:

Antidepressants have been shown to be effective in the treatment of panic disorder (PD) and obsessive compulsive disorder (OCD). In OCD clomipramine, a strong 5HT reuptake inhibitor, has proven to be especially effective. Thus far, serotonergic agents have not been investigated in other anxiety disorders.

We investigated the antianxiety properties of clomipramine and 5HTP, a 5HT precursor, in anxious patients, in a double blind controlled trial. Patients were randomly divided into three groups, one receiving clomipramine (150 mg/day), one receivng 5HTP and a decarboxilase inhibitor (150 mg/day each) and one placebo during the 8 week trial. 54 patients, 37 female, 17 male, participated. 10 patients dropped out. Diagnoses (DSM III) were: Agoraphobia with Panic Attacks: 30, PD: 5, OCD: 3, Generalized Anxiety Disorder: 7. There were no group differences in sex distribution, age, duration of illness or diagnoses. The Hamilton Depression Scale, Anxiety Scale, SCL-90, Spielberger State Trait Anxiety Inventory and Zung self rating scale for Depression were used. Clomipramine showed clear antidepressant and anti-anxiety ($p < 0.001$-$p < 0.01$) properties on all scales, compared to placebo. 5HTP showed significant anti-anxiety effects ($p < 0.05$) compared to placebo on all scales, but no antidepressant or other effects. The anxiolytic effects of 5HTP and clomipramine showed no significant differences. These findings suggest the involvement of 5HTergic systems in the treatment effect of antidepressants in anxiety states, especially panic attacks.

NR13 **Monday, May 12, 12:00 noon - 1:45 p.m.**

XANAX AND INDERAL IN PANIC AND PHOBIC OUTPATIENTS

C. Lewis Ravaris, M.D., Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03756; Matthew J. Friedman, M.D., Peter J. Hauri, Ph.D.

Summary:

This is the first double-blind controlled study to compare the efficacy of an established anti-panic, anti-agoraphobic drug alprazolam (Xanax) with a standard beta-adrenergic blocker propranolol (Inderal) whose efficacy in these syndromes is ambiguous. We present the interim results from sixteen patients between the ages of 18-60 years treated with either alprazolam 2-10 mg daily, or propranolol 120-300 mg daily for six weeks. All patients fulfilled DSM criteria for panic disorder and phobic avoidance behavior(s) extending to include housebound agoraphobics. Subjective and objective rating scales were completed before treatment and at each weekly visit. Each patient also completed three nights in the Sleep Disorders Clinic at the beginning and during the final week of drug treatment.

We find alprazolam and propranolol both exert clinically significant improvement in suppressing panic attacks and reducing generalized anxiety (anticipatory anxiety). Propranolol, however, seems to exert a less potent anti-phobic effect compared to alprazolam. The sleep pattern of the phobic patients is significantly different compared to control subjects. This finding which will also be presented may be significant in the differential diagnosis of phobic anxiety and generalized anxiety syndromes.

NR14 **Monday, May 12, 12:00 noon - 1:45 p.m.**

TRAZODONE IN THE TREATMENT OF PANIC AGORAPHOBIA

Matig Mavissakalian, M.D., Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh, PA 15213; James Perel, Ph.D., Kathleen Bowler, R.N., Robert Dealy, M.D.

Summary:

Eleven patients with panic disorder or agoraphobia with panic completed a ten week single-blind trial of two weeks placebo followed by eight weeks trazodone 300 mg/day without concurrent behavioral instructions. Measures of change included ratings of generalized and panic anxiety, phobias, depression, and a behavioral avoidance test which were administered at pretreatment, at two weeks (placebo), at six weeks (mid-trazodone) and at ten weeks (post-trazodone) of the trial. Repeated measures analysis of variance revealed significant time effects on all measures which, with rare exceptions, were already evident after two weeks of placebo. However, analysis which considered the two week assessment (placebo) as the baseline revealed statistically and clinically significant improvement in phobic and panic measures with trazodone proper. These pilot results suggest that trazodone may have specific antipanic and antiphobic action and underscore the importance of serotonergic mechanisms in these anxiety disorders.

NR15 **Monday, May 12, 12:00 noon - 1:45 p.m.**

CLINICAL ANXIOSELECTIVE ACTIVITY OF GEPIRONE

Jerry M. Cott, Ph.D., Bristol-Meyers, Pharmaceutical Research and Development, 5 Research Parkway, Wallingford, CT 06492; Neil M. Kurtz, M.D., Donald S. Robinson, M.D., Davis L. Temple, Ph.D.

Summary:

The first multi-center, single-blind study in anxious patients with gepirone (an analog of the anxioselective compound, buspirone) was recently completed. Forty patients at 4 centers completed this 6 week study. Sixty patients with *DSM-III* Generalized Anxiety Disorder were given a 1 week placebo run-in and placebo responders were excluded. Those patients with a HAM-A of at least 18 were started on gepirone at doses between 3 and 15 mg per day in divided doses. The dose was then individually titrated according to clinical response up to 60 mg per day. Safety and efficacy evaluations were done weekly. After 6 weeks treatment, placebo was substituted for an additional 7 days in order to assess the occurrence of any withdrawal symptoms.

The results with gepirone were encouraging. Mean HAM-A scores decreased from 24 at baseline to 18, 16 and 12 at days 4, 14 and 28, respectively. A reduction of at least 50% of baseline anxiety scores was seen in 81% of the patients. There was no evidence of any withdrawal symptoms during placebo substitution at the end of the treatment. There were 20 drop-outs: 9 for placebo response, 4 for adverse experiences, 6 were lost to follow-up and 1 dropped due to an abnormal ECG at baseline and week 1. The most common adverse experiences were: lightheadedness (37%), nausea (27%), drowsiness (16%) and headache (13%). Some of these effects, as well as the anxiolytic activity, are thought to be due to the selective affinity of gepirone for brain 5HT1A receptors.

NR16 **Monday, May 12, 12:00 noon - 1:45 p.m.**

LONG-TERM EFFECTS OF EXPOSURE WITH AGORAPHOBICS

Iver Hand, M.D., Psychiatric University, Clinic, Martinstrasse 52, D 2000, Hamburg 20 O, West Germany; Jorg Angenendt, Martina Fischer, Heidi Buttner-Westphal, Christa Maneke, Brigitte Friedrich

Summary:

This follow-up study with 175 agoraphobics, one to eight ($\bar{x}$ 5.5) years after exposure-in-vivo, differs in purpose, methodology and content from previous ones. 1. It constitutes a multiple, longterm replication of the first systematic "group exposure-in-vivo" (Hand et al., 1974), that already applied panic and depression management. 2. It includes a direct comparison of two main modes of exposure: therapist-aided (Hand et al., 1974) and manual-aided (Mathews et al., 1977). 3. Separate and detailed group statistical and single-case analyses of "gainers" (70%) and "losers" (30%) reveal that exposure: is a very effective intervention for phobic and panic anxiety as well as for depression; induces highly significant, multisymptomatic treatment and follow-up effects; and is followed by major changes in illness behavior and life style. 4. "Losers" remain resistant to change, even with additional treatments during follow-up. But, with the methodology applied, they can be detected early in treatment.

Results provide clear guidelines for effective, non-pharmacological treatment of agoraphobics, with and without panic attacks. They are "hard data" for a revision of *DSM III* classification of anxiety disorders.

NR17 **Monday, May 12, 12:00 noon - 1:45 p.m.**

BEHAVIORAL THERAPY EFFICACY FOR PANIC

M. Katherine Shear, M.D., Payne Whitney Clinic, 525 East 68th Street, New York,NY 10021; Gordon Ball, Ph.D., Bonnie Gitlin, M.S.W., Allen J. Frances, M.D.

Summary:

Behavioral therapy is known to be effective in treating patients with agoraphobia. However, outcome measures of most studies have not included the degree of panic attack reduction. Enhanced efficacy that results when pharmacotherapy is added to behavioral treatment supports the idea that panic is not maximally treated using standard antiphobic treatment. We report here the results of a prospective study of 15 patients using a behavioral treatment program aimed at treating panic attacks. *Subjects:* 15 patients who met *DSM IIIR* diagnoses of Panic Disorder. Two had uncomplicated panic disorder, 9 had limited phobic avoidance and 4 were agoraphobic. There were 6 males and 9 females. Mean age was 33 years and mean illness duration was 5.7 years. *Treatment:* was conducted by experienced behavior therapists and included (1) response modification techniques addressing both physiologic and psychologic components of panic and (2) programmed exposure to anxiety provoking stimuli. *Results:* 13 patients completed the study to meet termination criteria. The mean length of treatment was 17 weeks. Twelve patients (92%) were free of spontaneous fullblown panic attacks by the time of termination. In all cases there was a decrease in both situational panic and limited symptom episodes. 8 patients (60%) were free of all panic and panic related symptoms.

NR18 **Monday, May 12, 12:00 noon - 1:45 p.m.**

INDICATION FOR CARBAMAZEPINE IN MENTAL DISORDERS

Dietrich Blumer, M.D., Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202; Mary Heilbronn, Ph.D., Jonathan M. Himmelhoch, M.D.

Summary:

A series of 28 patients were successfully treated with carbamazepine for psychiatric disorders difficult to classify because of their atypical nature ("somatoform, anxiety and explosive disorders, schizoaffective and brief psychoses, dysphoric and amnestic syndromes"). The 18 females and 10 males, of average age 39, were treated for at least one year with carbamazepine; in 18 patients modest amounts of antidepressants were added.

Three patients were diagnosed temporal lobe epilepsy (TLE) for the first time, two had a history of TLE before adulthood, and in six the presence of complex partial seizures was judged probable. Among the 17 others who never had seizures, 11 had EEG abnormalities. 35% of all patients had a history of CNS insult and/or positive CT-Scan findings, and 37% had a family history of epilepsy. Psychiatrically, the entire group revealed mental changes characteristic for the interictal phase of TLE: excessive and labile emotionality with rapid mood shifts, circumstantiality-viscosity, and global hyposexuality.

The carbamazepine responders had either TLE or, in the absence of overt seizures, a Temporal Lobe Syndrome (TLS). Recognition of subtle seizures and of the TLS is crucial for identification of the carbamazepine responder. The TLS consists of: 1. evidence of CNS impairment, family history of epilepsy; 2. core mental changes related to the basic temporal-limbic interictal or subictal activity; 3. symptomatic atypical psychopathology of marked variety.

NR19 **Monday, May 12, 12:00 noon - 1:45 p.m.**

HETEROGENEITY, COEXISTENCE IN OBSESSIVE/COMPULSIVES

Steven A. Rasmussen, M.D., Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906; Ming T. Tsuang, M.D.

Summary:

Until recently, Obsessive Compulsive Disorder (OCD) has been thought of as a rare illness with a poor prognosis. Data from the National Epidemiology Catchment Survey has shown that OCD has a lifetime prevalence of 2.5% in the general population, double that of schizophrenia or panic disorder. We have identified and contacted 150 patients with a *DSM-III* diagnosis of OCD over the past two years and have begun a phenomenologic and epidemiologic study of these patients. The overwhelming majority of patients in our sample have both obsessions and compulsions. The most common compulsions are washing, checking and counting rituals. Eighty percent of patients follow a chronic waxing and waning course. Developing valid and reliable exclusion criteria is particularly difficult with OCD, due to the extensive overlap of OCD with schizophrenia, major depression and the other anxiety disorders. Fifty-five percent of the patients met criteria for a lifetime major depressive episode. A subgroup of 20% of the total sample was prone to other anxiety disorders including panic disorder, separation anxiety disorder, school phobia, social phobia, and simple phobias. A significant percentage of our patients report that nuclear family members have obsessive traits or symptoms. Several questions of particular relevance to the design of neuropharmacologic and treatment outcome studies are being pursued. These include (1) how heterogeneous is the syndrome and how can subgroups that are homogenous be identified, (2) what other psychiatric disorders and symptoms are most likely to coexist with OCD, (4) the importance of state vs. trait variables in the clinical manifestations of the illness, (5) the contribution of psychosocial factors to the phenotypic expressions of symptoms. Problems facing researchers interested in studying the neurobiology of the disorder are reviewed, and future clinical and epidemiologic studies that should proceed in concert with neurobiologic studies are suggested.

NR20 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PET-FDG GLUCOSE UPTAKE IN OBSESSIVE-COMPULSIVES

Lewis R. Baxter, Jr., M.D., Department of Psychiatry, University of California at Los Angeles-National Psychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024; Michael E. Phelps, Ph.D., John C. Mazziotta, M.D., Barry H. Guze, M.D., Carl E. Selin, M.S., Jeffrey M. Schwartz, M.D.

Summary:

We studied patients with obsessive-compulsive disorder (OCD) (n=11) with positron emission tomography (PET) and the fluorodeoxyglucose (FDG) method, looking for abnormalities in glucose metabolic rates in cerebral neuroanatomical structures which have been hypothesized to have abnormal functioning in OCD. These patients were compared to normal controls (NC) (n=13) and patients with unipolar depression (UD) (n=12), a disorder with phenomenological similarities to many aspects of OCD. The UD patients did not differ from the OCD patients in levels of anxiety, tension or depression. The first seven OCD patients were examined for abnormalities and the next four OCD patients examined prospectively to confirm these. Glucose metabolic rates in OCD patients were significantly increased in both cerebral hemispheres, in aggregate, and in the orbital gyri and caudate nuclei, bilaterally, when compared to normals and unipolar depressives. Relative to the metabolic rate of the ipsilateral hemisphere, the metabolic rates in the orbital gyri (orbit./hem.) were significantly elevated, while those in the caudate nuclei (caud./hem.) were decreased, compared to the ratios obtained for NCs. With improvement in OCD symptomatology on medication, caud./hem. increased, while there was no change in this ratio in patients who failed to improve. Possible relationships between altered metabolic activity in the caudate nuclei and orbital gyri and the symptomatology of OCD will be discussed.

NR21 **Monday, May 12, 12:00 noon - 1:45 p.m.**

SPECIFIC ANTIOBSESSIONAL EFFECT OF CLOMIPRAMINE

Joseph Zohar, M.D., LCS/National Institute of Mental Health, National Institutes of Health–Building 10, Room 3D/41, 9000 Rockville Pike, Bethesda, MD 20892; Thomas R. Insel, M.D., Ina S. Alterman, M.S., Edward A. Mueller, M.D., Dennis L. Murphy, M.D.

Summary:

Patients (n=10) with obsessive–compulsive disorder (OCD) who met DSM III criteria, and had been ill for at least one year were studied in a double–blind, randomized, crossover comparison of the tricyclic antidepressants clomipramine and desipramine.

Clomipramine (mean ± SD dose 235 ±67 mg/day, range 100–300 mg/day) was significantly ($p \leq .05$) more potent than desipramine (290 ± 32 mg/day, range 200–300 mg/day) for reducing obsessive–compulsive symptoms after both four and six weeks, as measured by the CPRS obsessive compulsive psychiatric rating subscale and the NIMH global scale for obsessive compulsive symptoms. In fact, no significant improvement in obsessive compulsive symptoms was evident during treatment with desipramine. No significant effects of clomipramine and desipramine were revealed on the Hamilton depression rating scale or the NIMH global scales for anxiety or for general functional impairment. Mean plasma level for both drugs were roughly equivalent and within the therapeutic range for antidepressant effects.

These results are consistent with earlier reports that clomipramine appears to have more potent anti–obsessional properties than a number of structurally related compounds; however, this is the first study that directly compares in a crossover fashion one tricyclic to another in patients with obsessive–compulsive disorder.

This difference between clomipramine and desipramine suggests that not all tricyclics are equipotent in their anti–obsessive–compulsive effects and therefore that some property of clomipramine, such as its potent serotonergic effects, may be of pathophysiologic relevance in obsessive–compulsive disorder.

NR22 **Monday, May 12, 12:00 noon - 1:45 p.m.**

SEROTONIN, BULIMIA, AND MIGRAINE: RESULTS WITH MCPP

Timothy D. Brewerton, M.D., Laboratory of Clinical Science, National Institute of Mental Health, Building 10, Room 3S229, 9000 Rockville Pike, Bethesda, MD 20892; Edward A. Mueller, M.D., David T. George, M.D., Dennis L. Murphy, M.D., David C. Jimerson, M.D.

Summary:

Altered serotonin (5–HT) function may play a role in the appetitive, affective and impulsive features of bulimia. In the course of inpatient neuroendocrine studies using the 5–HT agonist m–chlorophenylpiperazine (m–CPP) (0.5 mg/kg p.o.), we observed that 10 of 16 normal weight bulimics and 5 of 7 bulimic anorexics had severe migraine–like headaches. These headaches typically commenced 6–8 hours after drug administration and peaked between 10–12 hours post–challenge. This is in marked contrast to the absence of migraine–like headaches in seven healthy female controls in the present study, and in 14 controls described in a recently published report from our group. Migraine–like headaches in bulimics were associated with nausea, involuntary vomiting, photophobia, phonophobia, and/or unilateral headache initiation or predominance. Mild to moderate tension–like headaches did occur in some controls.

It was notable that 10 of the 15 patients who developed m–CPP induced migrainous headache had a family history of migraine, which was not found in other patients or controls. These results are of particular interest because of the 5–HT alterations that have been reported in migraine patients.

The finding of an unexpectedly high frequency of migraine headaches in the families of bulimic patients is in itself of note. This association is substantially higher than expected in the general population and suggests an important area for future research.

NR23 **Monday, May 12, 12:00 noon – 1:45 p.m.**

SLEEP ARCHITECTURE IN EATING DISORDER PATIENTS

Alan B. Levy, M.D., 473 West 12th Avenue, Columbus, OH 43210; Katharine N. Dixon, M.D., Helmut S. Schmidt, M.D.

Summary:

Recent interest in the apparent similarities between eating disorders and depression has led to a variety of studies investigating the potential overlap between these two psychiatric disorders. The sleep EEG, found to be abnormal in certain patients with depression, is a recent investigative tool in eating disorders. We recorded the sleep EEG on 2 consecutive nights in 9 women with anorexia nervosa, 10 with bulimia, and 10 healthy female controls. Data was analyzed for the second night of sleep recording. All subjects were between the ages of 16–38 and were free from medication for at least one month. Bulimic women did not differ from controls on any sleep architectural measure. However, anorectics demonstrated less S_4 sleep (ANOVA $p<.06$) and less sleep efficiency ($p<.001$) than did controls. Moreover, they had more S_1 sleep ($p<.001$) than did controls. Anorectics experienced more wakeful minutes after sleep onset ($p<.006$) and this was negatively correlated with %IBW ($p<.05$). Total sleep time for anorectics was also significantly diminished ($p<.01$) and was positively correlated with %IBW ($p<.05$). There were no differences in REM latency or REM density among groups. The sleep abnormalities found in some eating disorder patients do not appear to parallel those of patients with primary depression. Some of these abnormalities may reflect weight changes in anorectic subjects; however, follow-up polysomnography is necessary to determine the degree to which these changes are state-dependent.

NR24 **Monday, May 12, 12:00 noon – 1:45 p.m.**

CLONIDINE CHALLENGE TEST IN BULIMIA

Allan S. Kaplan, M.D., Eating Disorder Center, CW 1–G South 311, Toronto General Hospital, 200 Elizabeth Street, Toronto, Ontario, Canada M5G 2C4; Paul E. Garfinkel, M.D., Jerry J. Warsh, M.D., Gregory M. Brown, M.D.

Summary:

Bulimia has been linked to depression by a number of biologic and psychologic parameters. One such parameter is the metabolic response to clonidine. Differential responses to clonidine, an α_2-adrenergic agonist, have been found in depressed patients compared to controls. It is of importance to assess such responses in bulimia to elucidate its relationship to affective disorders.

We conducted the clonidine challenge test administering under controlled conditions, 1.3 mcgs/kg IV to a group of normal weight bulimics (n=14) and controls (n=11) matched on demographic and weight-related variables. We measured neuroendocrine effects with growth hormone and cortisol responses and biochemical effects with free and total MHPG, HVA and VMA responses.

All variables showed a significant response to the clonidine challenge (ANOVA $P<.01$). There were no significant differences between bulimics and controls in serum GH or plasma MHPG (free or total), or VMA responses. Plasma cortisol in healthy subjects (n=10) showed higher pre infusion values and greater decrements post infusion compared to bulimics (n=13). Baseline HVA values were higher in controls than in patients and demonstrated a greater drop in responses to clonidine in the control group. Since both groups displayed a drop in HVA after clonidine, this study is the first demonstration of an α_2-adrenergic agonist affecting dopamine metabolism.

These results are different from those found in depressed patients where there are blunted growth hormone responses to clonidine, differential responses in MHPG, and a greater decrease in cortisol in depressed patients compared to controls. This suggests reduced responsiveness of α_2 adrenergic receptors in depression.

From these data, bulimia appears to be biologically distinct from depression, with no evidence of α_2 adrenergic receptor subsensitivity.

NR25 **Monday, May 12, 12:00 noon - 1:45 p.m.**

NALTREXONE IN THE TREATMENT OF BULIMIA

Jeffrey M. Jonas, M.D., Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901; Mark S. Gold, M.D.

Summary:

Bulimia, the binge–purge syndrome, is a disorder of unknown etiology. The theory that bulimia is closely related to the affective disorders has led to the use of antidepressant medications in treating this disorder. An alternative hypothesis is that dysregulation of endogenous opioid peptides produces the abnormalities of eating and appetite seen in bulimia, as well as the "addictive attitudes" towards food often seen in these patients. To investigate this possibility, we administered the long–acting opioid antagonist naltrexone to 5 normal–weight bulimic women, in a 6–week, open trial of this medication. This represents, to our knowledge, the first test of an opiate antagonist in bulimia.

The patients were rated weekly for severity of depression, number of binge and purge episodes, and duration of binge episodes. At the end of 6 weeks there were significant decreases in the amount of binging (t_4=10.98, p<.001, two–tailed), (t_4=3.175, p<.05, two–tailed). Subsequent to the study patients maintained on naltrexone sustained their improvements, while 2 individuals who stopped the medication relapsed within 7 days. These preliminary data suggest that endogenous opioid peptides may play a role in the pathophysiology of bulimia, and that naltrexone may be a useful adjunct in the management of this disorder.

NR26 **Monday, May 12, 12:00 noon - 1:45 p.m.**

ALTERATIONS OF CSF, CRH AND POMC IN ANOREXIA NERVOSA

Walter H. Kaye, M.D., Western Psychiatric Institute, Room 1086, 3811 O'Hara Street, Pittsburgh, PA 15213; Wade H. Berrettini, M.D., Harry E. Gwirtsman, M.D., Ted George, M.D., David C. Jimerson, M.D., Philip W. Gold, M.D.

Summary:

Anorexia nervosa is an eating disorder associated with disturbances of mood, cognition, activity and multiple neuroendocrine disturbances (e.g., hypercortisolism, hypothalamic–hypogonadism). Little is known about the disturbances in brain transmitters that may contribute to such symptoms. Two related neuropeptide systems are of much interest in this disorder. The possibility of CRH hypersecretion in anorexia nervosa is of considerable theoretical interest since CRH administration in experimental animals produces many of the physiologic and behavioral changes classically associated with anorexia nervosa, including not only hypercortisolism, but also hypothalamic–hypogonadism, decreased sexual activity, decreased feeding behavior and hyperactivity. Brain CRH is known to regulate the degradation of the peptide precursor pro–opiomelanocortin into several sister peptides including beta–endorphin and ACTH. Beta–endorphin is of particular interest in anorexia nervosa because considerable animal literature has suggested it plays a role in the regulation of appetite. We measured CSF concentrations of these peptides in anorexics studied while underweight and at intervals following correction of the weight loss. Underweight anorexics (n = 20) had significantly elevated CSF CRH concentrations compared to healthy control women (n = 19). Underweight anorexics (n = 14) had a significant reduction of CSF beta–endorphin and ACTH compared to control women (n = 11). CSF concentrations of all three neuropeptides normalized after weight correction. It is not known whether abnormalities of these peptides reflects a defect intrinsic to anorexia nervosa or represents a response to weight loss per se. In any event, these findings may be relevant to certain components of the symptom complex. For example, increased activity of CRH and decreased activity of beta–endorphin may contribute to decreased feeding behavior and to several of the neuroendocrine disturbances typically found in this disorder. In addition, we found positive correlations between concentrations of all three peptides in anorexia nervosa and normal controls suggesting concentrations of these peptides in CSF reflect physiologic interrelationships of these systems.

NR27 **Monday, May 12, 12:00 noon - 1:45 p.m.**

NORADRENERGIC DISTURBANCES IN NORMAL WEIGHT BULIMIA

Walter H. Kaye, M.D., Western Psychiatric Institute, Room 1086, 3811 O'Hara Street, Pittsburgh, PA 15213; Harry E. Gwirtsman, M.D., C. Raymond Lake, M.D., David T. George, M.D., David C. Jimerson, M.D., Michael E. Ebert, M.D.

Summary:

Normal weight bulimia, an eating disorder of unknown etiology, occurs in association with disturbances of mood and neuroendocrine function and often responds to treatment with antidepressant medication. Norepinephrine (NE) is known to normally participate in the modulation of feeding behavior, mood, and several of these neuroendocrine systems. We measured plasma and CSF levels of NE in 13 normal-weight (85% to 120% average body weight) hospitalized bulimics to explore the possibility that there is a disturbance of noradrenergic function in this illness. We studied bingeing behavior just after inpatient admission. While basal plasma NE values of bulimics at the time of admission (each bulimic had been chronically bingeing prior to admission) were similar to controls, bulimics had significantly greater release of plasma NE (462 ± 254 pg/ml/min) while bingeing and vomiting than did controls when eating a large meal (186 ± 120 pg/ml/min). We restudied bulimics after a 30-day, inpatient, medication-free stabilization with abstinence from bingeing. Compared to their own values on admission, after 30 days of stabilization, we found that bulimics had a significant reduction in basal plasma NE (160 ± 87 pg/ml vs. 84 ± 18 pg/ml) and CSF NE (83 ± 40 vs. 67 ± 34 pg/ml). Furthermore, after 30 days of stabilization and abstinence from bingeing, bulimics had plasma NE values that were significantly less than controls (158 ± 60 pg/ml). These results suggest that bingeing produces sympathetic activation, and that there is a reduction in sympathetic and central NE activity after a month of stabilization and abstinence from bingeing behavior. It is not clear whether the reduction in NE concentrations after stabilization and abstinence reflect a disturbance in NE systems intrinsic to bulimia or is secondary to some variable known to effect NE metabolism. Nevertheless, these findings may explain several aspects of bulimia. Bulimics may binge to normalize NE activity. It is also possible that antidepressant medication corrects an intrinsic defect in NE metabolism or prevents recidivism by countering alterations in NE activity after bingeing stops. Finally, the self-reinforcing effects of bulimia, such as decreased anxiety or food craving, may be mediated through behavior-induced changes in NE functional activity.

NR28 **Monday, May 12, 12:00 noon - 1:45 p.m.**

BINGE-PURGE EPISODES INCREASE AMYLASE IN BULIMIA

Harry E. Gwirtsman, M.D., University of California at Los Angeles/Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024; Walter H. Kaye, M.D., Nicholas W. Carosella, M.D., David T. George, M.D., David C. Jimerson, M.D.

Summary:

Hyperamylasemia and parotid hypertrophy are found in bulimic patients. In order to further study the relationship of serum amylase to the phenomenology of eating disorders, we studied 52 patients with anorexia nervosa (30 restrictor type, 22 bulimic type), 21 normal weight bulimics with no previous history of anorexia nervosa, 17 patients with a previous history of anorexia nervosa (9 restrictor type and 8 bulimic type) 1 to 5 years prior to the study, and 24 age- and sex-matched normal volunteers.

Following an overnight fast, serum amylase and electrolytes were drawn at 8 a.m. on the day after admission on all patients and volunteers. Patients and volunteers were free of all medications for more than 2 weeks. Bulimic patients had significantly higher serum amylase (73.4 ± 8.0 I.U./L. Mean ± S.E.M.) than controls (40.8 ± 2.4). Additionally, the test distinguished between restrictor anorexics (44.7 ± 4.7) and bulimic anorexics (68.8 ± 8.6; $p < 0.05$). Recovered bulimic anorexics showed non-significantly higher serum amylase values than recovered restrictors.

In order to determine if increases in amylase were the consequence of the behavior of bingeing and vomiting, 7 bulimic patients had serum amylase measured before and after a series of binge/vomit episodes (3500 ± 229.5 KCal.) and 8 volunteers had serum amylase measured before and after a large meal (1700 ± 125 KCal.). Bulimics showed 2- to 4-fold increases in amylase following bingeing and vomiting, while normal volunteers showed no change in amylase values ($p < 0.001$).

Some bulimic patients ($N = 28$) were followed with multiple serum amylases during intervals on the treatment unit, while under close observation. Serum amylase declined significantly within 6 days of admission ($p = 0.002$) and declined further within 15 days of hospitalization ($p = 0.03$). However, following passes off of the unit, amylase values returned to admission values and remained elevated for up to 120 hours, presumably as a result of binge/vomit episodes.

These results indicate that modest increases of serum amylase are seen in a subpopulation of bulimic individuals of any weight and appear to be a consequence of the binge/vomit behavior. Serial amylase determination may be useful in monitoring the degree of abstinence in both inpatient and outpatient therapeutic programs.

NR29 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PLASMA DEXAMETHASONE LEVELS AND THE DST IN BULIMIA

B. Timothy Walsh, M.D., New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032; David C. Lindy, M.D., Ee Sing Lo, Ph.D., Thomas Cooper, M.A., Stephen P. Roose, M.D., Madeline Gladis, M.D., Sondra B. Dantzic, B.A., Alexander H. Glassman, M.D.

Summary:

Inadequate suppression of plasma cortisol following oral administration of dexamethasone (a positive dexamethasone suppression test, DST) has been reported in several studies of patients of normal body weight with bulimia. However, no significant association has been established between a positive DST and severity or chronicity of illness, presence of major depression, history of anorexia nervosa, current body weight or recent weight change.

We carried out a 1 mg dexamethasone suppression test (DST) in 66 women with bulimia and in 26 age- and sex-matched controls. Blood samples were obtained at 4 p.m. on the day following dexamethasone ingestion and levels of cortisol and of dexamethasone in the plasma were measured. Thirty percent of the patients vs. 8% of the controls had positive DSTs ($p < .05$). In the patient group, there was a significant inverse relationship between the plasma level of cortisol and that of dexamethasone ($r = -0.51$, $p < .001$), and the mean plasma dexamethasone level in the patient group was significantly lower than that in the control group (0.48 vs. 0.98 ng/ml, $p < .002$).

These results indicate: (1) in bulimia, the response to the 1 mg DST is determined, not only by the activity of the hypothalamic-pituitary-adrenal axis, but also by the factors which govern the plasma level of dexamethasone; and (2) the high frequency of abnormal DSTs in bulimia may be related to abnormally low levels of plasma dexamethasone.

NR30 **Monday, May 12, 12:00 noon - 1:45 p.m.**

ANOREXIA NERVOSA AND OBLIGATE RUNNING

Pauline S. Powers, M.D., University of South Florida College of Medicine, 12901 South 30th Street, Box 14, Tampa, FL 33612; Douglas D. Schocken, M.D., Peter O. Knight, M.D., Jeffrey Feld, M.D., Jeffrey T. Smith, B.S.

Summary:

Psychological similarities between male long-distance runners ("obligate" runners) and anorexia nervosa (AN) patients have been postulated. In this study, three groups were compared: 11 female AN patients, 11 female obligate runners (FR) and 19 male obligate runners (MR). We hypothesized that: (1) groups would have similar psychopathology, (2) all groups would have body image distortions, (3) AN patients would have more depression than runners, (4) fitness would be better in runners than AN patients. Subjects were given the MMPI, Leyton Obsessional Inventory (LOI), measures of body image, Beck Depression Inventory (BDI), a physical examination and an exercise stress test. The AN group had higher scores ($p<.05$) on several scales of the MMPI and higher scores on the LOI ($p<.05$) than either FR or MR groups. Females (AN and FR) overestimated hips on the Image Marking Technique compared to MR ($p<.05$). AN patients were more depressed ($p<.05$) than either group of runners. On the stress test, both FR and MR groups had greater work load capacity, longer exercise time and higher maximum blood pressure than the AN group ($p<.05$). We conclude that AN patients had significantly more psychopathology than either MR or FR. On body image tests, females shared some similarities, but no similarities appeared between AN patients and MR. Differences in depression and fitness were confirmed between AN patients and runners. However, we found fewer similarities between AN patients and runners than previously hypothesized. Our findings suggest that the appropriate comparison for future studies may be between AN patients and FR.

NR31 **Monday, May 12, 12:00 noon – 1:45 p.m.**

PREMENSTRUAL DYSPHORIA ACCORDING TO *DSM-III-R*

Sally Severino, M.D. NYH/CMC Westchester Division, 21 Bloomingdale Road, White Plains, NY 10605; Stephen W. Hurt, Ph.D., Margaret Anderson, M.D., Nancy A. Williams, Ph.D.

Summary:

The purpose of this study was to identify, in women who complained of a premenstrual disturbance, the prevalence and type of physical and emotional symptomatology. In particular, the authors utilized prospective data to explore the relationship between these symptom clusters.

Forty women agreed to undergo a three–month prospective study of the daily ratings of mood and physical symptoms. Prior to entry into the study, each woman completed a retrospective report of PMS symptomatology (PAF) and was extensively interviewed for the details of her psychiatric (SADS-L) and medical history. A complete physical examination including a bimanual pelvic examination, Pap smear, complete blood count and chemistry screen were obtained.

Data from the retrospective symptom ratings were used to classify women provisionally according to the proposed definition of premenstrual dysphoric disorder (PPD) of *DSM-III-R.* The data on prospective symptom change failed to support the provisional diagnosis in at least one-half of the sample. Retrospective symptom clusters, including those combinations which did or did not include physical symptoms, were differentially predictive of the prospective diagnosis of PDD.

These data support the need to consider the inclusion of PDD in *DSM-III-R* and the need to include physical symptoms as criteria for PDD.

In addition, the data should serve to educate the general clinician about criteria of and procedures for identification of premenstrual dysphoric disorder.

NR32 **Monday, May 12, 12:00 noon – 1:45 p.m.**

PREMENSTRUAL CHANGES IN ANXIETY PATIENTS

Diana P. Sandberg, M.D., NYS Psychiatric Institute, 722 West 168th Street, New York, NY 10032; Abby J. Fyer, M.D., Jean Endicott, Ph.D.

Summary:

There is good evidence that a lifetime history of major depressive disorder is related to dysphoric premenstrual mood changes. Although clinical observations suggest that panic attacks exacerbate premenstrually in some women, the relationship between anxiety disorders and premenstrual changes has not been well studied. This study describes such changes in anxiety patients.

The Premenstrual Assessment Form (PAF) was completed by women accepted for treatment at an anxiety disorders research clinic. Patients with various anxiety disorders were compared with both depressed patients and women without any mental disorder. Anxiety patients were further subdivided into those with and without a lifetime history of major depression.

Patients with panic disorder or agoraphobia with panic attacks met criteria for selected PAF typological categories of "autonomic physical syndrome," "organic mental features," "incresed well being," and "impaired social functioning" more often than did either comparison group. On the other hand, there was no difference in the percentage meeting criteria for PAF "water retention syndrome," indicating that there was not a general tendency for anxiety patients to endorse all symptoms. Comparison of anxiety patients with and without a past depression showed no difference in PAF scores.

There are both clinical and research implications of these findings. Awareness of their patient's usual premenstrual patterns will assist clinicians in preparing patients for temporary symptom increases and in assessing the need for supplemental medication. Investigators should be aware of the possible effects of premenstrual changes on the results of their evaluations and procedures.

NR33 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PREMENSTRUAL SYNDROME AND PSYCHIATRIC DISORDERS

Stephen W. Hurt, Ph.D., Psychiatry Department, NYH/CMC Westchester, 21 Bloomingdale Road, White Plains, NY 10605; Nancy A. Williams, Ph.D., Sally K. Severino, M.D., Margaret Anderson, M.D.

Summary:

Presently available data on the relationship between psychiatric disorders and premenstrual syndrome (PMS) have been difficult to interpret in the absence of prospective ratings of symptom change during the menstrual cycle.

The present study recruited 40 women who complained of marked premenstrual symptom exacerbation for a 3-4 month prospective study of daily symptom severity. Standardized rating forms were used to collect both retrospective and prospective data on symptoms related to psychiatric disorders and the menstrual cycle. Psychiatric disorders were classified using the Research Diagnostic Criteria. Although no association was found between psychiatric illness and kind of premenstrual disturbance, premenstrual syndromes were more prevalent among women with a present episode of an affective disorder. Symptom profiles were investigated to determine the presence of symptom clusters across menstrual cycles which discriminated between the presence or absence of a concurrent psychiatric disorder. These data suggest that affective disorders may represent an increased risk factor for the occurrence of PMS and that it can be reliably identified in prospective data in the absence of a psychiatric disorder.

The presentation should aid the listener in understanding the value of prospective data in establishing a diagnosis of premenstrual syndrome even in cases complicated by the co-occurrence of a psychiatric disorder.

NR34 **Monday, May 12, 12:00 noon - 1:45 p.m.**

ABNORMAL GLUCOSE TOLERANCE TEST IN PMS: A PILOT STUDY

Lee W. Vliet, M.D., 330 West Brambleton Avenue, #702, Norfolk, VA 23510

Summary:

This paper reports preliminary data on 32 consecutive patients aged 15-47 who were evaluated for the presence of premenstrual syndrome and evaluated for post-prandial (reactive) hypoglycemia as a contributing factor in their premenstrual mood, cognitive, and anxiety symptoms. The evaluation consisted of a standard psychiatric diagnostic interview, physical examination, Zung Depression Inventory, SMA 20, thyroid profile, 5-hour glucose tolerance test, and at least one cycle of menstrual symptom logs.

Twenty-six (81.2%) were found to have markedly abnormal 5-hour GTT results with a sharp drop in serum glucose to levels below 60 ng/ml. All patients kept a detailed symptom log during the GTT which enabled correlation of clinical symptoms with the serum glucose values throughout the test, and with symptoms which they experienced in the premenstrual (luteal) phase of their cycle. None of these patients had a previous history of diabetes and no other laboratory abnormalities were found.

The paper will discuss the specific patient symptoms, present additional epidemiological characteristics, and discuss the results of follow-up monitoring of the patients in response to the use of conservative treatment approaches (diet, exercise, relaxation training, etc.) in the amelioration of PMS.

NR35 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PREMENSTRUAL SYNDROME AND GALACTORRHEA: A NEW ENTITY

Bruce J. Biller, M.D., Medical Department, MIT, 25 Carlton Street, Cambridge, MA 02139; John H. Brandt, M.D.

Summary:

During evaluation of 18 women with premenstrual syndrome (PMS), we made the unexpected observation that 72% had galactorrhea. PMS was severe, manifesting depression, suicidal ideation, personality alterations, and emotional lability. These symptoms were also accompanied by non-psychiatric symptoms that surfaced 7-14 days before menses resulting in marked functional limitations. Notably, there was a three-generation family history of depression/psychiatric disease. Because of the galactorrhea and the severity of the PMS, we treated patients with bromergocriptine (Parlodel), a dopamine agonist. Galactorrhea resolved, irregular menses normalized, and hyperprolactinemia disappeared. All patients has either complete or near complete resolution of all of the major manifestations of PMS. Patients have been maintained on Parlodel in doses ranging from 5-30 mg/day, for an average of 32 months. All show continued absence of galactorrhea and control of PMS. There have been no significant side effects of long-term Parlodel therapy. Attempts at drug cessation resulted in recurrence of clinical/chemical abnormalities which resolved with resumption of medication. Our preliminary observations suggest an association between galactorrhea and severe PMS. We speculate that this reflects dysregulation of pituitary prolactin secretion due to a deficiency of hypothalamic dopamine. We speculate that this dopamine deficiency state may be more generalized in the CNS, creating the psychiatric manifestations of PMS which were treatable in this subgroup with Parlodel. Our results suggest a novel antidepressant effect of Parlodel in depressive states where dopamine deficiency may exist.

NR36 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PREMENSTRUAL DYSPHORIA: DISORDER? GONADAL IMBALANCE?

Uriel Halbreich, M.D., Department of Psychiatry, SUNYAB, 462 Grider Street, K-Annex, Buffalo, NY 14215; Jean Endicott, Ph.D., Susanna Goldstein, M.D.

Summary:

Physical, behavioral and mood changes during the premenstrual period are very common but their etiology is still obscure and even their existence is sometimes debated. Gonadal hormones have been postulated to be involved in (patho) physiology of premenstrual changes (PMC) but this is still unproven.

An update of our studies of the diversity of negative as well as positive PMC in normal women and their relationship to affective disorders will be presented. Then data on a subgroup of women with a wide range of severity of PMC as well as plasma levels of estradiol and progesterone will be used to demonstrate the possible dynamic, time-related relationship (as opposed to single blood drawings or averages) between these hormones and clinical changes.

It is shown that specific clinical dysphoric PMC are positively correlated with peak levels of progesterone, with its rate of change-over-time and the ratio between the relative rates of decrease-over-time (the angle between the two slopes) of levels of progesterone and estradiol, a time lag of 4-7 days between changes in plasma levels of progesterone and clinical symptoms has also been found. Plasma levels of estradiol per se were not associated with PMC.

These data and related animal studies suggest that dynamic, time-related changes in levels of gonadal steroid hormones are involved in the physiology of PMC. Their role in that multifactorial field and their contribution to vulnerability to develop symptoms will be discussed.

NR37 **Monday, May 12, 12:00 noon - 1:45 p.m.**

MASOCHISTIC PERSONALITY: DIAGNOSIS AND SEXIST BIAS

A. Kenneth Fuller, M.D., Department of Psychiatry, University of Florida, Box J-256, JHMHC, Gainesville, FL 32610; Roger K. Blashfield, Ph.D.

Summary:

Masochistic Personality Disorder (MPD) is a controversial category that has been proposed recently for inclusion in the *DSM-III-R.* The term has been criticized as having no scientific evidence for its validity and also as potentially sexually biased. The purpose of this research is to study the clinical relevance and possible sexist bias of MPD. Fifteen case histories have been chosen from previous research on the classification of the personality disorders by authors using the prototype model. Five of the case histories represent MPD; the remaining 10 case histories typify other selected personality disorders. The case histories have been sent to 450 psychiatrists, clinical psychologists and private practitioners. These clinicians are subdivided into three groups. The first group are asked to diagnose the case histories using the *DSM-III;* the second group diagnose the case histories using the *DSM-III-R;* for the third group, the gender of the case histories are reversed and the clinicians assign *DSM-III-R* diagnoses. If the diagnosis of MPD is not needed, the MPD cases should be consistently diagnosed using the *DSM-III.* Alternatively, if MPD is a clinically useful diagnosis, the Masochistic vignettes should be randomly diagnosed using the *DSM-III,* but consistently labeled as MPD under the *DSM-III-R.* The data received to date support the latter hypothesis. If sex bias exists, the diagnoses assigned to the cases should be changed when the gender is reversed. With the exception of one case history, the sex bias hypothesis has not been supported.

NR38 **Monday, May 12, 12:00 noon - 1:45 p.m.**

BORDERLINE AND NARCISSISTIC PERSONALITY DISORDERS

Eric M. Plakun, M.D., Austen Riggs Center, Inc., Stockbridge, MA 01262; John P. Muller, Ph.D.

Summary:

In a previous New Research presentation data from an Austen Riggs Center follow-up study of 237 inpatients were offered on borderline (BPD) and schizotypal (SPD) personality disorder functioning at admission and mean 14-year follow-up as measured by the Global Assessment Scale (GAS). The current study compares BPD to another related diagnosis, narcissistic personality disorder (NPD), to assess the validity of the DSM-III NPD diagnosis and determine whether it is distinct from BPD. Fifty–four BPD patients and 30 NPD patients are compared to each other and to major affective disorder (MAD) and schizophrenia patients in terms of (1) demographic and (2) psychiatric history variables, (3) admission and (4) mean 14-year follow-up GAS functioning. A discriminate function analysis of BPD and NPD criteria is performed to ascertain the most and least discriminating DSM-III criteria for these diagnoses. Finally, the impact of proposed changes in BPD and NPD criteria in *DSM-III-R* is examined in this patient sample. Results suggest NPD is distinct from schizophrenia but not MAD or BPD in terms of admission and mean 14-year follow-up functioning. The lack of demonstrable difference between BPD and NPD is consistent with Kerberg's notion that both diagnoses are manifestations of borderline personality organization. Proposed changes in *DSM-III-R* may decrease the ability to distinguish between these diagnoses.

NR39 **Monday, May 12, 12:00 noon - 1:45 p.m.**

COMPARISON OF *DSM-III* PERSONALITY DISORDER MEASURES

James H. Reich, M.D., University of Iowa, 500 Newton Road, Iowa City, IA 52242; Russell Noyes, Jr., M.D., Ed Troughton, B.S.

Summary:

In order to determine the comparability of three standardized measures of *DSM III* defined personality disorders they were compared on an acutely ill psychiatric outpatient population (N=128). The measures; the Structured Interview for *DSM III* Personality Disorder (SIDP), the Personality Diagnostic Questionnaire (PDQ), and the Millon Clinical Multiaxial Inventory (MCMI) had low agreement in both pairwise kappas and by correlation of personality disorder criteria. Kappas of agreement for a personality disorder for any two instruments exceeded .50 only twice. All instruments showed validity for "any" personality disorder and *DSM III* personality disorder clusters A and B. The PDQ and MCMI also showed validity for cluster C. Possible reasons for poor instrument agreement include possible problems with the *DSM III* criteria, state effects (depression, anxiety), methodologic difficulties and low base rates. The authors recommend that until further research clarifies the present difficulties, researchers should select the instrument(s) with the best reliability and validity for the particular disorder or cluster that they are studying.

NR40 **Monday, May 12, 12:00 noon - 1:45 p.m.**

CHILDREN'S PSYCHIATRIC SYMPTOM CATEGORIES

Marjorie McMeniman, Ph.D., 314 West 100th Street, #51, New York, NY 10025; Madelyn S. Gould, Ph.D., David Shaffer, M.B., Michael Rutter, M.D., Claire Sturge, M.B.

Summary:

The purpose of the research described here was to derive an empirically based classification of symptoms for this particular data set, and to compare this taxonomy to others similarly derived by other researchers. The data set used in this analysis is part of a larger study that was conducted in England for the World Health Organization on the multiaxial classification of child psychiatric disorders. Only the portion of the study used in the present analysis is described here.

The data derive from a "clinical study" in which the goal was to examine a large number of patients in a naturalistic setting. Psychiatrists were asked to diagnose and describe ten consecutive new cases from their clinical practice. Among the extensive data provided was information on the presence or absence (on a 4-point scale) of 35 different symptoms. The age range of the children was from 4 to 17 years old (N=320).

A six-factor solution was derived using Rao factor analysis of the symptoms. The factors were: (1) development delay, (2) anxiety, (3) attention deficit disorder, (4) delinquency, (5) autism, and (6) psychosis. Reliabilities ranged from .47 to .74. This solution was compared to those found in previous analyses (usually principal components on American children). Lisrel analyses of age-sex groups and cluster analysis were performed, but without satisfactory results. Reasons for this are discussed.

NR41 **Monday, May 12, 12:00 noon - 1:45 p.m.**

INFANT TEMPERAMENT AND INTELLIGENCE AT FOUR YEARS

Michel Maziade, M.D., Research Division, Hotel-Dieu Sacre Coeur, Avenue de Sacre-Coeur, Quebec PQ O, Canada G1N 2W1; Robert Cote, Ph.D., Pierrette Boutin, M.Ps., Hugues Bernier, M.Ss., Jacques Thivierge, M.D.

Summary:

This longitudinal study aims at measuring the association between the NYLS temperament assessed at 4 and 8 months and IQ assessed at 4.7 years, and at taking account of the effect of SES and family functioning (communication and behavior control). We selectd three subgroups of infants (matched for sex and SES) from our 1979 birth cohort (N=358): the initial 1979 sample was representative of all SES and consisted of all the babies born in a catchment district within a specific period (Maziade et al, 1984). Temperament was assessed by means of the Carey Infant Temperament Questionnaire. The infants were characterized on our easy-difficult Factor I (principal component analysis). We selected one subgroup of extremely easy, one of average and one of extremely difficult temperament (N=80); the temperament criteria had to be stable both at 4 and 8 months. The study was conducted double-blind to the 1979 temperament scores. Data show a strong effect of extreme temperament traits on IQ (WPSSI) development only in middle and upper SES (t test, $p<.005$; Bonferroni test, $p<.05$) and only in families presenting superior functioning in terms of communication (t test, $p<.002$; Bonferroni test, $p<.05$). Surprisingly the difficult infants displayed higher IQ. Conversely the already well replicated effect of SES on IQ was observed mainly in the temperamentally difficult subgroup. A robust regression approach also suggested the presence of a temperament X SES and a temperament X family communication interaction which produces an effect on IQ at 4 years. Besides, parental control does not interact with temperament. Data support the hypothesis that infants with difficult temperament activate special (especially linguistic) resources in the family, which stimulates their intellectual development over the years.

NR42 **Monday, May 12, 12:00 noon - 1:45 p.m.**

DECREASED IMIPRAMINE BINDING IN CHILD AGGRESSION

David Behar, M.D., Medical College of Pennsylvania, 3200 Henry Avenue, Philadelphia, PA 19129; David Stoff, Ph.D., Leafy Pollock, Ph.D., Benedetto Vitiello, M.D., David Yee, M.S., Wagner Bridger, M.D.

Summary:

Cerebral spinal fluid 5-HIAA levels have been found to be low in diverse groups of impulsive patients (e.g., violent suicides, impulsive murderers, and impulsive personality disorders). We recently presented data that platelet imipramine binding, thought to be a pre-synaptic marker of central serotonergic activity is also low in aggressive adolescents.

We selected 8 boys and 2 girls (mean age = 10.2 ± 1.4) with aggressive conduct disorders and hyperactivity according to the Diagnostic Interview for Children and Adolescents *(DSM-III)* and normal controls matched for age, sex, race and socioeconomic status. Subjects had a 31% lower maximal platelet imipramine binding ($p<.05$). There were no significant differences in total serum tryptophan or ratio of tryptophan to five other amino acids, differing from others' reports of aggressive alcoholics, who may have had liver damage.

Although there were highly significant differences between groups on ratings of hyperactivity, impulsivity and aggressiveness, correlations between Bmax and any of these measures were not robust, except the Conners conduct disorder factor ($r = -.44$; $p<.02$).

Because many of the subjects are expected to grow up to have the above adult disorders, low platelet imipramine binding may represent an early marker of an inability to modulate behavior.

NR43 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PSYCHOLOGICAL ASPECTS OF CHILDHOOD DEPRESSION

Margaret M. Rea, M.S., Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; John Sweeney, Ph.D., J. John Mann, M.D.

Summary:

Childhood depression continues to be poorly understood and even controversial as a diagnostic entity. One important question is whether adult and childhood depression are clinically similar; particularly in intrapsychic and cognitive dimensions. Three aspects of cognitive appraisal: low self-esteem, hopelessness, and an insidious depressive attributional style characterize adult depression. It remains unclear whether the configuration of these variables is similar in children. All 51 inpatients at a children's psychiatric hospital who were able to attend the hospital school and 56 comparison normal controls were administered the following tests: The Children's Depression Inventory, The Harter Perceived Competence Scale, The Hopelessness Scale, and The Children's Attributional Style Questionnaire. All children were of a least average I.Q. and ranged from 7-13 years of age. The psychiatric sample exhibited more severe depressive symptoms ($p=<.01$), lower cognitive self-esteem ($p<.05$), greater hopelessness ($p<.02$), but not a more depressive attributional style. Level of depression was correlated with feelings of hopelessness ($r = .60$, $p<.001$), dimensions of self-esteem ($r = -.38$, $p<.01$), and aspects of a depressive attributional style ($r = .27$, $p<.05$). The findings suggest the clinical validity of assessing these dimensions as indices of depression in children, however, a depressive attributional style, in which negative life events are attributed to enduring aspects of the self, seems less associated with depression than in adults.

NR44 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PATTERNS OF ADOLESCENT RAPE

Sophia Vinogradov, M.D., Department of Psychiatry, Stanford University Medical Center, Stanford, Ca 94305; Norman I. Dishotsky, M.D., Ann Doty, M.S., Jared R. Tinklenberg, M.D.

Summary:

The authors studied 67 rapes committed by 63 California adolescents, and devised a highly representative composite picture of the typical rape episode. Such a typical rape takes place on a weekend night, towards the end of summer, in the victim's home or a vehicle; the rapist is engaged in another activity, often some other crime, and there may be multiple assailants. The typical rapist is a young urban male of low socioeconomic status with a record of prior arrests. His victim is a young female who is a stranger to him. Most rapists are of the same race as their victim, but interracial rape occurs frequently and the typical victim is white.

Typological elements empirically derived from these data are presented. The authors show that a consistent, definable amount of violence is used in rape and that for a large subgroup of rapists, the amount of violence is high. The rape is primarily an act of assault and aggression that occurs opportunistically, although a subgroup of rapes are premeditated. A large number of adolescent rapists are intoxicated during the rape. Finally, a subgroup of rapists report difficulty relating to women, but the rape is not in repsonse to specific provocation by the intended victim.

NR45 **Monday, May 12, 12:00 noon - 1:45 p.m.**

THE COMMUNICATION DEFICIT IN ASPERGER'S SYNDROME

G. Bartolucci, M.D., St. Joseph's Hospital, 50 Charlton Avenue East, Hamilton, Ontario, L8N 4A6 Canada; Peter Szatmari, M.D., Lester Krames, Ph.D., Gordon Flett, M.A.

Summary:

Children who are socially isolated and show odd behavior have been described as having Asperger's syndrome; the diagnostic criteria by Wing emphasize the social and communicative defects of these patients. We have developed a battery of tests to describe objectively the communicative deficits under the categories of: nonverbal expressive (NVE), verbal expressive (VE), nonverbal receptive (NVR) and verbal receptive (VR). A modified Scale for the Assessment of Negative Symptoms (KSANS) was used to measure NVE, the Profile of Nonverbal Sensitivity (PONS)[2] to measure NVR, a word fluency test to measure VE and the children's version of the Token Test as a measure of VR. A sample of 20 Asperger's syndromes, mean age 14, 16M and 4F, was compared with a matched control group of mixed psychiatric patients with difficulties in peer relationships, but no odd behavior. Controlling for I.Q. the Asperger's syndromes showed more impairment on the KSANS in nonverbal communication: A=10.3 vs X, =2.4, pL0.0001, and alogia X=4.6 vs X, =.5, $p<0.0001$. Perception of facial expression on the PONS was also more impaired in the Asperger's syndromes ($p<0.04$). Data from standardized individual and family interviews and a comprehensive neuropsychological battery will also be presented.

NR46 **Monday, May 12, 12:00 noon - 1:45 p.m.**

INTELLIGENCE IN ADOLESCENT PSYCHOSIS

Terry E. Goldberg, Ph.D., NIMH, St. Elizabeths, WAW Building, Washington, D.C. 20031; Craig N. Karson, M.D., Jimmie P. Leleszi, D.O.

Summary:

While schizophrenia is associated with deficient performance on intelligence tests, the relationship of the impairment to the course of the illness remains uncertain. By studying psychotic adolescents, 90% of whom were hospitalized for the first time, we hoped to reduce the influence of such confounding variables as lengthy disease process, neuroleptic treatment, and institutionalization. Thirty-nine psychotic adolescent subjects who fulfilled *DSM-III* criteria for schizophrenia, schizophreniform psychosis, paranoid schizophrenia, or atypical psychosis were compared to 41 non-psychotic adolescent psychiatric controls.

Subjects were administered the Wechsler Intelligence Scale for Children — Revised, Peabody Individual Achievement Tests of reading, reading comprehension, and mathematics, Bender-Gestalt, and Purdue Pegboard Test within three weeks of admission to a psychiatric hospital. Performance IQ was significantly lower in the psychotic group (72 versus 93, p .001). Thus, the IQ pattern in adolescent psychotic patients at an early stage in their illness was similar to the pattern displayed by chronic adult schizophrenic patients. Results were not consistent with theories of left hemisphere involvement in schizophrenia. Academic achievement was similar in both groups despite marked differences in Performance IQ. Psychotrophic medication had little impact on the results. In summary, deficits in processing novel material seem at the very least to be present at the onset of the psychotic disorder, though they may be non-progressive thereafter.

NR47 **Monday, May 12, 12:00 noon - 1:45 p.m.**

PREATMENT OF HYPERACTIVITY WITH PHENYLALANINE

Alan Zametkin, M.D., Child Psychiatry Branch, NIMH, Building 10, Room 6N-240, 9000 Rockville Pike, Bethesda, MD 20892; Judith L. Rapoport, M.D., Farouk Karoum, Ph.D.

Summary:

Eleven hyperactive boys were treated with d-phenylalanine (20mg./kg./day for two weeks) or placebo in a double-blind crossover study. Phenylalanine is the dietary precursor of phenylethylamine, an endogenous trace amine that is excreted in smaller quantities by hyperactive children than by controls. Phenylalanine is also the major constituent of aspartame, a food additive now commonly ingested by school age children. Measures included parent and teacher behavior ratings, cognitive testing, and blood and urine measures of norepinephrine, amino acids, and trace amines. No significant improvement or deterioration in behavior or side effects were noted and only serum phenylalanine was increased significantly ($P<.0006$) by active treatment. This provides reassurance about dietary toxicity of aspartame, but argues against precursor loading treatment of hyperactivity.

NR48 **Monday, May 12, 12:00 noon - 1:45 p.m.**

CLINICAL OUTCOME AND THE DST IN DEPRESSED CHILDREN

Ronald A. Weller, M.D., Department of Psychiatry, OSU, 473 12th Avenue, Columbus, OH 43210; Elizabeth B. Weller, M.D., Mary Fristad, Ph.D., Michael Cantwell, M.D.

Summary:

Subjects were 28 prepubertal children hospitalized for depression who all had a positive Dexamethasone Suppression Test (DST) which was done as part of their diagnostic evaluation. All were moderately to severely depressed at admission on standard rating scales. After a one-week baseline evaluation period, all subjects began treatment for depression. Clinical evaluation and the DST were repeated for 21 of the patients after 6 weeks of treatment, remission had occurred in 9 of the 21 (43%) patients retested. Only one-third of these 9 in clinical remission normalized on the DST; 50% of the 12 subjects who remained clinically depressed normalized. Chi-square analysis did not show a significant correlation between the DST and clinical status at this point in time. At 5 months 6/14 (43%) subjects tested had clinical remissions, all 6 had normal DST's. Of the 8 who had not remitted, only 1 (12%) had normalized. Chi-square analysis indicated that DST results were now significantly associated with clinical outsome ($X=10.5$; $p<.01$; df, 1; two-tailed test). Results suggest that 6 weeks into treatment was too early to predict clinical status from DST results. However, the DST was clearly linked with clinical outcome 5 months after treatment had begun. At that time an abnormal DST was indicative of poor clinical status while a normal DST corresponded with clinical remission. In almost all cases where clinical improvement was noted, it coincided with or preceded normalization on the DST.

NR49 **Monday, May 12, 12:00 noon - 1:45 p.m.**

CORTISOL SUPPRESSION MEASURES IN CHILDREN

Ronald A. Weller, M.D., Department of Psychiatry, OSU, 473 West 12th Avenue, Columbus, OH 43210; Elizabeth B. Weller, M.D., Sheldon H. Preskorn, M.D., Mary Fristad, Ph.D., Michael Cantwell, M.D.

Summary:

The dexamethasone suppression test (DST) and cortisol suppression index (CSI) have been used to assess hypothalmic-pituitary-adrenal (HPA) axis dysfunction in depression. However, they have not been compared in prepubertal children. In fact, the CSI has not yet been tested in prepubertal depressed children. In this study the DST and CSI were both performed in 50 hospitalized depressed children, 18 psychiatrically hospitalized children without depression, and 18 psychiatrically well controls. All subjects were prepubertal aged 6-12. Baseline cortisol levels were measured at 8 a.m. and 4 p.m. Then .5 mg. dexamethasone was given at 11 p.m. and cortisol levels were measured at 8 a.m. and 4 p.m. the next day. The DST was abnormal if the post-dexamethasone cortisol levels were >5 ug/dl. The CSI was positive if the 8 a.m. CSI was <7.0 or 4 p.m.<2.5. Sensitivity, specificity, diagnostic confidence, and clinical utility of the DST and CSI were computed and compared. The 8 a.m. DST and 4 p.m. CSI lacked sufficient sensitivity and/or specificity to be clinically useful. However, the 8 a.m. CSI, 4 p.m. DST, and 2 point DST (8 a.m. or 4 p.m. positive) appeared to give useful results. Sensitivities were: 4 p.m. DST 70%, 8 a.m. CSI 75%, and 2 point DST 80%. Specificities were 8 a.m. CSI 78%, 2 point DST 81%, and 4 p.m. DST 86%. Clinical utility and diagnostic confidence were also similar. Furthermore, 94% of depressed subjects had either positive 8 a.m. CSI or 4 p.m. DST suggesting HPA axis abnormalities may be frequent in prepubertal depression. The concept that the CSI and DST may be complementary in assessing HPA abnormalities in depression should be the subject for further research.

NR50 **Monday, May 12, 12:00 noon - 1:45 p.m.**

METHYLPHENIDATE AND INFORMATION PROCESSING DEFICIT

David L. Braff, M.D., Department of Psychiatry M-003, UCSD, La Jolla, CA 92093; Leighton Huey, M.D.

Summary:

To examine the effects of methylphenidate on attention and information processing, 13 patients with clinical attentional deficits were tested in a double-blind, counterbalanced study. Patients received methylphenidate, oxazepam (15 mg bid), or placebo in 1-week blocks. They were further divided into high or low dose methylphenidate groups (1 or 0.5 mg/kg). Information processing measures consisted of 1) a stimulus identification task where visual perception was assessed, called the critical stimulus duration; and 2) a speed of information processing task, visual backward masking, in which a target stimulus is followed at varying interstimulus intervals by a noninformational mask limiting the availability of the target.

Data were analyzed by ANOVA and revealed that methylphenidate significantly impaired information processing. This effect was dose dependent: high dose methylphenidate caused more impairment than low dose, despite equivalent performance during the oxazepam and placebo treatment periods. The results demonstrate that methylphenidate does not adversely affect simple, initial stimulus registration that is theoretically linked to an uncomplicated and unstressed neural process. Methylphenidate does, however, impair more complex information processing tasks. The observed deficits resemble the performance deficits of schizophrenics. Results provide evidence that increased dopaminergic tone may account for the well-documented attentional and information processing deficits found in schizophrenia.

NR51 **Monday, May 12, 12:00 noon - 1:45 p.m.**

ELECTROCARDIOGRAM ABNORMALITIES AND PIMOZIDE

George Fulop, M.D., Department of Psychiatry, Mt. Sinai Hospital, 1 Gustave Levy Place, New York, NY 10029; Robert Phillips, M.D., Arthur K. Shapiro, M.D., J. Anthony Gomes, M.D., Elaine Shapiro, Ph.D., Johanna W. Nordlie, M.A.

Summary:

Pimozide is the only approved alternative to haloperidol for the treatment of Tourette Disorder (TD). However, reports of abnormal electrocardiograms (ECG) prompted FDA regulations advising "periodic" ECGs during dosage adjustment. This study evaluates the ECG changes associated with treatment of TD patients with pimozide.

Forty patients (mean age 21 years, range 8-47), with a *DSM-III* diagnosis of TD were treated clincially with haloperidol, pimozide, or placebo in a randomized, double-blind, crossover experimental study. Standard 12-lead ECGs were obtained at baseline, midpoint, and endpoint, and were read blindly by a cardiologist.

The QTc-interval (Bazett correction) was significantly prolonged for active drugs ($p=.0001$) but not for placebo (repeated measures analysis of variance), and for pimozide ($p=.0001$) compared to haloperidol (paired t-test). Rate, rhythm, QRS-interval, and u-wave or t-wave abnormalities were not significantly different among the three drug categories. There were no significant effects of age, sex, and dosage of medication (mg/kg) on the ECG (analysis of covariance).

Although the QTc-interval was statistically prolonged, treatment with pimozide up to a dosage of 0.3 mg/kg or 20 mg/day did not cause clinically significant cardiovascular adverse effects. The results suggest that pimozide can be administered safely during dosage adjustment and can be monitored by obtaining ECGs at baseline and clinical endpoint. Possible mechanisms of the effect of haloperidol and pimozide on the QTc will be discussed.

NR52 **Monday, May 12, 12:00 noon - 1:45 p.m.**

CHILD CUSTODY AND RELITIGATION IN RURAL SETTINGS

Bruce R. Berger, M.D., Department of Psychiatry, ECU Medical School, Brody Building, Greenville, NC 27834; Sudhakar Madakasira, M.D., Vivian Roebuck, Kevin F. O'Brien, Ph.D.

Summary:

Continued conflict and child custody arrangements are generally considered to be the major influences on children's adjustment to divorce rather than the divorce itself. Joint custody has been advocated in recent years to better facilitate children's adjustments. Postulating the rate of relitigation as a potential indicator of post-divorce parental conflict, a recent study done in an urban setting found joint custody to be associated with half as many relitigations as exclusive custody. The purpose of the present study was to assess in a rural setting the rate and type of relitigation after divorce in cases involving children, and to compare the rate of relitigation in joint versus exclusive custody. Between 1980 and 1984, there were 885 divorces that involved children. In 29% of the divorces child custody did not come up for adjudication because of prior satisfactory settlement. Exclusive custody was granted in 69% of the cases. Joint custody was noted in only 2.3% of the cases although joint custody has been legislated for more than 15 years in the state.

There were 171 relitigations after divorce. When the reasons for relitigation were examined, unsatisfactory monetary arrangement was more frequent with exclusive custody than with joint custody ($x^2 = 10.4$, $p<0.05$). Joint custody was associated with more relitigations for changing child custody ($x^2 = 74$, $p<0.001$) and for noncompliance with monetary obligations ($x^2 = 36.8$, $p<0.001$). Thus, joint custody, although very limited in prevalence in a rural setting, appears to be associated with increased relitigation and may not necessarily decrease family conflict.

NR53 **Monday, May 12, 12:00 noon - 1:45 p.m.**

SUICIDE BY CHILDREN: AN ANALYSIS OF 31 CASES

David N. Neubauer, M.D., 4940 Eastern Avenue, Baltimore, MD 21224

Summary:

The topic of adolescent suicide has received considerable popular attention recently; however, little research has focused on the problem of suicide by children. The present study examines all 31 suicides by children under age 15 in Dade County, Florida during the past 30 years. Demographic patterns and suicide method selection of the childhood cases are compared with the total population of suicides by individuals of all ages in this region during the same time period. The results of the analysis differentiate childhood suicides from completed suicides by adolescents. The rate has not significantly increased over recent decades, there is an overrepresentation of females and Blacks, and children often commit suicide in a violent manner. Since firearms and hangings account for 87% of their suicides, there are clear implications for suicide prevention which require immediate attention. Reduction of the availability of firearms alone will decrease the number of childhood suicides.

NR54 **Tuesday, May 13, 9:00 a.m.**

REARING CONDITION AND RESPONSE TO ANXIOGENIC DRUG

Thomas R. Insel, M.D., Laboratory of Clinical Science, NIH, 10/3D41, 9000 Rockville Pike, Bethesda, MD 20892; Maribeth Champoux, James M. Scanlan, Stephen J. Suomi, Ph.D.

Summary:

Socially housed rhesus monkeys (n=8) were raised in peer groups under two rearing conditions defined by their control over nonaversive stimuli. A control (CON) group had free access to toys and food treats. Identical items were presented to a yoked (YOK) group only when selected by an animal in the CON group. Testing in the third year of life revealed significant group differences ($p<.05$) in the response to social separation with individuals in the YOK group exhibiting more distress. The benzodiazepine inverse agonist, β-CCE (0, 50, 500 μ g/kg) was administered intravenously to individuals in both groups to investigate differences in "anxiogenic" responses. When given to individuals in their home groups, both doses of β -CCE were associated with increases in aggressive threats in the CON group, whereas animals in the YOK cage demonstrated increases in social withdrawal and "coo" (distress) vocalizations (differences between groups $p<.05$). Group differences in the behavioral response to β-CCE were also observed when drug was administered to individuals in an isolated condition. It appears that putative "anxiogenic" compounds have differential behavioral effects depending on rearing history, and that experiences of control and mastery early in life may have long-term consequences on coping behavior.

References:

[1]Insel T., Ninan P., et.al., Arch. Gen. Psych. 41: 741-750, 1984.

[2]Champoux M., Mineka S., Dev. Psychol. (in press).

NR55 **Tuesday, May 13, 9:15 a.m.**

INPATIENT FAMILY INTERVENTION: A CONTROLLED STUDY

Ira D. Glick, M.D., Payne Whitney Clinic, 525 East 68th Street, New York, NY 10021; Gretchen L. Haas, Ph.D., James H. Spencer, M.D., John F. Clarkin, Ph.D., Alfred B. Lewis, M.D., Veronica Lestelle, M.S.W.

Summary:

Family interventions are being used with increasing frequency and success in the treatment of major psychiatric disorders, such as schizophrenia and major affective disorder. This is the fourth report on an ongoing, long-term, controlled study designed to evaluate the relative effectiveness of Inpatient Family Intervention (IFI) added to a standard multimodal hospital treatment. Seventy-eight *DSM-III* Schizophrenic Disorder and 54 *DSM-III* Major Affective Disorder patients were randomly assigned to one of two treatments: an integrated multimodal hospital treatment *including* IFI, or comparison treatment including the same multimodal hospital treatment but with an emphasis on individual treatment and *excluding* IFI. Multidimensional measures of symptom severity and role-functioning as well as family attitudes toward patient and illness-related problems were obtained at admission, discharge, and at six- and eighteen-month follow up.

Results at discharge revealed a significantly better outcome for IFI patients (all diagnoses combined) on measures of global functioning, $F(1,130) = 7.17$, $p<.008$, and family willingness to accept help from professionals, $F(1,130) = 3.80$, $p<.05$. These effects were essentially restricted to the female patients who showed better global functioning, $F(1,73) = 8.34$, ($p<.005$), less severe symptoms, $F(1,73) = 6.97$, $p<.01$, and more positive attitudes of family toward patient, $F(1,73) = 4.29$, $p<.04$. Results for the full sample at six-months and a discussion of differences in outcome for the different diagnostic groups will also be presented.

References:

[1]Falloon IRH, Boyd JL, McGill CW, Williamson M, et.al. Family management in the prevention of morbidity of schizophrenia. Arch. Gen. Psychiatry 1985; 42:474-478.

[2]Glick ID, Clarkin JF, Spencer JH, Haas GL, Lewis AB, Peyser J, DeMane N, Good-Ellis M, Harris E, Lestelle V. A controlled Evaluation of Inpatient Family Intervention: I. Preliminary results of the six-month follow-up. Arch. Gen. Psychiatry 1985; 42:882-886.

NR56 **Tuesday, May 13, 9:30 a.m.**

FAMILY FUNCTIONING AND THE COURSE OF DEPRESSION

Gabor I. Keitner, M.D., Butler Hospital, Brown University Medical Program, 345 Blackstone Boulevard, Providence, RI 02906; Ivan W. Miller, Ph.D., Nathan B. Epstein, M.D., Duane S. Bishop, M.D.

Summary:

Although there is increasing awareness that families of depressed patients experience a wide range of difficulties, less is known about the relationship between the functioning of the family and the course of the depressive illness. Thirty–eight psychiatric inpatients with major depression and their families were assessed using the Family Assessment Device (FAD), a 60–item self–report questionnaire with established reliability and validity. All family members over the age of 12 filled out the FAD. Patients were followed until they recovered from the depressive episode (Modified Hamilton Rating Scale < 9 for three consecutive months) or for 12 months if recovery was not achieved, at which time the FAD was readministered to the patient and the family. The 28 families completing follow up were matched to 28 nonclinical control families. There were no differences between drop–outs and completers in general family functioning. 1) During the acute phase of the depressive illness, families of the depressed patients reported significantly worse family functioning, in a wide range of areas, than control families. 2) With resolution of the depression, there was some improvement in family functioning, but the depressed families still perceived their family life to be more problematic than those of nonpatient families. 3) In those families where there was some improvement in family functioning, the depressive episode lasted for a significantly shorter period of time (4.1 months) than in those families with no improvement (8.1 months) ($t=3.38$; $df=26$; $p<.0023$). 4) The family's perception of its functioning during the acute episode was not a good predictor of the length of depression for its family member.

References:

[1]Vaughn, C.E. and Leff, J.P.: The influence of family and social factors on the course of psychiatric illness. A comparison of schizophrenic and depressed neurotic patients. *British Journal of Psychiatry, 129:*125-137, 1976

[2]Rounsaville B.J., Prussof, B.A., and Weissman, M.M. The course of marital disputes in depressed women. A 48-month follow-up study. *Comprehensive Psychiatry, 21:*111-118, 1980.

NR57 **Tuesday, May 13, 9:45 a.m.**

SUICIDE ATTEMPTS BY SCHOOL-AGE ADOLESCENTS

Norma C. Josef, M.D., Lafayette Clinic, 951 East Lafayette, Detroit, MI 48207; R. John Kinkel, Ph.D., Charles W. Bailey, M.S.W.

Summary:

The prevalence of adolescent suicide attempts today remains relatively unknown. Although completed suicides for adolescents are generally considered a rare event (12.3 per 100,000 in 1980, ages 15–24), estimates regarding rates of suicide attempts have fluctuated considerably. Studies using private practice and/or hospital records contend there are 50 to 150 attempts for each completed suicide. According to these studies the rate of adolescent suicide attempts could be as high as 1845 per 100,000 (or 184.5 per 10,000). Dissatisfied with this approach for obtaining information on adolescent suicide attempts, a few studies have sought to examine the prevalence of suicide attempts using self–report instruments in a general population of adolescents. Until recently samples using this new approach have been relatively small (<500). In the Genesee County, Michigan, study (1985) we examined the prevalence of adolescent suicide attempts using: 1) a large probability sample (n=2,666); 2) self–report instruments; 3) focus on the general population of adolescents age 12–18 from a metropolitan statistical area (450,449; 1980). We found that 7.7 (201/2610) percent (or 770 per 10,000) of the sample reported attempting suicide at least once in the previous 12 months. Although more research is needed to determine the relative lethality of these reported attempts, our research suggests that previous studies may have underestimated adolescent suicide attempts by a factor of 4 (184.5 per 10,000 vs. 770 per 10,000). The Genesee County study grouped the data into attempters (n=201) and nonattempters (n=2409). The following factors were found to be statistically significant ($p<.05$) in predicting suicide attempts: 1) gender, 2.23 females to 1 male attempt; 2) parents' education — less educated more at risk; 3) drug use; 4) compulsive behavior; 5) life satisfaction index; 6) sexual abuse; 7) conflict with parents; and 8) suicide ideation. The implications these findings have for primary prevention and the identification of students at risk are discussed.

References:

[1]McKenry PC, Tishler CL, Kelley C: Adolescent Suicide. Clinical Pediat 21:266-270, 1982.

[2]Harkavy JM, Asnis G: Suicide attempts in Adolescence Prevalence and Implications. N Eng J Med 313:1290-1291, 1985.

NR58 **Tuesday, May 13, 10:00 a.m.**

ADOLESCENT SUICIDAL BEHAVIOR: PRELIMINARY STUDY

Jill M. Harkavy, Ph.D., MMC/AECOM, Psych OPD. 111 East 210th Street, Bronx, NY 10467; Gregory M. Asnis, M.D.

Summary:

Suicidal behavior among adolescents is not a new phenomenon. Over 7,000 adolescents in the United States are likely to kill themselves in this year alone. We have little knowledge regarding the nature, frequency and course of such self–destructive behavior in the general population and in this age group in particular. We conducted a study exploring the frequency and form of suicidal behavior among 382 high school students between the ages of 14 and 18. The study is unique in that suicidal thoughts, plans and attempts were asked about in specific detail. Sixty percent of students surveyed anonymously reported suicidal ideation, with over 20% reporting that these thoughts persisted for at least 7 days in a row and 35% reported suicidal plans. Most alarming was the finding that almost 9% reported having made at least one suicide attempt and less than half of these youths reached the attention of mental health professionals. The data suggest that suicidal behavior is not a discrete act. For example, almost half the students who reported making attempts stated that they had made multiple attempts and almost one–third reported that they had had suicidal thoughts in the week prior to the study. The results of this study have implications for the assessment, treatment and prevention of self–destructive behavior among our youth.

References:

[1]Vital Statistics of the United States. Washington, D.C.: Department of Health and Human Services, Government Printing Office, 1981.

[2]Harkavy, J.M., Asnis, G. Suicide attempts in adolescence: Prevalence and implications. *New England Journal of Medicine,* 1985, *313,* 1290-1291.

NR59 **Tuesday, May 13, 10:15 a.m.**

BIOLOGICAL MARKERS IN COGNITIVE AND PHARMACOTHERAPY

Gary D. Tollefson, M.D., Department of Psychiatry, St. Paul/Ramsey Medical Center, 640 Jackson Street, St. Paul, MN 55101; Erhard Haus, M.D., Michael Garvey, M.D., Joan M. Piasecki, B.A., Steve Hollon, Ph.D.

Summary:

A non–drug intervention, cognitive behavior therapy (CB), has proven effective for depression. This raises the question whether different interventions, imipramine (IMI) and/or CB, have a common impact on four potential biological markers in depression; melatonin (MEL), dehydroepiandrostereonesulfate (DHEA–S), cortisol (CORT), 6–methoxyphenylglycol (MHPG). A 12–week outcome study of 64 major depressed subjects (RDC criteria) was conducted. Three interventions were made: IMI only, CB only, or IMI plus CB. Subjects provided two consecutive 24–hour urine collections at baseline and 12 weeks. HAM–D and Beck Inventory were completed at intake, 6 weeks and 12 weeks by blinded raters. At study conclusion, only DHEA–S correlated with change in depression ($p=0.02$). Analyses of the three intervention strategies revealed: 1) IMI: DHEA–S change varied with HAM–D improvement ($p=0.06$) and 36% of the HAM–D change was accounted for by the pre–treatment urinary CORT; 2) CB: a trend emerged whereby symptom resolution (HAM–D) was related to increase in 24-hour urinary MEL ($p=0.08$); 3) IMI + CB: the DHEA–S relationship was again evident; however, the MEL:CB relationship was not apparent. A relationship emerged between HAM–D ($p=0.005$) and Beck ($p=0.02$) change scores and IMI dose (mean = 232 mg ± 198). IMI recipients demonstrated drug levels significantly related to the change in their 24-hour urinary CORT ($p<0.05$) and, by a trend, with MEL ($p=0.08$). In the pooled sample only DHEA–S correlated with depression change scores, principally represented by pharmacotherapy. Urinary MEL paralleled symptom remission in CB only; as a common denominator MEL correlated with subjects' IMI levels. This in turn significantly correlated with change in depression scores. IMI exerted a concentration–dependent effect upon 24-hour urinary CORT. Pharmacotherapy appeared singularly effective in impacting the corticosteroid axis.

References:

[1]Murphy, GE, Simons, AD, Wetzel RD, Lustman PJ: Cognitive therapy and pharmacotherapy; Singly and together in the treatment of depression. *Arch Gen Psychiatry* 1984; 41:33-41.

[2]Hansen, Jr. C.R., Kroll, J. and McKenzie T.B.: Dehydroepiandrosterone and Affective Disorders, *Am J. Psych* 139:386-387, 1982.

NR60 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

ENHANCED TSH RESPONSE TO TRH IN SONS OF ALCOHOLICS

David T. George, M.D., LCS, DICBR, NIAAA, Building 10, Room 3B19, 9000 Rockville Pike, Bethesda, MD 20205; Howard B. Moss, M.D., Sally Guthrie, Pharm.D., Jeannette Johnson, Ph.D., Markku Linnoila, M.D.

Summary:

Alcoholism is three times more prevalent in men than women. Adoption and cross-fostering studies show sons of alcoholic fathers to be four times more likely to become alcoholics than sons of non-alcoholics. The hereditability of alcoholism in women is less conclusive.

Previous studies measuring the thyroid stimulating hormone (TSH) response to thyrotropin releasing hormone (TRH) demonstrated a blunted TSH response during alcohol withdrawal and in 30% of abstinent alcoholics. To study whether the blunted response is a consequence of ethanol exposure or a pre-existing condition, we performed TRH tests on sons and daughters (aged 8-17) of familial alcoholics and on age- and gender-matched controls.

Our results, from nine sons and eight daughters of familial alcoholics and from eight control boys and seven control girls, showed the sons of familial alcoholics to have higher basal TSH levels (mean ± SEM) (3.71 ± 0.33 vs 2.48 ± 0.15, $P<.005$), higher peak TSH levels (16.98 ± 2.06 vs 12.16 ± 0.38, $P<.04$) and a greater area under the curve (22.31 ± 2.49 vs 15.78 ± 0.61, $P<.03$). The daughters of familial alcoholics showed no differences from control girls. Analysis of T_3, prolactin and growth hormone concentrations revealed no difference between the index children and controls.

Our results are suggestive of a male limited neuroendocrine difference between children of alcoholics and children of non-alcoholics.

NR61 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

NEUROELECTRIC CORRELATES OF RISK FOR ALCOHOLISM

Allan Tasman, M.D., Department of Psychiatry, University of Connecticut Health Center, Farmington, CT 06032; Sean J. O'Connor, M.D., Victor Hesselbrock, Ph.D.

Summary:

A study was conducted of healthy, young, adult male offspring of alcoholic fathers compared to age, education and drinking history matched controls with no alcoholism in first- or second-degree relatives. Recordings of neuroelectric activity were obtained during sober, placebo and mildly intoxicated states. Analyses of visual evoked potentials, resting power spectral topography, and peripheral expressions of autonomic arousal were performed. The Head Task, a visual odd-ball paradigm reported by Begleiter (1984), was chosen as an experimental paradigm in order to compare our results to those reported for a younger, non-drinking sample. In addition, evoked potentials were obtained during the completion of a tracking task. The evoked potential data were subjected to principle component analysis and grand mean evoked potential analyses, and between group comparisons were made on the basis of P3 component amplitude at three lead locations. It was found that the high-risk group had lower amplitude on the P3 component at Fz and Pz leads, but not at Cz in comparison to the control group. Between group comparison of the grand mean evoked potential data produced similar findings, but also suggested a laterality effect in that the increased amplitude demonstrated by the low-risk group was also more apparent in the right parietal temporal leads. The average amount of ethanol consumed during the experiment was not related to the amplitude of the P3 component. The tracking task also demonstrated a relative P3 deficit in the population at risk. This deficit was found to increase in relationship to the control group during mild intoxication. The high-risk and low-risk groups did not differ in reaction times to target stimuli in either sober, placebo or mildly intoxicated states.

NR62
WITHDRAWN

NR63 **Tuesday, May 13, 12:00 noon – 1:45 p.m.**

IDENTIFICATION OF SUBGROUPS AT RISK FOR ALCOHOLISM

V. E. Pollock, Ph.D., Psychiatric Hospital, Los Angeles County–University of Southern California Medical Center, 1934 Hospital Place, Los Angeles, CA 90033; Sarnoff A. Mednick, Ph.D., William Gabrielli, Ph.D., Donald W. Goodwin, M.D.

Summary:

The biological sons of male alcoholics constitute a group at high risk (HR) for alcoholism, and were the subjects of this study. Alcohol (0.5 g/kg) was administered to HR and control subjects, aged 18–21. Before and after alcohol administration, measures based upon EEG, subjective intoxication, and observer's ratings were obtained. The HR subjects showed greater EEG alpha changes following alcohol administration as compared to control subjects.

For purposes of this report, the magnitude of EEG alpha change that occurred before and after alcohol administration was used to identify two HR subgroups: those whose EEG alpha changes were large, and those whose EEG alpha changes were comparable to those of control subjects. The other measures were used as a basis for comparing the HR subgroups and control subjects, and revealed significant differences between them. Both HR subgroups reported feeling less intoxicated than the control subjects, and results based upon the observer's ratings were consistent with this. These findings demonstrate the utility of electrophysiological measures in high-risk alcoholism research, and suggest a strategy that can be used to identify subgroups of HR subjects, who may vary in their risk for developing alcoholism. At the end of this program, the learner will be able to recognize and identify the chief factors presently believed to be of etiological significance in alcoholism.

NR64 **Tuesday, May 13, 12:00 noon – 1:45 p.m.**

CLONIDINE VERSUS CHLORDIAZEPOXIDE IN ALCOHOL WITHDRAWAL

Gregory R. Baumgartner, M.D., 1425–B Confederate Avenue, Columbia, SC 29201; Randall C. Rowen, Phar.D., Martin R. Cohen, M.D.

Summary:

Recent studies have suggested the efficacy of clonidine in the management of alcohol withdrawal. However, no definitive comparison has been made with the accepted pharmacologic agent of choice, a benzodiazepine in the treatment of acute alcohol withdrawal. In a double–blind evaluation, 30 patients were randomly assigned to either clonidine or chlordiazepoxide. On study entry, both groups were similar regarding demographics, alcohol withdrawal symptoms (AWS), histories of prior alcohol use, physical findings and abnormal laboratory results associated with alcoholism. Once in significant withdrawal as measured by the AWS scale, the patients started on their respective study medication and then had observations made every 12 hours. Study scales administered were the AWS, the Hamilton Anxiety Rating Scale, the Cognitive Screening Exam, the Beck Depression Inventory and Subjective Self–Rating Scales. No clonidine study patients had to be withdrawn prematurely due to either intolerable alcohol withdrawal symptoms or adverse drug reactions. Analysis of the study data demonstrated more favorable AWS scores, blood pressure, pulse and respiratory rate changes for clonidine over chlordiazepoxide. In all of the remaining comparisons, clonidine was shown to be as efficacious as chlordiazepoxide. Considering also side effect profiles, clonidine may represent a new, and possibly even superior, pharmacologic treatment in the management of acute alcohol withdrawal syndrome.

NR65 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

RESPONSE TO CRF IN ALCOHOLICS FOLLOWING WITHDRAWAL

Bryon Adinoff, M.D., Clinical Science Laboratory, NIAAA, Building 10/3B19, 9000 Rockville Pike, Bethesda, MD 20892; Peter R. Martin, M.D., George H. A. Bone, M.D., Markku Linnoila, M.D., Philip W. Gold, M.D.

Summary:

Marked hypercortisolism has been reported in alcoholic individuals during the alcohol withdrawal syndrome. To further explore hypothalamic–pituitary–adrenal (HPA) function following alcohol withdrawal, we administered 1 ug/kg corticotropin–releasing factor (CRF) IV to 12 men with primary alcohol dependence one and three weeks after the cessation of drinking. CRF was chosen as a stimulus since it is a safe, potent, and specific stimulus to the HPA axis in man and has been shown to be capable of elucidating pathophysiologic mechanisms of HPA function in patients with disorders such as depression and Cushing's disease. All subjects were drug free (except ethanol) for at least two weeks prior to the studies and were studied on the NIAAA inpatient ward. CRF was administered at 8 p.m., and ACTH and cortisol were measured prior to and for three hours after CRF infusion. Baseline ACTH and cortisol and the ACTH and cortisol response to CRF did not significantly differ between one and three weeks following cessation of ethanol, nor did they significantly differ from the responses of eight healthy male volunteers. The results of our study suggest that the HPA axis returns to normal functioning within one week following the discontinuation of ethanol in chronic alcoholics.

NR66 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

MEMBRANE ADAPTATION IN ALCOHOLISM

Alan C. Swann, M.D., Department of Psychiatry, UTMS/MSI, P.O. Box 20708, Houston, TX 20708; Edward L. Reilly, M.D., John E. Overall, Ph.D.

Summary:

The sodium pump, Na,K–ATPase, is an integral part of the plasma membrane and has an important role in cell metabolism and excitability. We examined red blood cell Na,K–ATPase, its sensitivity to ethanol in vitro, and its relationship to clinical characteristics and history in 41 newly admitted alcoholic inpatients and 14 age–matched healthy controls. Sensitivity to ethanol was significantly lower in the alcoholic patients and correlated negatively with daily ethanol intake. In addition, sensitivity of enzyme activity to ethanol was lower in patients with high agitation–anxiety ratings and correlated negatively with agitation and anxiety scores on the BPRS. There were no significant correlations between measures of Na,K–ATPase and depressive symptoms, history of treatment for depression, or family history of depression. Multiple regression analysis and ANOVA showed that the correlations with ethanol intake and with behavior were not due to effects of age, red blood cell indices, or liver function abnormalities. These data suggest that membrane tolerance to ethanol can be demonstrated in man and may be related to the severity of ethanol dependence or withdrawal.

NR67 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

ANTIDEPRESSANT PHARMACOKINETICS IN ALCOHOLICS

Domenic A. Ciraulo, M.D., Box 1007, Tufts–New England Medical Center, 171 Harrison Avenue, Boston, MA 02111; Jamie G. Barnhill, B.S., Harold G. Boxenbaum, Ph.D., Jerome H. Jaffe, M.D.

Summary:

Recently detoxified, male, chronic alcoholics and matched controls were administered single intravenous (12.5 mg) and oral (50 mg) doses of imipramine (IMI) and desipramine (DMI), as well as intravenous (10mg/70 kg) doses of 2–hydroxyimipramine. Plasma samples obtained over 72 hours were assayed for parent drug and metabolite concentration by GC and HPLC methods. Unbound fraction was determined by equilibrium dialysis and the blood–to–plasma concentration ratio was measured directly. Following an intravenous infusion of IMI or DMI the alcoholic group (N=7) demonstrated shorter elimination half–lives and greater total body clearance than the control group (N=7). When referenced to unbound drug in blood, the alcoholics had a IMI clearance of 6.49±1.777 1/hr/kg and DMI clearance of 7.075±0.952 1/hr/kg. Controls had IMI clearances of 3.906±0.892 1/hr/kg and DMI clearances of 3.113±0.973 1/hr/kg. Terminal elimination half–life for IMI in the alcoholic group was 9.26 hr (harmonic mean), versus 20.63 hr in the control group. DMI half–life was 16.58 in the alcoholics and 22.43 in the controls. The alcoholic group also had greater mean clearance values and shorter half–life values following oral dosing of IMI and DMI. Data from the intravenous doses of 2–hydroxyimipramine indicate a biexponential plasma concentration fall–off curve with approximate terminal half–life of 10 hours. Metabolite measurement demonstrated rapid glucuronidation, as well as demethylation to 2–hydroxydesipramine.

NR68 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

NEUROPSYCHOLOGICAL AND RCBF RECOVERY IN ALCOHOLISM

Kenneth M. Adams, Ph.D., Neuropsychology, Henry Ford Hospital (K-11), Detroit, MI 48202; Igor Grant, M.D., Michael Boyle, D.O., Bobbe Kelly, D.O., Robert Simkins, D.O.

Summary:

This paper presents new longitudinal data on nine carefully screened abstinent patients studied in three phases of alcoholism recovery: (1) 21-24 days, (2) one year, and (3) two years following detoxification and successful treatment. Patients were examined using an extended Halstead-Reitan Neuropsychological Test battery supplemented with special memory issues. Regional Cerebral Blood Flow (rCBF) was accomplished using the Xe^{133} technique in both resting and activated conditions. We utilized an activation paradigm involving visual-spatial stimuli in an abstraction task (Raven's Progressive Matrices).

We found that patients found to be neurobehaviorally impaired at baseline examination will manifest a reduced pattern of resting condition blood flow in anterior regions which will become more apparent on behavioral activation. At follow up of one year, we found that patients having persisting neurobehavioral deficits will also be found to have reduced flows to the anterior regions in the behavioral activation condition even though resting flows may have normalized. Two-year follow-up data were similar to that at the one-year follow up. We hypothesize that both behavioral and cerebral blood flow impairments are more likely in those patients who resume their drinking in the rest-retest interval, although more data are needed to examine this hypothesis.

These data are consistent with previous replicated results suggesting loss of concept formation skills in alcoholic patients in early stages of treatment. The selective impairment of behaviors related to frontal lobe integrity and the causal possibilities are enunciated.

NR69 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

IMIPRAMINE BLOCKADE OF COCAINE EUPHORIA

Jeffrey S. Rosecan, M.D., Columbia/Presbyterian Medical Center, 38 East 61st Street, New York, NY 10021; Donald F. Klein, M.D.

Summary:

Tricyclic antidepressants have been advocated in the treatment of cocaine abuse since they appear to reduce cocaine craving and/or euphoria. In this study, 4 nasal cocaine abusers who were treated as outpatients with imipramine (IMI) for 12 weeks were given double-blind cocaine challenges while on IMI. Each subject was given 2 vials of clear liquid to be taken intranasally 1 hour apart. One vial contained 3 cc. of 1% procaine hydrochloride as active placebo, and the other contained 135 mg. of cocaine hydrochloride dissolved in 3 cc. water. Both authors and all subjects were unaware of vial content. Pulse and blood pressure were taken every 15 minutes, and subjects were asked what they felt subjectively after each vial and to what degree they felt euphoric. All reported a marked blocking of the cocaine euphoria, and the expected elevations in pulse and blood pressure from cocaine were also blocked in 3 of 4 subjects. There were no adverse side effects to the IMI-cocaine combination.

Subject	IMI dose (mg)	IMI level (ng/cc)	Euphoria	P	BP
1	250	160	minimal	0	0
2	25	34	none	-4	-2
3	400	175	none	16	10
4	150	55	minimal	4	-1

NR70 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

COCAINE DETOXIFICATION USING BROMOCRIPTINE

Irl L. Extein, M.D., Fair Oaks Hospital at Boca/Delray, 5440 Linton Boulevard, Delray Beach, FL 33445; David A. Gross, M.D., Mark S. Gold, M.D.

Summary:

The clinical picture of cocaine withdrawal has been identified, including intense cocaine craving, low energy and depression. Animal studies have suggested a central dopamine depletion hypothesis for cocaine withdrawal, which has been corroborated by the efficacy of single doses of the dopamine agonist bromocriptine in relieving cocaine withdrawal symptoms. Because withdrawal symptoms — particularly cocaine craving — are a major cause of treatment drop–out, a specific treatment for cocaine withdrawal would be useful. In order to study the clinical utility of bromocriptine, we administered bromocriptine to 10 consecutive patients hospitalized for cocaine abuse who manifested significant withdrawal symptomatology. Written informed consent was obtained. Patients were predominantly white male free–base or crack users in their 20s. Patients rated their mood, energy and cocaine craving using 100 mm lines before and during the bromocriptine trials. Dosage and duration were based on clinical response, ranging from 0.625 to 1.875 mgs po tid for 6–20 days. Mean baseline ratings of cocaine craving, energy and depression of 47 mm, 32 mm and 50 mm changed by the second day of bromocriptine treatment to 11 mm, 61 mm and 26 mm respectively. The most dramatic findings were decreased depression and craving for cocaine. Retrospective chart review using the Clinical Global Impression Scale showed a mean of 1.9 (much improved) by the second day of bromocriptine treatment, much more improvement than in untreated cocaine withdrawal. Bromocriptine's reversal of cocaine withdrawal distress was sustained for the duration of treatment with little recurrence after discontinuation of bromocriptine. No significant side effects were noted. All 10 patients completed the inpatient treatment program. The results of this preliminary open trial suggest a role for bromocriptine in detoxifying hospitalized patients addicted to cocaine and facilitating other aspects of the treatment program.

NR71 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

BROMOCRIPTINE TREATMENT FOR COCAINE CRAVING

Charles A. Dackis, M.D., Fair Oaks Hospital, 19 Prospect Street, Summit, NJ 07901; Donald R. Sweeney, M.D., John Byron, B.S., Robert Climko, M.D., Mark S. Gold, M.D., A. L. C. Pottash, M.D.

Summary:

We previously reported anti–craving action of bromocriptine in 2 cocaine addicts, based on single–blind challenges. We now have completed a double–blind placebo-controlled study of bromocriptine in 13 patients (4 females and 9 males, aged 27.7 ± 5.3 (SD) with *DSM III* cocaine abuse and no other substance dependence.

On 2 consecutive days, patients rated their cocaine craving before and after receiving either bromocriptine (1.25 mg) or placebo. Craving was rated by marking a line numbered from 1 to 100. After baseline ratings at 11:00 and 13:00, subjects handled cocaine paraphernalia (at 13:30) in order to provoke craving, and a third rating was made at 14:00. The mean of these 3 ratings was calculated and designated "baseline craving." Bromocriptine or placebo was administered at 14:15, double–blind, in a random order. Subsequent craving ratings were made at 15:00, 15:30, 16:00, and 16:30, and the mean of these 4 ratings was compared to "baseline craving."

Bromocriptine was significantly more effective in reducing craving than placebo. Both the absolute reduction ($t=1.84$, $p<.05$) and the average percentage drop of craving ratings ($t=2.01$, $P<.05$) were greater after bromocriptine than after placebo. A 55% average reduction of craving was found after the single bromocriptine dose.

These data further indicate the anti–craving efficacy of bromocriptine in cocaine addiction. Based on findings of hyperprolactinemia, pseudo–parkinsonism and sexual dysfunction cocaine addicts appear to be dopamine depleted. Cocaine craving has been hypothesized to result from dopamine depletion. Bromocriptine, through its dopamine agonist activity, reverses dopamine depletion and may thereby ameliorate cocaine craving.

NR72 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

COCAINE VERSUS MARIJUANA ABUSE IN ADOLESCENTS

Richard H. Schwartz, M.D., Pediatrics, Georgetown Medical School, 3800 Reservoir Road, NW, Washington, DC 20007; Mark S. Gold, M.D., Michael Lehrer, Ph.D., David M. Martin

Summary:

Cocaine abuse has emerged as a major public health problem in recent years kindling many studies into cocaine abuse patterns and its medical consequences. However, the majority of these studies have been done almost exclusively on adult populations providing little, if any, information on the impact of cocaine abuse on adolescents. Enticed by the powerful euphoric and exhilarating properties of cocaine, it has been estimated that 16% of all high school seniors have already used cocaine one or more times. We compared a group of middle-class white adolescents 14–17 years old who were in treatment for cocaine abuse (n=20) with a control group being treated for cannabis dependency with no history of cocaine abuse (n=20). A structured questionnaire was used to note any social, psychological or medical consequences of cocaine abuse. Some of the more remarkable findings were: suicide attempts in the cocaine group (45%) occurred almost twice as often than in the control group (25%), 10% of the patients develop generalized seizures after prolonged cocaine abuse, and the cocaine group was nearly four times as likely to be engaged in thefts of monies or material in excess of $1,000 as compared to the control group. These and other data will be presented illustrating the effects of cocaine abuse in adolescents and effective strategies in assuring abstinence and successful treatment for these patients.

NR73 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

EFFECTS OF COCAINE ON HUMAN CAUDATE D2 RECEPTORS

Godfrey Pearlson, M.D., Johns Hopkins Hospital, Meyer 279, 600 North Wolfe Street, Baltimore, MD 21205; Christopher A. Ross, M.D., Dean Wong, M.D., Marian Fischman, Ph.D., Henry N. Wagner, R. Foltin, M.D.

Summary:

Use of an exogenous ligand to measure brain receptor density by positron emission tomography presupposes that the ligand will not significantly be displaced by endogenous neurotransmitter. A high affinity ligand such as C11–3–N–methylspiperone (NMSP) may satisfy this supposition (since the endogenous neurotransmitter, dopamine, has an affinity several orders of magnitude lower than NMSP), but this has not yet been experimentally verified. We sought to determine whether acutely increasing synaptic dopamine availability with cocaine, a potent uptake inhibitor, could displace NMSP from human caudate. We have previously observed a linear relationship between the caudate/cerebellar ratio and time after NMSP injection (95% tolerance limits for change in slope of −0.0553 to 0.0473/min. or 5%–10% in 23 normal subjects). Two subjects received cocaine (48 mg IV) 30 minutes after the NMSP injection. Their changes in slope were only −0.009 and 0.0074 respectively. One subject received a baseline NMSP PET scan followed the next day by a scan in which subjects had substantial subjective and autonomic effects of cocaine. Further cocaine studies are in progress. These preliminary data suggest that acute elevations of synaptic dopamine concentration need not interfere with the binding of a high affinity ligand such as NMSP under normal PET scan conditions.

NR74 **Tuesday, May 13, 12:00 noon – 1:45 p.m.**

PSYCHIATRIC EFFECTS OF FOUR-HOUR INFUSIONS OF COCAINE

Michael Sherer, M.D., NIDA Addiction Research Center, 4940 Eastern Avenue, Baltimore, MD 21224; Karen Kumor, M.D., Jose DeBorja, B.A., Edward Cone, Ph.D., Loren Thompson, Ph.D., Jerome Jaffe, M.D.

Summary:

Previous research on cocaine in drug abusers has been limited to the effects of single doses on this short-acting substance. In six male volunteers aged 20–40 we have studied the behavioral and physiologic effects of cocaine using a 4-hour continuous infusion of cocaine. In contrast to the rapid decline of plasma cocaine after single injections, the infusions maintained constant cocaine plasma concentrations. All subjects were seen by a psychiatrist (M.S.) and were evaluated with the NIMH DIS interview. None had any *DSM III* axis I diagnosis other than substance abuse. Several had axis II pathology of which antisocial personality was most frequent. Blood pressure, pulse, EKG, subjective analog scales for mood and psychomotor effects, POMS and Addiction Research Center scales were completed by subjects. In addition, trained observers recorded subject behavior. As expected, peak cardiovascular effects were noted within ten minutes and were paralleled by maximal subjective ratings for euphoria, energy and anxiety. Despite the high plasma concentrations that were achieved and maintained, the intense euphoric effects of the drug subsided rapidly. Anxiety and energy did not decline to any significant degree. Suspiciousness as rated by blind observers gradually increased during the infusion and in three of six subjects paranoid symptomotology was noted. Cocaine infusions may offer a method to study the basis of psychiatric syndromes seen in cocaine abusers.

NR75 **Tuesday, May 13, 12:00 noon – 1:45 p.m.**

DEPRESSED OPIATE ADDICTS: DIAGNOSIS AND TREATMENT

Steven L. Batki, M.D., Department of Psychiatry, University of California at San Francisco, San Francisco General Hospital, San Francisco, CA 94110; Michael Rowbotham, M.D.,James L. Sorenson, Ph.D., Scott M. Wheeler, M.A., Kathy Brennan, M.A., Reese T. Jones, M.D.

Summary:

Undiagnosed depression may hamper the treatment of opiate addiction. This presentation reports on both diagnosis and treatment of depression among these patients. The authors examined 240 opiate addicts consecutively entering outpatient methadone detoxification, and assessed the prevalence of depression and its relationship to withdrawal intensity and treatment outcome.

At entry into treatment, patients completed the Beck Depression Inventory as well as an opiate withdrawal symptom self–rating form. They were also evaluted for Major Depressive Disorder, according to *DSM–III* criteria, using the NIMH Diagnostic Interview Schedule (DIS) section on depression.

Lifetime prevalence of MDD was found to be 29%. The Beck served as a good screening tool for MDD: a cutoff score of 15 identified 87% of addicts with MDD. Significantly, addicts with a history of MDD were found to have more intense withdrawal symptoms and were less likely to complete detoxification treatment.

Based on these findings, the authors are performing a double–blind, randomized, placebo–controlled clinical trial of doxepin as an adjunct to methadone in the detoxification of opiate addicts with MDD. The second part of the presentation will report the results from the first 50 subjects in this study, regarding outcome in terms of depression, retention in treatment, opiate withdrawal symptoms, and illicit drug use.

NR76 **Tuesday, May 13, 12:00 noon – 1:45 p.m.**

OPIUM ADDICTION AND DETOXIFICATION OF HMONG REFUGEES

Anthony G. Troiano, M.D., Department of Psychiatry, University of Minnesota, Box 393 Mayo, Minneapolis, MN 55455; James A. Halikas, M.D., Joseph Westermeyer, M.D., Marvin Seppala, M.D., Christian Schmidt, MS3

Summary:

Because of the high apparent incidence of opium addiction found in recent Laotian Hmong refugees to the twin city area, we have developed a model inpatient detoxification program and Research treatment protocol. The majority of the patients are married, unemployed, Hmong males. Their drug use has been limited to opium. They smoked 25–150 pipes per day. By self report, all patients began their opium use to self-medicate pain and all attempted self-detoxification but resumed use in order to alleviate withdrawal symptoms. With the use of our protocol, the clinical course demonstrated virtually no withdrawal symptoms and the entire sample has been successfully detoxified from opium.

The program involves the use of a 21 day methadone taper. Initial dose is determined based on clinical grounds and approximate daily use reported by the patients themselves, their families, and friends. After establishing the initial 24 hour methadone dose, the methadone taper is initiated. The daily dose is divided into two or three equal doses given in orange juice 12 or 8 hours apart. The daily dose is decreased by equal amounts per day such that by day 21 the methadone taper is completed. Seven to ten days after the last methadone dose, a narcan challenge is performed. If the patient shows no signs or symptoms of withdrawal, Naltrexone therapy is initiated. After discharge the patients attend an aftercare program where they receive their Naltrexone and support each other's continuing abstinence. The aftercare groups are specifically tailored to the needs of these refugees, but modeled on principals of A.A. and N.A.

The development of this protocol has enabled us to successfully detoxify Southeast Asian opium addicts in a 30 day inpatient period. To date, no relapses of opium use have occurred.

NR77 **Tuesday, May 13, 12:00 noon – 1:45 p.m.**

PCP RECEPTOR CHANGES AFTER PSYCHOTROPIC MEDICATION

James C. Byrd, III, M.D., Preclinical Pharmacy, National Institute of Mental Health/St. Elizabeth's, Washington, DC 20032; Victor Bykov, Richard B. Rothman, M.D.

Summary:

PCP, a widely abused psychotomimetic compound, is known to bind to specific CNS receptors. In this report we describe the effects of clinically relevant doses of iproniazide, an MAO inhibitor (3.4 mg/kg/24 hr.), etonidazine, a potent opiate agonist (0.2 mg/kg/24 hr.), and naloxone, an opiate antagonist (6.0 mg/kg/24 hr.) on PCP receptors in the rat. Medications were administered continuously by subdermal infusion (Alzet osmotic pumps) over a period of twelve days. Crude membrane preparations were made from whole brain (excluding cerebellum) using standard procedures. PCP binding was determined by displacing two concentrations of ^{3}H-TCP (1 nM and 5nM) with varying concentrations of cold TCP (1 nM – 100 nM). Displacement curves were analyzed using a curve fitting program. (*$p<0.05$)

Drug	K_d (nM) + S.D.	B_{max} (fmol/mg) + S.D.
Control	7.3 ± 0.5	657 ± 66
Iproniazide	6.0 ± 0.5*	589 ± 57*
Etonidazide	9.3 ± 0.9*	714 ± 98*
Naloxone	10.2 ± 0.6*	784 ± 66*

These results suggest that these psychotropic medications cause sensitization (iproniazide) or desensitization (etonidazine and naloxone) of the PCP receptor. The potential use of these medications in the study of the basic pharmacology of the PCP receptor and in the treatment of PCP abusers deserves further study.

NR78 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

INPATIENT VERSUS OUTPATIENT DETOXIFICATION

Arthur I. Alterman, Ph.D., Veterans Administration Medical Center, Philadelphia, PA 19104; Motoi Hayashida, M.D., Charles P. O'Brien, M.D., Edward Foulks, M.D.

Summary:

This paper will present preliminary findings of an ongoing study which investigates the relative efficacy of inpatient and outpatient medical detoxification. Patients found to be in need of detoxification, but not suffering from medical or psychiatric conditions requiring immediate hospitalization, were randomly assigned to either inpatient or outpatient medical detoxification treatment. Forty-six outpatients and 40 inpatients have thus far been treated. Seventy percent of the outpatients and 93% of the inpatients completed the detoxification treatment. Treatment duration averaged one week for outpatients and two weeks for inpatients. The sociodemographic and alcohol-related characteristics of the two groups of patients were generally not found to differ significantly. Furthermore, they were not found to differ in terms of the severity of alcohol withdrawal symptomatology, the extent of alcohol dependence, depression, and other related emotional states. Baseline assessment on the Addiction Severity Index (ASI) indicated no major group differences in medical, employment, legal, family/social, or psychological/emotional functioning nor differences in past and current alcohol and drug use. One month ASI follow-up data on approximately 75% of the patients failed to reveal group differences in any of the above areas of life functioning, with the exception of more reports of medical problems in patients who had received inpatient detoxification. Thus, our preliminary findings have revealed no major differences in the efficacy of outpatient and inpatient alcohol detoxification for appropriately screened patients.

NR79 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

EFFECT OF TRIHEXIPHENADYL ON EMOTIONAL STATE

Lawrence Plon, Pharm. D., Professor of Psychiatry, University of California Irvine Medical Center, 101 City Drive, South Orange, CA 92668; Daniel E. Bates, Ph.D., Richard D. Danson, M.D.

Summary:

It is commonly reported that patients who feign symptoms to obtain anticholinergics do so because of the drug's ability to induce euphoria. To our knowledge, this is the first systematic study aimed at determining if trihexiphenadyl induces pleasant or euphoric states with a typical clinical dosage. Twenty-three healthy male subjects served as their own controls in a 2 x 2 factorial design; independent variables were drug effect and drug set. Subjects received 5 mg of trihexiphenadyl at one session and an inconsequential dosage (0.001 mg) at another. Euphoria was operationally defined as a decrease of anxiety (State Trait Anxiety Scale) and an increase in elation (Elation Factor of the Mood Adjuctive Checklist). An analysis of covariance with multiple dependent variables using predrug measures as the covariate, showed that contrary to anecdotal reports, the drug significantly increased anxiety scores and significantly decreased average elation scores across pre to post measures. Instructional set had no effect on average scores for either measure nor were there any interactions. Trihexiphenadyl was found to increase state anxiety and decrease elation. It is suggested that the abuser may interpret an altered, drug induced state as desirable or that a sub-group of the population has altered cholinergic receptors and responds differently. The need for study in an abuse-prone population is noted.

NR80 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

ADDICTOGENESIS: A PROSPECTIVE LONGITUDINAL STUDY

Lawrence J. Hatterer, M.D., Department of Psychiatry, New York Hospital/Payne Whitney, 525 East 68th Street, New York, NY 10021; Raymond De Biase, Ph.D.

Summary:

A content analysis was performed on 131 archival records (male and female subjects) of the New York Longitudinal Study (NYLS) (which was begun in 1956 by Alexander Thomas and Stella Chess). Forty-eight items related to antecedent problem behavior, family pathology and intra-psychic factors were critically selected from a large pool of key variables posited by the authors and 50 other substance abuse researchers. These items were rated separately for age-periods birth to one, one to three, three to six, and six to nine. The raters were "blind" to all longitudinal information after age nine. When the antecedent data was completed, the outcome scores for substance use/abuse was provided by the original NYLS researchers for age periods 13 to 19+. A battery of statistical procedures including factor analysis, descriminant function and multiple regression/analysis, were used to test the hypothesis that early life developmental patterns would predict subsequent substance use/abuse behavior. Based on a clustering of the 48 items, three general factors were established which were associated with later substance use/abuse scores. Utilizing multiple regression analysis, these three factors, as correlated with the outcome scores, yielded a multiple correlation. R+.417 significant at the .002 level, accounting for 17.4% of the variance. Using a discriminant analytic procedure to further test the predictive power of these antecedent variables, high-score subjects were distinguished from lower-score subjects. At age group six to nine, 60% of the population fell into the high-score group. The results show that these variables correctly predicted 83.3% of the high-score subjects — CHI^2=6.4, P=.01. These preliminary findings suggest the possibility of detecting, at early ages, vulnerability to addiction in adolescence or later life.

NR81 **Tuesday, May 13, 12:00 noon - 1:45 p.m.**

HIPDM/SPECT IMAGES IN ALZHEIMER PATIENTS OVER TIME

Hugh C. Hendrie, M.B., Institute of Psychiatric Research, Indiana University Medical School, 791 Union Drive, Indianapolis, IN 46223; Henry N. Wellman, M.D., Martin R. Farlow, M.D., Kathleen S. Hall, Ph.D., Harry M. Brittain, Marian K. DeMyer, M.D.

Summary:

While PET scanning has shown promise in distinguishing Alzheimer's patients from other dementia patients, it is expensive and minimally available. Recently developed I-123 labelled bioamines, especially HIPDM, which are distributed in normal brains proportional to perfusion, when combined with SPECT techniques (HIPDM/SPECT) offer a less expensive means of providing similar clinical information. During an on-going longitudinal brain imaging study involving *DSM III* diagnosed Alzheimer's patients and age and sex matched healthy control subjects, 11 patients received HIPDM/SPECT images. All subjects had a thorough neuropsychiatric (NP) and neurological work up including CT and MR imaging. Results of the HIPDM/SPECT imaging proved surprisingly diverse. According to pre-determined criteria, only 4 patients had changes consistent with Alzheimer's disease, two patients had images suggestive of Alzheimer's disease but unilateral in nature, 2 patients had images consistent with MID, two patients had apparently normal images and one patient had a left frontal-parietal lesion. Several patients with atypical Alzheimer's images performed better on NP tests (particularly language) than cases with typical Alzheimer images. The atypical Alzheimer's cases were restudied after one year. In 3 patients, repeat images were now more consistent with Alzheimer's disease than baseline images. All patients had declined neuropsychologically. HIPDM/SPECT images of the only controls (n= 3) imaged so far were normal. The relative merits of HIPDM/SPECT imaging and the relationship over time between changes in the images, and the clinical status and NP scores will be discussed.

NR82 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

ALZHEIMER'S DIAGNOSTIC LABORATORY TEST

Frank P. Zemlan, Ph.D., Division of Geriatrics, UC College of Medicine, Cincinnati OH 45267; Ole Thienhaus, M.D., David Bienenfeld, M.D., H. Bruce Bosmann, Ph.D.

Summary:

It is well established that Alzheimer's disease is associated with degeneration of cholinergic neurons in several CNS regions. Recent neuropathological data in Alzheimer's patients indicate the presence of neurofibrillary tangles in numerous hypothalamic regions associated with regulation of pituitary hormone release. These hypothalamic regions, which receive a strong cholinergic projection, are located immediately caudal to the basal forebrain cholinergic cell bodies which degenerate in Alzheimer's patients. It is not known whether the cholinergic projection to hypothalamic regions controlling pituitary growth hormone release degenerates in Alzheimer's patients. The present study explores this hypothesis. Specifically, the present study examined whether Alzheimer's patients demonstrate a blunted growth hormone (GH) response to a presynaptic cholinergic challenge. Three baseline blood samples were taken prior to administration of the cholinesterase inhibitor, tensilon (0.15 mg/kg), and five samples taken during the 80 minutes following drug administration. A peak GH response of 17 ± 6 ng/ml was observed in 6 age-matched non-demented control patients, while a significantly blunted GH response of 2 ± 2 ng/ml was observed in 9 Alzheimer's patients ($p<0.02$). The implications of the present data for assessing cholinergic deficits in Alzheimer's patients will be discussed.

NR83 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

CIRCADIAN ACTIVITY RHYTHMS IN GERIATRIC DEPRESSION

Martin H. Teicher, M.D., Harvard Mailman Research Center, McLean Hospital, Belmont MA 02178; Janet Lawrence, M.D., Natacha I. Barber, Seth Finklestein, M.D., Harris Lieberman, Ph.D., Ross J. Baldessarini, M.D.

Summary:

Locomotor activity levels or rhythms may be disturbed in major depression, and vulnerable to disruption in old age. We compared activity rhythms of depressed geriatric inpatients and healthy elderly subjects admitted to a clinical research center. Depressed patients ($n= 8$; mean age $\pm$ SEm = 75 ± 1.4 years) had a mean Hamilton depression score (HDRS) of 27 ± 3.5; most received a variety of medications, but none received an effective thymoleptic regimen when studied. Controls ($n= 8$; 77 ± 2.4 years) were free of psychiatric or medical illness, previous psychiatric history, and current medications. All subjects chose their own sleep-wake times. Activity was measured using a modified NIMH-Colburn Ambulatory Activity Monitor worn on the non-dominant wrist. Activity counts were cumulated in 15 min. intervals over 48-64 hours, and transferred to a microcomputer for cosinor analysis.

Depressed patients had a 29% higher mean *activity* level ($p<0.02$), even though mean *circadian amplitude* was not different from controls ($p>0.1$). There was also an unexpected phase difference: the *acrophase* (time of daily peak activity) was at 1:50 pm in controls and 3:54 pm in depressed patients (2.04 h *phase delay*; $p < 0.0001$, with no overlap between the two groups). Depressed patients ($n= 4$) with the greatest phase delays (2.0–4.5 h) were also likely to be cortisol nonsuppressors at 4:00 pm of the day after 1 mg of dexamethasone (75% DST positive), and patients with smaller delays were not (0% DST positive), even though HDRS was similar in both groups. Phase delays and 4:00 pm postdexamethasone cortisol levels were highly correlated ($r= 0.76$ $p < 0.05$). These findings suggest that hospitalized depressed geriatric patients may have a prominent chronobiological disturbance in the modulation of activity levels, and possibly other circadian processes.

NR84 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

BRAIN ACETYLCHOLINE: A VIEW FROM THE CSF

Robert E. Becker, M.D., SIU School of Medicine, P.O. Box 3926, Springfield IL 62708; Ezio Giacobini, M.D., Roger Elble, M.D., J. Wesson Ashford, M.D., Kathy Sherman, Ph.D., Michael McIlhany, M.D., Jonathan Hess, Ph.D.

Summary:

Our studies of normal elderly and Alzheimer's (AD) patients suggest that the origins in CSF of 1) 85% of cholinesterase G_4 tetramer is brain AChE, 2) choline acetyltransferase is neuronal, 3) choline (CH) is multiple. Three cholinergic parameters, AChE, ChAc and Ch were decreased in CSF of AD patients. Further, changes at 3-6 month intervals in the same patient may accompany the clinical progression of the disease.

Our results using oral physostigmine (Phy) in AD patients are consistent with the findings of other investigators. Phy has some, but at the present clinically insignificant, beneficial effects. We have hypothesized that the effectiveness of Phy is limited by kinetic factors. To test this hypothesis we have compared the effect of two routes (intravenous and intracerebro-ventricular) administration of Phy in beagle dogs. Implanted reservoirs with silastic ventricular catheters were used. Significant (50-90%) and persisting (3-9 hrs) inhibition of CSF and brain AChE activity and increases in ACh levels were seen only with ICV administration. At comparable dosages, intravenous administration produced only small and short lasting effects. In conclusion 1) ACh metabolism in brain is reflected by variations of cholinergic parameters in CSF, 2) ACh metabolism is deficient in AD, 3) cholinergic parameters may correlate with the severity of AD, and 4) an adequate test of the ACh deficiency hypothesis by AChE inhibition may not be possible using peripheral routes of Phy administration.

NR85 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

A DISSOCIATIVE SPECTRUM IN PSYCHIATRIC ILLNESS

Frank W. Putnam, M.D., Neuropsychiatry, NIMH, St. Elizabeths Hospital, Washington, DC 20032; Eva Bernstein, Ph.D.

Summary:

Dissociation is manifest by a failure of the normal integration of thoughts, feelings and experience into the stream of consciousness and memory. The role of dissociation in psychopathology is hypothesized for a variety of psychiatric disorders including: post-traumatic stress disorder (PTSD), anxiety, phobic, and eating disorders, as well as the DSM-III dissociative disorders. While many clinicians have conceptualized dissociative experiences as lying on a continuum from normative phenomena (e.g., daydreaming) to major disorders (e.g., multiple personality disorder [MPD]), there has not been a systematic assessment of the form or frequency of dissociation in normals and psychiatric patients.

The Dissociative Experience Scale (DES) is a 28-item, self-administered scale. Reliability testing across a variety of normal and patient samples yielded a Spearman test-retest correlation coefficient of $r= 0.84$ ($n= 26$, $p<0.0001$) and Spearman-Brown split-half reliability ranged from $r= 0.71$ ($n= 34$, $p<0.0007$) to $r= 0.96$ ($n= 24$, $p<0.0001$). Criterion referenced validity was established by comparing six DSM-III/RDC diagnosed patient samples (alcohol abuse, agoraphobia, panic disorder, schizophrenia, PTSD, MPD) and two normal samples (adults, adolescents) with a Kruskal-Wallis yielding a Chi-square of 93.57 ($n= 192$, $df= 7$, $p<0.0001$).

The results demonstrate a continuum of dissociative experience and symptoms ranging from infrequent minor events in normal adults to frequent major dissociative phenomena in PTSD and MPD. The panic disorder and agoraphobic patient samples are composed of high and low dissociative subgroups. Normal adolescents report relatively frequent dissociative experience and display an item-by-item DES profile similar to schizophrenics. The highest DES scores were in the traumatically induced disorders, PTSD (combat) and MPD (child abuse and incest).

NR86 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

CSF SOMATOSTATIN IN DEMENTIA AND DEPRESSION

Trey Sunderland, M.D., LCS/NIMH, 10/3D41, 9000 Rockville Pike, Bethesda, MD 20892; David R. Rubinow, M.D., Pierre N. Tariot, M.D., Paul A. Newhouse, M.D., Alan M. Mellow, M.D., Edward A. Mueller, M.D., Robert M. Cohen, M.D., Dennis L. Murphy, M.D.

Summary:

Somatostatin (SLI) is a tetradecapeptide with possible neurotransmitter and neuromodulary functions throughout the central nervous system. In the elderly, diagnostic confusion sometimes exists between dementia of the Alzheimer type (DAT), especially in its early stages, and depression when it is accompanied by memory complaints. To investigate possible differences in SLI between diagnostic groups in the elderly, CSF samples were obtained from 12 DAT patients (61.2±3.3 yrs), 20 elderly depressives (DEP, 58.7±2.5 yrs) and 15 age-matched normal controls (NC, 59.5±2.0 yrs). The diagnosis of DAT or depression was made according to *DSM-III* criteria. All lumbar punctures were performed in the lateral decubitus positions between 8 and 9 am after an overnight fast. An aliquot of the 26th ml of CSF was assayed for SLI by radioimmunoassay using tyrosine (1) iodine 125, rabbit antisomatostatin antiserum, synthetic cyclic somatostatin standards and charcoal separation. The DAT and elderly depressives both showed marked reductions of SLI compared to the elderly controls (DAT= 39.3±3.5 ng/ml; DEP= 41.3±3.2; NC= 76.5±11.5; both $p<0.01$). No correlation between age and SLI ($r= 0.03$) or depression and SLI ($r= 0.15$) was found. There was a trend towards a positive correlation between SLI and cognitive performance as measured by the Weschler Memory Quotient (WMQ) ($r= 0.38$) in the DAT group. Thus, CSF SLI cannot be used to distinguish DAT patients from elderly depressives with cognitive dysfunction as both groups appear to have similar lumbar CSF reductions in this CSF peptide. While the association between WMQ and SLI is not strong, the trend towards a positive correlation in this small sample of DAT patients suggests that further study, perhaps with additional cognitive measures, may prove of value in linking the somatostatin deficit and cognitive abnormalities of DAT.

NR87 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

ABSENCE OF CORTISOL RESPONSE TO NALTREXONE IN ALZHEIMER'S DISEASE

Nunzio Pomara, M.D., Wayne State Univ., Lafayette Clinic, 951 E. Lafayette, Detroit MI 48207; Michael Stanley, Ph.D., H. Benjamin Rhiew, M.D., Matthew P. Galloway, Ph.D., Karl Verebey, Ph.D., Carol Tamminga, M.D.

Summary:

In previous work in which we assessed the cognitive effects of naltrexone (Nalt.) in Alzheimer's Disease (AD), we noted an absence of a cortisol response. Others using comparable doses of Nalt have shown increases in plasma cortisol. Conversely, opiate agonists have been shown to induce decreases in cortisol. Based on these findings, we have expanded our previous work to address the question of whether the lack of cortisol response to Nalt in AD was due to possible aging effects or more specifically related to the disease process. 20 individuals were included (10 normal elderly and 10 with AD). All received diagnostic evaluations. The two groups were of comparable age (demented, mean + S.D.,66.9±6.2; control 69.6±8.5) and sex ratio. Following a night of fasting, Nalt 100mg or placebo (PBO) were given orally in a double blind study design (the same time of day in two separate sessions at least 72 hrs apart). Vital signs and blood samples for determination of Nalt, βNaltrexol, its major metabolite, cortisol, prolactin and MHPG were taken at baseline, 90 min., and 3 hrs. post-drug. Nalt increased plasma cortisol in normal controls at 90 min. without a similar increase in AD (controls, PBO, mean plasma cortisol ± SD (μ g/dl) 12.22±3.69; Nalt 19.28*±7.22; AD, PBO 9.29±2.81, Nalt 10.62±4.46). In contrast, both controls and AD patients had increases in prolactin (ng/ml) (controls, PBO, 4.58±2.73, Nalt 6.35*±3.34; AD, PBO 7.21±2.82, Nalt 8.92*±2.35)*$p<.05$ compared to PBO. Measures sensitive to nonspecific stress were unaffected throughout the procedure. Thus, neither MHPG levels nor pulse or BP were significantly altered. Further, these findings cannot be attributed to pharmacokinetic differences between the two groups as neither Nalt nor βNaltrexol levels differed. These findings show what appears to be a differential effect of AD on the cortisol response to Nalt. Thus, while the cortisol response was absent, the prolactin response was preserved. Possible therapeutic and diagnostic implications of these findings will be discussed.

NR88 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

LOW AND HIGH DOSE NALOXONE IN OLDER NORMALS

Michael Gross, M.D., Clinical Brain Imaging, NIMH, Bldg. 10 Rm. 4N317, 9000 Rockville Pike, Bethesda, MD 20892; Pierre N. Tariot, M.D., Trey Sunderland, M.D., Julie Welkowitz, B.A., Robert M. Cohen, M.D., Dennis L. Murphy, M.D.

Summary:

Controversy over the potential benefits of naloxone for patients with dementia of the Alzheimer's type (DAT) recently led to an NIMH study of high dose naloxone, 2 mg/kg IV (up to 145 mg), in DAT patients. The results indicated naloxone induced significant clinical and cognitive impairment which was maximal at the intermediate dose of 100 mcg/kg. Another study with young normals administered doses up to 4 mg/kg IV demonstrated qualitatively similar effects, including anxiety, dysphoria, and impaired cognitive function. However, unlike the DAT group, the response of the young normals showed both a higher threshold dose and linear dose response relationship, suggesting age may be an important variable to examine in the endogenous opiate system. Consequently, we now report the results of a low (100 mcg/kg) and high (2 mg/kg) dose naloxone study of middle-aged and elderly normals age-matched to the DAT patients.

Eight normal subjects (ages 43 to 74, mean 66) were administered naloxone in a double-blind, placebo-controlled, random-day procedure. Days consisted of two sequential infusions 60 minutes apart: A) placebo-placebo, B) naloxone 0.4 mg and 100 mcg/kg, and C) naloxone 0.4 mg and 2 mg/kg. Behavior, measured by the BPRS, and cognitive function, assessed by a selective reminding task, a verbal vigilance task, and a dynamometer, were rated before and several times after the second infusion.

Preliminary analysis of the data shows a significant increase ($p \leq .01$) in the total BPRS following the infusion of the highest dose only, with elevations of the anergy, functional impairment, and activation subscales approaching significance. There is evidence suggestive of mixed activation and anergy, and subjective reports of drowsiness and fatigue. Analysis of the cognitive data reveals a significant impairment ($p \leq .01$) on two measures; one shows maximal impairment on the highest dose, the other an equal impairment on both the low and high doses.

Overall, the response of the middle-aged and elderly normals to naloxone suggests a threshold dose and dose response relationship closer to that seen with the young normals than with the age-matched DAT patients, in addition to some qualitative differences from the DAT group as well.

NR89 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

L-DEPRENYL IN ALZHEIMER'S DISEASE

Pierre N. Tariot, M.D., LCS/NIMH, 10—3D41, 9000 Rockville Pike, Bethesda, MD 20892; Trey Sunderland, M.D., Dennis L. Murphy, M.D., Paul A. Newhouse, M.D., Edward A. Meuller, M.D. Robert M. Cohen, M.D.,

Summary:

Monoamine neurotransmitters, as well as cholinergic pathways, play important roles in behavior and cognition, and are disturbed in dementia of the Alzheimer's type (DAT). This suggests that monoamine-enhancing drugs may ameliorate some symptoms of DAT. L-deprenyl is an MAO-B inhibitor which is relatively safe and specific for monoamine systems, which we have evaluated in DAT.

17 DAT patients were studied for 14 weeks in a double-blind, placebo-controlled, linear fashion. Patients received placebo, deprenyl 10 mg/day, deprenyl 40 mg/day, and placebo. BPRS ratings were performed regularly, along with global impressions of change. Episodic memory and learning (with measures of effortful and automatic processes), knowledge memory, attention, recognition, and performance on a complex visuomotor task were assessed.

The patients were able to acquire and recall new information more effectively on the task requiring the greatest cognitive effort while receiving 10 mg deprenyl ($p<.02$). There was a trend toward this effect on 40 mg ($p<.10$). No other cognitive measures changed. Total BPRS scores fell on 10 mg deprenyl ($p<.01$), associated with decreases in measures of anxiety/depression, tension, and anergia. 9 patients were judged to be globally improved, 7 on 10 mg/deprenyl. Responders were described as more energetic, more socially interactive, and less sad.

In sum, the administration of L-deprenyl resulted in improvement of ratings of behavior and mood and of performance on an effort-demanding task assessing episodic memory and learning. Such changes are generally what might be predicted to occur with monoamine-enhancing drugs, since they occur with these drugs in other populations. Improvement of some symptoms in DAT appears possible without necessarily etiologically specific interventions.

NR90 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

INTRAVENTRICULAR BETHANECHOL FOR ALZHEIMER'S DISEASE

Stephen L. Read, MD., West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073; John G. Frazee, M.D., Cheryll Smith, Ph.D., Jill Shapira, R.N., Jeffrey L. Cummings, M.D., Paul Satz, Ph.D.

Summary:

Acetyl-choline synthesis and choline acetyl transferase are characteristic of Alzheimer's disease (AD) and probably appear early in the course of this steadily progressive dementia. Therapeutic attempts to correct this deficiency have been disappointing, possibly because of consistent failure to penetrate the blood-brain barrier. The 1984 report of the intraventricular delivery of bethanechol (IVBC) by constant infusion pump overcomes this difficulty, but the reported symptomatic improvement remains unconfirmed and no objective measures have been reported.

Dose-response curves are not yet described for IVBC, but variations due to stage of progression or other unknown factors might be anticipated; certain functions, such as choline transport, have a dramatic bimodal distribution in AD. Which features of the memory impairment, behavioral changes, and other cognitive features in AD might be due to the cholinergic deficit also remains theoretical.

Data from an open dose-response study of IVBC in four patients with Stage I AD support the real, but incomplete symptomatic responses previously reported. Memory, visuo-spatial and language skills, problem solving and other cognitive tasks, body temperature and activity level show concurrent responses. Characterization of response and peak efficacy will enhance the evaluation of this novel, but invasive technique.

NR91 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

A GENETIC STUDY OF DEMENTIA OF THE ALZHEIMER TYPE

Ronald L. Martin, M.D., University of Kansas, School of Medicine, 39th and Rainbow Blvd., Kansas City, KS 66103; Gretchen Gerteis, M.S., William F. Gabrielli, Jr., Ph.D.

Summary:

This previously unreported family study of dementia of the Alzheimer type (DAT) found elevated lifetime risks of DAT in first-degree relatives of affected probands. The lifetime risk (aggregated to age 85) in 130 first degree relatives of carefully studied, clinically-defined DAT patients was 37.4% with a risk of less than half of that among relatives of non-demented control subjects. Risk to second degree relatives of DAT probands was not elevated when compared with relatives of controls. The relationship of these findings to those of other investigations is reviewed with a special emphasis on methodological problems in genetic studies of DAT which include specificity of diagnosis in index cases, and accurate detection of secondary cases. The late onset of the disease necessitates an extended longitudinal perspective. Death from competing causes often occurs before expression of the genome, necessitating age-corrected analyses such as the Weinberg Morbidity Method and the Kaplan-Meier Survival Estimator. Both methods yielded similar results in this study. Even with optimal methods, it is argued that the high risk of DAT among first degree relatives in this and most other studies represent, if anything, underestimates. Thus, actual lifetime risk may approximate the 50% rate expected if the genetic mechanism for DAT is autosomal dominant. The probability of this, and other mechanisms of transmission are discussed.

NR92 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

EARLY SYMPTOMS IDENTIFY SUBGROUPS OF ALZHEIMER'S DISEASE

Joe E. Thornton, M.D., Mental Hygiene C1, 116A8, Palo Alto, VA, 3801 Miranda Ave., Palo Alto, CA 94304; Helen D. Davies, R.N., Terry Miller, M.D., Jerome A. Yesavage, M.D., Philip A. Berger, M.D., Jared R. Tinklenberg, M.D.

Summary:

We have studied 40 patients with early dementia of the Alzheimer's type (DAT) for over three years. We have reported that the early clinical symptoms may identify subgroups of patients with DAT and predict the clinical course of illness. Empirically we found that patients with a copy deficit on the Mini-Mental State (MMS) yet with a total score of 18 or above were as a group younger, and two years later had a greater progression of dementia as measured by decline in total MMS score, functional ability, or survival. We call this group the copy deficit group, and they represented about 35% of our patients. We later reported that performance on a divided attention task, specifically pursuit tracking and reaction time, could be predicted by the cognitive subtype of dementia better than any global dementia score, and we suggested that other cognitive tasks may have a threshold for expression.

We now report extension of this data with an additional year for 25 patients and a year of data on 15 new patients. Autopsy results from 12 patients will be presented. Early symptoms may have prognostic value and different subgroups of DAT patients may respond to different drug therapies.

NR93 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

BEHAVIORAL CHANGES IN MILD DEMENTIA (SDAT)

Eugene H. Rubin, M.D., Dept. of Psychiatry, Washington Univ. Med. Sch., 4940 Audubon Ave., St. Louis, MO 63110; John C. Morris, M.D., Martha Storandt, Ph.D., Leonard Berg, M.D.

Summary:

As part of our Memory and Aging project and Alzheimer's Disease Research Center, we have been studying a carefully characterized group of physically healthy subjects with mild senile dementia of the Alzheimer's type (SDAT; Clinical Dementia Rating 1), questionable dementia (CDR 0.5) and healthy controls. Subjects with any history of a depressive syndrome or psychiatric illness were excluded, leaving a homogenous population in which to study behavioral changes associated with SDAT. Both open-ended questions and personality items from the Blessed Dementia Scale (BDS) were examined in 58 controls, 44 CDR 1 subjects and 16 CDR 0.5 subjects. The 17 items (6 summarized from open-ended questions and 11 from the BDS) were classified into 7 categories by factor analysis. These were then categorized into 4 clinically useful groups: passive, agitated, self-centered, and suspicious. Over 75% of those with mild SDAT had behavioral changes compared with 10% of controls. Passive symptoms occurred in ⅔ of mild SDAT subjects. Symptoms of agitation and self-centeredness each occurred half as frequently as passive symptoms. Suspiciousness was rare at this mild stage. Passive symptoms were the only ones to occur alone; agitated and/or self-centered symptoms most frequently occurred with passive symptoms. A similar pattern of behavioral changes occurred in our CDR 0.5 group. Characterizing the behavioral symptoms quantitatively in well-staged mild SDAT (not confounded by depression) has important clinical as well as brain-behavioral implications.

NR94 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

PSYCHIATRIC CARE NEEDS SURVEY OF NURSING HOMES

Michael Resinstein, M.D., Crises Stabilization Unit, Hartgrove Hospital, 520 N. Ridgeway, Chicago, IL 60624; Ben Gierl, M.D., Lawrence Lazarus, M.D., Lynne Jones, R.N., Lionel Dredze, A.C.S.W., Linda Gaibel, M.S.W.

Summary:

A large number of long term care (LTC) residents are known to have psychiatric illnesses. It seems their needs may not be adequately met, as few psychiatrists are involved in consultation to LTC facilities. In order to better understand psychiatric care needs of LTC residents a subgroup of the Illinois Psychiatric Society devised a questionnaire that was sent to LTC administrators in Illinois. It was mailed as a survey from the head of the Illinois Council on LTC and had a response rate of 25%. The tabulated results of 155 responses indicate that 10% of LTC residents are currently receiving a psychiatrist's services. An additional 10% not currently receiving psychiatric services are thought to be able to benefit from these services. All total, 25% of LTC residents receive medication for psychiatric problems. This means most psychotropic medications are not prescribed by a psychiatrist but instead by another physician. Half of all LTC facilities have no psychiatric services for any residents. It was not determined exactly why these LTC facilities do not have psychiatric services.

Our conclusion is that many LTC residents with known psychiatric needs are not receiving the benefit of psychiatric services. We cannot determine why this is so. The overwhelming interest in sending staff to a workshop on Psychiatric Management of the Elderly Resident suggests an educational conference as the next step toward alleviation of some of these inequities in the delivery of psychiatric services in LTC facilities. The above data indicate further research is necessary to understand how to better serve the psychiatrically impaired LTC resident.

NR95 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

MENTAL DISORDER IN ELDERLY PUBLIC HOUSING SITES

Peter V. Rabins, M.D., Johns Hopkins Hospital, Meyer 279, Baltimore, MD 21205; Pamela Fischer, Ph.D., Sam Shapiro, B.A., Morton Kramer, Sc.D.

Summary:

The recently completed Epidemiologic Catchment Area study (ECA) of the NIMH demonstrated a decreasing prevalence of mental disorder in late life. To determine whether high rates of disorder might be found in the elderly living in certain settings, we examined the 1 month and lifetime prevalence rates of persons over 65 living in public housing sites for the elderly. The prevalence of psychiatric disorder overall in these elderly housing projects was 31% at 1 month and 56% lifetime. These rates are significantly higher than the rates for age matched individuals living in the community ($X = 8.6, p<.005$; $X^2 = 11.3, p<.005$ respectively). Likewise rates among elderly subjects living in adult foster care were 33% and 52%. They were also higher than in community residing elderly ($X = 8.6, p<.005$; $X^2 = 6.0, p<.025$ respectively). To examine whether these rates were based on disorders which started early or late in life we compared the subjects on a variety of demographic characteristics. Men living in the senior high rise were less likely to have been in the armed forces when young compared to the general population living at home ($X^2 = 4.6, p<.05$). This suggests that the high rate of disorder in the elderly males residing in these settings is partially explained by lifelong difficulties. These early life problems could be initial manifestations of the disorder ascertained by the ECA study. Alternatively they could have led to diminished social and psychological supports and increased their likelihood of residing in public housing. Overall, these findings suggest that persons residing in public housing and foster homes for the elderly have higher rates of mental disorder than those residing at home and that community psychiatry services to the elderly consider them a priority in care delivery.

NR96 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

PRL REGULATION IN GERIATRIC DEPRESSION AND DEMENTIA

George S. Alexopoulos, M.D., NYH/CMC Westchester, 21 Bloomingdale Rd., White Plains, NY 10605; Robert C. Young, M.D., Jacob Kream, Ph.D., Russel Barakat, M.D., Robert Abrams, M.D. Charles Shamoian, M.D.

Summary:

Blunted prolactin (PRL) response to thyrotropin releasing hormone (TRH) has been reported in subgroups of young adults with depression, while elevated baseline plasma PRL has been found in some demented patients. We studied plasma PRL under baseline conditions and after challenge with TRH, and hypothesized that this test will distinguish patients with primary degenerative dementia (PDD) from similar age depressives.

The subjects were 26 elderly psychiatrically hospitalized patients who met *DSM-III* criteria for PDD (N = 13) or for unipolar primary major depression (N = 13). Men with PDD(N = 6) had higher baseline plasma PRL (Wilcoxon z = 2.01, $p<0.04$) and lower PRL percent change from baseline (percent E PRL) after TRH challenge (z = 2.09, $p<0.04$) than depressed men (N = 5). There was, however, no difference in the maximal plasma PRL after TRH (peak PRL) between the two groups. PRL maximal change from baseline after TRH challenge correlated with Hamilton Depression Rating Scale score in depressed men ($r= -0.97$, $p<0.005$). PDD women (N = 7) also had a trend towards higher baseline plasma PRL (z = 1.44, $p<0.15$) and lower percent Δ PRL (z = 1.20, $p<0.27$) compared to depressed women (N = 8). Peak PRL was comparable in PDD and depressed women. The data suggested the presence of differences in PRL regulation between PDD and depressed geriatric patients, probably due to different neurotransmitter abnormalities in these disorders.

NR97 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

CLINICAL PRESENTATION OF GERIATRIC DEPRESSION

George S. Alexopoulos, M.D., NYH/CMC, 21 Bloomingdale Rd., White Plains, NY 10605; Robert Abrams, M.D., Robert C. Young, M.D., Charles A. Shamoian, M.D.

Summary:

Demented patients frequently develop depression, but minimal information exists on the presentation of depression in these patients, in part because of the absence of a suitable rating method. We report a study of signs and symptoms of depression in demented and nondemented subjects using a recently developed instrument for rating depression in demented patients.

The subjects were elderly psychiatric inpatients (N= 65) and normal individuals (N= 15). Of the 65 patients, 24 were diagnosed by their psychiatrists as depressed and received antidepressant treatment. *DSM-III* and Research Diagnostic Criteria were used to confirm diagnoses. Signs and symptoms of depression were recorded with the Hamilton Depression Rating Scale and the Cornell Scale, an instrument which uses information from the subjects and their caretakers. Demented subjects with depression (N= 11) had depressive features comparable to cognitively unimpaired depressives (N= 13). Non-depressed demented subjects (N= 26) had significantly fewer depressive symptoms, with the exception of anxiety, irritability and agitation in 42, 50, and 50 percent of this population, respectively. The frequency of depressive symptoms in non-depressed demented patients was similar to that of patients with other psychiatric disorders (N= 15) and of normal controls(N= 15). The controls, however, had significantly less agitation ($p<0.05$) and irritability ($p<0.05$) than any of the patient groups. The data suggests that the presentation of depression in demented patients is similar to that of non-demented depressives and that it can be distinguished from other geriatric psychiatric entities. The similarity between depression in demented and non-demented elderly patients parallels the similarity between primary and secondary depression in younger adults.

NR98 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

TRIMIPRAMINE VERSUS IMIPRAMINE IN THE ELDERLY

Eric C. Dessain, M.D., McLean Hospital, 115 Mill St., Belmont, MA 02178; Jonathan O. Cole, M.D., Alan F. Schatzberg, M.D., Melinda Salomon

Summary:

Imipramine and trimipramine were compared under double-blind conditions in fifty elderly patients. Repeated measures analyses, covarying for baseline values, were used to examine the data. Trimipramine was significantly better than imipramine at weeks one through four of this thirty-five day trial on measures of depression, insomnia and anxiety. Overall, a significant drug difference ($p<0.02$) and time effect ($p<0.00$) was found on global measures of anxiety. At endpoint both drugs seemed equal on most clinical rating scales. However, eight of twenty-seven patients in the trimipramine group had a total remission of all symptoms. Only five of twenty-three patients on imipramine completely remitted. Six of seven patients in the imipramine group dropped out due to adverse reactions; two patients could not tolerate trimipramine. Analysis of blood pressure data were performed as well. Concomitant use of diuretics, allowed during the trial, had no effect on the overall analyses. Recumbent pulse rates at rest indicated a significant ($p<0.01$) drug difference, imipramine causing tachycardia. In an analysis of sitting systolic blood pressure, a significant time x drug interaction ($p<0.03$) and time effect ($p<0.05$) was again in favor of trimipramine. No overall drug effect was found, the hypotensive effects of imipramine being manifested in the last two weeks of the study. Standing systolic blood pressures, added later in the study ($N= 12$), also showed significant hypotension on imipramine but not trimipramine ($p<0.04$). These findings will be discussed in relation to differential effects of these drugs on biogenic amine reuptake properties and on relevant receptor sites.

NR99 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

AGING INCREASES HPA DYSREGULATION IN DEPRESSIVES

John F. Greden, M.D., Dept. of Psychiatry, Univ. of Michigan Hospital, 1405 E. Ann St., Box 011, Ann Arbor, MI 48109; Dolores Tiongco, M.D., Roger F. Haskett, M.D., Leon Grunhaus, M.D., Joan Kotun, M.D.

Summary:

Approximately eight cross-sectional studies have suggested that aged depressives have significantly more hypothalamic-pituitary-adrenal dysregulation than younger depressed controls. To determine whether this is due to aging itself or to interactions between aging and depression, evaluation of control groups of normals and non-depressed psychiatric patients is required. We conducted such a study by comparing post-dexamethasone plasma cortisol levels across five different age brackets (<30, 30-39, 40-49, 50-59, 60>) among five patient subgroups: 1) 100 patients with major depressive disorder (MDD), definite endogenous; 2) 102 patients with MDD, probable endogenous; 3) 84 patients with MDD, non-endogenous; 4) 106 psychiatric controls without depression; and 5) 18 normal controls. All Ss were hospitalized in the Clinical Studies Unit for Affective Disorders, were drug-free, diagnosed with SADS/RDC and rated blindly to DST (1 mg) results. Normal controls were studied in the University Hospital CRC.

Increasing age progressively and significantly increased DST concentrations in all *depressed* subgroups, but aging had no significant effects in non-depressed psychiatric patients or normal controls. These data suggest that the pathophysiologic changes associated with aging are synergistic with those that induce HPA dysregulation in patients with depression. They have relevance in designing future studies of neurobiologic mechanisms of depression. They also support the growing impression that neuroendocrine measures such as the DST will require different referent levels for different age ranges.

NR100 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

GERIATRIC BORDERLINE PERSONALITY DISORDER

Vivian Blotnick-Pender, MD., NYH/CMC Westchester, 21 Bloomingdale Rd., White Plains, NY 10605; Charles Shamoian, M.D.

Summary:

In a previous study of 800 geropsychiatric patient discharges, a zero incidence of borderline personality disorder was found. Tentative conclusions were: A) there was insufficient consideration of this entity in the elderly, B) current criteria were not applicable to this age group, or C) the entity simply did not exist in the elderly. Since then, increased interest in and awareness of this entity in the geriatric division of our institution has resulted in 10 cases with discharge diagnosis of borderline personality disorder.

In an attempt to independently validate this discharge diagnosis, a retrospective application of the Diagnostic Interview for Borderlines (DIB) to the hospital record was employed and scored by an independent reviewer. The reliability of this technique has been established. Using this technique in our study, a high degree of concordance in the accuracy of the diagnosis of borderline personality disorder between therapist and reviewer was found. The majority of geriatric borderline discharge diagnoses were deemed valid. Additionally, the result would appear to validate the concept of retrospective identification of the geriatric borderline personality disorder.

The conclusions of our earlier study can now be extended. Increased awareness has led to a greater consideration of borderline personality disorder as a geropsychiatric diagnosis. The applicability of current criteria (DSM-III, DIB) to the geriatric age group appears to be valid and fruitful. This preliminary study appears to indicate the existence of geriatric borderline personality disorder.

NR101 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

OMS SCREENING DEVICES

James J. Strain, M.D., 608 KCC, Mt. Sinai Hospital, 1 Gustave Levy Pl., New York, NY 10029; George Fulop, M.D., Barry Ginsberg, M.D., Michael Robinson, M.D., Anthony Stern, M.D., Peter Charap, M.D., Francesca Gany, M.D

Summary:

Organic Mental Syndrome (OMS) is one of the most common disorders encountered in medicine. The available screening devices are compromised by their high frequency of false negative and positive findings. This study examines the validity of three commonly used tests: Mini Mental State (MMS), Cognitive Capacity Screening Examination (CCSE), and Tachistoscope (T-Scope).

Ninety-seven medical/surgical inpatients at the Mount Sinai Hospital referred for psychiatric consultation had a Missouri Mental Status Examination performed by one attending psychiatrist who also rated the patient's organicity as mild, moderate, or severe. Within four hours, a team of three evaluators presented the screening devices in random order.

The 97 patients, 34 male and 63 females, significantly differed with regard to their degree of organicity and mean age: None -38.7, mild - 49.4, moderate - 59.5, and severe - 67.7. The CCSE, MMS, and T-Scope, respectively, showed: sensitivity - .54, .52, .68, specificity - .85, .76, .79, and positive predictive value - .83, .84, .79 The CCSE correlated with the MMS - .85, and the T-Scope - .50. The MMS also correlated with the T-Scope - .51. False negatives occurred more often among the "mild" organics in all instruments ($p<.05$) and the T-Scope could not be administered in 27% of the patients.

All instruments discriminated poorly between the critical "none" and "mild" categories. The Epidemiological Catchment Area studies omitted the important mild and moderate organic categories because of the MMS's questionable validity. OMS screening instruments with increased acceptability, sensitivity, and specificity, need to be developed to identify a potentially life-threatening disorder.

NR102 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

MUSCARINIC BINDING IN TEMPORAL LOBE EPILEPTIC FOCI

Ana Hitri, Ph.D., Dept. of Psychiatry, Medical College of Georgia, Augusta, GA 30912; Herman Flanigin, M.D., Gavin P. Reynolds, M.D.

Summary:

Pathological changes underlying temporal lobe epilepsy involve structural and functional changes in the temporal lobe nuclei of afflicted individuals. The degenerative neuropathological changes in the hippocampus related to cholinergic transmission have been implicated as the primary abnormality responsible for memory impairment. The aim of this study was to investigate the cholinergic muscarinic receptor site changes in the excised epileptogenic foci in patients undergoing temporal lobectomy, under local anesthesia. Seven patients with uncontrollable epilepsy were selected for surgery at the Georgia Epilepsy Center. Based on a series of preoperative and intraoperative evaluations of memory functions the decision was made for the removal of the hippocampus. The freshly frozen hippocampal tissue was homogenized and assayed for muscarinic receptors according to the method of Yamammura and Snyder (1974) using ^{3}H-QNB as the ligand. For the determination of kinetic parameters an 8-12 point scatchard plot was generated with each sample. The receptor density expressed as B-max ranged from 27-299 fmoles/mg protein and the affinity constant as K_D ranged from 66-81 pM. As compared to aged matched postmortem control hippocampal tissue there was a uniform decrease in the number of receptor binding sites in all seven patients. The magnitude of decrease was variable, from 23% to 93%. There was no change in the affinity of muscarinic receptors. The data suggest a strong relationship between the memory function prior to surgery and the abnormalities in cholinergic muscarinic receptor in the excised hippocampi.

NR103 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

EFFECT OF LITHIUM ON HUMAN STRIATAL D2 RECEPTORS

Christopher Ross, M.D., Johns Hopkins Hospital, Meyer 279, 600 N. Wolfe St., Baltimore, MD 21205; Godfrey D. Pearlson, M.D., Dean Wong, M.D., Henry W. Wagner, Robert F. Dannals, Ph.D., Jonathan M. Links, Ph.D.

Summary:

D2 dopamine receptors may be involved in affective illness. Lithium, which is widely used in the treatment of affective disorders, has been reported to have conflicting effects on brain dopamine receptors in different animal experiments. As part of an investigation of the role of D2 receptors in affective illness, we therefore sought to determine the effect of lithium on striatal D2 receptors in normal human volunteers. Subjects had C-11-3-N-methylspiperone (NMSP) PET scans before and after a minimum of one month of lithium at therapeutic levels (mean 0.74 mEq/l). Mean caudate/cerebellar ratio, (presumably related to Bmax) before lithium was 4.05 ± 0.557 and on lithium was 4.48 ± 0.60, an 11% increase. Mean slope of the caudate/cerebellar ratio with time (reflecting the rate of NMSP binding to receptors) was 0.0718 ± 0.011 before lithium and 0.0813 ± 0.12 while on lithium, for a 13% increase. The increase in the caudate/cerebellar ratios was not statistically significant, while the increase in the slope was statistically significant ($p<0.05$). These preliminary data suggest the possibility that chronic lithium treatment at therapeutic levels elevates human striatal dopamine D2 receptors. Further studies with more subjects are in progress.

NR104 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

LITHIUM, SODIUM, AND A POSSIBLE ANTIKINDLING MECHANISM

Alan G. Mallinger, M.D., Western Psychiatric Institute, 3811 O'Hara St., Pittsburgh, PA 15213; Israel Hanin, Ph.D., Jonathan M. Himmelhoch, M.D., Michael E. Thase, M.D., Steven Knopf, B.S.

Summary:

The therapeutic effects of lithium (Li) occur by an unknown mechanism. To investigate this area, we studied an action of Li on membrane sodium (Na) handling. Li is extruded from cells in exchange for external Na via a coupled Na-Li countertransport mechanism (Na-Li CT), which has been demonstrated in both erythrocytes (RBCs) and cultured neural cells. We hypothesized that during Li treatment, uncoupled entry of Li into cells, followed by Na-coupled Li extrusion via Na-Li CT, could lead to a significant augmentation of net cellular Na influx. To test this hypothesis, we measured Na influx *in vitro* using Li-free and Li-loaded RBCs from 27 drug-free bipolar patients. Basal Na influx (mean±SD) was 0.64±.13 mmoles/(liter RBCs x hr). Li-loading of cells significantly increased mean Na influx by more than 40%, to 0.92±.19 (paired t-test, $t= 9.57$, $p<0.0001$). However, these experiments were performed using cell Li levels that maximally stimulate Na-Li CT. To more closely approximate clinical conditions, we studied Na influx in RBCs from 8 subjects after loading with 0, 0.40, 0.66, and 1.55 mM Li. At these cell Li concentrations, Na influx increased significantly from a basal rate (mean±SD) of 0.72±.10 mmoles/(liter RBCs x hr) to 0.83±.12, 0.89±.16, and 1.05±.27, respectively (blocked ANOVA, $F= 6.96$, $p<0.002$). Thus raising cell Li content over a clinically relevant range led to a progressive increase of Na influx. The increased cellular Na load, in turn, can stimulate electrogenic activity of the membrane Na pump. Such an effect could stabilize the membrane electrophysiologically and thereby inhibit kindling phenomena, which have recently been proposed to occur in bipolar disorder. Moreover, patients having low Na-Li CT activity, whose cellular Na influx would be relatively less affected by Li, might be responsive only to alternative antikindling agents.

NR105 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

LITHIUM WITHDRAWAL EFFECT ON 5HTP CLONIDINE TESTS

Paul J. Goodnick, M.D., Columbia University, Box 77, 722 W. 168th St., New York, NY 10032; Annemarie Schlegel, R.N., Ronald R. Fieve, M.D.

Summary:

Lithium prophylaxis may influence trait abnormalities of bipolar disorder. Such traits may be serotonergic (the cortisol response to 5-hydroxytryptophan, 5HTP) or noradrenergic (the growth hormone response to clonidine). Both manic and depressed patients have been found to have similar abnormal elevations in response to 5HTP. Abnormal clonidine responses have been reported to persist in euthymic unmedicated patients after recovery from depression. Previous results indicate that lithium prophylaxis restores platelet 5HT uptake toward control levels and attenuates clonidine-induced hypotension. **METHOD:** 6 bipolar I & II patients (RDC) in remission at least one year while on lithium prophylaxis and 5 controls gave informed consent to be tested following 200 mg 5HTP and 1 ug/kg clonidine. Patients gave informed consent to be re-tested after two weeks of lithium withdrawal. Tests were done after overnight fast with bloods taken at t−15, 0, +30, +60, +90, +120, minutes. Clinical status was monitored weekly with BPRS, Ham-D, & Fieve Mood Scale; no patient relapsed during the study period. **RESULTS:** Preliminary findings are: 1) 5HTP-induced increases in cortisol were lower on lithium than after withdrawal (14.4 vs 10.3, P.05); 2) 5HTP-induced increases in cortisol were higher in patients than controls (3.5); 3) clonidine-induced hypotension was lower on lithium than after withdrawal (p.05). All growth hormone and a number of other results are still pending. **DISCUSSION:** 1) 5HTP-induced elevation of cortisol, since it continues to be abnormally elevated in the euthymic bipolar patient, may be a trait marker. 2) Lithium may succeed in prophylaxis partly because of influence of this trait abnormality to bring it closer to control levels. 3) Lithium prophylaxis may bring clonidine-induced hypotension under greater control; this could indicate an influence to stabilize presynaptic alpha-2 noradrenergic receptors. Discussion concerning clonidine and growth hormone awaits future results.

NR106 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

LITHIUM AFFECTS BALANCE OF BRAIN RECEPTOR ACTIVITY

Robert H. Lenox, M.D., Dept. of Psychiatry, Neuroscience Research, University of Vermont, Burlington, VT 05405; John Ellis, Ph.D., Daniel D. Hendley, Ph.D., Yigal H. Ehrlich, Ph.D.

Summary:

Accumulating evidence from animal models and clinical studies implicate an imbalance in central adrenergic/cholinergic activity in the mediation of affective illness. Muscarinic and alpha$_1$ adrenergic receptors in brain are coupled to a second messenger system involving the formation of inositol triphosphate, which mobilizes intracellular calcium; and diacylglycerol which stimulates protein kinase C activity. Lithium, which inhibits inositol-1-phosphatase can affect the dynamic balance of these phospholipid metabolites generated from phosphoinositide (PI) hydrolysis.

Our studies in hippocampal and cortical tissue slices demonstrate significantly different dose response and time course characteristics of muscarinic vs adrenergic receptor stimulated hydrolysis of PI. Further data indicate evidence for agonist-induced desensitization of the PI response in the muscarinic receptor system but not in the adrenergic system. Exposure of slices to phorbol ester (1 uM PDBu), which activates protein kinase C, results in a significant reduction of receptor-mediated activity; with greater inhibition noted in the alpha$_1$ adrenergic system (75%) vs the muscarinic (40%).

Recent studies in our laboratory have revealed that animals placed on chronic lithium diet and attaining therapeutic lithium levels in brain (1 meq/kg) and plasma (1 mM) show a significantly greater proportion of protein kinase C activity in the membrane fraction from cortex, as compared to control animals. This in turn, can differentially alter the regulation of the receptor systems in light of the *in vitro* studies described above. Such alterations in the balance of muscarinic/adrenergic activity may account for some long-term effects of chronic lithium in the treatment of major affective disorders.

NR107 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

LITHIUM EXTENDS SLEEP DEPRIVATION EFFECT IN DEPRESSION

Lewis R. Baxter, Jr., M.D., Dept. of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Edward H. Liston, M.D., Jeffrey M. Schwartz, M.D., Steven Richeimer, M.D., Lori L. Altshuler, M.D., Jeffrey N. Wilkins, M.D., Barry H. Guze, M.D.

Summary:

Partial sleep deprivation (PSD) acutely elevates the mood of 50% of depressed patients, but the effect does not last more than a day or two after "recovery" sleep. We studied PSD responders who were identified with a drug free, one night trial of PSD. Positive responders were randomized to receive PSD + lithium (PSD/Li), or PSD + placebo (PSD/Pl), double-blind, or lithium without PSD (LiOnly). All were given a loading dose of pills on day 1 of the study and thereafter kept on maintenance dosing as calculated from a previous lithium test dose given to predict requirements. PSD/Li and PSD/Pl patients had PSD on days 1 and 2. Patients were rated on the Hamilton Depression Scale (HAM-D) on days 0 and 5 by raters who only saw them on those days. Those on PSD who did not improve >50% by day 5 were taken off pill and crossed over to the other pill and the procedure repeated, as before, 3 days later. Significantly more patients on PSD/Li than on PSD/Pl improved 50% ($p<.05$). HAM-D scores declined a mean of 46% on PSD/Li, −6% on PSD/Pl and 7% on LiOnly (PSD/Li > PSD/Pl, $p<.002$; PSD/Li > LiOnly, $p<.02$; PSD/Pl = LiOnly, $p>.2$). Li may be able to prolong the effects of PSD long enough to make it a useful treatment.

NR108 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

INSOMNIA: VALIDATION OF SLEEP LABORATORY CRITERIA

E.O. Bixler, Ph.D., Sleep RSH & Treatment, Psychiatry Dept., Penn State, P.O. Box 850, Hershey, PA 17033; Anthony Kales, M.D., Joyce D. Kales, M.D., Rocco L. Manfredi, M.D., Roger J. Cadieux, M.D.

Summary:

There is controversy regarding both the clinical utility and validity in using the sleep laboratory for the confirmation of the diagnosis of chronic insomnia. Thus, we evaluated the diagnostic accuracy of two objective sleep laboratory criteria for the diagnosis of insomnia in 150 adults with a primary complaint of chronic insomnia (duration greater than 6 mo.) and 100 controls who were without any sleep complaints. Each subject was monitored for 8 hours in the sleep laboratory on four consecutive nights. The first criterion was a sleep latency of >20 min. and a total sleep time <6.5 hrs. while the second criterion was a sleep latency of >30 min. or a sleep efficiency of <85%. The overall diagnostic accuracy of these two criteria was quite similar and only slightly greater than chance. The two criteria differed in their accuracy in correctly classifying insomniacs (sensitivity) and controls (specificity). While the first criterion had low sensitivity and moderately strong specificity, the opposite was true for the second. In both cases the strongest sensitivity was obtained from the initial night of evaluation and the strongest specificity from the mean of the last three nights of evaluation. Sensitivity of these criteria increased with increasing patient age while specificity decreased. Sex of the patient, however, did not appear to influence either sensitivity or specificity. In summary, sleep laboratory assessment has little accuracy in classifying patients as having insomnia. Just as important, sleep laboratory evaluation in the majority of patients with chronic insomnia provides little information on the causative factors of this condition. Thus, the sleep laboratory has little validity in the diagnosis of chronic insomnia and limited clinical usefulness in determining the psychiatric disorders (anxiety, depression, somatization, etc.) and medical conditions (cardiovascular, arthritis, medication effects, etc.) usually associated with it.

NR109 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

SINGLE-DOSE KINETICS OF FLUPHENAZINE DECANOATE

George M. Simpson, M.D., Med. Coll. of PA, EPPI, 3200 Henry Ave., Philadelphia, PA 19129; Kashinath Yadalam, M.D., Douglas P. Levinson, M.D., Mary Jeanne Stephanos, R.N., Thomas B. Cooper, M.A., E-S Lo,Ph.D.

Summary:

Fluphenazine decanoate (FPZ-D) plays an important role in the maintenance treatment of schizophrenia. Although it has been available for over 20 years, little is known about its pharmacokinetic properties. This is because there have not been analytical techniques available for measuring the minute quantities of the drug often present in plasma (low nanogram or picogram levels). Also, the drug is not used to treat acute or drug-naive patients, creating logistical problems in evaluating its pharmacokinetic profile in patients. In this study, a sensitive FPZ assay was first used to demonstrate that haloperidol does not interfere with the analysis of FPZ. Then, 11 physically-healthy inpatients on maintenance haloperidol were studied. Haloperidol dosage was reduced by ⅓ and maintained at that level throughout the study. After two days on this reduced dosage, an injection of 12.5 mg FPZ-D was given. Blood specimens for assay of FPZ were drawn at 1, 3, 5, 8 and 24 hrs. after injection, and on days 2, 3, 4, 5 and then twice weekly through week 4. FPZ was measured by RIA method after prior extraction of the plasma. There was wide inter-individual variation in plasma levels (over tenfold at some time points). FPZ levels were still measurable at 26 days and 50% reduction of peak levels did not typically occur during the study period, so that elimination parameters could not be calculated. This suggests that long-term accumulation of FPZ may occur during FPZ-D treatment, and that levels may persist for long periods after drug discontinuation. Data from this study and from an additional study of discontinuation of chronic FPZ-D will be presented.

NR110 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

PERSISTANT FLUPHENAZINE AFTER DECANOATE WITHDRAWAL

Michael J. Gitlin, M.D., UCLA/NPI, 760 Westwood Plaza, Box 18, Los Angeles, CA 90024; David Fogelson, M.D., Keith Nuechterlein, Ph.D., Joanne MacKenzie, R.N., Kamal Midha, Ph.D.

Summary:

Fluphenazine decanoate, a long acting injectable phenothiazine, has been used for more than a decade in the maintenance treatment of schizophrenia. It is usually administered in doses ranging from 5 mg. to 50 mg. at one to four week intervals. Despite the wealth of clinical experience with this drug, our knowledge of its pharmacokinetics, its persistence in plasma and the optimal interval between injections remains poor, in large measure due to unreliable drug assays. In this study, using a double-blind, crossover design, we discontinued fluphenazine decanote in twelve recent-onset, clinically stable schizophrenics who had been given fluphenazine decanoate 12.5 mg i.m. every two weeks for at least one year prior to drug withdrawal. Each condition (drug or placebo) lasted 12 weeks. Using a radioimmunoassay (RIA) verified by gas chromatography/mass spectrometry (GCMS), we measured plasma fluphenazine levels every two weeks during drug and placebo conditions. In addition, we rated depression and akinesia. No patient relapsed over the 24 week period of the study. Mean fluphenazine levels between drug and placebo conditions showed a progressively larger difference over time, but significant differences were not seen until week eight. By week 12 after drug withdrawal, 44% of subjects still showed clearly detectable plasma fluphenazine levels. Both subjective and observer akinesia ratings tended to be higher in the drug condition. Side effects did not correlate with plasma fluphenazine levels. The potential implications of these results for future clinical use of fluphenazine will be presented.

NR111 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

DO NEUROLEPTIC BLOOD LEVELS HELP?

Joseph Zohar, M.D., LCS/NIMH, NIH-Bldg. 10, Rm 3D/41, 9000 Rockville Pike, Bethesda, MD 20892; Zecharia Shemesh, M.D., Robert H. Belmaker, M.D.

Summary:

Previous studies have reported a relationship between blood levels of neuroleptic drugs and clinical response in acute psychotic patients. We treated 22 acute psychotic patients with flexible doses of haloperidol, and had a knowledge of weekly neuroleptic blood levels for 12 of the patients, but were given no feedback information on blood levels for the other patients.

Mean BPRS scores over the five weeks of the trial showed no differences at any time points between the feedback and nonfeedback group, as measured by a blind rater. In fact, nonfeedback patients had blood levels within a "therapeutic range" of 10-20 ng/ml as frequently as the feedback patients.

These data do not contradict findings suggesting a correlation between clinical outcome and blood level, but rather suggest that responsible clinicians using clinical signs can maintain "the average patient" within the range of therapeutic blood levels, even without the laboratory monitoring of such levels.

Despite the absence of an overall benefit to the acute psychotic patients, measurement of haloperidol blood levels may be useful for specific patients such as non-complainers, those who have many side effects and non-responders. Cases which illustrate these specific conditions will be presented.

NR112 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

TARDIVE DYSKINESIA: CROSS-CULTURAL PREVALENCE RATES

Daniel E. Casey, M.D., Psychiatry Service 116A, VAMC, Portland, OR 97207

Summary:

Tardive dyskinesia (TD) prevalence rates average approximately 25%. However, the range varies widely from 0.5% to 80%. Special risk factors of patient variables (age, sex, psychiatric diagnosis), treatment factors (drug dose and type), and temporal aspects (duration of treatment and illness) may all substantially influence TD prevalence.

To identify the relative contributions of these different risk factors to TD prevalence, they were analyzed from studies across different cultural settings. Rates are lowest in the Far East, such as Singapore (2.5%) and Taiwan (4.5%). A study in India reported a 10% prevalence rate. Japanese TD rates average 20% (range = 0% to 36%). European rates are moderately high, but also vary considerably: Hungary = 23%; Sweden = 20%; France = 42%; and England = 50%-70%. North American TD rates are relatively high: Canada = 33%-53% and USA = 20%-70%.

An analysis of these data shows that TD is more commonly correlated with increasing age. When this factor is accounted for, higher neuroleptic doses for greater durations of time are associated with higher TD rates. Other patient, drug, and temporal factors will also be evaluated.

NR113 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

LONGITUDINAL ASSESSMENT OF INVOLUNTARY MOVEMENTS

Spyros J. Monopoplis, M.D., 8116 Bellona Ave., Towson, MD 21204; Douglas Heinrichs, M.D., William T. Carpenter, Jr., M.D., Jerry Levine, M.D.

Summary:

Recently there has been an increased interest in reference to the impact of various neuroleptic treatment approaches on involuntary movements (IMs) in general and tardive dyskinesia (TD) specifically. However, there is a considerable degree of difficulty in accurately assessing progression and long-term outcome given the high level of fluctuation in severity over time.

In an attempt to address some of these issues in the context of a longitudinal assessment of IMs, we studied the appearance and/or progression of IMs in an outpatient psychiatric population. AIMS data were collected over a 2-year period on 58 patients with an RDC diagnosis of schizophrenia. The subjects were randomly assigned to either a maintenance (MM) or a targeted medication (TM) group. The patients in the MM group were maintained on a minimum neuroleptic dose (equivalent to 300 mgm./24 hr. of chlorpromazine), except for periods of psychotic decompensation during which medication was adjusted accordingly. The patients in the TM group remained drug free while asymptomatic; neuroleptics were administered during decompensations. Linear trend analysis was used to examine change in AIMS scores during the study. Slopes representing the rate of change in IMs (progression or improvement) during the 2-year period were derived for each patient. One-way ANOVA was used to provide a preliminary assessment of the relationship between neuroleptic regimen (TM or MM) and the degree of change in AIMS scores.

Detailed results comparing the two treatment groups and their possible significance will be discussed.

NR114 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

AN OBJECTIVE MEASURE OF AKATHISIA

Mohamed Sabaawi, M.D., Dept. of Psychiatry and Human Behav., Brown Univ., Blackstone Blvd., Providence, RI 02905; Joseph H. Friedman, M.D., Richard L. Wagner, M.D., Thomas L. Kucharski, Ph.D., Farrel Klein, M.D.

Summary:

Akathisia is a common side effect of neuroleptics. It is difficult to define as it includes subjective complaints and objective signs which may overlap with both psychosis and tardive dyskinesia. In an attempt to improve clinical assessment and better monitor treatment response, we developed a new rating scale by modifying the checklist devised by Barnes and Braude. We introduced scales for subjective complaints and overall objective signs. We also added items to rate objective severity in each position (sitting, standing and lying) and percentage time of akathisia of different muscle systems in each position. Finally, an overall assessment scale based on all previous items was introduced. Eight patients with both subjective reports and objective signs of akathisia were selected from a chronic schizophrenic inpatient population receiving maintenance neuroleptics. Patients were videotaped and ratings were done by each of the five authors. Intra and inter-rater reliabilities were investigated. Reliability analysis was done by inter-item correlational matrix and a comparison of item mean and standard deviation. We found that: (1) subjective ratings did not correlate with any of the objective measures; (2) intra-rater reliability was enhanced by rating percentage time of akathisia of different muscle systems as opposed to merely rating overall severity in each position; and, (3) consistent ratings were obtained across raters in virtually all items. In conclusion, our new scale proved to be a reliable objective measure. Furthermore, we hypothesize that rating akathisia percentage time in different muscle systems may enhance the scale's sensitivity for measuring response to treatment.

NR115 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

NORADRENERGIC MECHANISMS IN AKATHISIA

Lenard A. Adler, M.D., Psychiatry Service 116A, NYVAMC, First Ave. and E. 24th St., New York, NY 10010; Burt Angrist, M.D., Eric Peselow, M.D., June Corwin, Ph.D., John Rotrosen, M.D.

Summary:

Lipinski et al. originally performed open studies which showed that propranolol was an effective treatment for neuroleptic-induced akathisia; we have reported a single-blind study corroborating this observation.

We have extended the assessment of the role of noradrenergic mechanisms in akathisia as follows:

1) Propranolol was compared to placebo in 12 patients under double-blind conditions; efficacy was demonstrated, with highly significant reductions in objective and subjective measures of akathisia, but not in Hamilton anxiety scores.

2) The effect of clonidine on akathisia was studied in a single-blind, on/off design in six patients. This agent reduced akathisia scores, but in contrast to propranolol caused sedation and reductions in Hamilton anxiety scores that paralleled akathisia decrements.

NR116 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

INFUSION PUMP ADMINISTRATION OF PSYCHOTROPIC DRUGS

Walter W. Winslow, M.D., Dept. of Psychiatry, Univ. of New Mexico, 2400 Tucker, NE, Albuquerque, NM 87131; Edward Reyes, Ph.D., Wayne Meyerowitz, M.D.

Summary:

The effectiveness of long term psychotropic administration in the prevention of relapse in certain chronically mentally ill patients is well established. However, patient non-compliance with medication regimens remains a barrier to successful long term management. Implantable, refillable infusion pumps are now available which can reliably deliver medications at fixed or variable rates over relatively long periods of time. This study is designed to determine the feasibility of administering certain psychotropic drugs via an infusion pump, first to experimental animals in preparation for later human trials.

Fluphenazine hydrochloride and lithium carbonate were administered for an extended period of time to experimental animals (dogs) via an implantable infusion pump manufactured by the Infusaid Corporation. Drugs were infused into the peritoneal cavity, and blood was drawn at regular intervals. Fluphenazine and lithium blood levels were measured by radioimmunoassay and flame photometry methods respectively. Pharmacokinetic parameters were developed from blood level versus time curves. The experimental animals were autopsied to determine tissue response at the infusion site, organ pathology due to the drugs and the biocompatibility of the pump system.

The presenters are prepared to discuss their preliminary findings.

NR117 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

SELECTION BIAS IN PSYCHIATRIC RESEARCH

Ann E. Pulver, Sc.D., Dept. of Psychiatry, Maryland Psych. Rsrch. Ctr., P.O. Box 3235, Baltimore, MD 21228; Paula Wolyniec, M.S., John McGrath, M.S., William T. Carpenter, Jr., M.D., Barton Childs, M.D.

Summary:

The importance of representative sampling in psychiatric research is demonstrated in this epidemiologic investigation of hospitalized psychotic patients in Maryland. Since June 15, 1983, psychiatric admissions to 15 different facilities have been monitored to identify a cohort of psychotic patients who will be involved in a long-term investigation of the heterogeneity of schizophrenia. Case identification will continue through 1988. Patients who meet the following criteria are entered into the sample: 1) caucasian; 2) ages 16-65; 3) hospitalized less than three times with a psychotic illness diagnosis or spectrum disorder diagnosis (*DSM-III*). Four types of facilities providing inpatient psychiatric services are represented in the 15 hospitals being monitored, i.e., state hospitals, university-affiliated hospitals, private hospitals, and community hospitals. Of the 30,913 patients who were admitted to these facilities since the study began, 988 have met the inclusion criteria, and 507 of these have consented to participate in the research. Basic demographic information is gathered for all patients who meet the inclusion criteria. Those patients who agree to participate in the research complete an extensive diagnostic interview (modified *Diagnostic Interview Schedule*) while they are in the hospital. The 988 patients meeting the inclusion criteria at the four types of facilities were compared with respect to 9 demographic variables. All 9 variables showed significant differences across facility types. The 507 patients at the four types of facilities who have entered the cohort were compared with respect to 44 clinical variables reported by the patient at the time of the hospital interview. 20 of the 44 variables showed significant differences including differences in premorbid functioning, age at oneset, and clinical signs and symptoms. In addition the total 6-month outcome functioning score was examined and was found to be significantly different across hospital types (N= 210). Differences in clinical manifestations suggest previously unreported patterns in disease expression (e.g., community hospital patients are more likely to experience rare forms of hallucinations). These data suggest that investigators of psychiatric illnesses who sample patients from one type of facility greatly limit the representativeness of their sample and hence the generalizability of their findings.

NR118 **Tuesday, May 13, 12:00 noon -1:45 p.m.**

CARBAMAZEPINE IN PTSD

Steven Lipper, M.D., Psychiatry Service, VAMC, 508 Fulton St., Durham, NC 27705; Jonathan R.T. Davidson, M.D., Tana A. Grady, B.S., Jack Edinger, Ph.D., Elliott B. Hammett, M.D., Steven L. Mahorney, M.D., Jesse O. Cavenar, Jr., M.D.

Summary:

Carbamazepine was evaluated in 10 veterans meeting DSM-III criteria for PTSD. Patients received no psychotropic medication other than carbamazepine, 600-1000 mg/day, for 5 weeks under non-blind, inpatient conditions. All had normal EEGs with nasopharyngeal leads and were drug-free for at least one week prior to the study. Symptomatology was assessed (a) on 6 interviewer-rated scales, including a 12-item PTSD Checklist derived from the DSM-III criteria for PTSD, and (b) on 9 self-report instruments, including a PTSD Index for recording frequency and severity of 11 symptoms. Data were analyzed with either paired, two-tailed t-tests or two-tailed Wilcoxon matched-pair signed-ranks tests. **Results:** Mean weekly serum carbamazepine concentrations were between 7.3 and 9.7 μg/ml. After carbamazepine treatment, mean total scores on the PTSD Checklist ($p<0.01$) and on the PTSD Index ($p<0.05$) for both frequency and severity of symptoms were significantly reduced. Among individual items on the Checklist, significant improvements occurred in recurrent and intrusive recollections ($p<0.05$), recurrent dreams ($p<0.01$), and sleep disturbance ($p<0.01$). Among items on the Index, significant improvements in frequency and intensity were found in dreams about combat ($p<0.01$), flashbacks ($p<0.01$), and "becoming upset by reminders" ($p<0.05$). The mean score for Intrusive, but not Avoidant, items on the Impact of Events Scale was significantly reduced ($p<0.001$). Anxiety but not depression ratings decreased on several rating scales; SCL-90 Hostility scores declined significantly ($p<0.05$). Seven patients responded "moderately" to "very much" on the Clinical Global Impression Scale. The results are consistent with the "'kindling model" of PTSD.

NR119 **Wednesday, May 14, 9:00 a.m.**

PROLACTIN IS ELEVATED IN SAD

Frederick M. Jacobsen, M.D., Clinical Psychobio., NIMH, Bldg. 10, Rm 4S239, 9000 Rockville Pike, Bethesda, MD 20892; David A. Sack, M.D., Thomas A. Wehr, M.D., Susan Rogers, R.N., Steven A. James, M.D., Norman E. Rosenthal, M.D.

Summary:

Prolactin is a pituitary hormone which triggers some seasonal rhythms in lower mammals. Seasonal affective disorder (SAD) is a recurrent winter depressive syndrome resembling some seasonal changes of lower mammals. Ten depressed patients with SAD and ten age and sex-matched normal controls were given 200 mg 5-hydroxytryptophan (5HTP) or placebo orally at 9:00 a.m. in a two-day, double-blind, random-ordered, placebo-controlled crossover study. On both study days, following an overnight fast, an intravenous line was inserted at 8:30 a.m. and serum samples were drawn at 8:40 a.m. and at 60-minute intervals from 9 a.m. until 3 p.m. Samples were assayed for cortisol, prolactin, growth hormone and melatonin. Blood pressure and pulse were recorded every half hour during the study.

SAD patients had significantly higher prolactin levels compared to normal controls at all timepoints on the placebo condition ($p<0.01$). 5HTP significantly lowered the prolactin levels in SAD patients but had no effect in the controls ($p<0.01$). No differences in cortisol, growth hormone melatonin, blood pressure or pulse were noted between the groups. Changes in prolactin may trigger winter depressions in SAD patients just as they trigger seasonal changes in lower animals. The effect of 5HTP on prolactin secretion in SAD patients appears to differ from that observed in normals.

References:

[1]Duncan MJ, Goldman BD: Physiological doses of prolactin stimulate pelage pigmentation in Djungarian hamster. Am J Physiol 1985; 248:R664-667.

[2]Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Mueller PS, Newsome DA, Wehr TA: Seasonal affective disorder: a sescription of the syndrome and preliminary findings with light therapy. Arch Gen Psych 1984; 41:72-80.

NR120 **Wednesday, May 14, 9:15 a.m.**

BRIGHT LIGHT TREATMENT OF WINTER DEPRESSION

Robert L. Sack, M.D., Oregon Health Sciences University, Portland, OR 97201; Alfred J. Lewy, M.D., L. Stephen Miller, M.S., Tana M. Hoban, Ph.D.

Summary:

We treated eight patients with winter depression and seven euthymic control subjects with bright artificial light (2500 lux), comparing AM and PM exposure using a 4-week crossover design. The patients suffered annual recurrences of depression in the winter with associated symptoms of lethargy, irritability, weight gain and hypersomnia. The treatment protocol was as follows: Week 1 - adaptation to a standard sleep and ambient light exposure schedule (sleep: 10 PM to 6 AM; dim light: 6 PM to 8 AM); Week 2 - random assignment to either AM (6 AM to 8 AM) or PM (8 PM to 10 PM) bright light treatment; Week 3 - crossover to the alternative treatment; Week 4 - both AM and PM light treatment. At the end of each week the evening rise in plasma melatonin production was measured in dim light conditions. At baseline, patients were found to have initially delayed melatonin onsets compared to the controls. AM light advanced the melatonin onset (caused an earlier rise) and was associated with alleviation of depression in most patients. PM light delayed the onset (caused a later rise) and had little benefit for most patients. AM and PM light together seemed to be less effective than AM light alone in many patients. We conclude that the underlying pathophysiology of winter depression involves delayed circadian rhythms that can be corrected by light treatment based on an hypothesized phase response curve (AM light advances circadian rhythms and PM light delays them).

References:

[1]Lewy AJ, Kern HE, Rosenthal NE, Wehr TA. Bright artificial light treatment of a manic-depressive patient with a seasonal mood cycle. Am J Psychiatry *139*:1496-1498, 1982

[2]Lewy AJ, Sack RL, Singer CM. Assessment and treatment of chronobiologic disorders using plasma melatonin levels and bright light exposure: The clock-gate model and the phase response curve. Psychopharmacol Bull *20*:561-565, 1984.

NR121 **Wednesday, May 14, 9:30 a.m.**

LIGHT THERAPY FOR SAD: DOSING REGIMENS

Michael Terman, Ph.D., NYS/Psy. Inst., 722 W. 168th St., New York, NY 10032; Frederic M. Quitkin, M.D., Jiuan S. Terman, Ph.D.

Summary:

Patients suffering seasonal affective disorder are being given daily bright-light exposure regimens between November and March: 6:00-8:00 am and 6:00-8:00pm; 7:30-8:00 am and 6:00-6:30 pm; 6:00-8:00 am alone; and 6:00-8:00 pm alone. Pre-treatment Hamilton scores (including Rosenthal's addenda for vegetative symptoms) range from 14-39 (mean = 26.7). Successful responses, always obtained within one week, lower the mean to 4.5. In addition, patients assess the various regimens as fully satisfactory, partially effective, or unsatisfactory:

	OUTCOME (%)		
	SATISFACTORY	PARTIAL	FAILURE
2 - hr morning +evening	91	9	0
2 - hr morning alone	67	16	16
30 - min morning + evening	27	55	18
2 - hr evening alone	0	0	100

Some patients experience transient benefit when evening-alone exposures follow a withdrawal period without lights. All patients have relapsed upon withdrawal from an effective lighting regimen, within 1 to 10 days. The pattern of results suggests a dose-dependent effect of light exposures, with individual patients showing differing sensitivity. The morning exposure is widely perceived by our patients as providing both antidepressant and activating effects throughout the daytime hours, which decline in late afternoon or early evening unless supplementary evening light is given.

References:

[1]Rosenthal, N.E., Sack, D.A., Gillin, J.C., Lewy, A.J., Goodwin, F.K., Davenport, Y., Mueller, P.S., Newsome, D.S., & Wehr, T.S. (1984) Seasonal affective disorder: A description of the syndrome and preliminary findings with light therapy. *Archives of General Psychiatry* 41:72-80.

[2]Wirz-Justice, A., Bucheli, C., Graw, P., Kielholz, P., Fisch, H., & Woggon, B. (1986) Light treatment of seasonal affective disorder in Switzerland. *Acta Psychiatrica Scandinavica,* in press.

NR122 **Wednesday, May 14, 9:45 a.m.**

TRANYLCYPROMINE VERSUS IMIPRAMINE IN MANIC DEPRESSION

Jonathan M. Himmelhoch, M.D., School of Med. Western Psychiatric Inst., 3811 O'Hara St., Pittsburgh, PA 15213; Michael E. Thase, M.D., Alan G. Mallinger, M.D., Carilyn Z. Fuchs, Ph.D.

Summary:

Neither the efficacy of tricyclics (TCA) nor that of monoamine oxidase inhibitors (MAOI) has been systematically demonstrated in pure samples of bipolar depressives. Several lines of indirect evidence suggest that MAOI's, particularly tranylcypromine (TRP), may be both better tolerated and more effective than standard TCA's, such as imipramine (IMI). We present preliminary results of an ongoing, or randomized, double-blind trial comparing TRP (n= 13) with IMI (n= 13) in bipolar depression. Only patients (mean age 37.2 ± 10.2 years) who had experienced at least one previous major episode of elations and who were in the midst of anergic depression with motor retardation, hypersomnia and/or weight gain were admitted to the protocol. Patients were moderately to severly depressed after a two-week, drug-free wash-out, with a mean score of 31.3 ± 4.4 on an expanded 25-item version of the Hamilton (HRSD). Mean dose of TRP was 37 mg/day, as compared to 190 mg/day for IMI. Significantly fewer IMI patients completed six weeks of treatment (5/13 versus 12/13, p= .005). Further, TRP was associated with significantly greater change on both the HRSD (ΔHRSD; TRP= 20.2±8.9, IMI= 5.23±13.1, F= 8.92, p= .002) and Beck (BDI) (ΔBDI; TRP= 19.2±10.5, IMI= 9.6±13.1, F= 8.92, p= .006), without induction of hypomania. Response to TRP also was more rapid than to IMI, with the TRP versus IMI difference on the HRSD apparent after only one week of treatment (ΔHRSD: TRP= 8.6, IMI= 1.46, p= .001). Tranylcypromine seems clearly more effective than IMI in anergic bipolar depression. In fact, such findings suggest that IMI may be relatively ineffective for this subform of depressive illness.

References:

[1]Himmelhoch JM, Fuch CZ, Symons BJ: A double-blind study of tranylcypromine treatment of major anergic depression. J Nerv Ment Dis 170:628-634, 1982.

[2]Quitkin FM, McGrath P, Liebowitz MR, et al: Monoamine oxidase inhibitors in bipolar endogenous depressives. J Chin Psychopharm 1:70-74, 1981.

NR123 **Wednesday, May 14, 10:00 a.m.**

BEAM IN MELANCHOLIA: VISUAL EVOKED POTENTIALS

Russel G. Vasile, M.D., NE Deaconess Hospital, Harvard Medical School, 110 Francis Street, Boston MA 02215; David M. Bear, M.D., Frank H. Duffy, M.D., Kerry Bloomingdale, M.D., Leslie K. Serchuck, M.A., Joseph J. Schildkraut, M.D.

Summary:

Brain electrical activity mapping (BEAM) is a computer-based technique for the topographic display and analysis of scalp-derived neurophysiologic data. BEAM, which included spectral topographic EEG, topographic flash visual evoked potential (VEP) and click auditory evoked potential (AEP), as well as standard EEG, was utilized in a preliminary study of 10 elderly (mean age ± SEM = 73.1 ± 1.9 yr) hospitalized patients, free of significant medical disease, who were admitted with *DSM-III* diagnoses of major depression with melancholia. Neurophysiologic abnormalities were detected by comparison to age-matched normative control data.

The major finding was a striking deviation from normative values of the late epochs of the flash VEP. These aberrant responses could be attributed to combinations of latency delay and amplitude augmentation in the posterior quadrant of every patient (10 of 10). Responses to single flashes were so dramatic they could often be seen in the raw EEG tracing. Less frequent and dramatic abnormalities were seen in the AEP (8 of 10), spectral EEG (7 of 10) and standard EEG (5 of 10). Flash VEP abnormalities were frequently asymmetrical (6 of 10), always coinciding with similarly lateralized AEP, spectral or EEG abnormalities. No hemisphere was more frequently involved (3 left, 3 right, 4 symmetrical). Further data from additional depressed patients are currently being analyzed and will be presented.

In summary, our findings suggest that the unusually consistent abnormalities in flash VEP observed in this study may represent a central neurophysiologic concomitant of major depression with melancholia. The possibility will be discussed that such abnormalities in flash VEP may be a manifestation of central catecholaminergic dysregulation.

References:

[1]Duffy FH, Burchfiel JL, Lombroso CT. Brain Electrical Activity Mapping (BEAM): A Method for Extending the Clinical Utility of EEG and Evoked Potential Data. *Annals of Neurology* 5:309-321, 1979.

[2]Onofrj N. Bodis-Wollner I. Dopaminergic Deficiency Causes Delayed Visual Evoked Potentials in Rats. *Annals of Neurology* 11:484-490, 1982.

NR124 **Wednesday, May 14, 10:15 a.m.**

D-TYPE SCORES AND RESPONSES TO ANTIDEPRESSANTS

Joseph J. Schildkraut, M.D., Mass. Mental Health Ctr., 74 Fenwood Rd., Boston, MA 02115; Alan F. Schatzberg, M.D. John J. Mooney, M.D., Benjamin Gerson, M.D., Jacqueline A. Samson, Ph.D., Jonathan O. Cole, M.D.

Summary:

The D-type equation is an empirically derived multivariate discriminant function equation based on urinary catecholamines and metabolites, that was found to provide a more precise discrimination of patients with bipolar depressive disorders than did urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) alone. In a validation sample of 144 depressed patients, whose data had not been used to derive this equation, the D-type score (using a criterion of D-type score <0.50) had a sensitivity of .85, and a specificity of .84, in identifying patients with clinically diagnosed bipolar/schizoaffective depressions. A wide range of D-type scores is seen in patients with clinically diagnosed unipolar endogenous depressions (i.e., depressed patients with no prior history of mania), and D-type scores are more effective than MHPG levels in predicting differential responses to antidepressant drugs in these patients.

In depressed patients treated with imipramine, mean drug-free pretreatment D-type scores were significantly lower ($p<.005$) in responders (0.501 ± 0.062) than in nonresponders (0.851 ± 0.066), and favorable antidepressant responses to imipramine occurred in 7 of 7 patients with pretreatment D-type scores <0.50, but in only 2 of 11 patients with D-type scores > 0.50— (Fisher Exact P= .005). Conversely, in depressed patients treated with alprazolam, mean drug-free pretreatment D-type scores were significantly higher ($p<.001$) in responders (1.169 ± 0.049) than in nonresponders (0.778 ± 0.100), and favorable antidepressant responses occurred in 9 of 10 depressed patients with D-type scores >1.0, but in 0 of 5 patients with D-type scores <1.0— (Fisher Exact P= .005). The pathophysiological implications of these findings will be discussed.

References:

[1]Schildkraut, J.J., Orsulak, P.J., Schatzberg, A.F., Gudeman, J.E., Cole, J.O., Rohde, W.A., LaBrie, R.A. Toward a Biochemical Classification of Depressive Disorders I: Differences in Urinary Excretion of MHPG and Other Catecholamine Metabolites in Clinically Defined Subtypes of Depressons. *Arch. Gen. Psychiat.* 35: 1427-1433, 1978.

[2]Schildkraut, J.J., Orsulak, P.J., LaBrie, R.A., Schatzberg, A.F., Gudeman, J.E., Cole, J.O. and Rohde, W.A. Toward a Biochemical Classification of Depressive Disorders II: Application of Multivariate Discriminant Function Analysis to Data on Urinary Catecholamines and Metabolites. *Arch. Gen. Psychiat.* 35: 1436-1439, 1978.

NR125 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

SLEEP AND CORTISOL IN ANERGIC BIPOLAR DEPRESSION

Michael E. Thase, M.D., Dept. of Psychiatry, Univ. Pittsburgh Med. Sch., 3811 O'Hara St., Pittsburgh, PA 15213; Jonathan M. Himmelhoch, M.D., Alan G. Mallinger, M.D., David B. Jarrett, M.D.,, David J. Kupfer, M.D.

Summary:

Clinical, genetic, and treatment response studies indicate that bipolar disorder is a distinct form of affective illness. It is not clear, however, if bipolar depressions also are characterized by distinct alterations in biological processes, such as EEG sleep or cortisol regulation. We report here results of 2-night EEG sleep studies (n= 26) and baseline 1600 hr plasma cortisol levels and 1 mg DSTs (n= 23) in outpatient bipolar depressives (mean age = 37.2 years). Overall, the sample was characterized by anergia and "atypical" features such as hypersomnia, hyperphagia, and/or weight gain. Sleep studies revealed few of the EEG changes commonly associated with endogenous depression: bipolar patients did not differ from age-matched controls on measures of sleep continuity, delta sleep, REM density, or REM latency, although they did show increased minutes of REM ($p<.05$) and stage 2 sleep ($p<.03$) and increased REM activity ($p<.03$). These patients also did not show striking abnormalities of cortisol regulation: Only 26% (6/23) had baseline 1600 hr cortisol values >10 mcg/dl and only 13% (3/23) had post-DEX 1600 hr cortisol values ≥ mcg/dl. Overall results suggest that pretreatment sleep and cortisol profiles in anergic bipolar depression are dissimilar from those in unipolar depression. Follow-up sleep (n= 5) and cortisol (n= 12) studies were repeated after 6-10 weeks of treatment in patients who experienced at least a partial response to either imipramine (n= 5) or tranylcypromine (n= 10). Both drugs were associated with significant suppression of REM activity ($p<.03$) and REM time ($p<.001$), prolongation of REM latency ($p<.001$), and decreased sleep efficiency ($p<.06$). Such treatment decreased baseline cortisol levels by an average of 5 mcg/dl ($p<.01$) in responders and normalized the DST in 2 of the 3 nonsuppressors.

NR126 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

NUCLEAR MAGNETIC RESONANCE IN BIPOLAR DEPRESSION

Arnold Winston, M.D., Beth Israel Med. Center, First Ave. at 16th St., New York, NY 10003; Jesse Rosenthal, M.D., Larry Minkoff, Ph.D., Abbey Strauss, M.D.

Summary:

The use of nuclear magnetic resonance as a clinical and research tool in psychiatry is becoming a practical reality.

Using nuclear magnetic resonance (NMR), Rangel-Guerra, et al (AJNR 4:229-231, 1983) found an elevated proton T_1 relaxation time in the temporal and frontal lobes of bipolar depressed patients which returned to normal after lithium therapy. Based upon this finding, this study tested the hypothesis that the more readily available red blood cells of bipolar depressed patients will also have elevated proton T_{10601} relaxation times. Red cells have already been shown to have clear physiological alteration in some depressed patients (Ostrow, et al, AM J Psych 135:1070, 1978). The effect of lithium on red cell proton T_{10601} relaxation time was also examined to determine if a group of lithium responsive bipolar depressed patients can be identified.

Results in six bipolar depressed patients revealed significantly elevated proton T_1 relaxation times, as compared to normal controls. After treatment with lithium there was a significant decrease in the proton T_1 relaxation time, and five out of six patients had a marked clinical improvement.

Additionally, two non-bipolar depressed patients did not have elevated proton T_1 relaxation times. Two other bipolar depressed patients not included in the original six had elevated proton T_1 relaxation times, but upon switching to a manic phase their proton T_1 relaxation times decreased to normal levels.

These preliminary findings suggest the possibility of increased intra-erythrocyte hydration which is being measured by NMR proton T_1 relaxation time. This technique may prove to be useful investigative tool in affective disorder research.

NR127 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

A HIGH-RISK STUDY OF PRIMARY AFFECTIVE DISORDER

John I. Nurnberger, Jr., M.D., NIMH, DIRP, Bldg. 10, Rm 3N218, 9000 Rockville Pike, Bethesda, MD 20892; Joel Hamovit, M.S.W., Euthymia Hibbs, Ph.D., Juliet Guroff, B.A., Elliot Gershon, M.D.

Summary:

Family studies of major affective disorder show that relatives of bipolar patients have about a threefold greater risk of unipolar (UP) or bipolar (BP) illness in comparison to relatives of controls. Data from our recent NIMH family study showed a mean age of onset of 27 for BP and 30 for UP. To be able to predict which young people are likely to get ill would provide valuable information clinically and etiologically. Retrospective studies of patients already ill are much less valuable from this point of view than prospective studies of persons at risk. We have begun a long-term follow-up study of 15-25 year olds with a manic-depressive parent (current N= 53) and age-matched controls (current N= 35). Persons with major psychiatric disorders at the beginning of the study were not included. Subjects have been interviewed at yearly intervals with the SADS-L (Spitzer and Endicott, 1975). In addition each subject has filled out an SCL-90R (Derogatis, 1975), a General Behavior Inventory (GBI) (Depue et al, 1981), and a Sensation-Seeking Scale (SSS) (Zuckerman and Neeb, 1979). Follow-up interviews during the first two years of study revealed five new cases of major affective disorder (1 BP, 4 UP), all among the index group. In addition six index subjects and two controls developed minor psychiatric disorders. An analysis of variance on the interview data was done using risk status (as defined by parental diagnostic category) as the independent variable and including age, sex, and presence or absence of minor diagnoses as covariates. Risk status was found to be related to the SSS total score, the experience-seeking and disinhibition subscales of the SSS, the hypomania subscale of the GBI, and the psychoticism subscale of the SCL-90. Further follow up will be helpful in establishing whether any of these instruments are in fact predictive.

NR128 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

BIPOLAR II FAMILY PATTERNS: A DIFFICULT CONDITION

Janice A. Egeland, Ph.D., Miami Psychiatry Dept., North Office, 49 Sylvania Rd., Hershey, PA 17033; Jean Endicott, Ph.D.

Summary:

Bipolar II disorder is difficult from many considerations: diagnostic criteria, reliability, severity, treatment and the issue of whether or not it belongs with bipolar I or recurrent unipolar depression. Some insights can be gained by examining a sample of BP II cases according to familial illness patterns.

The Amish Study (1976-1985) has ascertained a sample of 32 multigenerational pedigrees informative for bipolar affective disorder. These are high density families selected for genetic linkage study and consist of 372 first-degree and 557 second-degree relatives. Direct SADS-L interviews were done and medical records abstracted as two sources of information for diagnosis. A panel of four psychiatrists, plus Dr. Endicott, diagnosed cases blind to biologic relationships and diagnostic status of the proband.

This paper reports on the familial pattern for pedigrees with BP II cases and how those pedigrees differ from BP I pedigrees that have no bipolar II cases. Data will be given on differences in onset ages, sex, index features, morbid risks, comorbidity and diagnostic profiles. It will be shown that the BP II families are more ill or mixed with other medical and psychiatric conditions and have higher morbid risks, comorbidity and treatment problems. For the pedigrees with BP II patients, over 30% of all relatives had mental disorders. This compared to 18% of the relatives in pedigrees without any BP II disorder. Also, a wider spectrum of affective illnesses were represented, including much higher rates of depression, personality disorders and chronic hypomania. The BP II patients were difficult cases in difficult families.

NR129 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

RECONCILING BIPOLAR DISORDER WITH MENDEL'S LAWS

Susan E. Folstein, M.D., Johns Hopkins Hospital, Osler 320, Baltimore, MD 21205; J. Raymond DePaulo, Jr., M.D., Elsa Correa, M.D., Jeanne O. Gayle

Summary:

A consecutively ascertained case series of 26 bipolar probands was studied to address the following questions: 1) How often does clinically severe bipolar disorder show familial aggregation; and 2) is familial aggretaion in such unselected families compatible with dominant inheritance. All probands and many family members were interviewed and diagnosed according to RDC criteria. We also used Andreason's RDC-family history interview and medical records. Diagnoses on uninterviewed relatives were based on the method of Orvaschal and Thompson.

Twenty of 26 probands had at least one definitely affected bipolar or unipolar relative, 3 additional probands had a first-degree relative with probable affective disorder, and one further proband had a first-degree relative with an "affective equivalent." The proportion of affected first degree relatives approached 50% as inclusion criteria were broadened from bipolar and unipolar disorder to include clinical entities that have been suggested as "affective equivalents." Second-degree relatives followed a similar pattern.

The high number of probands (24/26) with affected relatives and the proportion of affected relatives suggest that dominant inheritance will be common in bipolar disorder. The failure of family patterns to closely follow Mendel's laws may be due to incomplete penetrance, age dependent penetrance, and variable expressivity of the phenotype. The variation in family transmission patterns (particularly presence or absence of male-to-male transmission) suggests multiple independent loci. We will discuss the resolvability of these hypotheses using a RFLP linkage map.

NR130 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

DIVORCE, DEPRESSION AND IMMUNE FUNCTION

Janice Kiecolt-Glasser, Ph.D., Dept. of Psychiatry, Ohio State Univ., 473 W. 12th Ave., Columbus, OH 43210; Laura Fisher, B.S., Paula Ogrocki, B.S., Julie Stout, B.S., Carl Speicher, M.D., Ronald Glaser, Ph.D.

Summary:

Divorce appears to be one of the most stressful life changes. As a group, separated and divorced individuals have higher rates of morbidity and mortality from a variety of causes (including some infectious diseases such as pneumonia) than widowed, single, or married adults. We wished to test hypotheses concerning continued attachment to the ex-spouse as a risk factor for depression and health, and to examine possible stress-associated immunological changes that might mediate the adverse health effects associated with divorce. Therefore, we collected blood samples and questionnaire data from a community sample of 40 recently divorced women.

Those women who scored higher on a scale measuring attachment to their ex-spouse were significantly more depressed and had poorer immune function (blastogenic responsiveness to two mitogens and higher antibody titlers to the latent Epstein-Barr virus (EBV) capsid antigen, reflecting poorer cellular immune system control of herpesvirus latency) than low scoring women. In addition, those women who were less attached to their ex-spouse were more likely to have been the initiator of the separation and were more likely to have subsequently formed a satisfying relationship with another man.

NR131 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

SOFT NEUROLOGICAL SIGNS AT AGE 7 AND DEPRESSION AT AGE 20

Nigel M. Bark, M.B., Nathan Kline Inst., Orangeburg, NY 109623; Mark Davies, M.P.H.

Summary:

A sample of 114 black, English-speaking males, half with neurological soft signs at age 7 and half matched controls without soft signs, from the Columbia Presbyterian sample of the Collaborative Perinatal Project were followed up at age 19-22. Of these, 103 were located, 91 contacted and 75 completed a 20-40 minute interview (65 by telephone) about symptoms of depression and conduct disorder, with 40 questions from the Psychiatric Epidemiology Research Instrument (PERI) as well as medical and family history questions.

No differences were found between the soft sign group and no soft sign group on any demographic or family variables nor on any questions about conduct disorder.

Depression, suicidal thoughts, and the sadness and psychophysiological subscales of the PERI were significantly associated with soft signs. These and the demoralization scale of the PERI were strongly associated with the number of soft signs and particularly with involuntary movement at age 7. Guilt and suicidal gestures were strongly associated with involuntary movements. Only computed major depression and sadness were significantly associated with incoordination. (No clinical features were significantly associated with sensory signs but there was a highly significant association between the number of times suspended from school and sensory signs.)

A diagnosis of anxiety, when depression was an exclusion criterion, showed no significant association with any soft signs (but a "trend" with sensory signs).

This study and others suggest that the associations found are not causal nor are they mediated by intelligence or birth factors. A common genetic factor is postulated.

NR132 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

THE NATURE OF COGNITIVE CONSTRICTION IN DEPRESSION

Kenneth R. Silk, M.D., Ann Arbor VAMC, 2215 Fuller Rd., Ann Arbor, MI 48105; Karen Saakvitne, M.A., Naomi Lohr, Ph.D., Kevin Kerber, M.D., Drew Westen, Ph.D., Margaret C. Buttenheim, Ph.D.,

Summary:

Studies of psychomotor retardation have emphasized the motor aspects while paying little attention to "psycho-" or cognitive aspects of the phenomenon. We examined Wechsler Adult Intelligence Scale-Revised (WAIS-R) results from 17 prospectively identified (RDC) inpatients with Major Depressive Disorder. We explored quality and consistency of perception and cognition across different tasks and stimuli. Well-diagnosed borderlines and carefully selected "normals"were controls. Profile and discriminate function analyses were used to identify discriminating variables. ANOVA (or ANCOVA) were used to evaluate group differences.

Depressives had significantly lower Verbal and Full Scale IQ scores despite equivalent education levels and Vocabulary Subtest scores, often the best predictor of intellectual capacity. Depressives did more poorly on untimed as well as timed tasks, and their performance suggested the effects of low self-esteem, increased helplessness, self-doubt and self-preoccupation on cognitive performance. For example, depressives (and borderlines) made significantly more early (easier) errors on the Comprehension Subtest when compared to normals. Depressives were more likely to give a correct answer if queried after saying "I don't know." Further they were more likely to give up and refuse to attempt a question whether or not they were urged to respond.

The effect of depression and psychomotor retardation on cognition does not appear in a distinct pattern as previous psychological literature implies, but it reveals itself through pervasive slowing down of and lowering of energy toward completion of intellectual tasks. Further clarification of this cognitive constriction can modify approaches to gathering information from depressed patients, either during structured interviews or psychotherapy sessions.

NR133 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

RESERPINE AUGMENTATION IN REFRACTORY MELANCHOLIA

Lawrence H. Price, M.D., Conn. Mental Health Ctr., Yale Univ. Med. School, 34 Park St., New Haven, CT 06508; Dennis S. Charney, M.D., George R. Heninger, M.D.

Summary:

Early studies of reserpine failed to document antidepressant effects, and some observations suggested that it could cause depression. However, Poldinger reported dramatic improvement in depressed patients using large doses of I.M. reserpine after nonresponse to imipramine. Recent studies of lithium augmentation in refractory depression prompted us to investigate the effects of reserpine augmentation of desipramine (DMI). *Methods:* Eight patients with *DSM-III* melancholic major depression were treated with DMI $\geq$ 2.5 mg/kg/day for $\geq$ 4 weeks with DMI plasma levels $\geq$ 125 ng/ml. After giving informed consent, patients received reserpine 5 mg IM b.i.d. over 2 days, in 7 cases as a placebo-controlled, double-blind trial. The Hamilton Depression Scale and the Short Clinical Rating Scale were completed before and after reserpine, and plasma was obtained for MHPG. Five patients underwent lumbar puncutre to assess CSF changes in MHPG, HVA, and 5-HIAA. *Results:* One patient had a dramatic resolution of depressive and psychotic symptoms within 48 hours of her last reserpine injection, but relapsed after 2 weeks. Two patients had transient hypomanic symptoms lasting <48 hours, followed by return to depressive states. The remaining patients failed to show substantial mood improvement. The relationship of these clinical effects to plasma and CSF measures will be presented. *Conclusion:* This pilot study suggests that reserpine augmentation lacks sufficient efficacy to compete with available treatments in the routine management of refractory depression. However, selected patients may benefit from this approach.

NR134 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

WHITE LIGHT IN SEASONAL DEPRESSIVES AND CONTROLS

Andreas C. Schmid, M.D., Psychiatric University, Clinic Basel, Switzerland; Anna Wirz-Justice, Ph.D., Peter Graw, Ph.D., Kurt Kraeuchi, M.S., Hans-Ueli Fisch, M.D., Claus Budderberg, M.D.

Summary:

Bright white light (2500 lux, Vitalite®, WL) effectively treats seasonal affective disorder (SAD). We replicated this finding in a Swiss-German population with 2 hrs WL am & pm. Controls improved mood after 1, but not ½ hr WL am & pm: morning tiredness was less that in SAD, who remained "tired in the morning" also in summer. This winter we attempted a WL dose-response study. SAD patients selected with depression scores >15 (HRS) were treated with WL for 1 week between 6-8 am. As found in the previous year, WL had a rapid antidepressant effect (in 32/41 trials as of 2.1.86). The response rate for 2 and 1 hr was higher than for ½ hr. Eating patterns of SADs and controls were followed throughout the year to provide data as to seasonal variations in the frequency of carbohydrate and protein intake.

NR135 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

DEPRESSION: EEG ABNORMALITIES AND CLINICAL OUTCOME

Alan G. Mallinger, M.D., Western Psychiatric Inst., 3811 O'Hara St., Pittsburgh, PA 15213; David J. Kupfer, M.D., Jonathan M. Himmelhoch, M.D., Ellen Frank, Ph.D., Victoria J. Grochocinski, Ph.D.

Summary:

In an effort to identify biological predictors of atypical responsiveness to treatment of unipolar depression, we examined pretreatment EEG findings of 117 outpatients, who were subsequently treated with imipramine (IMI) and interpersonal psychotherapy (PT). EEGs (drug-free) were diffusely abnormal (DA) in 19 subjects, and showed focal abnormalities or asymmetry in eight others. Depressive symptoms were rated using the Hamilton scale (HRS-D). Clinical outcome was assessed in two ways. First, an algorithm based on HRS-D scores was used to classify the initial response and its time course as normal (typical), slow, partial, or termination. Second, for subjects whose mood improved and remained stable for at least three consecutive sessions, continuation treatment was then initiated, and the means and standard deviations of HRS-D scores during such treatment were computed. Among subjects having DA EEGs, there was a greater frequency of slow responders and a lower frequency of normal responders, as compared to subjects having normal EEGs (Fisher's exact test, $p<0.025$). During continuation treatment, mean HRS-D scores were higher for slow responders than for normal responders, regardless of EEG status (ANOVA, $F= 7.56$, $p<0.001$). However, slow responders having DA EEGs had greater variability of depressive symptoms (and therefore higher standard deviation values for the HRS-D scores) as compared to the normal responder group (Kruskal-Wallis test, $p<0.015$). Among the remaining slow responders having normal EEGs, the standard deviation values were bimodal in distribution, but did not differ significantly from the normal responder group. Our findings suggest that subjects having DA EEGs prior to treatment with IMI and IPT may have an atypical clinical course characterized by slower initial response and greater lability of mood following apparent stabilization.

NR136 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

BRAIN WATER CONTENT IN DEPRESSION: AN MRI STUDY

Thomas A. Kent, M.D., Dept. of Neurology and Psychiatry, UTMB, Galveston, TX 77550; Eugenio C. Amparo, M.D., Raleigh F. Johnson, Jr., Ph.D., Adel Wassef, M.D., Robert M. Rose, M.D.

Summary:

One effect of adrenergic agents, such as tricyclic antidepressants (TCA), may be to alter the transport of water, and possibly other compounds between brain compartments and through the blood:brain barrier. These effects on water transport may be due to adrenergic mediated alterations in neuronal activity. Magnetic resonance imaging (MRI) is a method by which free water content can be determined noninvasively. Because of the effects of adrenergic agents on water transport, we were interested in the effect of antidepressant treatment (both TCA and ECT) on water content in the thalamus— a densely adrenergic innervated structure. Ten depressives (RDC), age 30-60, were studied by MRI after drug washout and 3 weeks after treatment was begun. Baseline and post-treatment Hamilton depression and anxiety scales were administered.

MRI was performed in a commercially available 0.6 Tesla imager (Technicare). T1-weighted (TR= 500, TE= 40,80) and T2-weighted (TR= 2000, TE= 40,80) spin echo sequences were obtained in the transaxial and coronal planes. An additional pulse sequence was used in some of the patients to obtain a single transaxial slice through the thalami that would allow T1 determinations (corresponding to water content) of any area by a region of interest cursor. External standards were simultaneously imaged. In the patients examined thus far, an increase in water content was seen within the thalamus in the medial and pulvinar regions, and a hemisphere asymmetry (R>L) was observed. This hemisphere asymmetry shifted sides after treatment (X change = 22 msec) which corresponds to known norepinephrine asymmetries within the human thalamus. Correlation with treatment response and analysis of additional patients are underway. These data indicate the ability of MRI to assess change in local water content which may correlate with neuronal density, activity, or integrity of adrenergic innervation.

NR137 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

CBF IMAGING IN PSYCHIATRY WITH T1-201 DDC AND SPECT

Barbara H. Byse, M.D., Dept. of Radiology, New England Deaconess, 185 Pilgrim Rd., Boston, MA 02215; Thomas C. Hill, M.D., J.F. de Bruine, M.D., Russell Vasile, M.D., Eric A. van Royen, M.D.

Summary:

Cerebral blood flow (CBF) is closely linked to neuronal metabolism, and initial studies have demonstrated that single photon emission computed tomography (SPECT) with Tallium-201 Diethyldithiocarbamate (T1-201 DDC) is an effective method for studying CBF. This method is examined with a pilot group of psychiatric patients as an alternative to the Xenon-133 CBF techniques.

Patients with major depression (N= 3), bipolar disorder (hypomanic, N= 3), schizophrenia (N= 1), Alzheimer's dementia (N= 1), and other psychiatric disorders (N= 4) were imaged, at the level of basal ganglia, with SPECT two minutes after the IV administration of 4 mCi of T1-201 DDC.

No difference in L/R hemispheric symmetry (L/R= 1.03±.02) was found. The ratio of non-dominant to dominant frontal cortex was significantly increased ($p<.01$) in the two symptomatic depressed patients, compared to normals or to the bipolar group. The other depressed patient, who was treated and was no longer symptomatic, did not show this asymmetry. The frontal/whole brain ratio (normals: R= 1.09±.04, L= 1.13±.02) was decreased in one actively delusional bipolar patient (R= 0.91, L= 1.05) and marketly increased in one actively delusional bipolar patient (R= 1.41, L= 1.39). Alzheimer's dementia showed biparietal decreased blood flow. These data indicate that psychiatric patients have measurable cerebral blood flow abnormalities, which may have diagnostic, prognostic or therapeutic utility, especially in differentiating some cases of depression from dementia.

Technical advantages of T1-201 DDC include 99% first pass extraction, stable count rates after 1½ minutes, and no redistribution after four hours. Acting as a chemical microsphere, T1-201 with SPECT demonstrates real CBF with higher resolution than Xe-133 functional washout images.

NR138 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

STEROID-CATECHOLAMINE INTERACTIONS IN DEPRESSION

Owen M. Wolkowitz, M.D., NIH Bldg. 10, Room 4N-214, 9000 Rockville Pike, Bethesda, MD 20892; Allen R. Doran, M.D., Alan Breier, M.D., David Jimerson, M.D., Rodrigo Labarca, M.D., Steven M. Paul, M.D., David Pickar, M.D.

Summary:

Hypercortisolemia is a commonly reported biological abnormality in major depression, although the pathophysiologic significance of this is unknown. Since evaluations in circulating corticosteriods may, in themselves, alter central neurotransmission, we administered dexamethasone to depressed patients and compared changes in plasma levels of homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) to those seen in normal controls. In normal controls, dexamethasone (1 mg p.o. at 11 pm) significantly increased plasma HVA ($p<0.01$) without significantly altering plasma MHPG. The depressed patients showed a significantly different response with decreased postdexamethasone plasma HVA ($p<0.05$) and increased plasma MHPG ($p<0l.05$) compared to controls. These abnormalities were most pronounced in the psychotically depressed patients. In addition, the magnitude of the increase in plasma MHPG in patients was directly related to the severity of the illness, measured by Hamilton depression ratings ($r= 0.573$, $p= 0.05$), and to cortisol nonsuppression ($r= 0.68$, $p= 0.02$). These results suggest abnormal corticosteroid-catecholamine interactions in depression and, in particular, in psychotic depression. These results may relate to findings of catecholaminergic abnormalities in some depressed patients.

NR139 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

AGE-RELATED IMMUNE CHANGES IN DEPRESSION

Steven J. Schleifer, M.D., Mt., Sinai School of Med. 1 Gustave L. Levy Place, New York, NY 10029; Steven E. Keller, Ph.D., Jacob Cohen, Ph.D., Marvin Stein, M.D.

Summary:

In an earlier study, we found decreased mitogen-induced lymphocyte stimulation in drug-free hospitalized patients with major depressive disorder (MDD) but not in ambulatory MDD patients who were younger and less severely depressed. To investigate the mechanisms of altered lymphocyte function as well as the role of age, sex, and severity of depression, a new sample of 61 patients with unipolar MDD was studied. Subjects were in good health and had not received antidepressant treatment for 3 months. Patient-control pairs were age and sex matched and studied on the same day. Severity of depression was assessed by the Hamilton Depression Scale.

Hierarchical regressions analyzing the effect of age, sex, severity, and hospitalization status on lymphocyte responses to PHA, ConA, and PWM and on T lymphocyte subsets were performed on patient and control data. Differences in mitogen response between patients and controls were found to be related to the subject's age and to severity of depression but not to sex or hospitalization. Older patients had significantly lower mitogen responses than controls, while responses of younger patients were higher than those of their controls. The pattern of age-related differences between patients and controls in T-helper cell numbers was comparable to that found for mitogen responses, suggesting that effects on the T-helper population may account for age-related functional lymphocyte changes. T-suppressor cells did not differ between patients and controls. Age-related differences were also found in cortisol levels, suggesting that adrenal— T-helper interactions may be involved. These findings may help elucidate underlying biologic processes in depression.

NR140 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

HEALTH OUTCOMES, IMMUNE STATUS, AND DEPRESSION

Marcia L. Daniels, M.D., Dept. of Psychiatry and Biobehavioral Science/UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; Michael Irwin, M.D., Herbert Weiner, M.D.

Summary:

Alterations in the immune response have been noted in both bereavement and depression. The relationship, however, of such alterations to subsequent individual health outcomes is not well defined. In this study, we have prospectively evaluated the health outcomes of 38 women and assessed the relationship of these outcomes to prior immune and mood states.

At baseline, 16 women were anticipating the loss of their spouse, 12 had recently experienced bereavement (within the past six months), and 11 were not bereaved. Data was obtained on sociodemographics, alcohol and drug use, illness occurrences, life events, and social support systems. The presence or absence of depression was determined using Research Diagnostic Criteria. The Hamilton Depression Rating Scale was used to measure affective severity. Immune parameters including natural killer cell activity, white blood cell counts, and T-cell subsets were assessed.

Immune studies separately reported document that natural killer cell activity was inversely correlated with both life events and severity of depression at baseline. The occurrence of bereavement per se did not predict immune status.

At follow-up one year later, no significant differences were found in the health outcomes of these women despite the baseline significant differences in immune status, mood states, and life events. Although a relationship among immune status, life events, and depression was initially demonstrated, the long-term clinical significance of this relationship remains unknown.

NR141 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

OLFACTION IN DEPRESSION AND RECOVERY: A NEW MARKER

Stephen C. Suffin, M.D., Dept. of Psychiatry, Sepulveda VAMC, 16111 Plummer St., Sepulveda, CA 91343; Michael Gitlin, M.D.

Summary:

Papez's hypothesis of a major involvement of the rhinencephalon in emotional behavior, together with the primary olfactory representation in this structure, were the basis for a preliminary study of quantitative olfactory threshold determinations in a population of depressed individuals. Twelve consecutive applicants to an ongoing study of psychopharmacologic treatment of depressed individuals were studied. All had major depressive disorder by *DSM III* criteria; with Hamilton (Ham) scores of 15 or greater. All patients were examined and characterized by laboratory tests and ECG to confirm the clinical impression of no major medical disorders. Prior to treatment, olfactory detection thresholds (ODT) for pyridine in oil employing Amoore's method were obtained. Imipramine in doses of 100 to 300 mg/day (mean= 183 mg) day was given which achieved plasma levels of 43 to 356 ng/ml (mean= 175 mg/ml). After four weeks of treatment the ODT and Hamiltons scales were repeated. Seven subjects were responsive to treatment (mean Ham= 3) and 5 were not (mean Ham= 20). The ODT for the responders improved 2.2 log steps while the ODT for the non-responders changed 0.4 log steps. ODT may be a non-invasive, clinically available state marker for depressive illness. The potential biologic significance of our results will be discussed.

NR142 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

OLFACTORY RECOGNITION AND MOOD IN MAJOR DEPRESSION

Paul J. Moberg, M.A., Johns Hopkins Hospital, 600 N. Wolfe St., Meyer 279, Baltimore, MD 21205; Godfrey D. Pearlson, M.D., Lynn J. Speedie, Ph.D., John R. Lipsey, M.D., J. Raymond DePaulo, M.D.

Summary:

Performance on 3 similarly structured standardized tasks of olfactory, verbal and visual recognition memory was compared to visual and analog mood ratings in 30 hospitalized inpatients with *DSM III* major depressive episode and 110 group matched normal controls. Depressed patients performed worse than controls on all 3 tasks, plus Mini-Mental State Scores (p values all $<.001$ by t-tests). Of the 3 recognition paradigms, only olfactory task performance significantly correlated with admission mood scores in the depressed group ($r= .43$, $p<.01$). As patients' moods normalized with treatment, so did scores on the olfactory battery, with change scores on both measures being significantly correlated ($r= .48$, $p<.01$). Verbal and visual recognition scores also improved, but yielded no similar associations with mood. Links between olfaction and the limbic system in depression are hypothesized.

NR143 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

PSYCHOBIOLOGY OF SLEEP ONSET REM PERIODS

James E. Shipley, M.D., Dept. of Psychiatry, U. of Mich., 1405 E. Ann St. Box 011, Ann Arbor, MI 48109; Anand Kumar, M.D., Alan Eiser, Ph.D., Micahel Feinberg, M.D., Pamela Flegel, B.S., John F. Greden, M.D.

Summary:

To further assess the frequency of occurrence of sleep onset REM periods (SOREM) in major depressive disorder (MDD) and to characterize the psychobiologic profile of such patients, we studied 62 in patients with MDD, all having HRS≥ 15. EEG sleep was recorded after a two-week drug washout, and using the shorter REM latency (RL) of the two recording nights, we stratified patients into three subgroups: SOREM-10 (RL<10 min), SOREM-20 (RL≥ 10 min but <20 min), and non-SOREM (RL≥ 20 min). A DST was completed at baseline, but not within 48 hours of the sleep recordings.

Results showed that the distribution of RL appeared bimodal, with 26 cases (42%) having at least one night with SOREM-10. Only six patients (9.7%) fell in the SOREM-20 group. SOREM-10 patients: a) were older at the time of study and at the time of their first depressive episode; b) had a longer hospital stay; and c) had a higher frequency of a family history of suicide (all $p<.03$). After controlling for age, comparison of EEG sleep variables showed that the groups differed only in that SOREM-10 had decreased stage 2 ($p<.01$) and increased REM activity/total sleep time ("REM intensity", $p<.05$). DST results showed SOREM-10 to have higher post-dex cortisol levels and a greater likelihood of nonsuppression (both $p<.01$), independent of age. Across all patients there was a negative correlation between RL and (log) post-dex cortisol ($r= -0.38, p<.01$).

To summarize, SOREM-10 occurred frequently in this inpatient MDD sample and was associated with certain clinical and neuroendocrine features. Other EEG sleep measures, however, did not distinguish SOREM-10 very well from non-SOREM. The impact of age on SOREM warrants further investigation.

NR144 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

THE EFFECT OF DMI AND 2-OH DMI ON NK CELL ACTIVITY

Andrew H. Miller, M.D., Klau-1 Psychiatric OPD, Montefiore Med. Ctr. 111 E. 210 St., Bronx, NY 10467; Gregory M. Asnis, M.D., Herman van Praag, M.D., Allen J. Norin, Ph.D.

Summary:

Mounting evidence suggests that the central nervous system and immune system are extensively interconnected. Of interest is that neurons and lymphocytes share surface receptors for hormones, peptides and neurotransmitters. Since psychotropic agents are active on nerve cell receptors, crossreactivity of these agents with similar lymphocyte receptors may result in specific immunologic effects. To explore this notion, the effect of the Tricyclic Antidepressant, Desmethylimipramine (DMI), on human Natural Killer (NK) Cell activity was examined *in vitro*. Serial half-fold dilutions of DMI ranging from 10,000 ng/ml to 78 ng/ml were incubated with a mixture of peripheral blood lymphocytes (2.5×10^6 cells/ml) and ^{51}Cr. labeled K562 target cells (effector to target ratio, 100:1) for 3 hours at 37°C. DMI at concentrations of ≥ 625 ng/ml inhibited NK activity. Pre-incubation of lymphocytes with DMI for up to 24 hours prior to the assay did not increase the inhibitory effect. Furthermore, removal of the drug from pre-incubated cells immediately prior to assay completely eliminated the inhibitory effect. These results demonstrate that DMI reversibility inhibits NK activity at serum concentrations which are not uncommonly found in depressed patients receiving this medication. To follow-up on this work, the *in vitro* effect of the main metabolite of DMI, 2-OH DMI, on NK cell activity has recently been examined. Like DMI, 2-OH DMI also exhibits an inhibitory influence. Implications of these findings will be discussed.

NR145 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

MELATONIN AND NORMAL SLEEP

Steven P. James, M.D., NIMH, Bldg. 10, Rm 4S-239, 9000 Rockville Pike, Bethesda, MD 20205; Wallace B. Mendelson, M.D., David A. Sack, M.D., Normal E. Rosenthal, M.D., Mary Lou Burch-Lien, R.N., Thomas A. Wehr, M.D.

Summary:

Clinical observation in various populations is that melatonin, an indoleamine produced in the pineal gland and secreted at night, is a naturally occurring sedative. Previous studies of melatonin and sleep have reported an enhancement of sleep in some, and a deterioration in others.

In this study ten medication-free normal subjects received 0, 1 mg. and 5 mg. doses of melatonin once a week in a randomized, double-blind study at night. After administration of the compound, their sleep was recorded by a polysomnogram. The day following the sleep study, subjects completed a Stanford Sleepiness Scale, Daily Sleep Questionnaire, and a 100 mm Visual Analogue Scale.

The Stanford Sleepiness Scale and the Visual Analogue Scale did not show any differences between the three conditions. The Daily Sleep Questionnaire revealed only a non-significant trend in an increased sense of deep sleep. Polysomnographic data are now being analyzed and will be presented.

Although melatonin apparently has no effect on the perception of sleep in normal subjects, this does not exclude the possibility that this pineal hormone may be important in pathological states.

NR146 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

MELATONIN AND MAO INHIBITORS

Gregory F. Oxenkrug, M.D., 951 E. Layfayette Ave., Detroit, MI 48207; Rob B. McCauley, Ph.D., Iain M. McIntyre, Ph.D., Richard Balon, M.D., Anil K. Jain, M.D., Arthur Yuwiler, Ph.D.

Summary:

Mechanisms of the antidepressant and hypotensive effects of MAO inhibitors are still obscure despite about 30 years of their clinical use. It is noteworthy that both effects are associated with the selective inhibition of MAO-A isoenzyme. Our recent studies revealed that selective inhibition of MAO-A but not MAO-B activity stimulated rat pineal melatonin synthesis. Current study aimed to explore the effect of MAO inhibition on human plasma melatonin (MAO-A), blood platelets MAO (B) and serotonin content (A?). MAO activity of blood platelets was suppressed by 80% one hour after administration of 10 mg of tranyl cypromine (Parnate) and remained inhibited up to six hours after drug intake. Melatonin and serotonin levels picked up between three and four hours after drug intake and returned to baseline within six hours of observation. Drop in blood pressure (20 mmHg) was observed in depressed patients 3 to 4 hours after drug administration. The stimulation of melatonin production during day time might postpone the beginning of the day phase for the endogenous circadian rhythms and therefore contribute to normalization of the advanced circadian rhythms in depression. The possible interaction between antidepressant and hypotensive effects of MAO inhibition will be discussed.

NR147 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

GH RESPONSE TO LEVODOPA AND PROPANOLOL IN PSYCHIATRIC PATIENTS

Patrick Rogue, M.D., Secteur VIII du Naut Rhin, 68250 Rouffach, France; Fabrice Duval, M.D., Marc-Antoine Crocq, Jean-Paul Macher, Madame Francois Fleck, Madame J. Gindein

Summary:

The responses of serum growth hormone (GH) to the ingestion of levodopa (1 gram) and propanolol (.75 mg/kg body weight) were studied in 27 hospitalized drug-free patients and 8 healthy controls. Mean (± standard deviation) values for maximal concentration of GH were significantly lower (F[3,31]= 27.42, p .001) in patients with *DSM-III* major depression (5.65±2.56 ng/ml, 10 unipolar and 1 bipolar) and schizoaffective disorder (3.86±3.32 ng/ml, n= 7) than in those with schizophrenia (33.91±20.04 ng/ml); both groups differed from controls (13.64±4.95 ng/ml). The statistical analysis (variance, covariance and multiple linear regression) showed that these differences were independent of age, sex, height, weight, Hamilton and BPRS rating scale scores, duration of illness, hospitalization status, or medication history. No correlation was found with the 24-hour urinary levels of the major monoamine catabolites.

We also studied the patients cortisol and TSH responses to dexamethasone and TRH respectively. No clear-cut relationship between these and the GH secretion patterns was found. However, the group with schizophrenia had significantly fewer abnormal responses than the other two (= 13.37, df= 6, p .05). The subclassification of the unipolar patients on the basis of family history showed that the FPDD cases had more endocrine abnormalities, though the limited sample size precluded any more definite conclusion.

These results point to the usefulness of the levodopa-propanolol GH stimulation test in the study of endocrine dysfunction in affective disorders. They are in agreement with several findings which on the one hand show links between major depression and schizoaffective disorder, and which validate Winokur's familial classification of unipolar depression on the other.

NR148 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

PITUITARY RESPONSIVITY TO TRY: CLINICAL STUDIES

James C. Garbutt, M.D., Clinical Research Unit, Dorothea Dix Hospital, Raleigh, NC 27611; James P. Mayo, Jr., M.D., Arthur J. Prange, Jr., M.D., George A. Mason, Ph.D., Gregory M. Gillette, M.D.

Summary:

The blunted TSH response to TRH, observed in both depressed and alcoholic subjects, has emerged as a major biological marker in the field of psychiatry. To date the underlying mechanism of the fault is obscure. One hypothesis is that the reducted TSH response may be secondary to down-regulated TRH receptors. Because TRH releases **both** TSH and PRL from the pituitary and because these two hormones exhibit different TRH dose-response relationships we have performed dose-response studies with TRH in major depressed, abstinent alcoholic and normal subjects. Four TRH dosages were given (25, 100, 500, 800 μg) using an intra-subject design and age- and sex-matched controls.

The most striking observation to emerge so far is the major disturbance in the TSH response to TRH in abstinent male alcoholics. This group had significantly lower TSH responses at all TRH dosages although the PRL response was similar to that in normals. In contrast depressed subjects (male and female) had nonsignificantly lower responses of both TSH and PRL compared to normals. These data suggest that the pituitary responsivity to TRH may be different between depression and alcoholism and, for alcoholism, does not support a broad down-regulation of TRH receptors.

NR149 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

IN VITRO GLUCOCORTICOID SENSITIVITY IN DEPRESSION

Anthony T. Reder, M.D., Dept. of Neurology, University of Chicago, Chicago, IL 60637; Martin T. Lowy, Ph.D., Jack P. Antel, M.D., Herbert Y. Meltzer, M.D.

Summary:

We have previously reported (Am J Psychiatry 141:1365, 1984) that nonsuppressors compared to suppressors were resistant to the immunosuppressive effect of dexamethasone (DEX) on the T cell mitogen response to phytohemagglutinin (PHA) and concanavalin A (Con A). In the present study we extended our work to examine the effect of *in vitro* DEX (10^{-10} *M*) as well as oral DEX (1 mg) administration on PHA- and Con A-induced lymphocyte proliferation. Following a 1 mg DEX dose, suppressors (N= 36) compared to nonsuppressors (N= 15) showed significant decreases in the PHA (84±3 vs. 103±2%; p 0.001) and Con A (81±3 vs. 103±5; p 0.001) response. *In vitro* DEX produced a dose-dependent decrease in both the PHA and Con A mitogen response, which did not differ between the depressed (N= 22) and nondepressed (N= 29) subjects. However, nonsuppressors were resistant to the immunosuppresive effect of low doses (10^{-10} *M*) of DEX on the Con A response compared to suppressors. Thus, glucocorticoid resistance in nonsuppressors could be detected using *in vitro* techniques, which further supports the hypothesis that glucocorticoid receptor abnormalities are associated with DST nonsuppression.

NR150 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

ANTIBODIES TO EPSTEIN-BARR VIRUS IN DEPRESSION

Jay D. Amsterdam, M.D., Depression Rsrch. Unit, Hosp./Univ. of PA, 36th and Spruce St., Philadelphia, PA 19104; Werner Henle, M.D., Owen Walkowitz, M.D., Andrew Winokur, M.D., Steven M. Paul, M.D.

Summary:

There has been considerable interest in the possibility that some psychiatric disorders may be caused by viral infections. There have been recent reports that Epstein-Barr virus (EBV) might result in chronic, recurrent illness with some symptoms suggestive of affective disorders. Investigators have observed higher antibody (AB) titlers to EBV viral capsid antigen (VCA) and early antigen (EA) in these subjects when compared to controls. We therefore studied the possibility that persistent EBV infection may be associated with major depression (MDD).

Serum AB to EBV-associated nuclear antigen (EBNA), VCA, and EA were determined in 43 patients with MDD: 30 unipolar and 13 bipolar depressed. All were drug free for at least 2 weeks, and were depressed for a minimum of 6 months. Sera for EBV antibodies were also obtained from 46 matched, healthy volunteers.

Results: Geometric mean titlers of AB to VCA and EBNA did not differ significantly between patients and controls. No patient had AB to the diffuse (D) component of EA, while the restricted (R) component of EA was higher in control and unipolar groups. These results suggest that an EBV etiology for MDD is not common. Furthermore, the data provide no evidence that MDD affects the immune system to the extent that a persistent EBV infection is activated. Therefore, routine determination of EBV AB profiles is not indicated in patients with MDD.

NR151 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

ACTH TEST IN DEPRESSION BEFORE AND AFTER TREATMENT

Jay D. Amsterdam, M.D., Depression Research Unit, Hosp. of the Univ. Penn., 36th and Spruce St., Philadelphia, PA 19104; Gregory Maislin, M.S., Ellen Abelman, B.A., Marian Droba, M.D., Andrew Winokur, M.D.

Summary:

Excessive cortisol secretion after cosyntropin (ACTH0$_a$1-24) infusion has been observed in some depressed patients. This has suggested the possibility that the adrenal cortex may be hyperresponsive to circulating ACTH and contribute, in part, to HPA axis activation in depression. Although several studies have shown a "normalization" of the DST with clinical improvement, few studies have examined possible changes in cortisol secretion after the ACTH infusion test before and after treatment.

We therefore measured serum cortisol concentrations after a 250μ g cosyntropin test, and after 1 mg DST, before and after treatment in 23 female and 9 male patients with major depressive disorder: 22 melancholic (MEL) and 10 nonmelancholic (NML). In addition, 19 were DST suppressors (S) and 13 were nonsuppressors (NS) prior to treatment.

Basal cortisol concentrations, and the maximum cortisol response to ACTH did not change significantly with treatment in any patient group. However, the MEL/DST-NS subgroup did have a significant decrease in cortisol response to ACTH after treatment ($p = .04$).

When the cumulative cortisol response (CCR) (area under the cortisol response curve) to ACTH was examined, a decrease was seen for the DST-NS group ($p = .05$). The DST-NS also had a greater CCR decrease than the DST-S ($p = .03$). In addition, the MEL group had a greater CCR decrease than the NML patients ($p = .02$). Finally, the MEL/DST-NS subgroup had the largest CCR decrease after treatment ($p = .03$), while the other subgroups had a nonsignificant increase in CCR. In conclusion, the MEL/DST-NS may represent a group of patients with adrenal cortex hyperresponsiveness to ACTH which tends to "normalize" with clinical recovery.

NR152 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

ACTH AND CORTISOL DISSOCIATION IN DEPRESSION

K. Ranga Rama Krishnan, M.D., Dept. of Psychiatry, Duke Univ. Med. Center, P.O. Box 3215, Durham, NC 27710; James C. Ritchie, MPH, Ananth N. Manepalli, M.D., Randal D. France, M.D., Charles B. Nemeroff, M.D., Bernard J. Carroll, M.D.,

Summary:

Dissociation between plasma cortisol and ACTH concentrations during the night time has been reported in normal individuals. As cortisol secretion has been reported to be increased in depression, we examined the question of whether there was a similar dissociation in depression.

METHODS: Ten drug-free, healthy patients who satisfied RDC criteria for major depression and ten normal were studied. Blood was collected for ACTH and cortisol at 15 minute intervals throughout the night and into the early part of the morning. Cortisol is measured by CPB. ACTH was measured by a highly sensitive and specific radioimmunoassay. CV minimal detectable concentration was 1 pg/ml. The inter-assay = 12% and the intra-assay CV = 7%. A dexamethasone suppression test was done on the following day in these patients.

RESULTS: There was an increased cortisol and ACTH secretion in depressed patients who were non-suppressors compared to normal volunteers. There were three types of dissociation between ACTH and cortisol secretion: 1) there was cortisol rise without a significant change in ACTH concentration; 2) ACTH rise without significant change in cortisol concentration; and 3) lack of a proportional correlation between ACTH and cortisol.

DISCUSSION: These findings suggest that mechanisms other than ACTH may be involved in the hypersecretion of cortisol in depression.

NR153 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

GRH STIMULATION TEST IN DEPRESSION

K. Ranga Rama Krishnan, M.D., Dept. of Psychiatry, Duke Univ. Med. Center, P.O. Box 3215, Durham, NC 27710; Ananth N. Manepalli, M.D., James C. Ritchie, MPH, Krishnaiah Rayasam, M.D., Jean Rivier, Wiley Vale, M.D., Michael Thorner, M.D., Charles B. Nemeroff, M.D.

Summary:

When compared to normal control subjects, endogenously depressed patients show a blunted growth hormone response to insulin induced hypoglycemia and to the alpha 2 adrenergic agonist clonidine. Currently, it is uncertain whether the defect is in the brain or at the level of the pituitary. We studied growth hormone releasing factor (GRF) induced growth hormone response in depressed patients and compared it to controls.

METHOD: Medically healthy patients who satisfied RDC criteria for major depression were studied. All patients were drug free for at least a week. Normal volunteers were age, sex, and weight matched to the patients. Premenopausal female patients were matched with female normal volunteers in terms of the menstrual cycle also. One mcg/kg of GRF was given at 0900h. Blood growth hormone was collected serially before and after at 15 minute intervals. Growth hormone was measured by immunoradiometric assay, intra-assay = 6.7% and inter-assay = 15%. The minimum detectable concentration = .2 ng/ml.

RESULTS: Nine patients were studied along with 9 age, sex, and weight matched controls. Seven of the 9 patients compared to their control had elevated growth hormone responses (Δ max). The mean Δ max of the patients was 13.04 ng/ml. For the controls 6.79 ng/ml ($t = 2.64$, $df = 16$, $p < .02$).

DISCUSSION: The hyper responsiveness of the somatotroph to GRF suggests that the blunted growth hormone response to clonidine is probably not due to a defect of the pituitary level.

NR154 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

CLINICAL UTILITY OF URINARY MHPG

Arnold L. Lieber, M.D., 250 W. 63rd St., Miami Beach, FL 33141

Summary:

One hundred inpatient RDC-diagnosed major depressives (68 unipolar, 27 bipolar and 5 secondary) underwent 72-hour urine collection for the measurement of 3-methoxy-4-hydroxyphenylglycol (MHPG). The average 24-hour urinary MHPG for these patients was compared by multivariate analysis of variance with the post-dexamethasone cortisol (DST), the delta thyroid stimulating hormone (thyrotropin releasing hormone stimulation test), six regional quantitative EEG (QEEG) measures of interhemispheric asymmetry and six focal QEEG measures of frequency on the same patients. Age, sex and diagnosis were included in the ANOVA. MHPG failed to discriminate among the three diagnoses. It showed no significant correlations with age, sex, post-dexamethasone cortisol or delta TSH. It failed to correlate with QEEG regional asymmetry or with focal QEEG frequency abnormalities. The average 24-hour urinary MHPG had no utility in the discrimination of diagnostic subtypes among these patients. It was shown to covary independently of the other diagnostic markers that were measured. Routine use of this relatively expensive and cumbersome laboratory test does not appear warranted.

NR155 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

SEVERITY OF DEPRESSION AND MULTIPLE HPA MEASURES

James H. Meador-Woodruff, M.D., Dept. of Psychiatry, Univ. Mich. Med. Ctr., 1405 E. Ann St., Ann Arbor, MI 48109; Roger F. Haskett, M.D., Huda Akil, Ph.D., Stanley J. Watson, M.D., Leon Grunhaus, M.D., John F. Greden, M.D.

Summary:

In patients with major depressive disorder (MDD), hypothalamic-pituitary-adrenal (HPA) axis dysregulation appears to be state related. We explored the relationship between severity of depression [reflected by Hamilton Rating Scale for Depression (HRSD) scores] and HPA function at multiple HPA levels. 108 patients with MDD, not psychotic, and drug-free for 2 weeks received 1 mg of oral dexamethasone at 11:30 pm and plasma cortisol was measured at 4:00 pm the next day. For analysis, the patients were grouped by severity (HRSD score 0-10, 11-15, 16-20, 21-25, 26 +). We found a highly significant correlation between HRSD score and cortisol levels ($F= 4.24$, $p= 0.0032$). We also measured beta-endorphin (BE) levels in another 42 patients with MDD. Each patient had 4 blood samples drawn between 3:30 and 4:30 pm on 2 successive days, before and after receiving 1 mg of oral dexamethasone. BE was determined in triplicate by RIA and the means ± SEM for each day were calculated. We found a significant ($F= 2.80$, $p<0.05$) relationship between HRSD scores and percent change from pre- to post-dexamethasone BE levels; patient groups with high HRSD scores had smaller changes after dexamethasone. We also determined the percentage of each group that "suppressed" their BE level after dexamethasone, defined as non-overlap between mean ± SEM of pre- and post-levels. Patient groups with higher HRSD scores contained more nonsuppressors ($X^2= 12.04$, $p<0.02$). There were no significant age, sex, or weight change differences between the groups in either the cortisol or BE study. These results suggest that severity of depression influences the degree of HPA dysfunction in MDD, at both the pituitary and adrenal levels.

NR156 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

THE DST AND PHASES OF DIAGNOSTIC MARKER RESEARCH

Andrew A. Nierenberg, M.D., Yale Univ. Med. School, Room 1E-61 SHM, P.O. Box 3333, New Haven, CT 06510

Summary:

After a period of popularity, the dexamethasone suppression test (DST) is no longer regarded as a clinically useful diagnostic marker for major depression (MD). We have reviewed 84 published articles to determine why the test became accepted and later rejected. From a consideration of test development procedures, we propose the following 5-phase classification of the process: 1) studies of basic mechanisms of test procedures; 2) studies of substantially diseased people (e.g., MD with melancholia by standard criteria) vs. healthy controls; 3) studies of an extended spectrum of disease type and severity (e.g., MD with and without melancholia and with ambulatory as well as hospitalized patients) vs. healthy controls; 4) studies with an expanded spectrum of cases and controls to include comorbidity in both groups and studies of just "controls" with comorbidity; 5) prospective "cohort" studies of large consecutive series of clinically pertinent patients. The DST became recommended for general use after several phase 2 and 3 studies, but without the completion of phase 1 or appraisal in the broader spectrums needed in phases 4 or 5. When phase 1 was completed years later, the absorption of oral dexamethasone was found to vary between people for unknown reasons and the initial assays for plasma cortisol were unreliable. When better comorbid spectrums were checked in phase 4 and phase 5, it became clear that the test was limited in differentiating depression from relevant comorbid conditions. This type of problem can be avoided in the future if diagnostic tests pass through the proposed series of evaluation phases before becoming widely accepted.

NR157 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

SEROTONERGIC ACTIVITY AND DRUG-INDUCED MYOCLONUS

James R. Merikangas, M.D., Temple Medical Center, 40 Temple St., New Haven, CT 06510; Kathleen R. Merikangas, Ph.D., Jonathan M. Himmelhoch, M.D.

Summary:

Myoclonus, the occurrence or rapid involuntary jerks of muscle unassociated with any obvious change in consciousness, can be caused by a variety of distinct clinical conditions. These conditions, which include viral infections, epilepsy, biochemical abnormalities, and intoxication by a variety of pharmacologic agents, vary in the prominence and severity of myoclonic jerks. The most prominent of the causative agents include imipramine, amitriptyline, lithium carbonate, carbamazepine and the monoamine oxidase inhibitors. Animal studies have demonstrated that myoclonus is directly related to the serotonergicity of the drug. The more potent the agent as a 5HT re-uptake inhibitor, the greater the occurrence of myoclonic seizures.

This paper presents the results of a study of the occurrence of myoclonus among 193 out-patients with affective disorders. The incidence of myoclonus is examined as a function of drug treatment including a variety of tricyclic antidepressants, monoamine oxidase inhibitors, lithium carbonate and combinations of the above. The findings indicate that similar to animal models, myoclonus is related to the degree of serotonergic activity induced by the particular pharmacologic agent. Interesting synergistic effects of drug combinations were also found. These findings have important implications for drawing inferences regarding the neurochemical activity and toxicity of these particular drugs.

Although myoclonus does not persist after discontinuation of the causative agent, it is also possible to maintain the drug with treatment of this side effect. Such treatment strategies will be described.

NR158 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

MHPG, MAO, AND CONTROL BELIEFS IN DEPRESSIONS

Jacqueline Samson, Ph.D., McLean Hospital, 115 Mill St., Belmont, MA 02178; Stuart Hauser, M.D., Steven Mirin, M.D., David Borelli, M.D., Benjamin Gerson, M.D., Joseph J. Schildkraut, M.D.

Summary:

In this study, 27 clinically depressed inpatients (9 male and 18 female, age range 17-57 years) completed the Kobasa Hardiness Questionnaire, Rotter Locus of Control Scale (LOC), and Sarason Life Experiences Survey (LES). Concurrently, we measured urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) levels, urinary free cortisol (UFC) and platelet monoamine oxidase (MAO) activity under drug-free conditions. Previously, we reported correlations of high MHPG with perceptions of powerlessness, and high MAO with internal LOC. Extending this work, we have expanded our data base and used factor analytic techniques to explore relationships among variables. Using varimax rotation with 10 selected variables, we obtained a 3-factor solution which accounted for 67% of the total variance in our dependent variables. (Factor 1 accounted for 29% and Factors 2 and 3 for 19% each.) **Factor 1** ("Life Stressors") = number of negative stressors (.98), impact of negative stressors (.98), impact of uncontrollable stressors (.94); **Factor 2** ("MHPG-Powerlessness") = high MHPG (.80), feelings of powerlessness (.72), high UFC (.54), external LOC (.42), male gender (.39); **Factor 3** (MAO-LOC) = high MAO (.69), greater social status (.67) internal LOC (.64), high UFC (.56), female gender (.47). The inclusion of high UFC on both Factor 2 ("MHPG-Powerlessness") and Factor 3 ("MAO-LOC"), is consistent with reports of associations between increased hypothalamic pituitary adrenal cortical activity and high platelet MAO activity, as well as high MHPG levels. We are now conducting further studies of these linkages between biological and psychological measures of adaptive response patterns. The hypothesis that Factor 2 ("MHPG-Powerlessness") and Factor 3 ("MAO-LOC"), reflect two distinct patterns of responses to environmental stressors will be discussed.

NR159 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

NEUROBIOLOGY OF HUMAN LEARNED HELPLESSNESS

Alan Breier, M.D., NIMH, Bldg. 10, Rm 4N214, 9000 Rockville Pike, Bethesda, MD 20892; Margot Albus, M.D., Theodore P. Zahn, Ph.D., David Pickar, M.D., Owen M. Wolkowitz, M.D., Steven M. Paul, M.D.

Summary:

The lack of control over aversive events results in the development of a variety of behavioral and neurobiological deficits, a phenomenon that has been termed "learned helplessness." Since the consequences of learned helplessness have been poorly defined in man, we have examined the behavioral and neurobiological effects of uncontrollable and controllable stress in 10 healthy volunteers.

All subjects participated in a nonescape (NES) and an escape (ES) test day which consisted of being exposed to 60 trials of loud (100 db) noise followed by an anagram learning test; in the ES the noise stress could be terminated by a learned response and in the NES termination of noise was not possible. The amount of noise was held constant in both conditions by "yoking" NES noise duration to ES noise durations.

The NES as compared to the ES condition increased self-ratings of helplessness ($F= 24.7$, $p= 0.001$), lack of control ($F= 196.8$, $p<0.0001$), depression ($F= 13.6$, $p= 0.006$), lack of success ($F= 33.9$, $p= 0.0004$), tension ($F= 8.6$, $p= 0.005$), unhappiness ($F= 8.1$, $p= 0.014$), and stress ($F= 11.2$, $p= 0.006$). These behavioral changes were accompanied by significant differences in ACTH secretion between the two conditions (condition vs time) ($F= 5.7$, $p= 0.006$); with ACTH elevations occurring in the NES but not the ES at 10 min ($p= 0.04$), and 45 min ($p= 0.02$) after the cessation of the noise stress. Plasma epinerphrine and norepinephrine levels in the two conditions will be presented. Skin conductance levels were significantly elevated in the NES in comparison to the ES ($F= 3.7$, $p<0.04$). The increase in ACTH levels in NES correlated with measures of increases in tension ($r= 0.82$, $p<0.01$), unhappiness ($r= 0.67$, $p<0.05$),and stress ($r= 0.62$, $p<0.06$). We conclude that the NES paradigm may be a useful method for investigating neurobiological correlates of mood in normal subjects and in various neuropsychiatric disorders.

NR160 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

NORADRENERGIC INDICES IN REMITTED DEPRESSIVES

Larry J. Siever, M.D., VAMC 116A, 130 W. Kingsbridge Rd., Bronx, NY 10468; Emil Coccaro, M.D., Oren Kalus, M.D., Karen Rubinstein, M.Ed., Kenneth L. Davis, M.D.

Summary:

Indices of noradrenergic release as reflected in basal concentrations of plasma norepinephrine and 3-methoxy-4-hydroxyphenyl glycol (MHPG) and of adrenergic receptor responsiveness as reflected in responses to clonidine, were measured in 17 acute and 10 remitted depressed patients as well as 8 matched controls. The data available to date indicates that the growth hormone (GH) response to clonidine, an index of post-synaptic adrenergic receptor responsiveness, was blunted in the majority of both acute (6/10 [60%]) and remitted (6/8 [75%]) patients compared to the normals (1/7 [17%]). The combined groups of depressed patients as well as the remitted depressed patients alone were more likely to demonstrate blunted GH responses to clonidine than the controls ($p<0.05$, Fisher's exact test). Preliminary results also are consistent with the possibility of reduced MHPG responses to clonidine in these remitted patients. These results will be contrasted to comparisons of basal indices of noradrenergic metabolism/release which tend to normalize in remitted depressed patients compared to acute depressed patients. They raise the possibility that reduced α_2-adrenergic receptor responsiveness as reflected in the blunted GH response to clonidine may constitute a trait or state-independent correlate of depression.

Educational Objectives: The goal of this presentation is to familiarize the psychiatrist with new research in the biology of depression and the research and clinical implications of trait markers of depression.

NR161 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

AUTOIMMUNE THYROIDITIS IN FEMALE DEPRESSIVES

Victor I. Reus, M.D., School of Medicine, UCSF, 401 Parnassus Ave., San Francisco, CA 94143; Jeffrey L. Berlant, M.D., Maurice Galante, M.D., Nathan Becker, M.D.

Summary:

Autoimmune thyroiditis (AT) is a remarkably prevalent but often undiagnosed disorder, achieving an incidence of 10% in the general female population. Several recent studies indicate a two- to threefold increase incidence in patients with major depression, but the relationship of elevation in thyroid antibodies to pertubations of thyroid function in a euthyroid psychiatric population has not previously been examined. 170 consecutive female patients were screened for the presence of antithyroid antibodies; 25% of females receiving a diagnosis of major depression were found to have an elevation in either antimicrosomal or antithyroglobulin antibodies. A battery of subjective and objective behavioral rating measures of these patients and a matched depressed control population revealed no specific identifying clinical symptomatology. However, patients with AT showed significant impairment on a selective reminding task while exhibiting no alteration in reaction time, continuous performance, or abstract thinking. Although measurements of T_3, T_4, FTI, and TSH in both the AT and control populations were within normal limits, the populations differed from each other in basal TSH level. Additionally, the TSH response to TRH was examined in 15 female depressed patients and a matched depressive cohort. AT patients had a significantly augmented TSH response to TRH (>26 lu/ml) suggesting subclinical hypothyroidism. Preliminary data on patients' likelihood of response to antidepressant treatment and the role of thyroid medication will be presented. The relevance of a diagnosis of AT to such clinical issues as rapid cycling and bipolar illness, the diagnosis of somatization disorder, and the onset of post-partum depression and anxiety will also be considered.

NR162 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

5HT UPTAKE EFFECT OF ANTIDEPRESSANT WITHDRAWAL

Jeffrey L. Rausch, M.D., Dept. of Psychiatry, M003 USCD School of Med., SDVAMC, La Jolla, CA 92093; S.C. Risch, M.D., David S. Janowsky,M.D., Lewis L. Judd, M.D.

Summary:

Platelet 5-HT uptake kinetics were characterized in remitted depressed outpatients candidate for trials off of medication after treatment with stable doses of different serotonin uptake blockers (imipramine, amitriptyline, desipramine, trazodone) for four months or longer. Platelet 5-HT uptake was measured twice while on drugs, weekly during tapering off of drugs, and at one day, and one, two, three, and four weeks after drug withdrawal. The data indicated Vmax and Km to be stable for a four week period after discontinuation of serotonin uptake blockers in the nonrelapsing patients. Data from the drug taper period found Vmax not to be significantly correlated with dose, although a highly significant positive correlation between dose and Km was found with multiple regression analysis of uptake parameters with partial F-tests for subject and drug differences. Km was significantly less than one half of the treatment value at one day drug-free with no significant differences between subsequent days, through the fourth drug-free week.

Tricyclic antidepressants are known to decrease serotonin uptake in platelets and synaptosomes. The data from this study indicate that the affinity constant for platelet serotonin uptake may be a functional indicator for the tissue response to the uptake blocking properties of these drugs, potentially useful as indicators of clinical dose effect in depressed patients during treatment with tricyclic antidepressants. A decreased maximum velocity (Vmax) of platelet serotonin uptake has been shown in depressed patients in several studies. These data indicate that Vmax does not change significantly in response to antidepressant withdrawal in patients remaining remitted from major depressive episodes.

NR163 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

CSF, CRH, AND PLASMA ACTH LEVELS IN DEPRESSION

Alec Roy, M.B., NIAAA, Bldg. 10, Room 3B19, 9000 Rockville, Pike, Bethesda, MD 20205; David Pickar, M.D., Steven M. Paul, M.D., Markku Linnoila, M.D., Allen Doran, M.D., Philip Gold, M.D.

Summary:

Although depressed patients (N= 22) and normal controls (N= 18) did not differ significantly for CSF corticotropin releasing hormone (CRH) levels (mean 39.19 ± 15.33 vs 37.21 ± 10.38 pg/ml) depressed patients who were DST nonsuppressors (N= 11) had significantly higher CSF CRH levels than DST suppressors (N= 11) (mean 45.73 ± 18.36 vs 32.63 ± 6.95 pg/ml, t= 2.1, $p<0.05$). Unipolar DST nonsuppressors (N= 8) had significantly higher CSF CRH levels than unipolar suppressors (N= 6)(mean 47.91 ± 18.34 vs 30.10 ± 6.81 pg/ml, t= 2.24, $p<0.05$). CSF CRH and postdexamethasone plasma cortisol levels were significantly correlated at 4 p.m. in the total (r= 0.66, $p<0.001$, N= 21), unipolar (r= 0.66, $p<0.001$, N= 14), and nonsuppressor (r= 0.56, $p<0.05$, N= 11) groups; at 11 p.m. in the unipolar (r= 0.46, $p<0.1$, N= 12) group; and at 4 p.m. predexamethasone in the total group (r= 0.35, $p<0.1$, N= 20). Among DST nonsuppressors CSF CRH levels correlated with CSF NE (n= 10, r= 0.59, $p<0.05$) and with plasma NE (n= 8, r= 0.51, $p<0.1$). CSF CRH correlated with urinary levels of NE (N= 9) (r= 0.67, $p<0.05$), NM (r= 0.72, $p<0.05$), VMA (r= 0.73, $p<0.01$), and urinary free cortisol (r= 0.81, $p<0.05$, N= 6). Depressed patients (N= 16) had significantly higher plasma ACTH levels than controls (N= 39) both at 4 p.m. predexamethasone (11.04 ± 4.85 vs 7.70 ± 3.85 pg/ml, $p<0.02$) and 4 p.m. postdexamethasone (6.84 ± 3.83 ± 2.80 ± 1.73 pg/ml, $p<0.01$). Among the 5 of these depressed patients who had an LP there was a significant negative correlation between the percent change in plasma ACTH levels and CSF CRH levels (r= −0.81, $p<0.05$). These results suggest that hypersecretion of endogenous CRH is associated with the dysregulation of both the HPA axis and NE system that occur in depression.

NR164 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

ADRENERGIC RESPONSIVENESS IN ENDOGENOUS DEPRESSION

J. John Mann, M.D., Payne Whitney Clinic, 525 E. 68th St., New York, NY 10021; Richard P. Brown, M.D., James P. Halper, M.D., John A. Sweeney, Ph.D., James H. Kocsis, M.D.

Summary:

Introduction: Animal studies suggest that desensitization of beta-adrenergic receptors may be a final common pathway for somatic antidepressant therapies. An abnormality in beta-adrenergic function may therefore be present in depressive disorders. Direct assessment of beta-adrenergic receptors in the central nervous system is currently not possible. We report here the measurement of lymphocyte beta-adrenergic receptor responsiveness in depressed patients as an indirect assessment of similar central mechanisms. **Methods:** Normal controls and 33 inpatients with endogenous depression (RDC criteria) and drug-free for at least 2 weeks were studied. Plasma catecholamines and lymphocyte beta-adrenergic receptor-mediated cyclic AMP production and binding indices were assayed. **Results:** Basal and isoproterenol-generated levels of cyclic AMP were significantly lower in depressed patients compared to controls (6.9 ± 0.9 vs 11.2 ± 2.7 pmol/10^6 cells for basal levels; 16.1 ± 2.2 vs 24.8 ± 2.2 pmol/10^6 cells at 10 uM isoproterenol; $p<.05$). Results of non-linear interative analyses of dose-response curves will be presented. Beta-adrenergic binding indices in depressed patients did not differ from controls. Overall severity of depression assessed by the Hamilton Depression Scale (HDS) did not correlate with cyclic AMP levels. The correlations of beta-adrenergic responsiveness to levels of plasma catecholamines and degree of psychomotor agitation and anxiety will be discussed. Treatment with ECT or tricyclics generated significant improvement (a 65% reduction in HDS Score) but only a small degree of beta-adrenergic receptor resensitization that may be due to a reduction in levels of catecholamines. **Discussion:** The results suggest a primary beta-receptor abnormality in endogenous depression. Supported by PHS grant MH 37907.

NR165 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

POSTRECEPTOR REGULATION OF ADENYLATE CYCLASE BY NE

John J. Mooney, M.D., Mass. Mental Health Ctr., 74 Fenwood Rd., Boston, MA 02115; Joseph J. Schildkraut, M.D., Alan F. Schatzberg, M.D., Benjamin Gerson, M.D., Kathleen Pappalardo, B.S., Jonathan O. Cole, M.D.

Summary:

In a series of 23 drug-free subjects (14 depressed patients and 9 controls), we found statistically significant inverse correlations between 24 hr. urinary levels of [norepinephrine (NE) + epinephrine (E)] and various measures of receptor-mediated and post-receptor-mediated platelet adenylate cyclase (AC) activity— 24 hr. urinary [NE + E] vs: basal AC, $r = -.43$, $p < .05$; NaF-stimulated AC, $r = -.53$, $p < .01$; prostaglandin D_2 (PGD_2)-stimulated AC, $r = -.57$, $p < .01$; E suppressed AC, $r = -.41$, $p < .05$. In leukocytes, statistically significant inverse correlations were observed between receptor-mediated and post-receptor mediated measures of AC activity and 24 hr. urinary E levels— basal AC, $r = -.51$, $p < .02$; NaF-stimulated AC, $r = -.54$, $p < .01$; PGD_2-stimulated AC, $r = 1.58$, $p < .01$; isoproterenol-stimulated AC, $r = -.48$, $p < .02$. Thus, catecholamines may regulate AC activities in both platelets and leukocytes by heterologous desensitization and modification occurring through post-receptor mechanisms.

In a series of depressed patients, alprazolam (APZ) significantly decreased urinary catecholamines ($p < .01$) and metabolites after one week of treatment, irrespective of clinical outcome. However, only those depressed patients who went on to show favorable antidepressant responses to APZ at the conclusion of the study, had significant increases ($p < .001$) in both PGD_2-stimulated and E suppressed platelet AC after one week of treatment; such changes were not seen in APZ nonresponders. Thus, enhanced signal transduction by the AC enzyme complex may play a role in the mechanism of action of APZ as an antidepressant. These findings will be discussed in relation to the post-receptor modulation of the AC enzyme complex by catecholamines.

NR166 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

DIMINISHED SEROTONERGIC FUNCTION IN DEPRESSION

Robert N. Golden, M.D., Dept. of Psychiatry, UNC School of Medicine, Chapel Hill, NC 27514; John Hsiao, M.D., Susan Rogers, R.N., Matthew V. Rudorfer, M.D., William Z. Potter, M.D.

Summary:

The neurohormone response to an acute "challenge" with the serotonin (5-HT) uptake inhibitor chlorimipramine (CMI) can provide a physiologic gauge of 5-HT function. In a pilot study of healthy volunteers, we found that low dose (10 mg.) CMI, administered intravenously over a 15 minute period, leads to a robust increase in plasma prolactin, ACTH, and cortisol concentrations without affecting norepinephrine, growth hormone, or melatonin concentrations and without eliciting cardiovascular or subjective indications of stress. We now report the results of a pilot study comparing the neuroendocrine response to the IV CMI "challenge test" in depressed patients and healthy volunteers.

Eight patients with RDC major depression were studied following a 4 week drug-free period, as well as 7 healthy volunteers. Plasma samples were obtained through an indwelling IV catheter at timed intervals before and after infusion of 10 mg. CMI.

Depressed patients showed a blunted prolactin response compared to healthy controls, with 15 minute post-infusion prolactin levels reaching $112 \pm 8\%$ and $186 \pm 38\%$ of baseline for the 2 groups respectively. Mean ACTH and cortisol responses were also lower in depressed patients compared to healthy volunteers, but there was considerable variance in each group. Depressed patients showed exaggerated growth hormone responses; 45 minute post-infusion plasma growth hormone concentrations reached $430 \pm 180\%$ of baseline for depressed patients compared to $59 \pm 19\%$ for controls.

The blunted prolactin response to the IV CMI challenge supports the concept of decreased serotonergic function in depressed patients. The unexpected finding of increased growth hormone output in these patients may reflect exaggerated responsivity to low levels of desmethylchlorimipramine due to increased alpha-adrenergic receptor sensitivity.

NR167 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

5-HT IN AFFECTIVE AND PERSONALITY DISORDERS

Emil F. Coccaro, M.D., Dept. of Psychiatry, Bronx VAMC, 130 W. Kingsbridge Rd., Bronx, NY 10468; Larry J. Siever, M.D., Howard Klar, M.D., Karen Rubinstein, M. Ed., Andrea Moskovitz, R.N., Kenneth L. Davis, M.D.

Summary:

CSF, platelet, and neuroendocrine studies suggest the presence of an abnormality in central 5-HT function in patients with major depressive disorder (MDD) and in patients with personality disorder (PD). We examined further the PRL response to the mixed 5-HT releaser/agonist, fenfluramine (FEN), in patients with acute (N= 10) and remitted (N= 10) MDD (assessed by SADS), in patients with *DSM-III* PD (N= 12; assessed by SIDP), and in 8 age/sex matched controls. Peak ΔPRL (ng/ml) for these groups were: 8.6 ± 8.9 (acute MDD), 9.1 ± 5.0 (remitted MDD), 8.6 ± 6.1 (PD) and 14.4 ± 8.0 (controls); p= NS. Half the MDD patients (10 of 20: six acute and four remitted MDD), and half the PD patients (7 of 12), however, demonstrated peak ΔPRL responses to FEN which were below 7.7 ng/ml (the lower limit of the 95% confidence interval for the ΔPRL response to FEN observed in controls) as compared to none among controls ($p<0.05$). Peak ΔPRL values in the 10 MDD (4.0 ± 1.8) and 8 PD (4.3 ± 2.3) patients who demonstrated reduced peak ΔPRL response to FEN were significantly lower than those of the remaining 10 MDD (13.6 ± 7.0) and 5 PD patients (14.8 ± 3.7) whose peak PRL response was indistinguishable from that of controls (14.4 ± 8.0; $p<0.001$). Further, the peak ΔPRL response to FEN was found to correlate inversely with behavioral variables related to physical aggression and motoric impulsivity in patients with PD but not with MDD. These data suggest that the ΔPRL response to FEN may identify a subgroup of MDD and PD with central 5-HT hypofunction which , in turn, may relate to an abnormality of mood, and impulse-control, regulation as seen clinically in these patients.

NR168 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

FLUOXETINE ALTERS BETA-ADRENERGIC, 5HT1, and 5HT2 RECEPTORS

William F. Byerley, M.D., Dept. of Psychiatry, Univ. of Utah Med. Ctr., 50 N. Medical Dr., Salt Lake City, UT 84132; James K. Wamsley, Ph.D., Tyler McCabe, B.A., Elizabeth McConnell, B.S., Fred W. Reimherr, M.D., Bernard I. Grosser, M.D.

Summary:

Long term administration of tricyclic antidepressants, MAOIs, "atypical" drugs, or repeated ECT decrease the sensitivity or number of postsynaptic βadrenergic receptors; alterations in serotonergic receptors are inconsistent. Third generation antidepressants are under investigation and may soon be released. One such compound, fluoxetine, is of heuristic interest because it appears to selectively and potently block serotonin reuptake. It, moreover, does not antagonize muscarinic, histaminergic, αadrenergic, or serotonergic-2 receptors. Norfluoxetine, the demethylated metabolite, is also a potent and selective blocker of serotonin reuptake. Long term administration of fluoxetine is reported not to affect βadrenergic receptors, while its effect on serotonin receptors has been discrepant. As a result, some investigators suggested that fluoxetine may not be a clinically effective antidepressant. Recently reported clinical trials, however, indicate that fluoxetine is efficacious. Using *in vitro* receptor autoradiography, we find that chronic administration of fluoxetine (10 mg or 30 mg/kg) produces alterations in βadrenergic and serotonergic receptors in discrete areas of rat brain. We will report data on the autoradiographic distribution of receptor changes as well as Scatchard plots.

NR169 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

EFFECT OF AGE ON MEASURES OF SEROTONERGIC FUNCTION

P. Anne McBride, M.D., Payne Whitney Clinic, 525 E. 68th St., New York, NY 10021; J. John Mann, M.D., Michael DeMeo, M.D., Jacob Kream, Ph.D., George Anderson Ph.D., Amy Wiley, B.S.

Summary:

Effect of age upon central and peripheral serotonergic function in normal subjects was assessed by multiple measures, including assay of serotonin receptors in postmortem brain and on the platelet, administration of a neuroendocrine challenge test, and assay of whole blood serotonin content. Scatchard analysis of ^{3}H-spiroperidol binding to 5-HT$_2$ receptors in frontal cortex revealed a decrease in Bmax with aging ($r = -0.61$, $N = 16$, $p \leq 0.01$), but no change in K_D. Binding of ^{3}H-5-HT to 5-HT$_1$ receptors in frontal cortex was not significantly correlated with age. Saturation studies of ^{125}I-LSD binding to 5-HT$_2$ receptors on platelets from 12 healthy subjects revealed a decline in Bmax with increasing age ($r = -0.55$, $p \leq 0.05$), with no change in K_D. In the same group of subjects, a significant inverse correlation was found between age and the amount of prolactin released in response to administration of the serotonergic challenge agent fenfluramine, in excess of levels following placebo administration ($r = -0.67$, $p \leq 0.02$). Correlations between whole blood serotonin content and age in normal subjects will also be presented. In a sample of 15 subjects with major depression, mean whole blood serotonin content was significantly lower in subjects older versus younger than 55 years ($t = 3.64$, $p \leq 0.005$). These data suggest a systemic decrease in 5-HT$_2$ receptor number with age, accompanied by a decline in central serotonergic responsiveness which might be secondary to decreased density of serotonin receptors and/or availability of releasable serotonin. Supported by NIMH grant MH 40210.

NR170 **Wednesday, May 14, 12:00 noon -1:45 p.m.**

URINARY FREE CORTISOL IN PSYCHOTIC DEPRESSION

Raymond F. Anton, M.D., Psychiatry Service, VAMC, Charleston, SC 29403

Summary:

The purpose of this study was to extend previous findings of abnormal cortisol secretion in psychotic depression. The subjects were male inpatients (N= 18) diagnosed by *DSM III* criteria as having major depression with psychotic features (MDPF) and a group of similarly aged male inpatients (N= 14) having major depression (MD) with (N= 12) and without (N= 2) melancholia. In the first week of hospitalization during a drug free or placebo period, at least one 24 hour urine was collected (6 am-6 pm) for urinary free cortisol (UFC) before and after 1 mg dexamethasone (DEX) at 11 pm. A Hamilton Rating Scale for Depression (17 item) was conducted within 48 hours of UFC collection. Urinary cortisol was assayed by RIA. Parametric and non-parametric tests were used to analyze the data. Results showed that 35% MDPF patients had UFC >100 μg/24 hr. compared to 7% MD patients ($p < .05$). After DEX, 44% MDPF patients had UFC >20 μg/24 hr. compared to 8% MD patients ($p < .02$). There was no significant correlation of UFC with age in the combined depressed groups. However, within the MDPF group, the patients who were in the high (>100 μg/24 hr.) UFC group were significantly older than those in the low UFC group. MDPF patients had significantly more psychomotor retardation, less weight loss, and similar agitation to the MD patients. The MDPF high and low UFC groups did not differ on these variables. These results suggest that older (>55 yrs) MDPF patients produce more cortisol than older MD patients. Although other clinical variables differ between MDPF and MD patients, these appear independent of UFC excretion.

NR171 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

MILITARY INDUCTION CAN CAUSE DST NON-SUPPRESSION

Mihaly Arato, M.D., National Institute for Nervous and Mental Disease, Budapest 27 Pf.1. 1281, Hungary; Istvan Magyar, M.D., Hedi Lukacs, M.D., Laszlo Mod, M.D., Antal Alfoldi, M.D.

Summary

It is a well known fact that stress is the most common cause of cortisol hypersecretion. Until recently, however, little attention has been paid to stress as a possible causal factor in the development of DST non-suppression/reduced suppressibility of cortisol hypersecretion/ in psychiatric diseases. Recent studies have shown that non-specific stress of acute hospitalization, surgical operations (Ceulemans et al. 1985) as well as public speaking (Baumgartner et al. 1985) may result in temporary DST non-suppression. We are presenting here further evidence that stressful events—obligatory induction into the army—can cause relatively frequent DST non-suppression in physically and mentally healthy, young males. The DST was given to 160 healthy, young (18 to 22 years) male inductees on the second day of the obligatory military service. One mg dexamethasone was administered orally at 22:00 hrs and the following morning at 8:00 hrs one blood sample was taken. Cortisol was measured by competitive protein-binding method. The cut-off point was 5 μg/dL. After one month military training the DST was repeated in the same way. All subjects underwent a complete physical, psychological and psychiatric check up. Thirty-eight subjects (24%) had an abnormal DST result within 2 days of starting their military service. One month later only 4% showed DST non-suppression. Considering the fact that only one morning blood cortisol measurement was used, an even higher non-suppression rate can be expected with the standard DST method.

NR172 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

EFFECTS OF DEPRESSIVE SYMPTOMS ON HPA FUNCTION

Richard P. Brown, M.D., Payne Whitney Clinic, 525 E. 68th St., New York NY 10021; Peter M. Stoll, Peter E. Stokes, M.D., Allen J. Frances, M.D., John A. Sweeney, Ph.D., James H. Kocsis, M.D., J. John Mann, M.D.

Summary

Goals: Although the dexamethasone suppression test (DST) has limited predictive power in a general psychiatric setting, it remains a useful tool for understanding the degree to which adrenocortical hyperactivity is associated with particular behavioral or other parameters in depressed patients. We determined the relative contributions to variance in DST nonsuppression from agitation, delusions, melancholic subtype, age, weight loss, and global severity of illness. Methods: We measured morning and afternoon cortisol levels before and after dexamethasone (DEX) in 93 prospectively studied unipolar major depressed inpatients. Patients met *DSM-III* criteria for major depressive disorder, with or without melancholia, with or without psychotic features and were rated on the 24 item Hamilton Depression Scale including an item for agitation. Results: Stepwise multiple regression showed that presence or absence of agitation predicted 22% of the variance in AM cortisol level after DEX. When melancholic subtype and then delusions were added, 27% and 34% of the variance in the cortisol variable was accounted for. Age, illness severity, and weight loss added no further significant predictive value. An agitated, delusional, melancholic group did not show significantly different cortisol levels compared to an agitated melacholic. Age, weight loss, and illness severity did affect cortisol levels when examined separately from the other variables. Rate of DST nonsuppression differed only between the nonmelancholic major depressive group and any other group with melancholia. Significance: These results suggest: that agitation in other psychiatric disorders may relate to DST nonsuppression; why discrepancies in DST results in delusional depression exist; but clinicians should avoid reliance on DST results in diagnosis of delusional depression; that greater consideration should be given to agitation in future studies.

NR173 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

MELATONIN RELATED TO DEPRESSED MOOD AND PSYCHOSIS

Richard P. Brown, M.D., Payne Whitney Clinic, 525 E. 68th St., New York NY 10021; James H. Kocsis, M.D., Stanley Caroff, M.D., Jay D. Amsterdam, M.D., Andrew Winokur, M.D., Peter E. Stokes, M.D., Alan Frazer, Ph.D.

Summary

Goals: Numerous abnormalities of nocturnal melatonin secretion including decreased amplitude, phase shifts, and association with hyperactive adrenocortical function have been reported in major depressed patients. We tested the hypothesis that melatonin hyposecretion is correlated with Hamilton factors of depressed mood/psychomotor retardation and reality disturbance, but not anxiety, sleep, or diurnal variation.

Methods: Serum melatonin was obtained at 11:00 p.m. from 28 inpatients hospitalized for major depressive disorder and measured by radioimmunoassay.

Results: The patients below the median for nocturnal melatonin secretion were less likely to somatize ($t = 2.1$, $df = 26$, $p < 0.01$) and showed a trend to more reality disturbances ($+ = 1.8$, $df = 26$, $p < 0.1$). There were significant inverse correlations between melatonin and depressed mood/psychomotor retardation and reality disturbance factors of the Hamilton Depression Scale (both $r = -0.4$, $p < 0.04$).

Significance: From these findings, which are consistent with two prior reports, it may be inferred that there may be a distinct subgroup of depressed patients with nocturnal melatonin hyposecretion and cortisol hypersecretion separate from an agitated/anxious group with morning cortisol hypersecretion after dexamethasone and normal melatonin.

NR174 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

DOES SEVERITY EXPLAIN MELANCHOLIA? A DST VALIDATION

John F. Greden, M.D., Dept of Psychiatry, Univ. of Michigan, Med Center, Ann Arbor, MI 48109; Roger Haskett, M.D., Leon Grunhaus, M.D., Hans Bendz, M.D., Pamela Flegel.

Summary

The *DSM-III* revision committee recently considered whether "melancholia" should be retained as a subcategory of major depressive disorder (MDD). The resolution of the question of whether melancholia has meaningful predictive value will depend on the study of external validators (family history, treatment outcome and laboratory variables). Although many HPA neuroendocrine studies have identified profound differences between melancholic and non-melancholic depressives, others fail to find such differences. Almost all studies, however, have failed to consider severity as a variable. To evaluate the validity of melancholia using hypothalamic-pituitary-adrenal variables as external validators while varying for severity of depression, we studied 91 depressed endogenous patients and 19 nonendogenous depressives. We collected eight DST variables as external validators (0800, 1600, 2300 hrs., maximum, minimum, and mean of these three samples, percentage of the three that were nonsuppressive, and pre/post ratio). We then subdivided all Ss into four subgroups on the basis of severity (17-item HRSD) and compared these eight variables. All Ss were drug-free and diagnosed with SADS/RDC as endogenous or nonendogenous.

We found that the most severe depressives had significantly higher DST profile values regardless of whether they had been diagnosed as "endogenous" or "nonendogenous" and that severe "nonendogenous" Ss had DST values that were equivalent or higher than those from mild "endogenous" patients. These data provide neuroendocrine validation for the historical impression that "endogeneity" may reflect a severity continuum rather than being a separate and unique subgroup, and suggest that severity measures should receive higher priority in future *DSM* revision.

NR175 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

THE DST IN THE LEARNED HELPLESSNESS PARADIGM

John L. Haracz, M.D., Brain Research Inst., 73-346, UCLA Med School, Los Angeles, CA 90024; Thomas Minor, Ph.D., Jeffery N. Wilkins, M.D., Emery G. Zimmermann, M.D.

Summary

One of the most widely replicated findings in biological psychiatry is that of cortisol resistance to dexamethasone (DEX) suppression in about half of depressed patients. Recently, elevated ratings of anxiety and agitation were associated significantly with positive DEX suppression tests (DSTs) in multiple medical centers in the NIMH collaborative study on depression (Kocsis et al., Am J Psychiatry 142:1291, 1985) and in an independent study at UCLA (Rubin, lecture presentation, Dec., 1985). These findings suggest an important role for psychological stress in the generation of DEX nonsuppression (Kocsis et al., 1985). We sought further evidence for such a role in the learned helplessness model of depression.

Adult male rats received 80 escapable tailshocks, 80 inescapable shocks, or no shock. Yoked pairs were shocked such that the rats received identical physical stress with the inescapably-shocked rats experiencing an additional psychological stress associated with a lack of control over the stressor. One of us (T.M.) found that this shock schedule induces typical "learned-helplessness" behavioral depression in the inescapably-shocked rats. Compared to nonshocked controls, both groups of shocked rats showed resistance to suppression of plasma corticosterone (CS) by DEX (100μg/kg, s.c. at 2 hr before shock). However post-DEX CS was significantly higher in the inescapably-shocked rats ($p < 0.01$), thus supporting a role for psychological stress in DEX nonsuppression of CS. These results are consistent with the early concept of pituitary-adrenal overactivity in association with psychological-defense breakdown (Sachar, Arch Gen Psychiatry 17:554, 1967). Prolactin data will be presented.

NR176 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

PLASMA DEXAMETHASONE LEVEL AND CORTISOL RESPONSE

Peter E. Stokes, M.D., NYH/CMC, 525 E. 68th St., New York, NY 10021; Peter M. Stoll, B.A., Betty J. Lasley, Ph.D., Carolyn R. Sikes, M.A.

Summary

Variability in diagnostic and laboratory assessment has been proposed to account for the limited diagnostic specificity of the dexamethasone suppression test in psychiatric patients. A few studies have examined the relation of plasma dexamethasone (DEX) level to cortisol response. Data in patients with Cushing's syndrome suggest that variability in DEX clearance may contribute to variability in DEX suppression of cortisol. To pursue this issue in psychiatric patients, we examined the relation between 9 a.m. plasma cortisol and DEX levels in 29 depressed patients who had taken 1 mg DEX at 11 p.m. There were 14 suppressors and 15 non-suppressors (9 a.m. cortisol $> 5\mu$g/dl). Radioimmunoassayed plasma DEX level varied considerably (range 32-313 ng/dl) but was higher than in 20 pre-dex plasma samples (range 1-12 ng/dl). Plasma DEX level correlated negatively with post-DEX cortisol level ($r = -.61$, $p < .001$) and was significantly lower in nonsuppressors than in suppressors ($t = 4.52$, $p < .0001$). A chi square analysis of plasma cortisol suppression/nonsuppression status versus high/low plasma DEX (cutoff 114 ng/dl) was significant ($X^2 = 18.54$, $p < .001$). Fifteen of 15 nonsuppressors had plasma DEX levels lower than 114 ng/dl versus only 2/14 suppressors, indicating that plasma DEX level accurately predicted cortisol response. These results suggest that individual differences in gastrointestinal absorption and/or hepatic metabolism of DEX strongly affect cortisol suppression by DEX. Further studies are underway to clarify this and other issues raised by these results.

NR177 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

SERUM DEXAMETHASONE LEVELS AND THE DST

Martin T. Lowy, Ph.D., Dept. of Psychiatry, Case Western Reserve, Cleveland, OH 44106; Anthony T. Reder, M.D., Jack P. Antel, M.D., Herbert Y. Meltzer, M.D.

Summary

Serum dexamethasone (DEX) levels were measured in 33 psychiatric patients and 12 normal controls during a standard overnight 1 mg DST and related to various biological variables including the effect of DEX on PHA and Con A induced lymphocyte proliferation. A wide range of DEX values were observed at both 8 a.m. and 4 p.m. Suppressors (N = 33) had significantly higher serum DEX levels compared to nonsuppressors (N = 12) at both 8 a.m. and 4 p.m. There was no difference between males and females nor between unhospitalized normal controls and hospitalized psychiatric patients in 8 a.m. or 4 p.m. serum DEX levels.

Significant negative correlations were observed between serum DEX levels and various post-DST cortisol values. In contrast, no correlations were observed with basal cortisol values. The PHA response, but not the Con A response, was negatively correlated with 8 a.m. or 4 p.m. serum DEX levels. No correlations between 8 a.m. or 4 p.m. DEX levels and age or body weight were observed.

Alterations in serum DEX levels appear to be a critical factor modifying the biological effects of administered DEX. However, the factor(s) responsible for modifying serum DEX levels remain to be elucidated.

NR178 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

DESIPRAMINE DOES NOT CAUSE WEIGHT GAIN

Stephen L. Stern, M.D., Dept. of Psychiatry, Ohio State Univ., 473 W. 12th Ave., Columbus, OH 43210; Thomas B. Cooper, M.A., Mark Johnson, Ph.D., Bruce Jones, M.D., Linda Nelson, Ph.D.

Summary

Weight gain, a common side effect of antidepressant drug therapy, is frequently cited by patients as a reason for discontinuing their medication. Weight gain can also exacerbate physical illnesses such as hypertension and diabetes. We report here a small but statistically significant mean weight loss in a group of 31 outpatients with primary major depression who were treated with desipramine (DMI) for five weeks.

There were 17 female and 14 male patients, with an age range of 20 to 51 years. The mean (± SD) daily dosage during the final four weeks was 162.9 (48.2) mg. Plasma samples drawn weekly 14 hours after the last dose were assayed for DMI and 2-hydroxy DMI by high-performance liquid chromatography.

The patient's mean (± SD) weight decreased during the course of the five weeks from 171.8 (35.5) to 169.6 (34.5) lb ($F = 9.38$; $df = 2,60$; $p < .01$). Twenty-four patients lost weight, while six gained weight and one had no weight change. There was no significant correlation between weight change and sex, dosage, clinical improvement, history of weight loss associated with the current depression, or mean steady-state DMI or 2-hydroxy DMI plasma levels.

These findings suggest that DMI may be indicated for many depressed patients in whom weight gain is not desired. Characteristics of DMI that may explain this lack of weight gain will be discussed.

NR179 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

ANTIDEPRESSANT PLASMA LEVELS AND DOSE PREDICTION

Sudhakar Madakasira, M.D., Dept. of Psychiatric Med., ECU School of Medicine, Greenville, NC 27834; David A. Ames, M.D., Prabhaker G. Khazanie, Ph.D.

Summary

Prediction of therapeutic dosage of nortriptyline utilizing a plasma level obtained after the first dose of the drug is a recent approach, also termed "Single-Dose Single-Point" (SDSP) method. It is not known whether the SDSP approach is clinically more advantageous than the traditional dose adjustment. To answer this, an ongoing study was designed in which outpatients diagnosed with major depression as per *DSM-III* criteria, were randomly assigned to treatment with nortriptyline by SDSP method or by traditional method. For the SDSP group, the dosage was predicted utilizing a 24-hour plasma level and for the traditional (T) group, dosage adjustment was entirely clinical and without the knowledge of plasma levels. Response was indicated by at least 50% improvement on the Hamilton Depression Scale.

Out of 20 patients who have completed the protocol, 11 (55%) were in the SDSP group and 9 (45%) in the T-group. The two groups did not differ significantly in age, mean dose, or mean plasma levels. Steady state plasma levels were in therapeutic range in 8 patients (73%) of SDSP group and 8 patients (89%) of T-group. All patients responded except for one in T-group, his plasma level remaining therapeutic however. The SDSP group had shorter duration of dose adjustment compared to the T-group ($\bar{x} = 6.2 \pm 3.4$ days vs. $\bar{x} = 11.7 \pm 8.5, t = 1.85, p > 0.05$) but not in the duration of onset of response ($\bar{x} = 14.6$ days vs. 14.9 days). Although the SDSP method appears to hasten the process of dose adjustment, our preliminary results do not suggest any clinical advantage of the SDSP approach over the traditional approach.

NR180 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

TRICYCLICS AND CARDIAC CONDUCTION DISEASE

Steven P. Roose, M.D., 72 W. 168th St., New York, NY 10032; Alexander H. Glassman, M.D., Elsa G. V. Giardina, M.D., B. Timothy Walsh, M.D., Sally Woodring, R.N., J. Thomas Bigger, Jr., M.D.

Summary

The observation that fatalities from tricyclic antidepressant (TCA) overdose are associated with heart block and/or arrhythmias has led to a longstanding concern about the cardiovascular effects of TCA's. Studies in patients without heart disease have established that although imipramine and nortriptyline prolong PR and QRS intervals, this is generally not of clinical significance. And, contrary to expectations raised by the overdose data, both drugs have been shown to have significant antiarrhythmic activity. Thus, in patients free from cardiovascular disease, the TCA's appear relatively safe. However, it is unclear whether these drugs are also safe in patients with heart disease. This prospective study compared the risk of cardiovascular complication at therapeutic plasma concentration of TCA's in 151 depressed patients with normal ECG's and 41 patients with 1° AV and/or bundle branch block. The frequency of 2nd degree AV block, a potentially fatal condition, was significantly greater ($p < .05$ by Fisher's exact test) in patients with pre-existing bundle branch block (9%) compared to patients with normal ECGS (0.7%).

Orthostatic hypotension (OH) was the most frequent cardiovascular complication for all patients treated with imipramine. Imipramine-induced OH was significantly greater in patients with conduction disease ($X^2 = 12.8, p < .001$) than in similar age patients free of cardiac disease. Nortriptyline caused negligible orthostatic problems compared to imipramine even in patients with conduction disease ($X^2 = 3.9, p < .05$).

If a TCA is necessary in a depressed patient with bundle branch block, measures of cardiac conduction (ECG's, 24-hour continuous ECG recordings), blood pressure recordings, and tricyclic plasma concentrations ought to be followed so that the antidepressant treatment is safe as well as effective.

NR181 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

NORTRIPTYLINE IN PATIENTS WITH HEART FAILURE

Steven P. Roose, M.D., 72 W. 168th St., New York, NY 10032; Alexander H. Glassman, M.D., Elsa G. V. Giardina, M.D., B. Timothy Walsh, M.D., Sally Woodring, R.N., Lynne L. Johnson, M.D.

Summary

Previous studies of the effect of tricyclic antidepressants on left ventricular function (LVF) in depressed patients with moderate to severe ventricular impairment, have focused primarily on imipramine. Though imipramine had no effect on ejection fraction as measured by first pass radionuclide angiography, the treatment could not be tolerated by 50% of patients because of intolerable drug-induced orthostatic hypotension (OH). Nortriptyline is an effective antidepressant that, in depressed patients without heart disease, causes significantly less OH than imipramine. To see if this advantage could be safely extended to patients with congestive failure, we measured the effect of nortriptyline on ejection fraction and blood pressure in 21 depressed patients with impaired LVF. Mean baseline ejection fraction was 33.5% (± 12.3%) and at therapeutic plasma concentration of nortriptyline, 32.3% (± 12.5%). Neither ejection fraction nor peak systolic pressure (ESV index), an index that is relatively independent of ventricular loading conditions, was affected by nortriptyline. Only 1 of 21 patients (5%) developed OH.

Thus, with the important exception of its potential to cause increasing degrees of AV block in patients with bundle branch block, nortriptyline would seem to be a relatively safe drug in the treatment of depressed patients with heart disease.

NR182 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

TCA ALONE CAN BE EFFECTIVE IN PSYCHOTIC DEPRESSION

Henry A. Nasrallah, M.D., Dept of Psychiatry, Ohio State Univ., Columbus, OH 43210; William H. Coryell, M.D., Mona McCalley-Whitters, M.A., Mark Zimmerman, M.D.

Summary

Several reports in the literature suggest that the combination of a tricyclic and a neuroleptic is more effective than the tricyclic or the nueroleptic alone in the treatment of psychotic depression. We conducted a double-blind comparison study of 26 consenting patients fulfilling *DSM-III* criteria for major depression with psychotic features. The patients were randomly assigned to amitriptyline (up to 300 mg/day) perphenazine (up to 48 mg/day) or the combination. Patients were evaluated at baseline and weekly for 6 weeks using the Hamilton Rating Scale, Beck Depression Inventory and the Clinical Global Impression.

There were no differences in the response rates of the patients in all three groups. Of particular interest is that with amitriptyline alone, depressive symptoms usually remitted within four weeks, while the psychotic features, even incongruent such as paranoid delusions, required the full six weeks to remit in the responders.

The data suggest that high dose amitriptyline for at least six weeks may be as effective in psychotic depression as the combination of amitriptyline/perphenazine, and with less risk for potential side effects, both immediate or delayed, such as tardive dyskinesia.

NR183 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

FAILURE OF T3 TO POTENTIATE TRICYCLIC RESPONSE

Michael J. Gitlin, M.D., UCLA NPI, 760 Westwood Plaza, Box 18, Los Angeles, CA 90024; Herbert Weiner, M.D., Lynn Fairbanks, Ph.D.

Summary

L-triiodothyronine has been recommended for use as an adjunctive therapy in treatment resistant depressions since the first evidence of its efficacy in 1968. However, among the ten prior papers examining this topic, only one used a doubleblind methodology. Because of this lack of documented efficacy, we treated 16 imipramine resistant outpatients (9 men, 7 women) with adjunctive T_3 using a doubleblind crossover design. All patients met criteria for RDC major depressive episode, unipolar subtype, and had Hamilton depression scores of $\geqq$ 16 (mean score = 23.1 ± 4.0) prior to four weeks of imipramine treatment. No patient was currently taking any thyroid preparation; baseline T_4 levels were normal for all patients. After four weeks of imipramine with a mean daily dose of 206 ± 54 mg and a plasma level of 220 ± 132 ng/dl, all patients had shown < 50% improvement in Hamilton scores (mean score = 19.6 ± 6.3) and no more than minimal improvement using global improvement scores. Patients were then treated with T_3 25μg and placebo for two weeks each in a doubleblind random order crossover design. Overall, there was no difference between T_3 and placebo in efficacy. Neither a drug effect nor a drug × week effect was seen. A strong time effect was seen, with patients showing a significant improvement over the four weeks of the study regardless of the drug condition or order of administration. No side effects were observed. These findings, their implications and the effect of T_3 on thyroid parameters will be discussed.

NR184 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

THE EFFECT OF ECT ON ENDORPHINS IN DEPRESSION

A. Missagh Ghadirian, M.D., 6875 Lasalle Blvd., Verdun PQ O, Canada H4H 1R3; Christina Gianoulakis, Ph.D., N.P. Vasavan Nair, M.D.

Summary

Pituitary opioid peptides have been implicated in the pathogenesis and treatment of psychiatric diseases. Administration of electroconvulsive treatment (ECT) in depression has been shown to increase the plasma levels of β-endorphin-like immunoreactivity (β-EPLIR) at 15 minutes after ECT. Since the previous studies did not explore the complete time course of the endorphin response at various stages of the ECT, the present study was undertaken with the objective to estimate the plasma β-ELPIR level at various stages of pre- and post-ECT (before atropine, before Na barbital, immediately before ECT and at 15, 60 and 120 minutes after ECT). Six depressed patients diagnosed according to *DSM-III* and rated with Hamilton Depression Scale were treated with ECT. The time course study of the endorphin response to ECT was carried out at the first and sixth ECT. Results confirmed previous reports suggesting a significant rise of plasma β-ELPIR levels at 15 minutes after ECT. However, we found this β-ELPIR increase transient approaching the pre-ECT levels one hour after ECT. Furthermore, the plasma β-ELPIR content immediately before ECT was higher than that of either before atropine or two hours after ECT. This increase was probably stress related in anticipation of ECT. A similar increase in plasma β-ELPIR was observed in a patient undergoing full preparation for ECT without receiving electric current. Clinical implications of the results will be discussed.

NR185 WITHDRAWN

NR186 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

NEUROENDOCRINE RESPONSES TO ECT

Richard D. Weiner, M.D., Psychiatry Service (116A), Durham VAMC, Durham, NC 27705; C. Edward Coffey, M.D., James C. Ritchie, M.P.H., Jonathan R. T. Davidson, M.B., K. Ranga Rama Krishnan, M.B.

Summary

Electrically induced seizures are associated with numerous, predominately transient physiologic, chemical, and endrocrinologic consequences. Ictal changes in plasma prolactin, ACTH, and cortisol were measured during the first or second and sixth or seventh treatments in a group of 19 subjects receiving ECT for treatment of an endogenous depressive episode. All subjects were also involved in a protocol randomly assigning them to unilateral nondominant versus bilateral electrode placement and to brief pulse versus sine wave stimuli. Consistent robust rises in all three measures were observed regardless of ECT type (mean peak elevations over baseline: prolactin, 34 ng/ml; ACTH, 25 fm/mol, cortisol, 14 μg/dl). The data were further investigated in terms of ECT modality and relationship to seizure duration. In effect, all of these factors appear to be involved, at least in terms of the degree of prolactin response, though inter- and even intra-individual variabilities were high. These findings will be discussed in terms of recent evidence suggesting that prolactin serves as a marker for extent of generalization of seizure activity.
Supported by NIMH grants MH 30723 and MH 40159, and the Veterans Administration.

NR187 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

UNILATERAL VERSUS BILATERAL ECT IN MELANCHOLIA

Rajiv Tandon, M.D., Dept of Psychiatry, Univ. of Mich. Hospital, 1405 E. Ann St., Box 011, Ann Arbor, MI 48109; Leon Grunhaus, M.D., Tina Krugler, John F. Greden, M.D.

Summary

There is ongoing controversy as to whether unilateral nondominant electroconvulsive therapy (ECT) is clinically as effective as the traditional bilateral ECT in the treatment of endogenous depression. To study this issue, we compared their therapeutic efficacy in 46 drug-free patients with endogenous depression who received bilateral ($n = 30$) or unilateral ($n = 16$) ECT. Seizure length was monitored and when seizures were less than 25 seconds, ECT was readministered immediately.

After 5 treatments, blind assessment on the Hamilton Rating Scale for Depression showed a 53% improvement in the bilateral group as compared to a 19% improvement in the unilateral group. The unilateral group received more total treatments (mean = 11.5) than the bilateral group (mean = 7.6). At the conclusion of all ECT treatments, 85% of the bilateral group were clinically improved as compared to 40% of the unilateral group. Normalization of the dexamethasone suppression test was more rapid in the bilateral group. There were more missed seizures requiring restimulation with unilateral ECT. Even when seizure length was equivalent between unilateral and bilateral groups, bilateral ECT was found to be significantly more effective and patients receiving bilateral ECT recovered more rapidly than those receiving unilateral ECT and required significantly fewer treatments. These results were independent of age, sex or severity of illness.

Although unilateral ECT may be associated with fewer side-effects, these data suggest that bilateral treatments are more effective.

NR188 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

CARROLL AND HAMILTON RATING SCALES FOR DEPRESSION

Rajiv Tandon, M.D., Dept of Psychiatry, Univ. of Mich. Hospital, 1405 E. Ann St., Box 011, Ann Arbor, MI 48109; Pamela Flegel, B.S., John F. Greden, M.D.

Summary

The Carroll Rating Scale for Depression (CRSD) is a direct, self-rated adaptation of the original Hamilton Rating Scale for Depression (HRSD). The 52 individual CRSD items closely match the information content of the 17 scales from the HRSD. The two scales, however, have not been adequately compared to determine if the CRSD has acceptable reliability, validity, transferability and sensitivity to change in the assessment of severity of depression. We studied 1460 concurrent CRSD and HRSD weekly ratings obtained from 133 inpatients with major depressive disorder (SADS/RDC). The CRSD and HRSD total scores correlated highly ($r = +0.82, p < .001$) and matching items of the two scales correlated significantly ($p < .001$) in 16 of 17 items compared. The internal consistency of the CRSD was similar to that of the HRSD. Factor analyses of the two scales revealed similar factor loadings for the respective first and second factors. The CRSD correlated very significantly ($p < .001$) with four validating depression rating measures in the assessment of both baseline severity and change of severity during treatment. High CRSD scores predicted endogeneity (SADS/RDC) and DST nonsuppression as well as high HRSD scores. High correlations ($r = +0.70$) between CRSD and HRSD aggregate scores also were found in 127 non-MDD inpatients representing a range of psychiatric diagnoses. These data suggest that the self-administered CRSD is a credible alternative to the HRSD in the assessment of severity of depression. The CRSD has the advantages of being administered inexpensively and conveniently in clinical and research settings, and of being available for use in home settings.

NR189 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

BIOCHEMICAL EFFECTS OF ECT VERSUS ANTIDEPRESSANT DRUGS

Matthew V. Rudorfer, M.D., NIMH/LCS, Bldg 10 Room 2D46, 9000 Rockville Pike, Bethesda, MD 20892; John K. Hsiao, M.D., Emile D. Risby, M.D., Markku Linnoila, M.D., William Z. Potter, M.D.

Summary

Electroconvulsive therapy (ECT) and a variety of antidepressant drugs all reduce norepinephrine (NE) turnover in patients. In rat cortex, a common noradrenergic effect (beta receptor down regulation) is contrasted with a disparity in the rotonergic (5HT) system: antidepressant drugs reduce but electroconvulsive stimulation increases $5HT_2$ receptors. In order to address this issue in humans, lumbar punctures were performed before and one week following a course of ECT in depressed patients completely medication-free for one month. All patients showed good clinical response. In our first 4 patients ECT produced no effect on cerebrospinal fluid (CSF) MHPG (43.5 ± 2.8 pmol/ml pre vs 42.7 ± 5.4 post), while increasing 5-HIAA (90.2 ± 8.2) by 28% to 115.7 ± 19.1 and HVA by 40% (157.8 ± 32.5 to 221.0 ± 46.0). These data are in sharp contrast to our findings that several types of biochemically dissimilar antidepressants decrease CSF MPHG and 5-HIAA in all patients without consistently altering HVA. Moreover, one of the ECT patients had earlier undergone an unsuccessful trial of desipramine, during which all measured CSF monoamine metabolites fell: MHPG by 31%, 5-HIAA by 18%, and HVA by 19%. In the group, despite the lack of ECT effect on CSF MHPG, changes in plasma NE reactivity to an orthostatic challenge were observed, with a reduction in the initially exaggerated positional NE change by 44% following completion of ECT. These findings suggest that in humans, as in rats, ECT and antidepressant drugs produce contrasting effects on different transmitter systems. Further probing of the 5-HT system may shed light on the mechanism(s) of action of ECT. Prolactin responses to a 5-HT challenge before and after ECT will be presented.

NR190 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

ECT IN SUBCORTICAL ARTERIOSCLEROTIC ENCEPHALOPATHY

C. Edward Coffey, M.D., Duke University Med Ctr, P.O. Box 3920, Durham, NC 27710; Phillip Hinkle, M.D., Richard D. Weiner, M.D., Charles B. Nemeroff, M.D., K. Ranga Rama Krishnan, M.B., Indu Varia, M.D., Burton P. Drayer, M.D.

Summary

Subcortical arteriosclerotic encephalopathy (SAE) is a form of cerebrovascular disease characterized pathologically by necrosis and demyelination of the subcortical white matter. Recent brain imaging studies indicate that SAE is common, especially in the elderly. Clinically, SAE may be associated with subacute motor deficits, dementia or affective disorder. Safe and effective therapy for affective disturbances in patients with SAE has not been defined however.

We will describe a series of patients with depression unresponsive to drug therapy who were found to have SAE on brain CT and/or magnetic resonance (MR) imaging. The leukomalacia was more apparent and estensive on MR than CR, and was characterized by periventricular long-T2 lesions that caused high MR intensity on spin echo images. All of the patients received ECT with a good clincial response and, in general, the therapy was well tolerated. The neuroradiology and pathophysiology of SAE will be reviewed and the treatment of affective disturbances in patients with SAE discussed.

NR191 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

AUGMENTATION OF ECT SEIZURES WITH CAFFEINE

C. Edward Coffey, M.D., Duke University Med Ctr, P.O. Box 3920, Durham, NC 27710; Phillip Hinkle, M.D., Richard D. Weiner, M.D., Martha Cress, R.N.

Summary

In electroconvulsive therapy (ECT), a seizure with a minimum duration of 30 sec. is considered essential for clinical efficacy. Frequently during a course of ECT however, seizure duration may shorten to less than 30 sec. The typical clinical approach to lengthening the seizure is to increase the electrical energy of the ECT stimulus. The higher stimulus energy may produce more CNS toxicity however, and is not an option when the ECT device is already at maximal settings.

We recently reported that pretreatment with caffeine IV produced therapeutic seizures in patients whose seizures had been too short despite maximal settings on 3 different ECT devices. These findings raised the possibility that caffeine could be used routinely to avoid any increase in stimulus intensity during a course of ECT. In a series of 8 drug-free depressed inpatients with declining seizure times, pretreatment with caffeine IV lengthened the seizures and obviated the need for any further increase in ECT stimulus intensity. Indeed, in 2 cases caffeine actually permitted a lowering of the stimulus energy. Placebo had no effect on seizure duration. Caffeine was well tolerated, even in patients with cardiovascular disease. Possible neurobiologic mechanisms to explain caffeine's effect will be discussed.

NR192 **Wednesday, May 14, 12:00 noon - 1:45 p.m.**

EEG IMAGING IN PSYCHIATRY: ARTIFACT CONSIDERATIONS

Michael W. Torrello, Ph.D., Dept of Psychiatry, OSU Medical School, 473 W. 12th Ave., Columbus, OH 43210; Henry A. Nasrallah, M.D.

Summary

The emerging technology of topographic mapping of EEG has many potential applications in psychiatry. Topographic maps of spectral and evoked potential data have provided new insights into the biological basis of psychopathology. However, caution must be exercised in the identification and reduction of extra-cerebral signal sources (e.g., eye blink, eye movement, etc.) to be assured that the topographic images of electrical activity measured from scalp electrodes emanate only from brain activity. Artifacts are of special concern in studies using subjects with psychiatric or neurological problems.

In order to begin to understand the influence of artifacts on topographic maps of EEG we collected EEG data from normal subjects, who sat quietly and fixated their eyes forward. Different topographic artifact signature maps were constructed when the subjects blinked lightly, moved their eyes laterally, moved their eyes vertically, gently raised their eyebrows or tightened their jaw muscles. These artifacts, when topographically displayed along with the EEG, represented a potentially serious confounding factor interferring with the assessment of brain electrical activity.

The conclusions are that artifacts must be closely monitored, using dedicated electrodes, and minimized during the course of testing and eliminated during computer analyses. Using this strategy, artifact-free topographic maps of brain electrical activity can be produced leading to a more accurate understanding of electrophysiological abnormalities in psychopathology.

NR193 **Thursday, May 15, 9:00 a.m.**

ANIMAL MODELS OF SENSORY GATING AND SCHIZOPHRENIA

David L. Braff, M.D., Dept. of Psychiatry, M-003, USCD, La Jolla, CA 92093; Neal Swerdlow, M.D., Mark A. Geyer, Ph.D., George Koob, Ph.D.

Summary

We have previously found that rats with overactive mesolimbic dopamine show a loss of sensory gating functions reflected by a decrement of prepulse inhibition (PPI) of the acoustic startle response (ASR). This loss strikingly paralells our findings in schizophrenic patients. Dopamine overactivity in rats was induced by 6-OHDA lesions of nucleus accumbens followed by systemic apomorphine challenge. Lesions were confirmed by regional biochemical analyses of dopamine metabolites. The loss of PPI in rats with mesolimbic dopamine overactivity and schizophrenics is important in that: 1) it occurs in the prestimulation conditions of 60 and 120 msecs, a time base thought to be important in information processing deficits observed in schizophrenics, and 2) it is temporally similar to the sensory gating deficits observed in evoked potential paradigms. We are able to confirm that supersensitive mesolimbic dopamine stimulation following treatment with 0.1 mg/kg apomorphine is more effective in inducing the sensory gating disturbance than dopamine manipulations in the striatum or frontal cortex.

We replicated our findings of the loss of PPI of the ASR with mesolimbic dopamine overactivity and report on the normalizing effects of antipsychotics (haloperidol and thioridazine). These results will be discussed as they clarify the relationship of dopamine overactivity, information processing deficits, sensory gating dysfunction, and schizophrenia.

References:

[1]Braff DL, Stone C, Callaway E, et al: Prestimulus effects on human startle reflex in normals and schizophrenics. Psychophysiology 15:339-343, 1978.

[2]Swerdlow NR, Braff DL, Geyer MA, et al: Central dopamine hyperactivity in rats mimics abnormal acoustic startle response in schizophrenics. Biol Psychiatry 21:23-33, 1986.

NR194 **Thursday, May 15, 9:15 a.m.**

EVOKED POTENTIAL AND BRAIN METABOLISM CORRELATIONS

Henry H. Holcomb, M.D., Nuclear Medicine, Johns Hopkins Univ., 615 N. Wolfe St., Baltimore, MD 21205; William E. Semple, Ph.D., Monte S. Buchsbaum, M.D., Robert M. Cohen, M.D., Lynn E. DeLisi, M.D., Anna C. King.

Summary

Schizophrenia is marked by multiple perceptual and cognitive performance deficits. In our research with schizophrenic (sczs) patients we have described behavioral, electrophysiological, and metabolic (regional cerebral glucose metabolism [RCMGluc measured with positron emission tomography, PET]) abnormalities which parallel somatosensory confusion. An inability to consistently indicate which levels of cutaneous, electrical stimulation are painful, is this condition's principal clinical manifestation. We now report the results of a correlational analysis designed to determine the relationship between somatosensory evoked potential (SEP) amplitude (16 leads, 3 latencies, 4 stimulus intensities), and RCMGluc in normal volunteers (nmls, n = 21) and unmedicated patients (szcs, n = 17). In conjunction with repetitive, aversive, cutaneous, electrical stimulation (30 min duration), SEP's were measured from 16 leads placed on the left side of the head. About 20 seconds after initiating stimulation 18F-2deoxyglucose (FDG) was administered. PET imaging commenced about 50 min. after FDG injection. Correlations between SEP and LCGU differed markedly in the two groups: 1) Whereas nmls exhibited 7 fold more correlations at the $p < .01$ level than predicted by chance alone, sczs had fewer than chance would predict; 2) One class of SEP (P200,23 milliamps stimulation, a noxious level) provided all $p < .01$ correlations in the normal group; 3) Only SEP acquired during the first 4 1/2 minutes of stimulation provided $p < 0.01$ correlations. This dramatic difference suggests a fundamental disturbance in this group's temporal/spatial brain dynamics.

References:

[1]Buchsbaum, M.S., DeLisi, L.E., Holcomb, H.H., et al. (1984). Anteroposterior gradients in cerebral glucose use in schizophrenia and affective disorders, Arch. Gen. Psychiatry 41:1159-1166.

[2]DeLisi, L.E., Holcomb, H.H., Cohen, R.M., et al. (1985). Positron emission tomography in schizophrenic patients with and without nueroleptic medication, J. Cereb. Blood Flow and Metabol. 5:201-206.

NR195 **Thursday, May 15, 9:30 a.m.**

UNDERRECOGNITION OF NEUROLEPTIC MOVEMENT DISORDER

Peter J. Weiden, M.D., Payne Whitney Clinic, 525 E. 68th St., New York NY 10021; Gretchen Haas, Ph.D., J. John Mann, M.D., Allen J. Frances, M.D., Marlin Mattson, M.D.

Summary

Goals: This study investigates 1) the relative accuracy of clinical assessment and diagnoses of neuroleptic-induced extrapyramidal syndromes (EPS) compared to research diagnosis in acutely psychotic inpatients 2) clinical features of underrecognized EPS. Methods: A battery of structured standard ratings for Parkinsonism, akinesia, akathisia, dystonia and tardive dyskinesia were adminstered to 58 acutely psychotic inpatients by a researcher blind to clinician EPS diagnosis and management. Clinician EPS assessments were determined by chart review after discharge. Research EPS ratings were compared to clinician diagnoses. Clinical errors were classified as: nondiagnosis, failure to recognize the degree of EPS severity, or delay in diagnosis. Results: EPS diagnoses made by research criteria were missed clinically in 9 out of 10 patients with tardive dyskinesia ($p < .005$), 12 out of 29 patients with Parksinsonism ($p < .005$), 9 out of 23 patients with akinesia ($p < .005$), 20 out of 27 patients with akathisia ($p < .0001$) and 3 out of 8 patients with acute dystonias (n.s.). All clinical errors were in the direction of underdiagnosis. EPS diagnoses that were made clinically were always present on research ratings. The potential reasons for these differences in diagnostic sensitivity will be discussed. Significance: There is a high rate of clinician underrecognition of all EPS sub-types. This study documents the value of the use of systematic EPS assessments by clinicians to enhance diagnostic sensitivity to EPS symptoms and thereby reduce morbidity from these syndromes.

References:

[1]Asnis, GM, Leopold, MA, Duvoisin, RC, Schwartz, AH: A survey of tardive dyskinesia in psychiatric outpatients. Am J. Psychiatry 134:1367-1370, 1977.

[2]Rosen, MA, Mukherjee, S, Olarte, S, et al: Perception of tardive dyskinesia in outpatients receiving maintenance neuroleptics. Am J Psychiatry 139:372-373, 1981.

NR196 **Thursday, May 15, 9:45 a.m.**

TD PREVALENCE: RESEARCH AND CLINICAL DIFFERENCES

Thomas E. Hansen, M.D., Portland VAMC 116 A-P, P.O. Box 1034, Portland OR 97207; Daniel E. Casey, M.D., Ronald M. Weigel, Ph.D.

Summary

Researchers report tardive dyskinesia (TD) prevalence rates of about 25% (above 50% in special populations). These rates may seem high to practicing psychiatrists. In our study we compare researcher determined TD prevalence with recognition of TD by clinicians on an acute treatment Veterans Administration Medical Center ward. We also examine the associations of age, diagnosis, and parkinsonism with TD. Of 250 patients admitted during six months, all patients with prior neuroleptic exposure ($n = 103$) were evaluated for TD and parkinsonism with the AIMS and Sct. Hans scales (i.e., researcher determined cases). Charts were reviewed to determine whether TD was noted in the admitting physical or as a diagnosis in the discharge summary (i.e., clinician determined cases). Researchers diagnosed TD in 47.6% of patients when a single mild score was used to define a case, and 27.2% of patients if two mild or one moderate score was required. Clinicians recorded TD on admission in 12 patients (11.7%), and in discharge summaries for 8 cases (7.8%), with 5 patients included in both groups. The clinician prevalence rates were significantly less than the researchers' in all comparisons ($p < 0.001$). Researcher determined TD was more prevalent in older patients and those with psychotic diagnoses. No association with affective disorders was found. Age, diagnosis, and parkinsonism were not correlated with the discrepancy between researchers and clinicians. Logistic regression did reveal a positive correlation ($p = 0.053$) between researcher determined severity and clinician recognition of cases. We discuss the implications of and possible explanations for the large discrepancy in prevalence rates found by researchers and clinicians. Recommendations for evaluating patients and reading the literature are made.

References:

[1] Kane JM, Smith JM: Tardive dyskinesia: prevalence and risk factors, 1959 to 1979. Arch Gen Psychiatry 39:473-481, 1982

[2] Hansen TE, Casey DE, Vollmer WM: There is an epidemic of tardive dyskinesia? Proceedings of the American Psychiatric Association Annual Meeting, 43A:85-86, 1985.

NR197 **Thursday, May 15, 10:00 a.m.**

RUBIDIUM AND NEUROLEPTIC DOSAGE REDUCTION

Guy Chouinard, M.D., Allan Memorial Inst., 1025 Pine Ave., Montreal PQ O, Canada H3A 1A1; Lawrence Annable, B.Sc., Pierre Mercier, Ph.D., Luc Turnier, M.D.

Summary

Rubidium, like lithium, is an alkaline metal of group 1A in the periodic table. We arried out three controlled clinical trials of RbCl which suggest that this substance may have a beneficial effect when added to the maintenance neuroleptic medication of chronic schizophrenic patients. We report the results of a fourth double-blind controlled study of RbCl in which the neuroleptic dosage was reduced gradually by 50%. Method. Thirty-two chronic hospitalized schizophrenic patients were randomly assigned to a monthly dose of 1 g RbCl or Rb placebo added to their regular neuroleptic medication. Patients underwent a staged withdrawal of 50% of neuroleptic and antiparkinsonian dosage over a 9-month period. Results. During neuroleptic withdrawal Rb-treated patients needed less ($p = .01$) supplementary neuroleptics to control psychotic agitation and less ($p < .05$) antiparkinsonian medication than placebo treated patients. Female patients treated with Rb ended the trial with a lower mean score for schizophrenic symptoms ($p = .08$) and parkinsonian ($p < .05$) than those treated with placebo. No change in tardive dyskinesia was observed. Discussion. Rubidium permitted 50% neuroleptic reduction without relapse. No increase in tardive dyskinesia was observed despite the neuroleptic reduction which has been found to uncover covert dyskinesias. Rubidium may have a therapeutic action on schizophrenia and extrapyramidal symptoms by slowly increasing dopamine turnover.

References:

[1] Chouinard G, Annable L: The effect of rubidium in schizophrenia. Commun Psychopharmacol 1:373-383, 1977.

[2] Chouinard G: Rubidium in the treatment of schizophrenia. New Research Abstracts of the 136th Annual Meeting of the American Psychiatric Association, No. NR52, 1983.

NR198 **Thursday, May 15, 10:15 a.m.**

ANDROGYNY IN SCHIZOPHRENIA: MRI EVIDENCE

Henry A. Nasrallah, M.D., Dept of Psychiatry, OSU, 473 W. 12th Ave., Columbus OH 43210; Nancy C. Andreasen, M.D., Jeffrey A. Coffman, M.D., Stephen C. Olson, M.D., Val D. Dunn, M.D., James C. Ehrhardt, Ph.D.

Summary

Gender-related differences have been described in the human brain structure and function. A larger splenium in females vs. males was reported in a post mortem study (Delacoste-Utamsing et al., Science 1982), a finding consistent with bihemispheric representation of visuo-spatial functions in females, requiring a larger number of interhemispheric fibers in the visual cortex region of the corpus callosum. We conducted a magnetic resonance imaging (MRI) study of 41 control and 38 schizophrenic subjects. Using the midsagittal view, the area of the posterior quartile of the corpus callosum was measured and its ratio (x 100) to the total callosal area was considered the splenial proportion. In control subjects, right handed females had a significantly larger splenium than males (36.3% vs. 33.45%), thus confirming the post mortem study. However, schizophrenic females tended to have a smaller mean splenial proportion than schizophrenic males (32.8% vs. 34.4%) and significantly smaller than control females. Male schizophrenics were found to be bimodally distributed, one group having a large splenium like control females and another group having a small splenium similar to control males. The data suggest the possibility of a genetic or developmental neuroendocrine disorder that produces a "virilized" splenium in the brains of schizophrenic females, and "unvirilized" splenium in the brain of some schizophrenic males. The findings are discussed in light of the psychoneuro-endocrine literature, some of which suggests the existence of androgyny in schizophrenia.

References:

[1]DeLacoste-Utamsing C, Holloway RL: Sexual dimorphism in the human corpus callosum. *Science* 216:1431-1432, 1982.

[2]Nasrallah HA, Andreasen NC, Coffman JA, et al: A controlled magnetic resonance imaging study of corpus callosum thickness in schizophrenia. *Biological Psychiatry* 21:274-282, 1986.

NR199 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PET OF ACUTE AND CHRONIC SCHIZOPHRENICS (SCZ)

John M. Cleghorn, M.D., Dept of Psychiatry, McMaster University, 1200 Main St., W. Hamilton ON, Canada L8N 3Z5; Edmund Stephen Garnett, M.B., Ronald D. Kaplan, Ph.D., Janice Mitton, R.N., Peter Cook, M.D., Stanley W. Dermer, M.D.

Summary

STUDY 1: 8 drug free, first episode RDC SCZs who never received neuroleptics were compared with 10 age and sex matched normal controls on 2 occasions using PET with 18F FDG. On first examination, middle prefrontal cortical slice revealed asymmetrical uptake of 18F FDG in all patients and 4/10 controls ($p = .01$). On second examination all controls were asymmetrical but 5/8 patients were symmetrical ($p = .01$). When 6 other brain regions were compared for asymmetries on 2 occasions controls tended to be symmetrical on the first and asymmetrical on the second. Conversely, patients were the opposite ($p = .05$). Data demonstrate an order effect and imply differences in brain mechanisms involved in tuning and switching. Data on neuroleptic effects after one year will be presented. Data on 18F fluorodopa is now available on 3 of these patients and 10 controls. Additional data may be forthcoming prior to presentation. STUDY 2: 12 neurolepticized chronic SCZ patients were examined by PET using 18F FDG: 6 with chronic auditory hallucinations and 6 who previously had auditory hallucinations which responded to neuroleptics and were absent at examination. The two groups were similar on SADS positive and negative symptom scores and neuropsychological assessment. 4/6 hallucinators had greater glucose uptake in right superior temporal region than left and 2 the opposite. 4 controls showed bilaterally symmetrical temporal lobes and one each showed dominance of either lobe. Sample size is being enlarged to determine statistical significance. These patients demonstrated strikingly increased glucose uptake in caudate nuclei compared with subjects in STUDY 1.

NR200 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SCHIZOPHRENIA AND INCREASED BASAL GANGLIA ACTIVITY

Susan M. Resnick, Ph.D., Brain/Behavior Lab, U of Pennsylvania, 205 Piersol, Philadelphia, PA 19104; Raquel E. Gur M.D., Abass Alavi, M.D., Ruben C. Gur, Ph.D., Martin Reivich, M.D.

Summary

Local cerebral glucose metabolism was determined with 18F-FDG using positron emission tomography in a sample of 17 schizophrenics and 12 normal volunteers. All patients were off medications for at least 7 days before the PET study. Qualitative and quantitative analyses were performed comparing basal ganglia to cortical activity. Ten of 17 patients were found to have prominent basal ganglia activity on blind radiologic reading. This included 4 of the 7 patients who had been off medications for greater than 6 months before PET study and 6 of the 10 patients who had been washed off medication prior to study. Relative increase of basal ganglia activity was confirmed by quantitative analysis. Comparisons between patients and controls indicated that schizophrenics had significantly higher ratios of basal ganglia to mean cortical metabolism for both right and left hemispheres ($p < .05$) Absolute metabolic rates, showing a trend toward decreased metabolism in patients, suggest that these findings may be due to a relative sparing of the basal ganglia. Although patients were off medication at the time of this study, the extent to which prior medication may contribute to these findings is uncertain. It is notable, however, that prominence of basal ganglia activity was unrelated to duration of time off medication.

NR201 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

CEREBELLAR ATROPHY IN SCHIZOPHRENIA BY MRI METHODS

Jeffrey A. Coffman, M.D., OSU Dept of Psychiatry, 473 W. 12th Ave., Columbus OH 43210; Henry A. Nasrallah, M.D., Nancy C. Andreasen, M.D., Stephen C. Olson, M.D., Val D. Dunn, M.D., James Ehrhardt, Ph.D.

Summary

Utilizing computed tomographic techniques limited to assessment in the transverse plane, a number of investigators have reported finding evidence of cerebellar atrophy in schizophrenics (Nasrallah & Coffman, 1985). In the context of a larger study of schizophrenics and controls using magnetic resonance imaging we undertook a reevaluation of cerebellar size in the midsagittal plane. Thirty-eight schizophrenics and 41 controls underwent examination using a 0.5 tesla Picker NMR imaging system. Structures on the midsagittal image were projected and measured by planimetry. We compared midsagittal cerebellar area in schizophrenics and controls as a group and divided by sex and handedness. We also computed a ratio of cerebellar/cerebral size. We found that no significant differences emerged between schizophrenics or controls in cerebellar area for the full group or when divided according to sex and handedness. However, the cerebellar/cerebral ratio was significantly greater ($p < .01$) among schizophrenics than controls.

NR202 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

III VENTRICULAR ENLARGEMENT IN CHRONIC SCHIZOPHRENICS

Shigenobu Kanba, M.D., Dept of Psychiatry, Mayo Clinic Foundation, Rochester MN 55905; Satoru Shima, M.D., Yutaka Masuda, M.D., Taizo Tukumo, M.D., Toshinori Kitamura, M.D., Masahiro Asai, M.D.

Summary

The third ventricular enlargement in schizophrenia was first found in 1927 by means of pneumoencephalography. Since then, the third ventricle has been a focus of neuropsychiatric research of schizophrenia. For the third ventricular atrophy could reflect morphological deficits in the surrounding areas such as the diencephalon and the limbic system which have been suspected to be neuroanatomical loci for schizophrenia. Recently several CT studies have confirmed this early findings; although there are controversial findings. In this study, the selective enlargement of the third ventricle was found in 37 chronic schizophrenic patients (the area $= 70.8 = 31.8$, the VBR $= 0.00492 \pm 0.00224$) as compared with 37 controls (the area $= 54.5 \pm 22.4$, the VBR $= 0.00369 \pm 0.00145$). However, the width of the third ventricle did not show statistically significant differences. There was no correlation between the third ventricle size and the clinical variables such as age, age of onset, duration of illness, neuroleptic dosage, and administration of ECT. In this sample, we previously found no significant differences in the lateral ventricular size between the patients and the controls when the VBR, the Ewans' index, and the CMI were measured; but the schizophrenics had the significantly lower CT density in the bilateral frontal and the occipital regions. However, no correlation was found between the frontal CT density and the third ventricle size. In summary, our study confirmed third ventricular enlargement independent of the disease process or the treatments of schizophrenia. However, the clinical or etiological significance and the pathogenesis of this structural abnormality remain to be explored further.

NR203 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

VBR IN LATE ONSET SCHIZOPHRENIA (PARAPHRENIA)

Peter Rabins, M.D., Johns Hopkins Hospital, Meyer 279, Baltimore MD 21205; Godfrey Pearlson, M.D., Jayaram Geetha, M.D., Cynthia Steel, R.N., Larry Tune, M.D.

Summary

29 elderly patients meeting all *DSM III* criteria for schizophrenia except for symptomatic onset at greater than 59 years of age underwent cranial CT scans. Mean age of the patients was 73 ± 7.4 years. 86% of the sample was female, 55% black. 48% had at least one significant sensory impairment and 45% were socially isolated. 31% of the sample had Schneideran first-rank symptoms, 31% had a probable family history of schizophrenia in a first or second relative and 86% had a clinical response to neuroleptic medications. Mean ventricular-to-brain ratio (VBR) was 13.0 ± 3.4, compared to 18.1 ± 5.4 in 23 age-matched patients who had NINCDS/ADRDA probable senile dementia of the Alzheimer's type plus hallucinations and delusions. This difference in VBRs was highly significant (2-tailed t value = 4.2, DF = 50, $p < .0001$). Mean VBR in 37 normal elderly was 8.8 ± 5.2. This value was significantly lower than that of the late onset schizophrenics (2-tailed + value = 4.0, DF = 64, $p < .001$). 17% of these late onset schizophrenic patients had a VBR equal to or exceeding 2 standard deviations above the age-appropriate normal mean calculated from a normative CT aging volunteer population (N = 153). This compared with 28% of a sample of 50 young schizophrenics. Those elderly schizophrenic patients with a positive family history for schizophrenia did not have larger VBR values than those without a family history.

NR204 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

EEG SPECTRA IN SCHIZOPHRENICS-TOPOGRAPHIC ANALYSIS

E. Michael Kahn, M.D., Western Psychiatric Inst, 3811 O'Hara St., Pittsburgh PA 15213; Richard D. Weiner, M.D., Richard Ulrich, M.S., Harold S. Kudler, M.D.

Summary

Many experimenters have attempted to correlate EEG abnormalities in schizophrenic patients with symptom status, medication response, and underlying "traits." Topographic mapping techniques, with multichannel recording, careful artifact rejection, and improved statistical methods have increased our ability to characterize patterns of brain activity. The authors studied 16 stable *DSM-III* schizophrenic patients on medication, and 11 age-matched controls. EEG, awake, eyes closed, was recorded from 19 scalp sites. Eye movement and EKG were monitored in additional polygraph channels. EEG data were digitized and stored on hard disk by a DEC 11-24 computer. Three minutes of data, divided into 5-second epochs, were gathered for each subject. Artifact-contaminated epochs were excluded from further analysis. A variety of spectral parameters were computed and reviewed using topographic techniques in the Duke/DVAMC Neuropsychiatry Lab. Alpha power was higher frontally in schizophrenics; this difference was most pronounced at Fz. Alpha power, grouped into frontal, central/temporal, and occipital regions (derived by factor analysis) predicted group assignment (discriminant analysis) correctly in 74% of cases ($p < 0.05$). No differences in left-right symmetry were found between groups, and mean frequency did not differ by region. These findings differ from many studies, which report frontal slowing and parieto-temporal beta in schizophrenics. Differences in alpha may reflect alterations in attentional processes.

NR205 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

USING CEREBRAL LATERALITY TO SUBTYPE PSYCHOSIS

Bruce E. Wexler, M.D., Yale U. Dept of Medicine, VAMC, 116A-1, West Haven CT 06516; Earl L. Giller, Jr., M.D.

Summary

Dichotic listening tests were administered to 41 acutely psychotic inpatients, RDC diagnosed as depressed, manic, schizophrenic or schizo-affective. Subsets of patients were retested after recovery. One test consisted of nonsense syllables; the other of words. Previous studies of psychotic patients found that right ear advantage (REA) on the nonsense test increased with recovery while REA on the word test decreased. This study examined the relationship between clinical symptoms and dichotic scores. As in past studies, REA increased on the nonsense with recovery and decreased on the words. The extent to which patients showed this pattern was inversely correlated with improvement in BPRS ratings of unusual thought content ($r = -.62$, $p = .003$) and hallucinatory behavior ($r = -.37$, $p = .09$) and positively correlated with improvement in emotional withdrawal ($r = .42$, $p = .05$) and hostility ($r = .39$, $p = .07$). When patients were divided into groups based on recovery-related changes in laterality, they differed on two of four BPRS factors. The group with recovery-related increases in REA on nonsense and decreases on words showed less improvement in thinking disorder ($p = .02$) and more in withdrawal-retardation ($p = .08$). When the full group of 41 patients was divided according to dichotic scores upon admission, patients with greater REA on words and lower REA on nonsense showed more withdrawal-retardation ($p = .05$) and less thinking disorder ($p = .05$). Associations between dichotic scores and symptomatology extended across RDC diagnostic groups. These results are consistent with suggested similarities between fluent aphasia and schizophrenic language, and with the putative association between posterior cerebral pathology and positive schizophrenic symptoms.

NR206 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

ANOMALOUS MOTORIC DOMINANCE AND SCHIZOPHRENIA: CLINICAL IMPLICATIONS

Peter Hauser, M.D., Dept of Psychiatry, Georgetown Univ Hospital, Washington, DC 20007; Jane Hood, M.A., Craig Hudson, B.S., Mary Seeman, M.D.

Summary

Studies of anomalous motoric dominance (AMD) in schizophrenia have reported widely varying and contradictory results. Assuming the possibility that schizophrenia is mainly a left brain disorder and recognizing the above mentioned contradictions, the obscure etiology of AMD, and the dimorphic organization of male and female brains, we hypothesized that AMD might serve different prognostic functions in women and men. In a replication of a study by Nasrallah, we evaluated the handedness of 66 RDC chronic schizophrenic patients (20 women, 46 men) and 66 non-psychiatric controls (matched for age and sex) with an 11 item laterality scale and asked about family history of sinistrality. Patients were further questioned about age at first hospitalization, and details about each hospitalization. Patients were also divided into paranoid and non-paranoid sub-types using Tsuang Winokur criteria. Our results showed there were significantly more non-right handed female schizophrenics than female controls. For males the distribution was equivalent. In our female sample left/mixed handedness was associated with two indices of poor outcome: (1) higher frequency of hospitalizations and (2) more time spent in hospital. It was also associated with early onset of illness and non-paranoid subtype of schizophrenia, both of which are known to predict poor outcome. Results will be discussed for their clinical and theoretical relevance.

NR207 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

NEGATIVE SCHIZOPHRENIC SYMPTOMS AND BRAIN DAMAGE

John A. Sweeney, Ph.D., New York Hospital, Payne Whitney, 525 East 68th St., New York, NY 10021; John G. Keilp, M.A., Paul Jacobsen, Ph.D., Carla M. Solomon, Ph.D., Michael Deck, M.D., J. John Mann, M.D.

Summary

A number of recent studies of schizophrenia have suggested an association among negative symptoms, neuropsychological impairment, and structural brain abnormalities. Studies examining all three systematically, though, have been infrequent. We examined the relationships among these variables in 21 chronic, recently admitted, inpatient schizophrenics. These patients were diagnosed (SCID) and their symptoms rated (SANS, SAPS) by structured interview. Each was then given a brief, comprehensive battery of neuropsychological tests and a CT scan. Patients in this sample were predominantly (17 of 21) mixed positive and negative symptomatology. Nonetheless, an index of these patients' cognitive (neuropsychological) impairment was bimodally distributed. The more impaired group was found to have significantly greater ($p < .05$) negative symptomatology. No relation to positive symptoms was found. Performance on brief, timed, conceptual-motor tests (WAIS-R Digit Symbol subtest, Trails A & B) distinguished this more impaired, greater negative symptom group with 100% efficiency. Blind preliminary ratings of sulcal and ventricular abnormalities on CT (planimetry ratings in progress) defined a subgroup of patients with both neuropsychological impairment and the most severe negative symptomatology. These results support the validity of Crow's (1980) Type II syndrome in schizophrenia, in that negative symptomatology is found to be closely associated with presumptive evidence of brain damage, regardless of positive symptom status.

NR208 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

TRAIT AND STATE ATTENTION DEFICITS IN SCHIZOPHRENIA

David L. Braff, M.D., Dept. of Psychiatry, M-003, USCD, La Jolla, CA 92093.

Summary

Schizophrenic patients were compared with schizoaffective, bipolar, and non-psychotic depressed patients in a visual masking paradigm in which an informational target stimulus was followed at varying intervals by a non-informational masking stimulus. The masking paradigm, by controlling the pulse of information supplied to the CNS, serves as a useful marker or stress test of the individual's CNS attentional capacity. The use of a masking paradigm has been very productive in specifying the information processing/attentional deficits in schizophrenics and schizophrenia spectrum patients. Current results confirmed previous findings of a performance deficit in schizophrenics when compared to non-psychotic controls. The data allow us to make strong inferences about trait and state contributions to the observed schizophrenic attentional dysfunction. Schizoaffective and bipolar patients also showed evidence of slow information processing and these results are interpreted in terms of a unifying trait-state formulation where impaired information processing is seen as a fundamental trait of schizophrenic spectrum disorders and as a state that can covary with multiple psychotic illnesses. More severely ill schizophrenics are burdened with relatively greater trait-linked vulnerabilities to information processing disruptions. Data from a variety of sensory gating paradigms are consistent with those of the masking paradigm in revealing that the processing deficits are time dependent and occur in the 500 msecs following stimulus input. These gating studies also support the hypothesis that there are trait and state dependent contributions to the schizophrenics' information processing deficits. The putative casual mechanism of overactive mesolimbic activity is also discussed.

NR209 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

EYE MOVEMENTS IN CHRONIC SCHIZOPHRENIC PATIENTS

Takuya Kojima, M.D., UCI Med Center, Psychiatry, 101 City Dr. S., Rte 88, Orange, CA 92668; Steven G. Potkin, M.D., Mohammad Kharazmi, Eisuke Matsushima, M.D.

Summary

The eye movements of 20 chronic schizophrenic patients (CS) and 10 normal controls (NC) were examined using an eye mark recorder. The CS patients were diagnosed according to *DSM-III* criteria. The NC were matched for age and gender with the CS patients. Fifteen of the CS patients were on neuroleptic medication and 5 were drug-free. Each subject was shown an "S" shaped figure projected on a screen and then shown two other figures partially different from the original one to ascertain differences. The eye movements during comparative viewing were analyzed by the procedure of Kojima et al. (1985). The CS patients had less frequent eye movements and a much more limited area of inspection than the NC. The mean responsive search score for the CS patients, measured after verbal stimuli, was 6.4, while for the NC it was 10.7 ($+ = 6.321, P < .001$). There was no difference in the responsive search score between the unmedicated and medicated CS patients. These results were consistent with Japanese studies which have shown a similar difference between chronic schizophrenics and normal controls (Kojima et al. 1985). Further Japanese studies have demonstrated that the relatives of schizophrenics also had less frequent eye movements than normal controls. These data indicate limited eye movements can be considered as a marker for susceptibility to schizophrenia.

NR210 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

EYE TRACKING AND NUCLEAR SCHIZOPHRENIA

Carla M. Solomon, Ph.D., Payne Whitney Clinic, 525 E. 68th St., New York, NY 10021; John A. Sweeney, Ph.D., J. John Mann, M.D.

Summary

Deviant eye tracking is a marker of vulnerability for some forms of schizophrenia. This study examined the relationship between deviant tracking and familial, premorbid, cognitive and clinical features of the illness. Twenty-four chronic schizophrenics (SCID *DSM III* diagnosis) were administered an eye-tracking task and a battery of clinical interviews. Deviant tracking was characterized by intrusive saccadic activity and/or poor sinusoidality. Intrusive saccadic activity was correlated with a family history of schizophrenia ($p < .01$), later age of first treatment ($p < .05$), childhood social withdrawal ($p < .05$), and poor adolescent peer relations ($p < .01$). Poor sinusoidality was correlated with poor grooming ($p < .05$) and emotional withdrawal ($p < .05$). Both poor sinusoidality and saccadic intrusions tended to be associated with inappropriate affect, difficulties with intimacy, decreased spontaneous movements and poor affective responsivity. Deviant tracking was negatively correlated with depression ($p < .01$) and helplessness/hopelessness ($p < .05$). No correlation was found between poor tracking and global measures of clinical state. On a pilot sample of eleven subjects deviant tracking was correlated with *DSM III* prodromal symptoms of social withdrawal ($p < .01$), poor hygiene ($p < .05$) and unusual perceptions ($p < .05$). Deviant tracking thus identifies schizophrenics with consistent premorbid, prodromal and clinical features of insidious onset, interpersonal and affective deficits as well as other negative symptoms, and family history. The study provides further evidence identifying deviant eye tracking as a trait marker of nuclear schizophrenia.

NR211 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

TRAINING SCHIZOPHRENICS IN MEDICATION MANAGEMENT

Robert P. Liberman, M.D., Dept. of Psychiatry, UCLA/NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Thad Eckman, Ph.D., Catherine C. Phipps, M.S.

Summary

The Medication Management Module is a structured, behaviorally based method of teaching reliable and self-directed use of neuroleptic drugs to chronic schizophrenic patients requiring maintenance pharmacotherapy. The module contains a therapist's manual, a patient's workbook, and a professionally made videotape demonstrating the knowledge and skills to be learned. It comprises four skill areas: (1) benefits of neuroleptics; (2) self-administration techniques; (3) side effects; and (4) negotiating drugs and dose with physician. Using modeling, role-playing, coaching, feedback, in vivo and homework assignments, therapists can teach the knowledge and skills in groups of up to 10 patients over a 30-hour course. After pilot testing and empirical validation at the Brentwood VA Hospital, the Module was field-tested at 30 clinical sites throughout the USA and Canada. Data will be presented from over 200 patients and 50 professionals regarding efficacy of training on compliance, predictors of outcome, and fidelity of delivery of the training. Results indicated that the Module can be readily used by a wide variety of mental health professionals in both inpatient and community-based facilities.

NR212 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

TIASPIRONE IN TREATMENT OF SCHIZOPHRENIA

Anil Kumar Jain, M.D., Lafayette Clinic, 951 E. Lafayette, Detroit, MI 48207; Norman C. Moore, M.D., Elaine Meyendorff, M.D., Samuel Gershon, M.D.

Summary

Tiaspirone is a new antipsychotic drug which possesses potent dopamine receptor blocking property in animals, without causing receptor super-sensitivity. Our center recently reported the efficacy of this drug in an uncontrolled single blind study conducted on 28 schizophrenic patients. In the investigation reported here we compared the efficacy of tiaspirone with standard neuroleptics using a single blind crossover design.

Following a placebo washout period of 7-10 days 6 young schizophrenic males were treated with tiaspirone (maximum average dose 217.5 mg/day) for 6 weeks. All the patients were then crossed over, after a week of placebo washout, to standard neuroleptics (maximum average dose in CPZ equivalents 1018 mg/day) for 4 weeks. Efficacy parameters were BPRS and CGI.

On both treatments patients showed significant improvement. One way ANOVA with repeated measures over time performed on BPRS scores for pretreatment, baseline and weekly for 6 weeks indicated a significant overall improvement ($p < .01$) for tiaspirone; baseline scores significantly differed from week 4, 5, and 6 ($p < .01$). Similar analysis for neuroleptics showed a significant overall improvement ($p < .01$); baseline scores significantly differed from week 4 ($p < .01$). There was no significant difference between tiaspirone and neuroleptics at week 4 on BPRS and CGI. No neurological side effects were noticed with tiaspirone. Two patients developed EPS on neuroleptics. One patient was taken off tiaspirone at week 4 due to evelation in liver enzymes.
A double blind control study is in progress at our center to further evaluate the efficacy and safety of tiaspirone.

NR213 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

STRESSFUL LIFE EVENTS AND SCHIZOPHRENIC RELAPSE

Joseph Ventura, M.A., Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Los Angeles, CA 90024; Keith H. Neuchterlein, Ph.D., David Lukoff, Ph.D.

Summary

The relationship between life events and schizophrenic episodes has been the focus of a substantial amount of research. Some evidence exists to support the hypothesis that life events may "trigger" the onset or relapse of schizophrenic episodes. However, most studies have been plagued by methodological limitations, primarily due to the retrospective design that characterizes much of this previous work.

In this study, a prospective, longitudinal design is employed in the monthly collection of life events data utilizing the Psychiatric Epidemiology Research Inventory for Life Events. Fourteen recent-onset schizophrenic outpatients who met outcome criteria for release or significant exacerbation during a period of standardized outpatient maintenance (12.5 mg fluphenazine decanoate every two weeks) comprised the sample. Utilizing a within-subjects design, we evaluated the two-month period prior to a relapse or significant exacerbation of symptomatology (prerelapse period) and a two-month period which was not followed by a relapse or significant exacerbation of symptomatology (nonrelapse period).

A significant increase in the number of independent life events (those not under the patient's control nor the result of insidious return of symptomatology) was found in the one-month period just prior to a relapse or significant exacerbation relative to the comparable time during the nonrelapse period.

The methodological advances of this design as well as the consistency of these findings with those of previous studies and a vulnerability/stress model of schizophrenic episodes will be presented.

NR214 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

A PREVENTION PROGRAM FOR YOUNG SCHIZOPHRENICS

James J. Gange, Ph.D., VAMC 116B, Indiana University Med School, Indianapolis, IN 46202; Randall C. Jordan, M.D., Paul A. Schneider, Ph.D.

Summary

The term "revolving door" has been used to describe the readmitted schizophrenics who continue to comprise more than one quarter of all admissions to state and county mental hospitals (Rosenfeld, 1982). Several innovative and cost effective programs have been successfully implemented with this population (e.g., Paul & Lentz, 1977), utilizing psychosocial principles in treatment allowing for successful placement in the community. Far less attention has been devoted to the younger patient. In the present study, a prevention strategy was adopted in which social skills and stabilization of life events were addressed through an intensive inpatient hospitalization relatively early in the patient's life. By focusing on the young, schizophrenic patient, an attempt was made to successfully disrupt the cycle of multiple hospitalizations before pathological behaviors and family adjustments associated with the disorder are entrenched. We examined the effectiveness of a multi-component strategically planned social learning based intervention in an inpatient setting with young schizophrenic patients. All subjects in the study received the currently available treatment program on the inpatient unit. Those subjects randomly assigned to the experimental condition received the following enhancement procedures: 1) assignment to the "Young Vets Mini-Unit"; 2) an early (within 24 hours of admission) Orientation & Preparation for Treatment program; 3) a Family Orientation program; 4) Skills Acquisition Groups; and 5) an intensive aftercare program. The preliminary results suggest that in comparison to the "regular" treatment control condition, subjects receiving the experimental procedures: 1) were more willing to stay longer in the hospital during the inpatient phase of the study; 2) scored higher on social skills measures at the end of the inpatient phase of the program; 3) scored higher on Quality of Life measures after discharge; and 4) were not rehospitalized (to date).

This investigation was supported by a grant to the first author from the Veterans Administration Research Advisory Group.

NR215 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

CHILDHOOD HEAD TRAUMA AND SCHIZOPHRENIA

James Wilcox, D.O., Dept. of Psychiatry, University of Iowa, Iowa City, IA 52242; Henry A. Nasrallah, M.D.

Summary

There are several reports suggesting that schizophrenia-like psychoses may develop following head injury. However, many of these reports are not properly controlled, and do not specify whether diagnostically reliable schizophrenia is associated with head injury. We report here a study of childhood head injury comparing rigorously diagnosed schizophrenics vs. two psychiatric, as well as a nonpsychiatric, control groups.

The medical histories of 200 schizophrenic, 203 depressed, 122 manic and 134 nonpsychiatric surgical subjects were compared. All diagnoses were made by the criteria of Feighner et al., and all subjects were hospitalized. We recorded the occurrence of head injury prior to age ten years, and which required medical attention or caused loss of consciousness. The frequency of such head injury among the groups were statistically compared.

Schizophrenics had significantly more history of head trauma compared to the surgical controls ($p = .0001$), depressives ($p = .0001$) and manics ($p = .06$). There were no differences among the affective and surgical control groups.

The results suggest that serious head trauma during childhood may be a contributing factor to the development of schizophrenic psychosis. The implications of the findings for the assessment and treatment of schizophrenic patients are discussed.

NR216 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

GENDER DIFFERENCES IN SCHIZOPHRENIA

Karen K. Bardenstein, Ph.D., Chestnut Lodge, 500 W. Montgomery Ave., Rockville, MD 20850; Thomas H. McGlashan, M.D.

Summary

Does gender affect the clinical profiles (demographics, premorbid functioning, baseline symptoms, long-term course and outcome) of major mental illnesses? Data from the Chestnut Lodge Follow-up Study are used to examine gender differences in six systematically rediagnosed *(DSMIII)* study cohorts: schizophrenia (S), schizoaffective psychosis (SA), bipolar (BI), and unipolar (UNI) affective disorders, and schizotypal (SPD) and borderline (BPD) personality disorders (Total N = 491). Outcome data were collected by interview 2-32 years post discharge. Baseline clinical assessment involved independent ratings of abstracted medical records. Major Findings: (1) the interaction between gender and disease is strongest in S. Males are poorly related loners without affect who become ill earlier and pursue a more relentlessly downhill course. By contract, S in females is more heterogeneous and benign; (2) Gender differences within SPD mimic those for S and provide further evidence validating SPD as part of the S spectrum; (3) For BI and BPD, outcome is superior for males—a new finding for both diagnostic groups; (4) Some differences (masochistic self-destructiveness in females and antisocial acting out in males) persist across diagnostic groups and therefore appear more specific to gender than to psychopathology. Other findings, including results for SA and UNI, will be presented and discussed. Significance: This is the first study of gender differences using multiple diagnostic groups that are systematically rediagnosed according to current criteria and compared over a multidimensional clinical profile that included long-term functional outcome.

NR217 WITHDRAWN

NR218 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

CHARACTERISTICS OF VERY POOR OUTCOME SCHIZOPHRENIA

Richard S. E. Keefe, B.A., VAMC, 116A, 130 W. Kingsbridge Rd., Bronx, NY 10468; Richard C. Mohs, Ph.D., Michael Davidson, M.D., Jeremy M. Silverman, M.A., Kenneth S. Kendler, M.D.

Summary

The biological, genetic and phenomenological characteristics of 21 "Kraepelinian" schizophrenics and 86 other chronic schizophrenics were compared. The Kraepelinians met the following criteria for the past 5 years: 1) either (a) continuous hospitalization, or (b) dependence on others for food, shelter, clothing; 2) no useful work or employment; and 3) continuous illness. Kraepelinians met criteria for schizophrenia by more diagnostic systems ($p < .001$), were less responsive to haloperidol ($p < .001$), had more severe negative symptoms ($p < .01$), and a similar severity of positive symptoms than exacerbated schizophrenics. Kraepelinians had cerebral ventricles that were more asymmetrical ($p < .02$), and a greater incidence of family history of schizophrenia spectrum disorders than other chronic schizophrenics ($p < .05$). These data suggest that patients with 5 years of illness and complete dependency on others may represent a subgroup of schizophrenia.

NR219 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PROGNOSTIC SCALE FOR CHRONIC SCHIZOPHRENIA

Wayne S. Fenton, M.D., Chestnut Lodge, 500 W. Montgomery Ave., Rockville, MD 20850; Thomas H. McGlashan, M.D.

Summary

Although prognostic scales are available for schizophrenia, these focus on acute or subacute populations where premorbid functioning and established chronicity are the best predictors of outcome. Their usefulness in chronic schizophrenia is limited. The authors describe a simple and reliable, 5-item, 12-point prognostic scale for chronic schizophrenia independept of chronicity. It measures prognosis as the product of a dynamic interplay between the highest level of adaptive occupational and social functioning ever achieved by the individual and the "invasiveness" of the Axis I disorder as manifest by genetic loading (family history of schizophrenia), erosion of reality testing (psychotic assaultiveness), and preservation of affect in psychopathology (depressed mood). Among chronic schizophrenic patients in the Chestnut Lodge Follow-up Study (N = 163), the prognostic score (based on history and admission clinical picture) allowed strong probabilistic statements to be made concerning long-term outcome. Tables present the conditional probability or risk of specific outcomes in the domains of institutionalization, work functioning, social relations, and global outcome for patients at varying levels along the prognostic spectrum. Close examination of these predictor-outcome relationships suggests that (1) prognosis in chronic schizophrenia may be thought of as the variability (as opposed to fixedness) remaining in the individual's future life course, and (2) poor outcome can be predicted with greater sensitivity than good outcome.

NR220 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SUSTAINED REMISSION IN DRUG-FREE SCHIZOPHRENICS

Wayne S. Fenton, M.D., Chestnut Lodge, 500 W. Montgomery Ave., Rockville MD 20850; Thomas H. McGlashan, M.D.

Summary

In view of the risks of long-term neuroleptics, our inability to determine which schizophrenic patients can be medication free is a significant gap in current knowledge. This report from the Chestnut Lodge Follow-up Study details the characteristics of a subgroup of largely chronic *DSM-III* schizophrenic and schizoaffective patients who, after discharge, were able to sustain good outcome without hospitalization over an average 15 year period with no maintenance antipsychotics. Relevant patients were identified by multiple regression and discriminant function analysis of their history and admission clinical picture. Distinguishing characteristics included better premorbid social and occupational adjustment, a higher level of accrued psychosocial competence and acquired skills, higher intelligence (IQ), fewer hebephrenic traits (Elgin Scale), and an absence of somatic preoccupations and motor symptoms. Of note, level of chronicity was not predictive. Hence, even among largely chronic patients, classical predictors of good outcome also appear useful in predicting sustained remission without medication. A marked tendency of these patients to drop out of and avoid further psychiatric treatment may result in clinicians and researchers substantially underestimating the overall proportion of chronic schizophrenic patients able to function without continuous medication.

NR221 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SINEMET CHALLENGE AND RELAPSE IN SCHIZOPHRENIA

Michael Davidson, M.D., VAMc 116A, 130 W. Kingsbridge Rd., Bronx NY 10468; Richard S.E. Keefe, B.A., Richard C. Mohs, Ph.D., Thomas B. Horvath, M.D., Kenneth L. Davis, M.D.

Summary

Neuroleptic administration has been shown to be superior to placebo in prolonging schizophrenic remission. However, individual patients are able to maintain long periods of remission in the absence of neuroleptic treatment, while others relapse soon after neuroleptic withdrawal. Based on the acute effect of a dopaminergic challenge, this study attempted to predict time to relapse in 28 schizophrenic patients withdrawn from neuroleptics and challenged with Sinemet for 7 days, then followed until relapse. Time to relapse correlated significantly with Sinemet-induced increase in BPRS score ($p = .006$) Five of 6 "positive responders" to Sinemet relapsed within four weeks from the time of Sinemet administration, while only 4 of 22 "negative responders" relapsed in a comparable period.

NR222 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

LYMPHOCYTE FUNCTION IN MANIA

Ziad Kronfol, M.D., Dept of Psychiatry, Univ. of Mich. Med Ctr, (AGH 9C), Ann Arbor MI 48109; J. Daniel House, Ph.D.

Summary

The central nervous system and the immune system are intimately connected. Recent evidence indicates both structural and functional relationships between the brain and the reticuloendothelial system. The implication for psychiatry is that the immune system may play a role in the etiology of certain psychiatric conditions. Conversely, specific psychiatric disorders may be accompanied by impaired immune regulation. We have earlier reported a decrease in lymphocyte mitogenic activity in patients with depressive illness. These findings have been replicated by independent investigators. We now report on the immunological status of patients with mania. Hospitalized manic patients ($n = 11$) were compared on a variety of immunological variables with hospitalized schizophrenic patients ($n = 19$) and normal controls ($n = 33$). The immune variables include total lymphocyte counts, percentage of T cells, B cells, T helper and T suppressor cells as well as *in-vitro* lymphocyte response to mitogen stimulation. Diagnoses were made in accordance with *DSM-III*. We found no major differences in lymphocyte populations or lympocyte subsets among the groups. Lymphocyte mitogenic responses, however, were significantly reduced in the manic group. Relation of mitogenic activity to serum cortisol levels and drug status will be discussed. These results expand previously reported abnormalities of immunological function in psychiatric patients and suggest that extreme mood states (not merely depression) be accompanied by impairment of immune function.

NR223 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

ECT IN MANIA: EFFICACY AND TREATMENT FREQUENCY

Steven D. Roth, M.D., NYS Psychiatric Inst., Box 72 722 W. 168th St., New York NY 10032; D.P. Devanand, M.D., Sukdeb Mukherjee, M.D., Harold A. Sackeim, Ph.D., Carl Lee, M.D., Sidney Malitz, M.D.

Summary

It has been claimed frequently that manic patients require at least daily ECT treatment, often extending to 20 or more seizure inductions to achieve clinical response (e.g. Ottosson 1985). This claim is related to the view that symptomatic remission is secondary to an ECT-induced organic mental syndrome. The efficacy of ECT in mania was examined in two samples. One group of 6 patients received unilateral ECT three times per week. In a second group, patients received unilateral or bilateral ECT 5 times per week, with 3 non-responders to unilateral treatment crossed over to bilateral ECT. Patients were medication free 7-10 days prior to, and during, ECT. Ratings of manic symptomatology were made blind to treatment modality. In the total sample, responders required a mean of only 6.1 (SD = 2.1) treatments and 11.1 (SD = 4.0) days to recover. Responders to 3x/week treatment (n = 5) required an average of 5.1 (SD = 2.1) treatments to recover, while responders to 5x/week ECT (n = 4) required 7.3 (SD = 1.7) treatments (t = 1.69, n.s.). Mean duration in treatment to response also did not differ between groups (3x/week, x = 11.1 ± 5.4 days; 5x/week, x = 11.0 ± 2.2 days). Our preliminary findings do not support the need for large numbers of treatment nor do they support the superiority of daily relative to conventional 3 per week treatment.

NR224 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

THIOTHIXENE VERSUS CHLORPROMAZINE FOR ACUTE MANIA

Philip G. Janicak, M.D., Ill. State Psych Inst, 1601 W. Taylor St., Chicago IL 60612; David B. Bresnahan, M.D., John M. Davis, M.D., Charles Malinick, M.D., Rajiv Sharma, M.D., Joseph E. Comaty, M.S.

Summary

Many investigators advocate low dose, high potency neuroleptics in combination with lithium to treat acute mania, reasoning that their side effect profile allows for more rapid dose escalation and therefore more rapid symptom resolution. We tested this hypothesis using a double blind, random assignment, titration design comparing thiothixene (THX) to chlorpromazine (CPZ) in 24 bipolar manics on a standard dose of lithium. Washout period ranged from 12 hours to 14 days (m = 4.5 days). Neuroleptic dose was established by giving blind fixed dose capsules (THX = 5 mg; CPZ = 100 mg) every two hours and titrated upward to a maximum dose of 100 mg THX or 2000 CPZ in order to achieve the highest dose possible, in the shortest time, based on clinical need and side effects. GAS, BPRS, Biegel-Murphy Mania Scale, Serial New Haven Schizophrenia Index, and Global Sedation Scale ratings were obtained at baseline, days 1-5, 7, and 14. Change from baseline was calculated at days 4, 7 and 14. CPZ and THX produced identical rates of improvement. As expected we were able to give a higher dose of thiothixene, an average of 6 tablets on day 4 (30 mg) in comparison to an average of 3.8 tablets (380 mg) chlorpromazine. Similar differences were also seen on day 7 (THX = 38 mg; CPZ = 580 mg) and 14 (THX = 36 mg; CPZ = 486 mg) but were not statistically significant. We found that roughly 1 mg of THX was as efficacious as 13 mg of CPZ. Although some patients were titrated to the maximum dose, many patients had good clinical responses on lower doses, and showed only minimal sedation. Without the titration design, we would not have appreciated that most of the patients could be managed on much lower doses. Implications for the less aggressive use of high potency neuroleptics and our observed CPC/THX ratio are discussed.

NR225 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SCHIZOPHRENIA VERSUS MANIA: NEUROENDOCRINE DIFFERENCES

John Mason, M.D., Psychiatry—116A, West Haven VAMC, West Haven CT 06516; Earl Giller, M.D., Thomas Kosten, M.D.

Summary

Although schizophrenia (S) and mania (M) can be symptomatically indistinguishable during an acute episode, several differences have been suggested in central catcholamine activity, for which hormones such as cortisol, catecholamines, thyroid hormones and gonadotrophins have been used as indices. We assessed these hormones at admission and biweekly during hospitalization in male veterans with paranoid schizophrenia ($n=9$) and bipolar I, mania ($n=7$) by Research Diagnostic Criteria. The two groups differed at admission in 24 hour urinary cortisol (S = 32 vs M = 82 μg, $t=6.1$, $P<0.0001$), epinephrine (S = 14 vs M = 26 μg, $t=2.2$, $P<0.05$) and norepinephrine (S = 44 vs M = 86 μg, $t=2.4$, $P<0.05$) and in serum free thyroxine (S = 1.3 vs M = 1.8 μg%, $t=4.3$, $P<0.001$) and testosterone (S = 570 vs M = 390 ng%, $t=2.0$, $P<0.07$). Because of overlap in hormone levels, any single hormone correctly classified only 75% of the patients as M or S. To improve classification, the hormones were combined using discriminant function analysis (DFA) and multi-dimensional scaling (MDS). With the admission hormone levels, correct classifications were obtained on all patients using DFA and 14 patients (two S misclassified) using MDS. Mean hormone levels (2-10 samplings per hospitalization) yielded 100% correct classifications with both DFA and MDS. The manics were older than the schizophrenics (26 vs 34 years, $t=2.1$, $P<0.05$), but age was not correlated with levels of hormones in the DFA (mean variance due to age = 9%). No medications were used at admission except antipsychotics in 14 patients, and the M (680 ± 226 mg, $n=7$) and S (640 ± 200 mg, $n=7$) did not differ in chlorpromazine (Cpz) equivalents ($t=0.1$, ns). In spite of contrasting statistical methods, both DFA and MDS correctly classified diagnoses and were substantially better than any single hormone.

NR226 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

THE SCHIZOPHRENI-FORM DIAGNOSIS: CONSTRUCT VALIDITY

J.A.E. Fleming, M.D., Dept. of Psychiatry, Shaughnessy Hosp. UBC, 4500 Oak St., Vancouver B.C. O, Canada; Tsung-yi Lin, M.D., Morton Beiser, M.D., William T. Iacono, Ph.D.

Summary

The usefulness of the schizophreniform diagnosis has been the subject of controversy. In *DSM-III*-R the schizophreniform diagnosis is retained along with the six-month duration criterion. However, additional criteria, thought to be predictive of good outcome, are included. The Markers and Predictors of Schizophrenia (MAP) study at the University of British Columbia focuses on the longitudinal course of first episode schizophrenia and predictors of outcome. Thirty-two subjects, assessed with the Present State Examination as well as a variety of procedures including psychophysiological testing and CT scans, received a diagnosis of schizophreniform psychosis utilizing a standardized diagnostic algorithm. At an 18-month follow-up subsequent to the initial evaluation, one-third of the schizophreniform subjects had recovered completely. Of the remaining two-thirds, most exhibited symptoms of sufficiently long duration to qualify for a diagnosis of schizophrenia. The following characteristics (some of them proposed as criteria for schizophreniform in the *DSM-III*-R) discriminate those schizophreniforms who go on to recover from those who develop the schizophrenic syndrome: good premorbid work history, evidence of a larger and more supportive social network, a more positive self-image and being perceived more favorably by family and friends. Symptoms of predictors of unfavorable course include: paranoia, loss of control and disorganized behavior. Implications for including duration and predictor criteria as part of a diagnosis are discussed.

NR227 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PREDICTING OUTCOME IN SCHIZOAFFECTIVE PSYCHOSIS

Paul V. Williams, M.D., Chestnut Lodge, 500 W. Montgomery Ave., Rockville MD 20850; Thomas H. McGlashan, M.D.

Summary

We studied the prediction of long-term follow-up (FU) diagnosis and functional outcome in a schizoaffective (SA) cohort (N = 68) from the Chestnut Lodge Follow-up study who satisfied *DSM-III* criteria for both schizophrenia (S) and affective disorder (AD). Outcome and FU clinical diagnosis was assessed by interview 2-32 years postdischarge. Independent assessment of abstracted medical records provided reliable baseline ratings of multiple (N = 153) predictor variables, including demography, premorbid characteristics, psychopathology, and illness course up to index admission. Predictors of functional outcome were identified using correlation, multiple regression, and discriminant function analysis (DFA). Prediction of FU diagnosis (SA, S, or AD) used DFA. Main Findings (1) Functional Outcome. Predictors accounted for half the global outcome variance. Superior outcome was best predicted by good pre-morbid instrumental skills and fewer "typically schizophrenic" symptoms as measured by the New Haven Index, thus confirming the common clinical belief that better prognosis SA patients have fewer "schizo" and more "affective" elements. (2) FU diagnosis demonstrated marked diagnostic instability over time. Only 18% of the baseline SA patients received a FU diagnosis of SA while 56% changed to S, and 25% changed to AD. Furthermore, by DFA, the diagnositically stable SA was not distinctive at baseline (sensitivity = 36%). Results strongly question SA as a stable diagnostic entity or as a distinctive third psychosis in Axis I. SA patients appear to resolve either toward S or toward AD over time.

NR228 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

BIOLOGICAL STUDIES OF PARANOIA

Kenneth L. Davis, M.D., VAMC, 130 W. Kingsbridge Road, Bronx, NY 10468; Bonnie M. Davis, M.D., Gordon Campbell, Ph.D., Richard C. Mohs, Ph.D., Michael Davidson, M.D., Thomas B. Horvath, M.D.

Summary

Potential parameters of noradrenergic activity were measured in plasma and CSF of RDC paranoid schizophrenics, chronic undifferentiated schizophrenics with paranoia, other chronic schizophrenics, and normal controls. CSF cyclic-AMP levels were significantly elevated ($p = .003$, $N = 24$) in the paranoid schizophrenic group than compared to normal controls. Similarly, paranoid schizophrenics had significantly higher CSF cyclic AMP than nonparanoid schizophrenics ($p = .003$, $n = 26$). The variability in plasma growth hormone concentrations with 20 minute sampling over a three hour period was assessed primarily due to an increased number of peaks in growth hormone secretion ($p = .002$, $n = 49$). In contrast, serum prolactin did not differentiate these groups. These results are compatible with an interpretation that noradrenergic activity is elevated in paranoid schizophrenics and other schizophrenics with paranoid features. However, CSF, MHPG did not differ between any subgroup of schizophrenics and normals, suggesting that enhanced activity can be most easily ascertained by focusing on post-receptor parameters.

NR229 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

BIOGENETIC ASPECT OF BORDERLINES AND SCHIZOTYPALS

Howard Klar, M.D., Dept of Psychiatry, Mt. Sinai Pl., One Gustave Levy Pl., New York NY 10029; Larry J. Siever, M.D., Emil F. Coccaro, M.D., Miklos Loconszy, M.D., Jeremy Silverman, M.A., Kenneth L. Davis, M.D.

Summary

Evidence from both genetic and biologic studies suggest that there may be a biogenetic contribution to both borderline and schizotypal personality disorder. One to two relatives of patients with a variety of personality disorders (25 schizotypal patients and 23 borderline patients) as diagnosed by two interviewers using The Structured Interview for *DSM III* Personality Disorder (SIDP) were evaluated for a family history of schizophrenic disorders, affective disorders, and related personality disorders. Schizotypal patients were more likely to have a family history of schizophrenia-related disorders and borderline patients to have a family history of affective-related disorders ($p < 0.05$, test of difference between two proportions). Schizotypal patients were also more likely to have biologic abnormalities associated with schizophrenia such as impaired smooth pursuit eye movements (SPEM) ($p < 0.05$, chi square). A trend towards elevated ventricular brain ration (VBR) was observed in these patients and psychotic-like symptoms as reflected in the Chapman Perceptual Aberration Scale correlated positively with CSF HVA ($r = 0.86$, $df = 9$, $p < 0.05$). Borderline patients, however, did not show increased biologic abnormalities associated with major affective disorder such as DST non-supression or blunted responses to TRH. Thus, familial studies are consistent with a familial and biologic relationship between schizotypal personality disorder and schizophrenia and a familial relationship between borderline personality and affective disorder, not reflected in traditional biologic markers for depression.

NR230 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SIGNIFICANCE OF BORDERLINE AND SCHIZOTYPAL OVERLAP

Eric M. Plakun, M.D., Austen Riggs Center, Inc., Stockbridge MA 01262; John P. Muller, Ph.D.

Summary

In a 1984 New Research presentation we reported on 14-year follow-up of borderline (BPD) and schizotypal (SPD) personality disorders, comparing admission and follow-up Global Assessment Scale (GAS) functioning to major affective disorder (MAD) and schizophrenia. Six BPD patients simultaneously met criteria for SPD, a group whose admission GAS functioning was worse than other BPD or SPD patients and similar to schizophrenia. At mean 14-year follow-up BPD with SPD patients lost their similarity to schizophrenia, manifesting the highest mean GAS of any group. In the current study a multiple regression analysis on BPD with SPD patients revealed two BPD and two SPD criteria accounting for 99% of the total GAS score variance at follow-up. BPD criteria were "physically self-damaging acts" and "inappropriate and intense anger." SPD criteria were "recurrent illusions" and "suspiciousness or paranoid ideation." Among all study participants with all diagnoses a New Group of 18 met these four criteria. The New Group is compared to schizophrenia, MAD, SPD, and BPD at admission and follow-up. At admission, the New Group GAS is significantly higher than schizophrenia, but significantly lower than MAD, SPD or BPD. At follow-up the New Group performed significantly better than schizophrenia and had the highest GAS overall. This replicates with a larger sample the finding of poor functioning at admission but high functioning at follow-up compared to other BPD or SPD patients. BPD appears to remain a heterogenous group. Four core BPD and SPD criteria are demonstrated to predict good follow-up functioning irrespective of diagnosis.

NR231 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

CLASSIFICATION OF PSYCHOSIS IN MARYLAND STATE HOSPITALS

Lawrence W. Adler, M.D., Epidemiology Section, Maryland Psychiatric Res, P.O. Box 21247, Baltimore, MD 21228; Ann E. Pulver, Sc.D., William T. Carpenter, Jr., M.D.

Summary

There is a longstanding concern that schizophrenia is overdiagnosed and the affective disorders underdiagnosed in American hospitals. An aim of *DSM III* is to correct this situation, but a recent study from a public hospital suggests that a major problem continues and pharmacotherapeutic decisions are consequently sub-optimal. As part of an ongoing program in epidemiology we are able to contrast research diagnoses (RD) with clinical diagnoses (CD) in five public hospitals. RD were based on review of medical records, application of a structured diagnostic interview, and six month follow-up evaluations. *DSM III* criteria were used for both RD and CD. Reliability for RD ranges from $k = .67$ to $k = .71$. Concordance of admission CD and working CD with RD was 52% ($k = 0.32$, $P = 0.10$). However, discharge CD were 64% concordant ($k = 0.48$, $p = 0.015$), far in excess of that previously reported. The dynamic shift of CD in the course of hospital stay and the improved concordance of discharge CD with RD is encouraging. The most interesting aspect of the discordance relates to affective disorders. Here admission CD concordance of 42% rises to 71% by discharge CD. Twenty discordant cases at admission include 13 who received pharmacotherapy with antidepressant drugs, carbamazepine or lithium. Eight of these cases were diagnosed affective disorders at discharge. These results are on the first 157 cases. This is an early psychosis sample, predominantly first admission, where differential diagnosis is most vexing. Analyses to be reported will include all additional cases. Discussion will focus on the diagnostic and treatment implications.

NR232 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PET AND CLINICAL STATUS IN SCHIZOPHRENIA

Raquel E. Gur, M.D., University of Pennsylvania, Brain and Behavior Laboratory, 205 Piersol, Philadelphia, PA 19104; Susan Resnick, Ph.D., Ruben C. Gur, Ph.D. Abass Alavi, M.D., Martin Reivich, M.D.

Summary

A number of positron emission tomography (PET) studies have reported regional metabolic abnormalities in schizophrenics. However, there is still need to establish the reliability of these findings and their association with clinical status. We examined a sample of 18 schizophrenics who were off medication studied with 18-FDG for measuring local cerebral glucose metabolism. A follow-up PET was performed at 6-8 weeks later on patients and controls.

Patients differed from matched controls in metabolism at initial evaluation. Differences in cortical and subcortical regions were observed and some corresponded to clinical status. Differences in regional metabolic rates between the two studies were related to clinical status.

NR233 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

NEUROPSYCHOLOGIC DYSFUNCTION IN HTLV SEROPOSITIVES

Charles Silberstein, B.A., Albert Einstein Coll Med, 202 W. 85th St., New York NY 10024; F. Patrick McKegney, M.D., Mary Alice O'Dowd, M.D., Peter A. Selwyn, M.D., Ernest Drucker, Ph.D., Gerry H. Friedland, M.D.

Summary

To test the hypothesis that cognitive impairment may present early in the course of HTLV-III infection,* 232 intravenous drug abusers (IVDAs) without overt symptoms of AIDS-related illness have been tested with standard neuropsychological and psychosocial measures. This study is part of a large ongoing prospective study of the natural history of HTLV-III infection in this high risk population. Of 204 subjects initially evaluated blind to serologic status 68 (33%) were HTLV-III seropositive and 136 (67%) were seronegative. Proportion of males and females were equal among seropositives and seronegatives. The mean ages were: seropositives 34 ± 5 (range 26-52); seronegatives 33 ± 5 (range 21-55). The seropositives were 55% Hispanic, 38% Black and 6% White. The Seronegatives were 43% Hispanic, 22% Black and 34% White. At the baseline, the seropositive IVDAs on 4 of 7 measures examined: Finger Tapping—dominant hand ($p = .004$), Digit Span Forward ($p = .03$), Digit Span Backward ($p = .048$), Trail Making A ($p = .014$). Trends in the same direction were found in the other 3: Trail Making B, Finger Tapping—non-dominant hand and the Family APGAR. Data from additional subjects and measures including subsections of the WAIS and Wechsler Memory Scales, the Brief Symptom Inventory and the Life Events Scale as well as early follow-up data will be presented. These preliminary results suggest the seropositive IVDAs may show evidence of impaired neuropsychologic function even in the absence of AIDS related symptoms and may provide further evidence of the neurotopism of HTLV-III. Multivariate analysis will be performed to further assess the relationship between neuropsychologic function, serologic status, demographics, socioeconomics, drug use and affective state.

NR234 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

CORONARY BYPASS: DENIAL IMPROVES ADAPTATION

Arthur M. Freeman, III, M.D., Dept of Psychiatry, Univ. of Alabama Med School, Birmingham AL 35294; David G. Folks, M.D., Roberta S. Sokol, M.A.

Summary

We examined the relationship between denial of illness and outcome from surgery in 55 patients undergoing coronary artery bypass grafting (CABG). Six month postoperative measures of anxiety, depression, and psychosocial adjustment to illness were analyzed with respect to preoperative denial. In order to determine whether denial is an adaptive or maladaptive coping style for CABG patients, we utilized a modified version of the MGH Denial Scale, originally developed for evaluation of patients undergoing cardiac catheterization. This scale measures conscious as well as unconscious components of denial. The Spielberger State Anxiety Inventory (SSAI), the Zung Self-Rating Depression Scale (SDS) and the Psychosocial Adjustment to Illness Scale (PAIS) were administered preoperatively and six months postoperatively. Based upon the Denial Scale measures, patients were divided into three groups: high, average and low deniers. Analysis of variance yielded significant differences among the three groups in six months postoperative measures of anxiety ($p < .01$), depression ($p < .01$) and psychosocial adjustment to illness ($p < .05$). Preoperative denial scores were inversely correlated with postoperative measures of anxiety, depression and psychosocial adjustment to illness among all three groups. In general, high levels of denial are correlated with good outcome following bypass surgery. Results of this study indicate a need for recognizing preopera;tive levels of denial in CABG patients.

NR235 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

THE CONSULTATION PSYCHOPATHOLOGY RATING SCALE

Penelope Krener, M.D., Dept. of Psychiatry, Univ. of Calif., Davis, 2315 Stockton Blvd., Sacramento CA 95817; Mary Kay Simmons, M.S., Rebecca True, R.N.

Summary

Sixty pediatric patients for whom child psychiatry consultation was requested and 30 controls were assessed with a new Consultation Psychopathology Rating Scale. It quantitatively rates 30 patient variables and 15 parent variables. Global scales (0-100) are assigned to both. Ten consultation variables were logged and cross-tabulated with psychopathology. Interrater reliability was established for this instrument. Results showed that consult requests evolved over the training year, the day of the consult request shifts toward Monday from Friday. The consult questions became more specific but the reason the consultation was requested was frequently more limited than the actual problems identified by the consultants. Overall, children for whom psychiatric consultation was requested were older than controls, suggesting that psychopathology is more easily identified in older children or that chronic illness may beget psychopathology as the child grows older. Mean global ratings were 43.20 for consult children, 75.20 for ward controls and 58.25 for intensive care unit controls, indicating more severe psychopathology in youngsters for whom consultation was requested. Consultations were more frequently requested in pediatric settings because of child psychopathology. Parents of children for whom consultation was requested also had lower mean global ratings (53-75) than did parents of ward controls (77.8) and intensive care unit controls (77.0). *DSM-III* Axis 4 and Axis 5 showed no significant difference between consult children and controls, but the percent of consult patients with one or more *DSM-III* psychiatric diagnoses was higher than that for controls, indicating that pediatricians successfully identified psychopathology against a background noise of stress secondary to illness and hospitalization.

NR236 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

DEVELOPMENT OF A NEW ALEXITHYMIA SCALE

R. Michael Bagby, Ph.D., Dept of Psychiatry, Mt. Sinai Hosp, 600 University Ave., Toronto ON O M5G 1X5; Graeme Taylor, M.D., David Ryan, Ph.D.

Summary

This study reports the results of the first phase of a program of research to develop a new self-report alexithymia scale—the Toronto Alexithymia Scale (TAS). The new scale was devised with concern for theoretical congruence with the construct of alexithymia, internal consistency, and independence from social desirability response bias. Initially, 41 items were written and administered to 542 college students. Twenty-six items meeting pre-established psychometric guidelines were retained, yielding an internal consistency (Cronbach's alpha) of .79. Factor-analysis produced four interpretable factors - (1) the ability to identify and distinguish between feelings and bodily sensations; (2) the ability to describe feelings to other people; (3) daydreaming; (4) externally oriented thinking. Each of these factors is theoretically consistent with the construct of alexithymia. Test-retest reliabilities across one-week ($r = .82$, $p < .001$) and five-week ($r = .75$, $p < .001$) periods were obtained. TAS scores were not significantly associated with intelligence, age, education and socioeconomic status; nor were the items influenced by a social desirability response set. Convergent and divergent validity were examined in a second study using a sample of 81 college students. TAS scores showed nonsignificant correlations with depression and anxiety, significant negative correlations with the personality variables psychological mindedness (-.34, $p < .002$) and need-for-cognition (-.46, $p < .001$) and a significant positive correlation with a scale of somatic concern (.36, $p < .001$). The pattern of these correlations provide initial evidence of construct validity. These preliminary results suggest that the TAS may be used as a clinical screening device in both psychiatric and general medical settings.

NR237 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

WORK ON CORE THEME AS MEASURE OF CHANGE IN THERAPY

Dinko Podrug, M.D., Downstate Medical Ctr, 450 Clarkson Ave., Box 1203, Brooklyn, NY 11203.

Summary

The core conflictual relationship theme (CCRT) method, as developed by Luborsky over the past decade, admirably achieves its main purpose of guiding raters' clinical judgment to arrive at a reliable formulation of the patient's main relationship pattern. Luborsky has demonstrated that the individual CCRT remains stable throughout therapy and across many different objects, including the therapist, becomes more deeply experienced as therapy progresses, and that the high improvers are differentiated from the non-improvers by a greater sense of mastery of their theme and some increase in "positive" responses. Although potentially attractive as a psychotherapy change measure, CCRT is primarily a content-analysis system, and can be vague in identifying change. Hoping to make it capable of more definitely registering small changes inherent in the evolving psychotherapy process, the author has developed an elaboration of CCRT by shifting the emphasis beyond formulating to assessing what the patient does with it in the course of therapy. This "Work (on) CCRT" (CCRTw) rating system starts by arriving at CCRT and then proceeds to systematically assess the conflict and contradictions within and across CCRT components, the patient's awareness of it all, and the extent of current efforts expanded towards understanding it better. To establish reliability of CCRTw and how it measures psychotherapy change in this single-case study, independent raters applied CCRTw to the entire audiotape transcript of a 14-session time-limited dynamic psychotherapy. Results demonstrating changes patient undergoes throughout therapy, differential response to transference and extratransference interpretations, and methodological implications for psychotherapy change research are discussed.

NR238 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

MASSACHUSETTS LAWS AND SECLUSION RATE CHANGES

Steven J. Spitz, M.D., 15 Magazine St., Cambridge, MA 02139

Summary

Between January 1984 and April 1985 there were three legal changes in Massachusetts (a federal and supreme state judicial finding, a federal judicial consent decree, and a new state law) which made use of involuntary seclusion, restraint, and medication more rigorous. This paper studies the 5028 seclusions from the population of the maximum security state hospital between April 1983 and December 1985, a period chosen to include a nine month baseline through a nine month observation period following the final change. Most noteworthy findings are that, while the average length of a seclusion episode decreased by about 25%, the total number of episodes doubled. Also, the subgroup of repetitive users of seclusion markedly increased and accounted for a much higher percentage of the seclusion episodes. There appear to have been numerous undesired changes.

NR239 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PATIENT PERCEPTIONS OF CIVIL COMMITMENT

Gail A. Edelsohn, M.D., Johns Hopkins Dept of Ment Hygiene, 615 N. Wolfe St., Baltimore, MD 21205; Virginia Aldige Hiday, Ph.D., Jo Anne Earp, Sc.D., Gary A. Chase, Ph.D.

Summary

Concerns over the negative effect of involuntary commitment on patients are frequently voiced, but there are relatively few studies where patients were asked about their own perceptions. We interviewed adult civil commitment respondents who had hearings in North Carolina in 1984-1985. Six months after discharge, in a phone interview, respondents were asked standardized precoded questions about their perceptions of commitment. Likert-type scales were developed for the following constructs: consequences of hospitalization; perceived need of commitment; perception of treating physician; and medication effects. To date, this phone interview has been administered to 161 patients who came from a larger sample of 1224. This subsample is similar to the larger sample with respect to diagnoses and sociodemographic characteristics. Patients had a mixed view of commitment. The experience was seen as helpful by 53% and necessary by 56%. Forty-nine percent also reported that the experience had given them hope. Sixty-three percent said that if at some time in the future they became sick and appeared dangerous, they would want to be committed to the hospital. Negative descriptors of the experience were also expressed. The experience was described as depressing by 48%, unpleasant by 42%, degrading by 30%, and embarrassing by 27%. All four scales derived from the constructs outlined above had moderate internal consistency and reliability. Future work will explore if such scales have predictive value, e.g. for follow-up with community outpatient services. Further awareness of patient concerns has implications for psychiatric resident education, treatment practices, and approaches to improving precommitment procedures.

NR240 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

FACTORS INVOLVED IN A SUCCESSFUL INSANITY PLEA

Caryl E. Boehnert, Ph.D., Dept. of Psychiatry, UM, Box 393 Mayo Bldg., 420 Delaware St., SE, Minneapolis, MN 55455

Summary

Thirty men given verdicts of "not guilty by reason of insanity" (NGRI) were matched on type of violent crime and compared to thirty men whose plea of insanity failed. Groups did not differ by race, occupation, reliance on a public defender, or prior arrests: the majority in both groups were white, skilled or unskilled laborers, represented by a public defender, and had prior arrests. The two most important factors which discriminated groups were a finding of incompetency to stand trial in the legal history and choosing of judge as trier of fact. 80% of NGRI's had been found incompetent to stand trial, compared to 33% of those found guilty ($p < .001$). 96% of acquittees appeared before a judge in an uncontested trial, compared to 24% in the guilty ($p < .001$). A subset of individuals, those men in the guilty group who had a jury trial, appeared to be significantly different on personality test measures. These men had a higher IQ, good reality testing, poor impulse control, a high potential for aggression, and were classified as psychopathic rather than psychotic on the MMPI and clinical interview. These findings were compared with similar studies from Oregon and New York. The ability of the legal system to identify persons meeting criteria for the insanity defense is discussed.

NR241 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SUICIDE AND UNEMPLOYMENT IN CANADA

Isaac Sakinofsky, M.D., Psychiatry Department, St. Michael's Hospital, 30 Bond St., Toronto ON O, Canada M5B 1W8; Professor Robin Roberts

Summary

We carried out a time-series study across the decade 1969-71 to 1979-81 of 122 ecological factors and their relation to male and female suicide in the provinces of Canada. The variables described social and family organization, employment, education, income, religion and ethnicity, etc. Discriminant function analysis indicated the variables which distinguished those provinces with low and high increases in suicide over the ten-year period (during which Canadian suicide rates had overtaken and exceeded those of the United States). For male suicide, change in the following variables were discriminators: the proportion of males not registered in the work force; crimes of rape; households occupied 6-10 years; deaths due to alcoholic liver disease; and the proportions of non-family persons. In the case of female suicide the discriminators which emerged were: males not registered in the work force, females not registered in the work force; neonatal death rates; females in jobs such as technology; and population density. The paper discusses these aggregate findings and their interpretations.

NR242 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SUICIDE AND VIOLENCE RISK IN PSYCHIATRIC PATIENTS

Robert Plutchik, Ph.D., Dept of Psychiatry, Albert Einstein Med Sc, 1300 Morris Park Ave., Bronx, NY 10461; Herman van Praag, M.D., Hope R. Conte, Ph.D.

Summary

Clinical experience suggests a close relationship between violence directed against others and violence directed towards oneself in the form of suicide attempts. A small but growing body of clinical research indicates that anywhere from 5 to 40 percent of murderers make subsequent suicide attempts. In addition, studies of prisoners and psychiatric patients reveal that approximately one-fourth of violent prisoners have made some prior suicide attempt, and that a similar proportion have acted violently toward others. The present study has developed and used psychometric measures of a large number of variables that have been reported to be possible predictors of either violence or suicide risk. These include: life problems, physical symptoms, feelings of depression, hopelessness and dyscontrol, family problems and childhood discipline. Measures of violence risk and suicide risk were also obtained. The scales were administered to 100 psychiatric inpatients. Item analyses revealed that the scales had high internal reliability. Twenty-nine variables were found to be significant predictors of both violence risk and suicide risk. Because measures of suicide and violence were moderately correlated, partial correlations were computed. It was then found that depression, hopelessness and family violence were predictors of suicide risk but not violence, while impulsivity, legal problems, and menstrual problems were predictors of violence risk but not suicide. The results are consistent with a two-stage vectorial model of interacting variables.

NR243 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

OPERATIONAL CRITERIA FOR SUICIDE CLASSIFICATION

Lucy Davidson, M.D., Violence Epidemiology, CDC, Atlanta, GA 30333; Mark L. Rosenberg, M.D., Jack C. Smith, M.S.

Summary

As the eighth leading cause of death in the United States, suicide is a major public health concern. Without explicit criteria for the classification of suicide, coroners and medical examiners do not reliably code suicides; medical examiners have estimated that half of all suicides may be inaccurately classified. The Operational Criteria for the Classification of Suicide was developed by a group of individuals representing organizations involved in the compilation, analysis, and utilization of suicide statistics. Beginning with a definition of suicide as a death arising from an act inflicted upon oneself with the intent to die, this group elaborated criteria for the separate and sequential determinations of the death as being self-inflicted and intentional. These criteria were refined using a Delphi process and incorporating the evaluative comments of experts in suicidology and death certification. The criteria incorporate four types of evidence that could be available to the certifier: pathological, toxicological, investigational, and psychological. Disseminating these criteria will promote complete reporting and accurate classification of suicides on death certificates. Their implementation will enhance our ability to estimate the true extent of suicide, identify risk factors, and plan preventive interventions.

NR244 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

UNTREATED SUICIDAL BEHAVIOR: SUBSTANCE ABUSERS

Deborah Hasin, M.S., NYS Psychiatric Inst., 722 W. 168th St., New York, NY 10032; Bridget Grant, Ph.D., Jody Weinflash, M.P.H.

Summary

While the association of substance abuse and suicidal behavior has been documented, helpseeking for suicidal behavior has not been previously studied. We therefore interviewed 123 alcohol and drug inpatients about suicide gestures and attempts. Twenty-nine percent of the sample had engaged in suicidal behavior. Suicide attempters were younger, although not significantly different from non-attempters on other demographic variables. Two-thirds of those with suicidal behavior had had episodes of Major Depression (SADS-L/RDC), although attempts were not always limited to periods of major depression. About 40% of the attempters went untreated for their attempts or gestures. Age, sex, and education did not distinguish those seeking treatment from those who did not, although married subjects were treated significantly more often. Treated subjects had significantly higher mean levels of suicidal intent and seriousness of medical consequences (measured by the SADS-L) than untreated subjects, apparently indicating that those receiving treatment for suicidal behavior were at higher risk for eventual suicide. However, illustrations from the clinical material may indicate some subjects whose risk was higher than that indicated by their scores on these suicide predictors (for example, a subject indecisive about suicide toying with his gun while alone and drinking, who communicated this only in the interview for this study). Given the poor impulse control of many such subjects, circumstances of their suicidal behavior and any subsequent communications to others about such behavior may provide important additional predictors of eventual suicide. Follow-up research on such subjects is needed to investigate this hypothesis.

NR245 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SUICIDE IN BORDERLINE PERSONALITY DISORDER

Minna R. Fyer, M.D., 722 W. 168th St., New York, NY 10032; Allen J. Frances, M.D., Timothy Sullivan, M.D., Steven Hurt, Ph.D., John F. Clarkin, Ph.D.

Summary

Purpose: Although self-destructive behavior is part of the *DSM-III* criteria set for borderline personality disorder (BPD), there have been few empirical studies of suicidal behavior in *DSM-III* BPD. Attempts to determine suicide risk in BPD should take into account concurrent Axis I diagnoses which independently carry a risk for suicide. This study determines the extent of suicidal behavior in patients with BPD and whether the presence of comorbidity with affective disorder and/or substance abuse/dependence affects suicide rates in BPD.

Method: Diagnostic, demographic and course data were gathered on 180 BPD inpatients. Lifetime suicidal behavior was rated as none, gestures or serious attempts based on lethality. Interater reliability for diagnostic and suicide categories was acceptable.

Results: 19% of BPDs had no history of suicidal behavior, 32% had made gestures and 49% serious attempts. BPDs with concurrent affective disorder and substance abuse/dependence had a significantly higher rate (21%). Intermediate rates were found in patients with BPD plus affective disorder (50%) and those with BPD plus substance abuse/dependence (43%).

Significance: Both suicide gestures and serious attempts are common, but not ubiquitous, in *DSM-III* BPD. Comorbidity with affective disorder and/or substance abuse/dependence greatly increases the risk for serious suicide attempts in BPD patients. These data suggest that treatment of concurrent Axis I disorders may decrease the risk of suicide in BPD.

NR246 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

NEUROLEPTIC DOSE ADJUSTMENT BY DOPAMINE BLOCKADE

R. J. Hitzemann, Ph.D., Psychiatry Service 116A, VAMC, Northport, NY 11768; J. Hirschowitz, M.D., D. C. Garver, M.D.

Summary

This pilot study explores the usefulness of monitoring D2 receptor blockade by measuring growth hormone (GH) response to apomorphine in patients receiving antipsychotic drugs. Our working hypothesis is that the dose of antipsychotic drug which just blocks the apomorphine induced rise in GH will be the minimum dose with full antipsychotic effect.

Method: Eleven *DSM III* Schizophrenic patients were studied during an acute exacerbation of their illness. After a two week drug free period, patients received apomorphine (10 μg/kg). Baseline GH levels and peak past apomorphine GH levels were obtained. Patients were then started on Haloperidol 60 μg/kg daily. Clinical status was monitored with Serial New Haven Schizophrenic Index (SNHSI). The GH test was repeated weekly and if the post APO rise in GH was not blocked, the dose of Haloperidol was increased, first to 200 μg/kg daily, and then to 600 μg/kg.

Results: a) Six of the eleven patients showed complete blockade at 60 μg/kg daily, and had a good outcome. (One patient received concommitant Lithium). Average plasma Haloperidol levels were 1-2 ng/ml; b) One patient showed a partial response at 200 μg/kg (blood level 7 ng/ml). Higher doses did not produce further improvement; c) One patient who responded at 60 μg/kg did not show blockade of the GH response, and; d) three patients who showed blockade of the GH response at 60 μg/ml had a poor outcome even at doses of 200-600 μg/kg of Haloperidol.

Conclusion: These preliminary results suggest an association between blockade of the GH response and maximum antipsychotic effect.

NR247 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PSYCHOPATHOLOGY IN VIETNAM VERSUS VIETNAM ERA VICTIMS

Glenn C. Davis, M.D., 10701 East Blvd., Cleveland, OH 44106; Naomi Breslau, Ph.D.

Summary

We compared psychiatric morbidity in 69 Vietnam veterans and 76 Vietnam era veteran (who had not served in Vietnam) inpatients in a psychiatric VA hospital during a three month period in 1984. NIMH-DIS was used to ascertain 10 *DSM III* Axis I diagnoses. Vietnam veterans were indistinguishable from Vietnam era veterans in age, race, marital status, level of education and family SES. The rate of PTSD in Vietnam veterans was 68%. Vietnam veterans had significantly higher rates ($p < .01$) of Major Depressive Disorder, Mania, Panic and Phobic disorders than era veterans. Vietnam veterans had, on the average, 5.55 $\pm$ 1.83 diagnoses, whereas Vietnam era veterans had 3.59 $\pm$ 2.05 ($t = 6.05$ $p < .000$).

Vietnam veterans with PTSD were predominantly of the chronic subtype; only 21% were delayed. PTSD positives reported, on the average, 5.2 of the six miscellaneous symptoms in Criterion D (only two required). The specificity of re-experiencing was low (54.4%), with half of Vietnam veterans who were PTSD negatives reporting it. In contrast, numbing of responsiveness had a high specificity (85.5%), with only one PTSD negative reporting the symptom. Of 22 Vietnam veterans who were PTSD negatives, 9 failed to meet diagnostic criteria because they did not experience numbing of responsiveness, although they reported re-experiencing of the trauma and more than the necessary number of symptoms to meet Criterion D. The implications for the definition of *DSM III* PTSD of the extensive concurrence of affective and anxiety diagnoses and the chronologic proximity of age of onset of the various disorders are discussed.

NR248 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SAAB: A SCALE FOR ASSESSING AGGRESSIVE BEHAVIOR

David A. Brizer, M.D., Dunlap 14A-Research Dept., Manhattan Psychiatric Center, Ward's Island, NY; Antonio Convit, M.D., Menahem Krakowski, M.D., Jan Volavka, M.D.

Summary

Violence is a major problem in psychiatric institutions today. Ward reports completed by ward aides and nurses underestimate the incidence of inpatient violence and are poorly standardized and have low reliability. Although several scales for rating inpatient violence exist, none identify all participants in violent incidents and therefore they fail to account for the interactional nature of such events.

The frequency and nature of violent events occurring on a 15-bed state hospital ward for the treatment of violent patients were recorded on a rating scale for the assessment of aggressive behavior (SAAB) over a 4 month period. Raters recorded the identity of both initiators and targets of violent behavior, and classified these behaviors as either (i) agitation, (ii) verbal assaults, (iii) assaults vs. self, (iv) assaults vs. others, or (v) assaults vs. property, on the basis of operational criteria. Additional items on the scale included the number of staff and patients present on the ward at the time of the event; extent of injury to participants; general level of agitation on the ward; and staff response to the event. SAAB raters achieved highly significant [$p < .001$) reliability for each item rated, and recorded more total events than did ward staff (444 vs. 281 events, respectively). The use of the SAAB scale replicated previous findings of underreporting of violent events on a psychiatric ward, and provides a means of studying the effect of treatment interventions on individual and dyadic violent behaviors.

NR249 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PHYSOSTIGMINE: MEMORY VERSUS PLASMA CHOLINESTERASE

J. Wesson Ashford, M.D., Dept. of Psychiatry, SIU School of Medicine, P. O. Box 3926, Springfield, IL 62709; Rodger Elble, M.D., Kathleen Sherman, Ph.D., Jonathan Hess, Ph.D., Sandy Best, M.A., Connie Higgins.

Summary

In patients with Alzheimer's disease, we have sought to delineate the relationship between drug induced inhibition of plasma butyrylcholinesterase (BuChE) and enhancement of cognitive functions. Phy was administered orally to 7 patients (probable Alzheimer's Disease; Mini-mental State scores: 9-25; 1 at 30 μg/kg; 4 at 40 μg/kg; and 2 at 50 μg/kg). BuChe activity was measured every 30 minutes after drug. Short- and long-term memory in verbal and visuo-spatial domains, attention, and tapping (10 tests in total) were tested at baseline, 30-60 min., 90-120 min., and 150-180 min. post-drug. BuChe inhibition was maximal at 60 minutes (11-26%), and dose dependent. Baseline performance and response to Phy varied considerably. Yet, when each test was averaged across patients, all tests were positive relative to baseline in the 90-120 minute epoch (ranging from 1% for Rey word-list learning to 55% for category association; $X = 23.1\%$, S.D. 18). The average of the memory test scores in the 90-120 min. epoch was improved for all 7 cases (range 1-57%; $X = 18$, S.D. = 19). Average cognitive performance peaked at the 90-120 epoch, approximately 30 min. after the peak BuChE inhibition. Despite the considerable inter-patient variability, these data confirm the enhancing effect of Phy on memory. Moreover, these data show that plasma BuChe inhibition provides a valuable indication of Phy absorption and efficacy and begin to define the kinetic relationship between this measure of blood level and psychological effect.

NR250 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

MEASURING TREATMENT RESPONSE BY COMPUTER INTERVIEW

D. Robert Fowler, M.D., VAMC, 4500 S. Lancaster Rd., Dallas, TX 75216; Allan S. Finkelstein, Ph.D., Walter Penk, Ph.D., William Bell, M.S.

Summary

The Dallas Problem Rating Interview (DPRI) was developed to take advantage of two of the most powerful features of computers—the ability to perform repetitive tasks accurately and reliably, and the capacity to manage and sort large amounts of data rapidly. The DPRI is a computer-administered psychiatric interview, using branching logic to increase efficiency, that permits a patient to endorse the presence and rate the severity of up to 245 "problem indicators" (symptoms, behaviors, or dysfunctions). Using the patient's response on the DPRI and its followup form (the DPRI-F), the computer then sorts and synthesizes the data into 21 empirically-derived (by cluster and factor analyses) "problems" and calculates a severity score for each problem. Concurrent validity of the DPRI problems with both a self-report instrument, the (MMPI) and a widely-used clinician-administered rating scale (the BPRS) has been previously established. The present study examines concurrent validity of the DPRI as a change measure, using interview responses of 80 patients hospitalized on acute psychiatry and substance abuse units. The DPRI was administered within one week after admission; the DPRI-F, at least 14 days later. Residual scores were determined for each of the 21 "problems", using weighted severity scores from each administration of the interview. Similar residual scores were determined for the concurrently administered BPRS ratings. Correlation between residuals for the DPRI and the BPRS were determined, using canonical correlation analysis, and showed a high correlation ($r = 0.75$, $p < .02$) between the DPRI and the BPRS. Specific overlaps between the two instruments will be presented in greater detail.

NR251 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

A COMPARISON OF DSM-II AND DSM-III IN 10,000 CASES

Armand W. Loranger, Ph.D., NYH/CMC Westchester, 21 Bloomingdale Rd., White Plains, NY 10605.

Summary

DSM-III has attracted more interest than any previous nosology in the history of psychiatry. Its impact on clinical practice, education, and research are inescapable. This study attempts to gauge that effect at one of the largest university hospitals in the United States, the Westchester Division of The New York Hospital-Cornell Medical Center. The frequencies of various diagnoses during the last five years of the *DSM-II* era were compared with those during the first five years of *DSM-III* in more than 10,000 patients. In the *DSM-II* period schizophrenia accounted for 25.2% of all cases compared to only 14.5% after the introduction of *DSM-III*. There was a corresponding increase in the diagnosis of affective disorders. Unipolar forms of depression increased from 15.3% to 25.5%. Bipolar disorder increased significantly but less dramatically from 7.4% to 10.8%. There was no change in schizoaffective disorder. About one-half of the *DSM-III* sample was given an Axis II diagnosis. Most common were the atypical-mixed-other and borderline types. Details will be presented on the relationships of age, sex, and Axis I diagnoses to Axis II conditions. There are indications that the multiaxial system may encourage the confusion of personality traits with personality disorders and contaminate the assessment of personality traits with Axis I clinical states.

NR252 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

DIAGNOSIS BY CONTENT ANALYSIS: SYSTEMS COMPARISON

Thomas E. Oxman, M.D., Dept. of Psychiatry, Dartmouth Medical School, Hanover, NH 03756; Paula P. Schnurr, Ph.D., Stanley D. Rosenberg, Ph.D., Marc Clemente, M.D.

Summary

A variety of investigators have suggested that content analysis may be preferable to assessment by self-report or observer-rating scales, or clinical interview because content analysis is less susceptible to distortion by denial or social desirability while still permitting rigorous quantitative measurement. The Gottschalk-Gleser (G-G) schema is the best known content analysis method in psychopathology research; however, it requires human scorers, raising reliability and cost issues. It is also based on somewhat different linguistic assumptions than computer scored systems such as the General Inquirer using the Harvard III Psychosocial Dictionary (GI/HIII). In this study, we compared the diagnostic abilities of the GI/HIII with both the G-G method and psychiatric raters.

Five minute free speech samples were obtained from 71 patients (Somatization Disorder, n = 17; Paranoid Disorders, n = 25; Cancer, n = 17; Major Depressive Disorder n = 12). Each content analysis method produced frequences of different psychosocial themes in each speech text sample. The frequency results of both methods were entered into stepwise discriminant and classification analyses. The GI/HIII and G-G methods correctly classified 77% and 54% respectively. These hit rates were compared to a classification analysis by a psychiatrist who read the transcripts and correctly identified 55% of the diagnoses. These results imply that a simple word classification method, which can be inexpensively and reliably scored by computer, may be superior to more inferential hand scoring in identifying linguistic cues for diagnostic classification. The mechanism for this appears to be that patterns of lexical choice are determined by affective and connotative components of words, a dimension that may be rather independent of sentences' formal meanings.

NR253 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

PRELIMINARY VALIDATION OF A FAMILY ATTITUDE SCALE

Gretchen L. Haas, Ph.D., Payne Whitney Clinic, 525 E. 68th St., New York, NY 10021; Anthony T. DiVittis, M.A., Marylin Levitt, D.S.W., James H. Spencer, M.D., John F. Clarkin, Ph.D., Ira D. Glick, M.D.

Summary

Recent investigations of family variables associated with relapse and the long-term course of schizophrenia point to the need for reliable and sensitive measures of family attitudes and family functioning. Data from several controlled studies of family intervention reveal that family attitude variables, in particular, Expressed Emotion (EE)—as measured via the Camberwell Family Interview procedure—predict rate of rehospitalization and response to family intervention. Unfortunately, the length of the interview and the intensive training of the clinical interviewer/raters has restricted the general use of the CFI. The need for more economical and effective procedures for assessing family attitudes toward the psychiatric patient has been indicated by recent efforts to construct abbreviated versions of the CFI as well as alternate assessment instruments.

This report summarizes preliminary data on the Family Attitude Scale (FAS), a 53-item inventoy of relatives' attitudes toward patient and illness, willingness to seek help from professionals, and family reliance on social support. The instrument includes a modified version of Kreisman's (1979) Patient Rejection Scale, items from the Family Evaluation Form (Spitzer et al.) and questions assessing attitudes toward the hospital and psychiatric treatments in general. A principal components analysis of data gathered on a sample of families of 170 psychiatric inpatients at time of hospital admission and discharge yielded five factors with moderate to high internal reliabilities (with Cronbach alpha values ranging from .66 to .91) and substantial internal stability over time (as assessed via independent principal components analyses for data at three times of assessment). Results of repeated measures analyses of outcome from a controlled study of Inpatient Family Intervention (IFI) will be presented in discussion of the construct validity of the instrument.

NR254 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

THE EVANS-BROWN RATING SCALE

Susan Evans, R.N., Payne Whitney Clinic, 525 E. 68th St., New York, NY 10021; Richard P. Brown, M.D.

Summary

Goals: To develop a nurses rating scale that 1. effectively and reliably differentiates changes in mood and behavior in psychiatric inpatients 2. assesses symptoms representative of *DSM III* Axis I and II diagnoses 3. can be programmed for daily nurse's use on the personal computer.

Methods: The Evans-Brown Rating Scale is a 25 item, 5 point instrument assessing Depression, Borderline Personality Disorder, Mania, Organic Brain Syndrome, Schizophrenia and Global functioning. Ratings, based on observations and data obtained by the RN during the course of a shift, takes approximately 3 minutes to complete. Reliability training requires brief interviews of 4-7 patients followed by discussion. Twenty psychiatric inpatients were rated on admission, discharge and twice weekly by trained RN's. Two RN's rated the same patient on the EBRS and one of the pair also rated the patient on the "NOSIE-30" and Patient Rating Form (PRF).

Results: Intra-class correlations on items ranged from .23-1.0 with 90% of items showing robust agreement. Grouped into subscales, total correlations improved (.71 - .91, $p < .001$). Global assessment and EB Global scores were highly correlated ($p < .001$). Construct validation analysis correlated PRF, NOSIE and EBRS subscales. Spearman correlation coefficients ranged from .22-81. EB-PRF Depression, Mania, Schizophrenia and EB - NOSIE OBS subscales were highly correlated [$p < .001$). Other subscales showed significant trends.

Significance: Advantages of the EBRS over other rating scales is its ability to measure a wide range of psychopathology including character pathology. Analysis of these observations offers a means of extracting clinically significant information, leading to timely decisions in the treatment of psychiatric inpatients. Data collected in the computer is available for research study.

NR255 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

INCREASED SPECIFICITY IN MEASURING SATISFACTION

Barbara Urquhart, R.N., 525 E. 68th St., New York, NY 10021; John A. Sweeney, Ph.D., Barbara Bulow, M.S.W., M. Katherine Shear, M.D., Allen J. Frances, M.D.

Summary

Goals: 1) To increase the specificity in measurement of patient satisfaction; 2) to determine if satisfaction is unitary or multidimensional; 3) to determine which patient, treatment, setting and interacting variable most correlate with outpatient satisfaction; 4) to determine test/retest reliability of satisfaction ratings. Methods: A consumer satisfactions survey was administered to 380 Payne Whitney Clinic outpatients. Questions tapped levels of satisfaction and dissatisfaction in patients who were receiving a variety of different types of treatment, with and without medication, performed by therapists of different disciplines, experience and sex.

Results: Overall satisfaction was high and principal component factor analysis revealed that satisfaction appeared to be unitary dimension. Nonetheless, ways of increasing variance of measurement of satisfaction and determining differential satisfaction did emerge. Patients were not influenced in their global satisfaction by the physical appearance of the clinic or clerical staff courtesy. Satisfaction was significantly higher for individual therapy, longer therapies, same sex patient/therapist matches and for staff Social Workers as compared to Psychiatry Residents. Even though ratings were generally very high, a third of patients preferred a form of treatment than the one they are receiving. Conclusion: By studying patients receiving a variety of different treatments with an instrument that taps different types of satisfaction and dissatisfaction, it is possible to increase the variance of satisfaction measurement and to target particular areas of consumer satisfaction that may be valuable in treatment, and program planning.

NR256 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

ESTIMATES OF SERVICE NEED FROM COMMUNITY SURVEYS

Philip J. Leaf, Ph.D., Yale University, 350 Congress Ave., New Haven, CT 06519; Gary L. Tischler, M.D.

Summary

Although work is currently underway to estimate the prevalence of psychiatric disorders and to improve the utility of epidemiologic data for estimating treatment needs, data from one recent study, the Epidemiologic Catchment Area (ECA) Project are already being used to plan for services in several states. Although the pressure to use any available data, especially data generated by a large, multisite study funded by NIMH is great, efforts to date indicate a serious misunderstanding of the nature of the design of the ECA project, the assessment procedures used in the study, and the functioning of the mental health service system.

In this presentation, we describe the fiscal and clinical implications of misuse of these data. We first describe why the overall rate of disorder in a community is not the best indicator of need for specific psychiatric services. Criteria for establishing caseness for planning purposes are generated. We then discuss how prevalence estimates should be modified to better reflect the specific types of cases for which planning is being undertaken. Next we describe how to interpret the epidemiologic data in light of existing services. Finally, we discuss alternative procedures for allocating services and funds that do not rely on ECA data.

NR257 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

EVALUATION OF A SEXUAL ABUSE PREVENTION PROGRAM

Renee L. Binder, M.D., 401 Parnassus Ave., San Francisco, CA 94143; Dale E. McNiel, Ph.D.

Summary

In response to increasing reports of child sexual abuse, many schools and community groups have implemented educational programs designed to teach children about how to prevent sexual abuse. In fact, recent legislation in California (AB 2443) makes child assault prevention programs mandatory in schools. Nevertheless, there has been little study of the effectiveness of these programs. In addition, some parents have expressed concern that these programs could have harmful effects, eg., provoking unreasonable mistrust or anxiety in their children. This paper presents very recent findings obtained from ongoing research which evaluates a child assault prevention program in two middle class communities and answers the following questions: How much do the children know about preventing sexual abuse prior to the program? How much do the children know about preventing sexual abuse after the program? Did parents or teachers notice changes in children's behavior as a result of the program? Do parents have an accurate idea of how much their children know about preventing sexual abuse? 106 children (ages 5-12), their parents and teachers completed interviews and questionnaires which provided information relevant to these questions. Children showed increases in knowledge about how to protect themselves after they participated in the program. Neither parents nor teachers reported noticeable negative changes in children's behavior after the program. There were significant discrepancies between what parents thought their children knew and what they actually knew, in that parents tended to underestimate their children's knowledge. In summary, this study supports the value of providing sexual abuse prevention programs to children.

NR258 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

SHORT REM LATENCY IN IMPOTENCE WITHOUT DEPRESSION

Helmut S. Schmidt, M.D., Sleep Disorder Evaluation Center, 473 W. 12th Ave., Columbus, OH 43210; Kathy Shy, M.D.

Summary

The most characteristic findings in the sleep EEG of patients with major depression have been the short REM latencies (RL) and the increased duration and REM density (RD) of the first REM period. The occurrence of short RL (< 70 min) was observed with surprising frequency in patients presenting to our Sleep Disorders Clinic with impotence. Twenty-five patients, mean age 53.8 ± 10.3, were found to have variably impaired noctural penile tumescence (NPT). The mean RL using the shortest one of two consecutive nights, was 42.1 min ± 19.6, shorter than for most groups of major depressives described in the literature. Fourteen of the twenty-five patients had their shortest RL on the first night, in contrast to what has been described as a "first night effect" in normal subjects. Only two of the twenty-five patients could be diagnosed to have a major depression (age 27, RL 37.5 and age 64, RL 48.5). Five patients, or 20%, had RL < 20 min (mean age 50.4) with the shortest RL of .5 min in a 38 year old subject. Absence of tumescence during REM sleep in some of these patients is followed by partial or full tumescence in the subsequent awake or non-REM period, thus strongly suggesting psychogenic inhibition of NPT. Repetitive REM Awakenings, not infrequently coinciding with the onset of tumescence, were consistently noted. The fact that several of these patients appeared to have regained their waking erectile capability following brief psychosexual therapy provides further documentation for psychogenic inhibition of their NPT studies. We conclude that short RL is not specific for depression and that short RL with REM interruptions (awakenings) is a useful biologic marker identifying the presence of probable psychogenic NPT inhibition. Although sleep continuity disturbance is frequently mentioned as being prominent in depressed patients, repetitive awakenings out of REM sleep has never been mentioned in such patients.

NR259 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

MENTAL HEALTH TRAINING FOR PHYSICIANS

James J. Strain, M.D., 608 KCC, Mt. Sinai Hospital, 1 Gustave Levy Pl., New York, NY 10029; Linda K. George, M.D., Harold A. Pincus, M.D., Leslie H. Gise, M.D., Jeffrey Houpt, M.D.

Summary

Since the Epidemiological Catchment Area study demonstrated that 19% of all Americans have alcohol, drug abuse, and/or mental (ADM) disorders in any six-month period and are seen primarily in general medical care settings, it is imperative to know the quality and quantity of mental health training for primary care residents. A series of general and specific hypotheses regarding training models developed before data collection to preclude post hoc interpretations were tested.

Method: Using a random sample technique stratified for 4 geographical regions, 147 training programs were examined: 67 Family Practice, 42 Primary Care Internal Medicine, and 38 Internal Medicine. Data was collected using a structured mail questionnaire previously pilot-tested in 35 primary care training sites.

Results: Eight hypotheses were tested regarding model types and critical variables: primary care specialty, program cost, program size, intensity of informal and formal training, teaching performed by primary care physicians, use of inpatient settings, use of block rotations, amount of training by consultation, and the disciplines of mental health teachers. Using bivariate and multivariate analyses all hypotheses across program model types were supported. Multiple discriminant analyses revealed that the relationships between 12 training program characteristics (independent variables, all of which were included in the tests of the bivariate model hypotheses) and the 5 program model types (dependent variables) were such that the former could explain 57% of the variance in the latter and correctly classify 89% of the programs.

NR260 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

THE PSYCHIATRIC IMPACT OF AIDS ON PHYSICIANS

James Dilley, M.D., AIDS Health Project, 333 Valencia, 4th Fl., San Francisco, CA 94103; Leon McKusick, Ph.D., William Horstman, Ph.D., Donald Abrams,. M.D., Thomas J. Coates, Ph.D.

Summary

Of 150 San Francisco Bay Area physicians sampled who engaged in AIDS related professional activity, 82 (55%) returned our August 1985 survey of psychological reactions to working with AIDS. 40 also consented to be interviewed. 33% identified themselves as heterosexual, one respondent was bisexual, and 63% indicated they were gay or homosexual. The average length of time working with AIDS was 3.2 years. Mean per cent of professional patient contact time with AIDS or ARC was 44%.

We found that 36% experienced more depression, 34% more anxiety, 39% overwork, 46% more stress, and 36% felt more fear of death since first working with AIDS. Increased intellectual stimulation was felt by 46%, and greater career satisfaction reported by 45% of these physicians since they began working with AIDS.

When asked by pretested check list how they cope with the emotional aspects of working with AIDS, 66% indicated that they talk to a friend, lover, spouse, or family member. 65% teach others about AIDS, 54% remain objective, and 48% get support from other physicians.

We found that gay identified physicians are more likely than their heterosexual counterpatrs to have experienced increased anxiety depression, stress, overwork, and fear of death since first working with AIDS. Through interviews, we determined that this differing psychological response is due to the gay physician's self perception as being at risk for AIDS. The number of years working with AIDS does not correlate with psychological distress, although percentage time inpatient per week with AIDS patients is related to depression, overwork as well as intellectual stimulation. AIDS practitioner burn out appears to be less a function of longitudinal contact with the disease and more related to amount of concentrated exposure. Implications for physician education are discussed.

NR261 **Thursday, May 15, 12:00 noon - 1:45 p.m.**

COMPLIANCE WITH CHEMOTHERAPY PROTOCOLS

Sushil Bhardwaj, M.D., Psychiatry, KCC 608 Mt Sinai, 1 Gustave Levy Pl., New York NY 10029; Madelyn R. Messe, Ph.D., Allen H. Lebovits, Ph.D., Steven J. Schleifer, M.D., James J. Strain, M.D.

Summary

Since optimal therapeutic results and accurate research findings require uncompromised protocol adherence, this National Cancer Institute-funded study examines the frequency of and psychological correlations with noncompliance in both patients with breast cancer and their physicians. METHOD: A semi-structured interview and a battery of psychological measures were given to 94 women with Stage I, II, III, or IV breast carcinoma before the first chemotherapy treatment and at 2, 4, 13 and 26 week intervals. Measures included were: RDC assessment, Multidimensional Health Locus Control, SCL-90 analog, Karnofsky, Mini-Mental State, and DOTES. Physicians' prescribing behavior for oral and intravenous medications was obtained from patients' medical records. A specially-trained staff oncologist evaluated whether the physician adhered to the protocol or whether unjustified modications were made. RESULTS: Of 51 patients on oral cytoxan and prednisone 51% (N = 26) varied their doses 10% or more on at least one prescribing event: cytoxan 20% (N = 10), prednisone 10% (N = 5), cytoxan and prednisone 21% (N = 11). The psychological measures did not distinguish between the compliant and the noncompliant patient groups. Of 29 prescribing physicians 38% (N = 11) had unjustified modifications for 10% or greater of the prescribed dose. Physician nonadherence to protocol across six drugs (cytoxan, prednisone, adriamycin, methotrexate, vincristine, and 5 flourouracil) varied according to location: Academic 9%, private office 12%, and clinic 18%; and, stage of illness: I 1.5%, II 26.4%, III 3.6%, IV 9.4%. Staff and patient adherence to protocols has been insufficiently measured or considered in the interpretation and recommendation from research findings in clinical trials.

INDEX